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Integrated Science Assessment for Particulate Matter

Includes Errata Sheet created on 2/10/2010

National Center for Environmental Assessment-RTP Division
Office of Research and Development
U.S. Environmental Protection Agency
Research Triangle Park, NC

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for the document titled
Integrated Science Assessment for Particulate Matter, December 2009, Final

Table or Figure	Page	Erratum
	iv-v	Table of contents for Chapter 2 updated to correct page numbers.
	xv, xxiii	Page numbers for Chapter 2 figures and tables corrected.
	2-9	Replaced reference to "Table 6-14" in the text with "**Table 6-15**"
	2-10	Replaced reference to "Table 6-14" in the text with "**Table 6-15**"
	2-11	Replaced reference to "Table 6-14" in the text with "**Table 6-15**"
	2-12	Replaced the reference to "Figure 7-8" in the text with "**Figure 7-7**" (cited 3 times)
Figure 2-2	2-15	Mean concentration for Laden et al. (2006, 087605) corrected from 14.8 to **16.4.** Deleted "conducted in locations where the mean annual $PM_{2.5}$ concentrations were <17 $\mu g/m^3$ " in caption.
	2-17	Replaced reference to "Table 6-17" in the text with "**Table 6-18**"
Figure 6-4	6-72	Figure replaced. Lisabeth et al. (2008, 155939) correctly moved to $PM_{2.5}$ study group.
Figure 6-15	6-148	Updated HERO ID numbers.
Figure 7-6	7-85	$PM_{2.5}$ concentrations for Laden et al. (2006, 087605) corrected from 17.6 to **16.4**

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Acronyms and Abbreviations

α	alpha, ambient exposure factor
α-HCH	alpha-hexachlorocyclohexane
Å	Ångström
A	surface albedo
AAC	abdominal aortic calcium
AAS	atomic absorption spectrophotometry
AB	Alcian Blue stain
ABC	Asian Brown Cloud
ABI	ankle-arm or resting blood pressure index
AC	air conditioning
Ace	acenaphthene
ACE-1	angiotensin converting enzyme-1
ACEAsia	(Asian Pacific Regional) Aerosol Characterization Experiment
ACGIH	American Conference of Governmental Industrial Hygienists
ACh	acetylcholine
Acl	acenaphthylene
ACP	accumulation mode particle
ACS	American Cancer Society
Ad4BP	adrenal-4-binding protein
ADEOS-1	Advanced Earth Observing Satellite-1
A-DEP	automobile diesel exhaust particles
ADM	angular distribution model(s), angular dependence model
ADMA	asymmetric dimethylarginine
AD-Net	Asian Dust Network
Ae	AERONET
AeroCom	Aerosol Comparisons between Observations and Models
AERONET	NASA AERosol RObotic NETwork
AF	atrial fibrillation
AGA	appropriate for gestational age
AGE	advanced glycation end product
AHR	airway hyperresponsiveness, airway hyperreactivity
AhR	arylhydrocarbon receptor

AHSMOG	California Seventh Day Adventist study
AI	aerosol index
AIC	Akaike's information criterion
AIM	ambient ion monitor
AIOP	2003 Aerosol Intensive Operating Period
AIRS	Aerometric Information Retrieval System
Al	aluminum
ALI	air liquid interface
AM	alveolar macrophage(s)
AM, AMF	arbuscular mycorrhizal
AMAP	Arctic Monitoring and Assessment Programme
AMDP	annual maximum of daily precipitation
AMI	acute myocardial infarction
AMS	aerosol mass spectrometry
Ang II	angiotensin II
ANOVA	analysis of variance
ANP	atrial natriuretic peptide
ANS	autonomic nervous system
Ant	anthracene
AOD	aerosol optical depth
AP-1	activator protein 1
APC	antigen presenting cell(s)
APCS	Absolute Principal Components Scores
APEX	Air Pollutants Exposure Model
APHEA	Air pollution and Health: a European Approach
APO	apocynin
ApoE	apolipoprotein E
APS	aerodynamic particle sizer, aerosol polarimetry sensor
aPTT	activated partial thromboplastin time
AQCD	Air Quality Criteria Document
AQI	Air Quality Index
AQM	air quality model
AQS	U.S. EPA Air Quality System database
Aqua	NASA satellite
AR4	Fourth Assessment Report (AR4) from the IPCC

ARCTAS	Arctic Research of the Composition of the Troposphere from Aircraft and Satellites
ARD	Air Resources Division
ARDS	adult respiratory distress syndrome
ARI	acute respiratory infection
ARIC	Atherosclerosis Risk in Communities study
ARIES	Aerosol Research and Inhalation Epidemiology Study
ARM	Atmospheric Radiation Measurement program
ARQM	Air Quality Research Branch (Meteorological Service of Canada Toronto)
ARS	Air Resource Specialists
As	arsenic
ASDNN5	mean of the standard deviation in all 5-min segments of a EKG 24 h recording
ASOS	Automated Surface Observing System
ATOFMS	aerosol time-of-flight mass spectrometry
ATP	adenosine triphosphate
A-Train	a group of 5 afternoon overpass satellites (Aura, PARASOL, CALIPSO, CloudSat, Aqua)
ATS	American Thoracic Society
AURA	NASA satellite
avg	average
AVHRR	Advanced Very High Resolution Radiometer
ß	beta, beta coefficient, slope
β-HCH	beta-hexachlorocyclohexane(s)
3βHSD	3β-hydroxysteroid dehydrogenase
βTGF	β transforming growth factor
b_{ag}	absorption by gases coefficient
b_{ap}	absorption by particles coefficient
b_{ext}	light extinction coefficient
b_{sg}	scattering by gases coefficient
b_{sp}	sum of light scattering by (aerosol) particles coefficient
Ba	barium
BaA	benz[a]anthracene
BAD	bronchial artery diameter
BAL	bronchoalveolar lavage
BALB/c	albino inbred mouse strain

BALF	bronchoalveolar lavage fluid
BALT	bronchus-associated lymphoid tissues
BAM	beta attenuation monitor
BaP	benzo[a]pyrene
BASIC	Brain Attack Surveillance in Corpus Christi
BASE-A	Burning Airborne and Spaceborne Experiment - Amazon and Brazil
BbF	benzo[b]fluoranthene
BC	black carbon
BCC-CMI	Beijing Climate Center – Carbon Mitigation Initiative
BCCR	Bjerknes Centre for Climate Research
BeP	benz[e]pyrene
BghiP, BpPe	benzo[g,h,i]perylene
BGT	beta-gauge technique
BH_4	tetrahydrobiopterin
bhp	brake horsepower
BkF	benzo[k]fluoranthene
BMI	body mass index
BMP	bone morphogenetic protein
BN/BR	Brown Norway rat strain
BNP	brain natriuretic peptide, B-type natriuretic peptide
BOSS	BYU Organic Sampling System
BP	blood pressure
BPM	blowing $PM_{2.5}$
BpPe	benzo[ghi]perylene
BPQ	benz(ayrene (BaP)-quinone
Br	bromine
BRAVO	Big Bend Regional Aerosol and Visibility Observational (Study)
BrdU	bromodeoxyuridine
BS	black smoke
BUC	bucillamine (N-[2-mercapto-2-methylpropionyl]-L-cysteine)
BVAIT	B-Vitamin Atherosclerosis Intervention Trial
BYU	Brigham Young University
C	carbon
C^4	Center of Clouds, Chemistry and Climate
^{12}C	carbon-12

^{13}C	carbon-13
^{14}C	carbon-14
$C_{60}(OH)_{24}$	water-soluble fullerene
Ca	calcium
CAA	Clean Air Act
CAAA	1977 Clean Air Act Amendments
CAAM	continuous ambient mass monitor
CAC	coronary artery calcification
$CaCO_3$	calcium carbonate
CAD	coronary artery disease
CALINE	California Line Source Dispersion Model
CALIOP	Cloud and Aerosol Lidar with Orthogonal Polarization
CALIPSO	Cloud-Aerosol Lidar and Infrared Pathfinder Satellite Observations
CAM	Community Atmosphere Model
CAMM	continuous ambient mass monitor
CAMP	Childhood Asthma Management Program
CAMx	comprehensive air quality model with extensions
$Ca(NO_3)_2$	calcium nitrate
CAP	concentrated ambient particle
CAPMoN	Canadian Air and Precipitation Monitoring Network
CASAC	Clean Air Scientific Advisory Committee
$CaSO_4$	calcium sulfate
CASTNet	Clean Air Status and Trends Network
CATS	cumulative air toxics surface
CB	carbon black, chronic bronchitis
CB-Fe	carbon black particles artificially coated with Fe(II) salt.
CB(P)	carbon black (particles)
CBSA	Core-Based Statistical Area
CB-V	carbon black particles artificially coated with a targeted concentration of Vanadium (IV) salt
CBVD	cerebrovascular disease
CC16	Clara cell protein, Clara cell 16 protein
CCCma	Canadian Centre for Climate Modeling and Analysis
CCM3	Community Climate Model
CCN	cloud condensation nuclei
CCPM	continuous coarse particle monitor

CCSM3	Community climate system model, version 3
CCSP	Climate Change Science Program
Cd	cadmium
CDC	Centers for Disease Control and Prevention
CDE	conjugated diene
CDNC	cloud droplet number concentration
CDPHE	Colorado Department of Public Health and Environment
Ce	cerium
CEN	European Committee for Standardization
CenRAP	Central Regional Air Planning Association
CERES	Clouds and the Earth's Radiant Energy System
CERFACS	European Centre for Research and Advanced Training in Scientific Computation
CF	coronary flow, cystic fibrosis
CFA	coal fly ash
CFD	cystic fibrosis disease
CFR	Code of Federal Regulations
CGCM3.1	Coupled global climate model
cGMP	cyclic guanosine monophosphate
CH_2Cl_2	methylene chloride
CH_2O	formaldehyde
CH_4	methane
CHAD	Consolidated Human Activity Database
CHD	chronic heart disease
CHF	congestive heart failure
CHL	crown heel length
CHO	Chinese hamster ovary cells
Chr	chrysene
CHS	Children's Health Study
CI	confidence interval
CIF	carbon-impregnated charcoal filter
CIIT	Chemical Industry Institute of Toxicology
CIMT	carotid intimal-medial thickness
Cl	chlorine
CL	chemiluminescence
CLAMS	Chesapeake Lighthouse and Aircraft Measurements for Satellites

CM	conditioned medium, cell culture medium
CMAQ	Community Multi-scale Air Quality modeling system
CMAR	CSIRO Marine and Atmospheric Research
CMB	chemical mass balance
CMD	count median diameter
CNES	Centre National d''Etudes Spatiales
CNP	carbon nano particle
CNRM	Centre National de Recherches Meteorologiques
CNRM	Center National Weather Research
CNS	central nervous system
Co	cobalt
CO	carbon monoxide
CO_2	carbon dioxide
COD	coefficient of divergence
COH, CoH	coefficient of haze
CONUS	continental United States
COO^-	carboxyl group
COPD	chronic obstructive pulmonary disease
CoPP	cobalt protoporphyrin
COX-2	cyclooxygenase 2 enzyme
CPC	condensation particle counter
CPZ	capsazepine
Cr	chromium
C-R	concentration-response (relationship)
CRP	C-reactive protein
Cs	cesium
^{137}Cs	cesium-137
CS	cigarette smoke
CSA	Combined Statistical Area
CSC	cigarette smoke condensates
CSE	cigarette smoke extract
cSHMT	cytosolic serine hydroxymethyltransferase
CSIRO	Commonwealth Scientific and Industrial Research Organization
CSN	Chemical Speciation Network
CTM	chemistry-transport model, chemical transport model

Cu	copper
$CuSO_4$	copper sulfate
Cu/Zn SOD	Cu/Zn superoxide dismutase
CUP	Current Use Pesticide
CV	cardiovascular, coefficient of variation
CVD	cardiovascular disease(s)
CVM	contingent valuation method
CYP	cytochrome P450
CYP 1A1	cytochrome P450 1A1
Δ	delta, change, difference
ΔFEV_1	change in forced expiratory volume in one second
d_{50}	50 percent cut point or 50 percent diameter
d_{ae}	aerodynamic diameter of a particle
D	diameter
D_a	Dalton
DAAC	Distributed Active Archive Center
DAASS	Dry Ambient Aerosol Size Spectrometer
DABEX	Dust and Biomass-burning Experiment (in West Africa)
DAR	denuded aortic ring
DAX-1	x-chromosome gene-1
DBA	dibenzo(a,hnthracene
DBP	diastolic blood pressure
DC	dendritic cell
DC	diesel exhaust particles + cigarette smoke condensates
DC8	Douglas aircraft
DCF	direct climate forcing, 2',7'-dichlorofluorescin
DDT	dichlorodiphenyltrichloroethane
DE	diesel exhaust
DEE	diesel exhaust extract
DEP	diesel exhaust particle
DEPAL	diesel exhaust particles aliphatic (extract)
DEPAR	diesel exhaust particles aromatic (extract)
DEPE	diesel exhaust particles extract
DEPM	diesel exhaust particles methanol (extract)
DEPME	diesel exhaust particles methylene chloride extract

DEPPO	diesel exhaust particles polar (extract)
Dex	dexamethasone
*d*Fld	change fold, unit change in property
DFO	desferrioxamine (Desferral) an iron chelator
DFX	deferasirox (Exjade) an oral iron chelator
DHR	dihydrorhodamine 123
DLCO	carbon monoxide diffusing capacity
DMEM	Dulbecco's modified Eagle's medium (culture medium)
DMSO	dimethyl sulfoxide
DMT1	divalent metal transporter-1 protein
DMTU	dimethylthiourea
DNA	deoxyribonucleic acid
DOE	U.S. Department of Energy
dpc	days post conception
DPC	dodecylphosphocholine
DPCC	1,2-dipalmitoyl-SN-glycero-3-phosphocholine
DPI	diphenyleneiodonium
DPM	diesel particulate matter
DPPC	dipalmitoylphosphatidylcholine
DRE	direct radiative effects
DRF	direct radiative forcing
DRUM	Davis Rotating Uniform size-cut Monitor
DS	diffusion screens
DSP	daily sperm production
DTMA	Dynamic mechanical thermal analysis
DTPA	diethylene triamine pentaacetic acid
DU	dust
dv	deciview(s)
DVT	deep vein thrombosis
EAD	electrical aerosol detector
EANET	Acid Deposition Monitoring Network in East Asia
EARLINET	European Aerosol Research Lidar Network
EarthCARE	Earth Clouds, Aerosols and Radiation Explorer
EAST-AIRE	East Asian Study for Tropospheric Aerosols
EBCT	electron beam computed tomography

EC	elemental carbon
ECE-1	endothelin converting enzyme-1
ECG, EKG	electrocardiogram
ECHAM5	European Centre Hamburg with Hamburg Aerosol Module
ECHO-G	(ECHAM4 + HOPE-G):
ECRHS	European Community Respiratory Health Survey
EC/TC	ratio of elemental carbon to total carbon
ED	emergency room, emergency department
EDGAR	Emissions Database for Global Atmospheric Research
EDTA	ethylenediaminetetraacetic acid
ED-XRF	energy dispersive X-ray fluorescence
EGM	electrogram
EGU	electricity-generating unit
EHC-93	Ottawa dust; urban air particulate matter PM_{10}, collected in 1993 in Ottawa, Canada
EKG, ECG	electrocardiogram
ELISA	enzyme-linked immunosorbent assay
EMECAS	Spanish Multi-centric Study on the Relation between Air Pollution and Health
EMEP	European Monitoring and Evaluation Programme
eNO	exhaled nitric oxide
eNOS	endothelial nitric oxide synthase
EOS	Earth Observing System
EPA	U.S. Environmental Protection Agency
ER	estrogen receptor
ERBS	Earth Radiation Budget Satellite
ERK1/2	ERK-1 (MAPK p42) and ERK-2 (MAPK p44)
ESRL	Earth System Research Laboratory
ESTR	expanded simple tandem repeat
E_T	forcing efficiency
ET	extrathoracic region
ET	endothelin
ET_A	endothelin A receptor subtype
ET_B	endothelin B receptor subtype
ETS	environmental tobacco smoke
EU	endotoxin units

F	breathing frequency
f	the ratio of ambient aerosol mass (wet) to dry aerosol mass M.
fσsp(RH)	total light scattering coefficient at given relative humidity(RH) values
faf	anthropogenic fraction of fine-mode fraction
ff	fine mode fraction
f(RH)	the unitless water growth term that depends on relative humidity
F	fine particles
F344	Fisher 344 strain of rats
*F*a	adjusted forcings
FA	filtered air
FAC	ferric ammonium citrate
FBI	Federal Bureau of Investigation
FBS	fetal bovine serum
FCS	fetal calf serum
FDMS	Filter Dynamics Measurement System
FDMS-TEOM	Filter Dynamics Measurement System - Tapered Element Oscillating Microbalance
F*e*	effective (F*e*) forcings
Fe	iron
$Fe_2(SO_4)_3$	ferric sulfate
$FeCl_3$	ferric chloride
FEF	forced expiratory flow
FEF_{25-75}	mean forced expiratory flow over the middle half of the forced vital capacity
$FEF_{50\%}$	mid-expiratory flow
FEM	Federal Equivalent Method
FeNO	fractional exhaled nitric oxide
FERA	Fire and Environmental Research Applications (Team)
FEV_1	forced expiratory volume in one second
FGA	one fibrinogen alpha chain
FGB	one fibrinogen beta chain
FGOALS-g1.0	Flexible Global Ocean-Atmosphere-Land System Model
*F*i	instantaneous forcing
FID	flame ionization detection
FIMS	fast integrated mobility scanners
F_{inf}	infiltration factors

FKHR	Proapoptotic Factor FOXO1
Fle	fluorine
Flu	fluoranthene
FMD	flow-mediated dilation
FPG	formamidopyrimidine-DNA glycosylase
f-PM, FPM	fine particulate matter
FR	Federal Register
FRM	Federal Reference Method
FROSTFIRE	The landscape-scale prescribed research burn in the boreal forest of interior Alaska, July 1999; conducted by FERA.
Fs	SST forcing(s), forcing driven by sea surface temperature (SST)
Fsfc	mean net solar flux at the (Earth) surface
FT	free troposphere
FTIR	Fourier transform infrared spectrometry
F/UFP	mix of fine and ultrafine particles, all < 2.5 μm
FVC	forced vital capacity
γGCS	gamma glutamylcysteine sythetase
Ga	gallium
GAM	generalized additive model
GATOR	Gas, Aerosol, Transport, and Radiation model
GATORG	Gas, Aerosol, Transport, Radiation, and General circulation model
GAW	Global Atmospheric Watch network
GBS	group B streptococcus
GC	gas chromatography
GCM(s)	general circulation model(s), global climate model
GCMOM	General Circulation, Mesoscale and Ocean Model
GC/MS	gas chromatography/mass spectrometry
GCS	gamma glutamylcysteine sythetase
GD	gestational day
GDF	growth differentiation factor (e.g., GDF-9)
GEE	generalized estimating equations, gasoline engine exhaust
GEIA	Global Emissions Inventory Activity
GEM	gaseous elemental mercury
GEOS-Chem	Goddard Earth Observing System-CHEMistry
GFAAS	graphite furnace atomic absorption spectrometry
GFAP	glial fibrillatory acidic protein

GFDL	Geophysical Fluid Dynamics Laboratory
GFDL-CM2.x	GFDL Climate Models
GFED	Global Fire Emission Database
GGT	gamma-glutamyltranspeptidase
GHG	greenhouse gas
GIS	Geographic Information System
GISS	Goddard Institute for Space Studies
GISS-AOM	GISS Atmosphere-Ocean Model climate prediction model
GISS-EH	GISS AOM for sea ice model
GISS-ER	GISS AOM for liquid sea model
GLAS	Geoscience Laser Altimeter System
GLM	generalized linear models
GM	geometric mean
GM-CSF	granulocyte macrophage colony-stimulating factor
GMD	Global Monitoring Division
GMS	Greater Mekong Subregion
GOCART	Goddard Chemistry Aerosol Radiation and Transport
GOES	Geostationary Operational Environmental Satellite
GoMACCS	Gulf of Mexico Atmospheric Composition and Climate Study
GPS	Global Positioning System
GSD	geometric standard deviation
GSFC	NASA Goddard Space Flight Center
GSH	glutathione
GSH:GSSG	ratio of reduced glutathione to glutathione disulfide (oxidized glutathione)
GSO, GSNO	S-Nitrosoglutathione
GSSG	glutathione disulfide; oxidized glutathione
GST	glutathione-S-transferase
GSTM1	glutathione S-transferase polymorphism M1
GSTP1	glutathione-S-transferase polymorphism P1
GSTT1	glutathione-S-transferase polymorphism T1
GWP	global warming potential
h	hour
H	atomic hydrogen, hydrogen radical, height, heart rate, high dose, high exposure
H^+	hydrogen ion

HR	heart rate
H_2	molecular hydrogen
H_2CO	formaldehyde
H_2O	water
H_2O_2	hydrogen peroxide
H_2S	hydrogen sulfide
H_2SO_4	sulfuric acid
H9c2	rat embryonic cardiomyocytes cell line
HA	hospital admission
HAEC	Human Aortic Endothelial Cell
HAPC	Harvard ambient particle concentrator
HBE, HBEC	Human Bronchial Epithelial cells
HC	hydrocarbon(s); head circumference
HCB	hexachlorobenzene
HCH	hexachlorocyclohexane(s) (e.g. α-HCH, β-HCH)
HDL	high density lipoprotein
HEAPSS	Health Effects of Air Pollution among Susceptible Subpopulations study
HEI	Health Effects Institute
HEPA	high efficiency particle air (filter)
HERO	Health and Environmental Research Online, NCEA Database System
HF	heart failure, high frequency (HRV parameter), high (dose/exposure) filtered
HFCD	High-Fat Chow Diet
HFE	HFE gene, HFE protein
Hg	mercury
Hg(0)	gaseous elemental mercury
Hg(II)	gaseous divalent (oxidized) mercury
HH	hereditary hemochromatosis
HNRS	Hans Nixdorf Recall Study
HO-1	heme oxygenase-1
hOGG1	8-hydroxyguanine DNA-glycosylase
HOPE-G	Hamburg Atmosphere-Ocean Coupled Circulation Model
hPA	hectopascal
hPAEC	human pulmonary artery endothelial cells
hPBMC	human peripheral blood mononuclear cells

HPLC	high pressure liquid chromatography
HPMF	high particulate matter filtered
hPMVEC	human pulmonary microvascular endothelial cells
HR	heart rate, hazard ratio, high level DE
HRV	heart rate variability
HSD	17β-hydroxysteroid dehydrogenase
HSP-70	heat shock protein
HSPH	Harvard School of Public Health
HSRL	High Spectral Resolution Lidar
HUVEC	human umbilical vein endothelial cells
hν	photon
HWS	hardwood smoke
Hz	hertz
IC	ion chromatography
ICAM-1	intercellular adhesion molecule-1
ICARTT	International Consortium for Atmospheric Research on Transport and Transformation
ICAS	Inner-City Asthma Study
ICD	implantable/implanted cardioverter defibrillator
ICD-9	International Classification of Disease 9th revision
ICD-10	International Classification of Disease 10th revision
ICESat	Ice, Cloud and land Elevation Satellite
ICP-AES	inductively coupled plasma-atomic emission spectroscopy
ICP-MS	inductively-coupled plasma-mass spectrometry
ICR	imprinting control region, mouse strain
ICRP	International Commission on Radiological Protection
IDP	indeno[1,2,3-c,d]pyrene
IFN-γ	interferon-gamma
IFS	Integrated Forest Study
Ig	immunoglobulin (e.g., IgE)
IGS	International Genetic Standard
IHD	ischemic heart disease
IIASA	International Institute for Applied Systems Analysis
IL	interleukin
iMDDC	immature monocyte-derived dendritic cells

IMPACT	Interactive Modeling Project for Atmospheric Chemistry and Transport
IMPROVE	Interagency Monitoring of Protected Visual Environment
IN	ice nuclei
INAA	instrumental neutron activation analysis
INCA	Interactions between Chemistry and Aerosol
INDOEX	Indian Ocean Experiment
INGV-SXG	Istituto Nazionale di Geofisica e Vulcanologia coupled to SINTEX-G
INM-CM3.0	Institute of Numerical Mathematics climate model
iNOS	inducible nitric oxide synthase
INTEX	Intercontinental Chemical Transport Experiment
I/O	indoor-outdoor ratio
IOM	Institute of Medicine
i.p.	intraperitoneal
IP	inhalable particle
IPCC	Intergovernmental Panel on Climate Change
IPSL-CM4	Institut Pierre Simon Laplace climate model
IQR	interquartile range
Ir	iridium
IR	incidence rate, infrared radiation
IRE	iron responsive element
IRMS	isotope ratio mass spectrometer
ISA	Integrated Science Assessment
ISO	International Standards Organization
ISO	isoprene, 2-methyl analog of 1,3-butadiene
IT	intratracheal, intratracheally
IUGG	International Union of Geodesy and Geophysics
IUGR	intrauterine growth restriction, intrauterine growth retardation
i.v.	intravenous
JNK	c-jun N-terminal kinase
κB	kappa B
K	potassium
KC	local neutrophil chemoattractant protein
kHz	kilohertz
kJ	kilojoules
KLH	keyhole limpet hemocyanin

km	kilometer
km^{-1}	inverse kilometer
K_{ow}	octanol-water partition coefficient
L, dL, mL, µL	Liter, deciLiter, milliLiter, microLiter
L	low
La	lanthanum
LAC	light-absorbing carbon
LACE98	Lindenberg Aerosol Characterization Experiment 1998
LBA-SMOCC	Large-Scale Atmosphere-Biosphere Experiment in Amazon
LBW	low birth weight
LC	lethal concentration
LC_{50}	median lethal concentration
LDH	lactate dehydrogenase
LDL	low-density lipoprotein
LDLR	low-density lipoprotein receptor
LDVP	left developing ventricular pressure
LES	large eddy simulations model
LF	low frequency an HRV parameter
LF/HF	ratio of LF to HF an HRV parameter
LIBS	laser induced breakdown spectroscopy
LIF	leukemia inhibitory factor
LITE	Lidar In-space Technology Experiment
LMD	Laboratoire de Meteorologie Dynamique
LMDz	LMD with Zoom
LMDZ-INCA	LMDZ INteractive Chemistry and Aerosols model
LMDZ-LOA	LMDZ with Laboratoire d'Optique Atmosphérique model
L-NAME	arginine analog; N(G)-nitro-L- arginine methyl ester
L-NMMA	N(G)-mono-methyl-L-arginine
LnRMSSD	natural log of RMSSD; measure of HRV
lnSDNN	natural log of the standard deviation of NN intervals in an EKG
LOA	Laboratoire d'Optique Atmospherique
LOESS	locally weighted scatterplot smoothing
LOSU	level of scientific understanding
Lpm	liters per minute (L/min)
LPMF	low particulate matter filtered

LPO	plasma lipid peroxides
LPS	lipopolysaccharide
LRAT	long range atmospheric transport
LROT	long range oceanic transport
LSCE	Laboratoire des Sciences du Climat et de l'Environnement
LSDF	low-sulfur diesel fuel
LTB_4	leukotriene B_4
LTE_4	leukotriene E_4
LUA NRW	The North Rhine-Westphalia State Environment Agency
LUDEP	LUng Dose Evaluation Program
LUR	land use regression
LV	left ventricle
LVEDP	left-ventricular end-diastolic pressure,
LVSP	left-ventricular systolic pressure, left ventricular developed pressure
L/W	ratio of lumen to wall
LWC	liquid water content
LWDE	Low Whole Diesel Exhaust
LWP	liquid water path
µg	microgram
$\mu g/m^3$	micrograms per cubic meter
µm	micrometer, micron
m, cm, µm, nm	meter(s), centimeter(s), micrometer(s), nanometer(s)
M, mM, µM, nM, pM	Molar, milliMolar, microMolar, nanoMolar, picoMolar
M	dry aerosol mass, medium dose/exposure
ma	moving average
MAM	March-April-May
MAN	Maritime Aerosol Network
MANE-VU	Mid-Atlantic/Northeast Visibility Union
MAP	mitogen-activated protein, mean arterial pressure
MAPK	mitogen-activated protein kinase(s), MAP kinase
MARAMA	Mid Atlantic Regional Air Management Association
MATCH	Model of Atmospheric Transport and Chemistry
max	maximum
MBP	major basic protein
MCAPS	Medicare Air Pollution Study

Mch	methacholine
MCN	mixed carbon nanoparticle
MCP-1	monocyte chemoattractant protein 1
MCV	mean corpuscular volume
MD	mineral dust
MDA	malondialdehyde
MDCT	multidetector computed tomography
ME	Multilinear Engine
MEE	mass extinction efficiency
MEF	maximal expiratory flow
MEF_{50}	maximum expiratory flow rate at 50% of vital capacity
MeHg	methyl mercury
MENTOR	Modeling Environment for Total Risk Studies
MEP	motorcycle exhaust particulate(s)
MEPE	motorcycle exhaust particulate extract (particle-free)
MESA	Multi-Ethnic Study of Atherosclerosis
MFFSR	multifilter rotating shadowband radiometer
mg/m^3	milligrams per cubic meter
Mg	magnesium
MI	myocardial infarction
MIROC3.x	Model for Interdisciplinary Research on Climate
MILAGRO	Megacity Initiative: Local and Global Research Observations, study of air pollution in Mexico City
min	minute(s), minimum
MINOS	MPI Mediterranean INtensive Oxidant Study
MIP-2	macrophage inflammatory protein-2
MIRAGE	Megacities Impact on Regional and Global Environment program
MIS	mullerian inhibiting substance
MISR	Multi-angle Imaging SpectroRadiometer
Mm	megameter
Mm^{-1}	inverse megameter
MM	monocyte-derived macrophages
MM5	mesoscale model
MMAD	mass median aerodynamic diameter
MMD	mass median diameter
MMEF	maximal mid-expiratory flow

mmHg	millimeters of mercury
MMP	mitochondria membrane potential
MMP(2,9)	matrix metalloproteinase (2, or 9)
MMT	million metric tons
Mn	manganese
MN	micronuclei
$MnSO_4$	manganese sulfate
MnSOD	manganese superoxide dismutase
MnTBAP	manganese tetrakis (4-benzoic acid) porphyrin
mo	month
MOA	mode(s) of action
MODIS	MODerate resolution Imaging Spectroradiometer
MOUDI	Micro-Orifice Uniform Deposit Impactor
MOZART	MOdel for Ozone and Related chemical Tracers
MP	mid polar, myelopeptide
MPC	mean platelet component
MPF	median power frequency
MPG	N-(2-mercaptopropionyl) glycine
MPI	Max Planck Institute for Meteorology
MPLNET	Micro-Pulse Lidar Network
MPO	myeloperoxidase
MPPD	Multiple-Path Particle Dosimetry model
MPV	mean platelet volume
MRI	Meteorological Research Institute
MRI-CGCM	MRI coupled general circulation model
mRNA	messenger RNA
MRPO	Midwest Regional Planning Organization
ms	millisecond
MSA	metropolitan statistical area
MSH	melanocyte stimulating hormone
MSHA	Mount St. Helen ash
MSU	monosodium urate crystals
MT	metric ton
MTHFR	methylenetetrahydrofolate reductase
MTT	methyl thiazol tetrazolium

MV	motor vehicle
MWNT	multiplewall nanotube
M/Z	mass-to-charge ratio
N	nitrogen
N_2O	nitrous oxide
Na	sodium
Na_2SO_4	sodium sulfate
NAAQS	National Ambient Air Quality Standards
NAC	N-acetylcysteine, a thiol antioxidant
NaCl	sodium chloride
NADPH	reduced form of nicotinamide adenine dinucleotide phosphate
NAG	N-acetyl-β-D-glucosaminidase
Na,K-ATPase	sodium-potassium adenosine triphosphatase
NAMS	National Ambient Monitoring Stations
NaN_3	sodium azide
$NaNO_3$	sodium nitrate
nano-BAM	low pressure-drop ultrafine particle impactor coupled with a Beta Attenuation Monitor
NAPAP	National Acid Precipitation Assessment Program
NAPCA	National Air Pollution Control Administration
NAS	National Academy of Sciences
NASA	U.S. National Aeronautics and Space Administration
NASDA	National Space Development Agency, Japan
NATA	U.S. EPA's National Air Toxics Assessment
2-NB	2-nitrobenzanthrone
NC	total (particle) number concentration
NCAR	National Center for Atmospheric Research
NCC-MPSP	negatively charged carboxylate-modified polystyrene particle(s)
NCD	Normal Chow Diet
NCEA	National Center for Environmental Assessment
NCHS	National Center for Health Statistics
NCICAS	National Cooperative Inner-City Asthma Study
NCore	National Core
Nd	drop number concentration
Nd:YAG	neodymium-doped yttrium aluminum garnet laser
NDDN	National Dry Deposition Network

NEAQS	NOAA New England Air Quality Study
NEI	National Emissions Inventory
NESCAUM	Northeast States for Coordinated Air Use Management
NET	National Emissions Trends database
NFκB	nuclear factor kappa-B
NG	neutrophil granulocytes
NH	northern hemisphere
NH_3	ammonia
NH_4^+	ammonium ion
NH_4NO_3	ammonium nitrate
$(NH_4)_2SO_4$	ammonium sulfate
NHANES	National Health and Nutrition Examination Survey
NHBE(C)	normal human bronchial epithelial cells
NHPAE	normal human pulmonary artery endothelial cells
NHS	Nurses' Health Study
Ni	nickel
NIOSH	National Institute for Occupational Safety and Health
NIST	National Institute of Standards and Technology
NMHC	non-methane volatile hydrocarbon
NMMAPS	U.S. National Morbidity, Mortality, and Air Pollution Study
NO	nitric oxide
NO_2, $NO_2^{\cdot}$	nitrogen dioxide, nitrogen dioxide radical
NO_3^-	nitrate
NOAA	National Oceanic and Atmospheric Administration
NOAEL	no observed adverse effect level
NOS	nitric oxide synthase
NOS3	nitric oxide synthase 3
NOx	nitrogen oxides, oxides of nitrogen ($NO + NO_2$)
NP	National Park
NPM	non-blowing $PM_{2.5}$
NPOESS	National Polar-orbiting Operational Environment Satellite System
NPS	National Park Service, U.S. Department of the Interior
NR	not reported
NR5A1	nuclear receptor subfamily 5, group A, member 1
NRC	National Research Council

NRPB	National Radiological Protection Board
NSA	North Slope Alaska
NT	neurotrophin, nitrotyrosine
NWS	National Weather Service
NYHA	New York Heart Association
O	oxygen
O_2	molecular oxygen
O_3	ozone
OAQPS	Office of Air Quality Planning and Standards
OC	organic carbon
OCM	organic carbon mass
OE	organic extracts
OGG1	8 oxo-guanine repair enzyme
OH, OH•	hydroxyl group, hydroxyl radical
8-OHdG	8-hydroxydeoxyguanosine
OM	organic matter
OMI	Ozone Monitoring Instrument
OMM	organic molecular marker
OR	odds ratio(s)
OSM	oncostatin M, a cytokine
OSPM	Operational Street Pollution Model
OVA	ovalbumin
oxLDL	oxidation of LDL, marker of oxidative stress
8-oxodG	8-oxo-7-hydrodeoxyguanosine
ox-PAPC	oxidized 1-palmitoyl-2-arachidonoyl-sn-glycero-3-phosphorylcholine
P450	cytochrome P450
P450c17	cytochrome P450 17-α-hydroxylase
P450scc	cytochrome P450 cholesterol side chain cleavage enzyme
P90	90th percentile; Printex 90
p	probability value
P	phosphorus
PA	photoacoustic analyzer, physical activity, plasminogen activator, pulmonary arterial, alveolar pressure
PAF	platelet-activating factor
PAH	polycyclic aromatic hydrocarbon(s)
PAI	plasminogen activator inhibitor, (e.g. PAI-1)

PALMS	NOAA Particle Analysis by Laser Mass Spectrometry instrument
PAMCHAR	Chemical and Biological Characterisation of Ambient Air Coarse, Fine, and Ultrafine Particles for Human Health Risk Assessment in Europe
PAMS	Photochemical Assessment Monitoring Stations network
PAR	photosynthetically active radiation
PAR(s)	Pulmonary Artery Rings
PARASOL	Polarization and Directionality of the Earth's Reflectances, coupled with observations from a Lidar, a CNES satellite
PARP	poly(ADP-ribose) polymerase
PAS	Periodic Acid Schiff stain
Pb	lead
^{207}Pb	lead-207
PBDE	polybrominated diphenyl ether
PBL	planetary boundary layer
PBMC	peripheral blood mononuclear cell
PBMM	peripheral blood monocyte-derived macrophages
PBP	primary biological particle(s)
PBS	phosphate buffered saline
PC	synthetic carboxylate-modified particles
PCA	principal component analysis
PCA-MPSP	positively-charged amine modified polystyrene particle
PCB	polychlorinated biphenyl(s)
PCDD	polychlorinated dibenzo-p-dioxin
PCIS	Personal Cascade Impactor Sampler
PCM	NCAR Parallel Climate Model
PCPSP	positively charged polystyrene particle
PCR	polymerase chain reaction
PDF	probability distribution functions
pDR	personal DataRam
PE	post exposure, post exercise, phenylephrine
PEACE	Pollution Effects on Asthmatic Children in Europe study
PEC	particulate elemental carbon
PECAM-1	platelet endothelial cell adhesion molecule 1
PEF	peak expiratory flow (L/min)
PEFR	peak expiratory flow rate

PEFT	time to peak flow
PEM	personal exposure monitor
PEM-West	NASA Pacific Exploratory Missions in the western Pacific
Penh	enhanced pause
Per	perylene
PESA	particle elastic scattering analysis
PFDE	particle free diesel exhaust
PGE_2	prostaglandin E_2
PGI_2	prostacyclin
Phe	phenanthrene
PI	post instillation, posterior interval, pulmonary inflammation
PICT	pollution-induced community tolerance
PILS	Particle Into Liquid Sampler
PILS-IC	Particle Into Liquid Sampler-Ion Chromatography
PIXE	Particle Induced X-ray Emission
PKA	protein kinase A
PLS	partial least squares, projection to latent structures
PM	particulate matter
PMx	particulate matter of a specific size range. X refers to the diameter at which the sampler collects 50% of the particles and rejects 50% of the particles. Collection efficiency increases for particles with smaller diameters and decreases for particles with larger diameters. The variation of collection efficiency with size is given by a collection efficiency curve. The definition of PMx is frequently abbreviated as "particles with a nominal mean aerodynamic diameter less than or equal to x µm.
PMx-y	particulate matter with a nominal mean diameter greater than x µm and less than y µm where x and y are the numeric mean aerodynamic or mobility diameters (µm).
$PM_{0.1}$	particulate matter with a nominal mean mobility diameter less than or equal to 0.1 µm (referred to as ultrafine PM)
$PM_{2.5}$	particulate matter with a nominal mean aerodynamic diameter less than or equal to 2.5 µm (referred to as fine PM)
PM_{10}	particulate matter with a nominal mean aerodynamic diameter less than or equal to 10 µm
$PM_{10-2.5}$	particulate matter with a nominal mean aerodynamic diameter greater than 2.5 µm and less than or equal to 10 µm (referred to as thoracic coarse particulate matter or the course fraction of PM_{10}) Concentration may be measured with a dichotomous sampler or calculated as the difference between measured PM_{10} and measured $PM_{2.5}$ concentrations.
PMA	phorbol 12-myristate 13-acetate
PMF	particulate matter filtrate, positive matrix factorization

PM-HD	particulate matter at high concentration
PM-LD	particulate matter at low concentration
PMN	polymorphonuclear leukocytes
PN	particle number
PNC	particle number concentration, particle number count
PND, pnd	post-natal day
PNMD	particle number median diameter
PNN	proportion of interval differences of successive normal-beat intervals in EKG
pNN50	proportion of interval differences of successive normal-beat intervals greater than 50 ms in an EKG
PNNL	Pacific Northwest National Laboratory
pNO_3	particulate nitrate
POA	primary organic aerosol
POC	particulate organic carbon
POLDER	POLarization and Directionality of the Earth's Reflectance
POM	particulate organic matter
POP	persistent organic pollutant
P_p	particle density
PP	pulse pressure
ppb	parts per billion
PPFL	percent predicted lung function
ppm	parts per million
ppt	parts per trillion
PRB	policy-relevant background
PRE	AeroCom Experiment
PRELC	Primary Rat Epithelial Lung Cells
PRIDE	Puerto RIco Dust Experiment
PS	public school
PSAS	The French National Program on Air Pollution Health Effects
PSO	Public Service Company of Oklahoma
pSO_4	particulate sulfate
PSS	physiologic saline solution
PSU	Pennsylvania State University
PT	prothrombin time
PTT	partial thomboplastin time

PTV	programmable temperature vaporization
PVD	peripheral vascular disease
Pyr	pyrene
Q	cardiac output
Q	coronary flow of the heart
QAI	QA interval
QBQ	backup quartz-fiber filter behind a quartz-fiber filter
QEEG	quantitative electroencephalography
Qext	the extinction coefficient (a function of particle size distribution and refractive index)
r	correlation coefficient
R^2	coefficient of determination
RAIN	Regional Aerosol Intensive Network
RAMS	real-time total ambient mass sampler
RANTES	regulated upon activation, normal T cell expressed and secreted
RAPS/RAMS	Regional Air Pollution Study / Regional Air Monitoring Study
RAR	rapidly activating receptor(s)
RASMC	rat aortic smooth muscle cells
RAW 264.7	mouse macrophage cell line
RBC	red blood cell
RD	respiratory disease
REALM	Regional East Atmospheric Lidar Mesonet
RF	radiative forcing(s)
r_{eff}	particle effective radius
RFL	Fetal Lung Fibroblasts
RH	relative humidity
RHMVE	rat heart micro-vessel endothelial cell
RHR	Regional Haze Rule
RLF	rat lung fibroblasts
RMC	rat cardiomyocyte(s)
RME	rapeseed oil methyl ester
RMSSD	root mean squared differences of successive normal-beat to normal-beat (NN or RR) time intervals between each QRS complex in the EKG
RMV	respiratory minute volume
RNA	ribonucleic acid

RNS	reactive nitrogen species
RO	residual oil
ROCK	rho associated kinase
ROFA	residual oil fly ash (particles)
ROFA-L	residual oil fly ash leachate
ROI	reactive oxygen intermediates
ROS	reactive oxygen species
RPO	Regional Planning Organizations
RR	risk ratio, relative risk, normal-to-normal (NN or RR) time interval between each QRS complex in the EKG
RS	resuspended soil
RSV	respiratory syncytial virus
RTI	respiratory tract infection
RTM	Radiative Transfer Model
RTP	Research Triangle Park, North Carolina
RV	right ventricular
RVCFB	right ventricular cardio fibroblasts
RVCM	right ventricular cardiomyopathy, rat ventricular cardiomyocytes, reduced volume culture medium
σ	sigma, standard deviation
1σ	one sigma; one standard deviation
σ_g	sigma-g; geometric standard deviation
s	second
S	sulfur
SAB	(EPA) Science Advisory Board
SAFARI	South African Fire-Atmosphere Research Initiative
SAGE	Stratospheric Aerosol and Gas Experiment
SALIA	German study on the Influence of Air Pollution on Lung Function, Inflammation, and Aging
SAM	Stratospheric Aerosol Measurement
SAMUM	Saharan Mineral Dust Experiment
SAP2.3	Synthesis and Assessment Product 2.3
Sb	antimony
SB	strand breaks
SBL	stable boundary layer
SBP	systolic blood pressure

Sc	scandium
SC	summer curbside particles
SCAB	California South Coast Air Basin
SCAR	Smoke/Sulfates, Clouds and Radiation
SCARPOL	Swiss Study on Childhood Allergy and Respiratory Symptoms with Respect to Air Pollution
sCD40L	soluble CD40 ligand
SCE	sister chromatid exchange
SCS	Harvard Six Cities Study
SD	standard deviation; Sprague-Dawley rat
SDANN5	standard deviation of the average of normal to normal (N:N) intervals in all 5-min intervals in a 24-h period
SDNN	standard deviation normal-to-normal (NN or RR) time interval between each QRS complex in the EKG
SDNN24HR	standard deviation of the average of all normal to normal intervals in a 24-h period
Se	selenium
se	standard error
SEARCH	Southeastern Aerosol Research and Characterization
sem	standard error of mean
SEM	scanning electron microscopy
SES	socioeconomic status, sample equilibration system
SF-1	steroidogenic factor -1
SF-UFID	suspension, particle free ultrafine industrial exhaust
SGA	small for gestational age
sGC	soluble guanylate cyclase
SGP	Southern Great Plains
-SH	sulfhydryl group
SH	Mount Saint Helen's ash
SH, SHR	spontaneously hypertensive disease model rat
SHADE	Saharan Dust Experiment
SHEDS	Stochastic Human Exposure and Dose Simulation model
Si	silicon
sICAM-1	soluble intercellular adhesion molecule
SIDS	sudden infant death syndrome
SiO_2	silicone dioxide
SIPS	State Implementation Plan

SJV	San Joaquin Valley
SLAMS	State and Local Air Monitoring Stations
SME	soybean oil methyl ester
SMOCC	Smoke Aerosols, Clouds, Rainfall and Climate
SMOKE	Spare-Matrix Operator Kernel Emissions system
SMPS	scanning mobility particle sizer
SMPS-APS	scanning mobility particle sizer– aerodynamic particle sizer
SMRA	small mesenteric rat arteries
SNP	single-nucleotide polymorphism, sodium nitroprusside
SNS	sympathetic nervous system
SO_2	sulfur dioxide
SO_3	sulfur trioxide
SO_4^{2-}	sulfate
SOA	secondary organic aerosol
SOC	semi-volatile organic compound
SOD	superoxide dismutase
SOPHIA	Study of Particulates and Health in Atlanta
SO_X	sulfur oxides, oxides of sulfur
SP	surfactant protein (e.g., SPA, SPD)
SPA	surfactant protein A
SPD	surfactant protein D
SPEW	Speciated Pollutant Emission Wizard
SPG	Southern Great Plains site
SPM	suspended particulate matter
SPRINTARS	Spectral Radiation-Transport Model for Aerosol Species
SRM-154b	NIST standard reference material 154b; (TiO_2 Titanium dioxide)
SRM1648	NIST standard reference material 1648; (urban particulate matter)
SRM-1649	NIST standard reference material 1649 (Washington, D.C. urban air particulate matter, urban dust)
SRM-1650	NIST standard reference material 1650 (diesel exhaust particulate matter)
SRM-1879	NIST standard reference material 1859; (silicone dioxide, respirable cristobalite [respirable crystalline silica])
SRM-2975	NIST standard reference material 2975 (diesel exhaust particulate matter)
s-ROFA	soluble portion of residual oil fly ash
SS	secondary sulfate, sea salt

SSA	single-scattering albedo
SSR	standardized sex ratio
SST	sea surface temperature
STEM	Sulfur / Sulfate Transport Eulerian Model
STN	EPA Speciation Trend Network
STP	standard temperature and pressure
STZ	Streptozotocin
SUB	summer urban background particles
SURFRAD	NOAA GMD Surface Radiation network
SVA	supraventricular arrhythmia
sVCAM-1	soluble vascular adhesion molecule 1
SVEB	supraventricular ectopic beats
SWNT	singlewalled nanotube
SXRF	Synchroton X-ray fluorescence
SZA	solar zenith angle
τ	photochemical lifetime
T	body temperature
TAR	IPCC 3rd Assessment Report
TARC	thymus and activation-regulated chemokine
TARFOX	Tropospheric Aerosol Radiative Forcing Observational Experiment
TAT	thrombin-anti-thrombin complexes
TB	tracheobronchial
TBA	thiobarbituric acid
TBAP	tetrakis(4-benzoic acid) porphyrin
TBARS	thiobarbituric acid reactive substances
TBQ	backup quartz-fiber filter behind a Teflon-membrane filter
^{99m}Tc	Technetium-99m
^{99m}Tc-DMTA	^{99M}Tc Dynamic mechanical thermal analysis
^{99M}Tc-DTPA	^{99M}Tc-diethylenetriaminepentaacetic acid
T_{co}	core temperature
TD	thermal desorption, tire debris extracted in methanol
TD-GC/MS	thermal desorption-gas chromatography/mass spectrometry
TEAC	Trolox Equivalent Antioxidant Capacity assay
TEOM	Tapered Element Oscillating Microbalance
TexAQS	Texas Air Quality Field Study

TF	tissue factor
TFPI	tissue factor pathway inhibitor
Tg	teragram
TG	terminal ganglion (neurons)
TGF	transforming growth factor
TGF β	β transforming growth factor
Th	thorium
Th1	T helper cell type 1
Th2	T helper cell type 2
tHcy	total homocysteine
Ti	titanium
TIA	transient ischemic attack
TiFe	iron-loaded fine titanium oxide
TIMP-2	tissue inhibitor of MMP
TiO_2	titanium dioxide
TK	thymidine kinase
TM	transition metals
TM5	Thematic Mapper, a sensor on Landsat5 satellite
TMTU	tetramethylthiourea
TNF-α	tumor necrosis factor alpha
TOA	top of the atmosphere
TOF-SIMS	time-of-flight - secondary ion mass spectrometry
TOMS	Total Ozone Mapping Spectrometer
TOT/GC	thermal optical transmission analyzer coupled with gas chromatography
TOVS	TIROS-N Operational Vertical Sounder
tPA, t-PA	tissue plasminogen activator
TRACE	Transition Region and Coronal Explorer
TRP	transient receptor potential
TRPV1	transient receptor potential vanilloid-1 receptor
TR-XRF	total reflection X-ray fluorescence
TSA	trichostatin A
TSP	total suspended particulate
TSS	WRAP Technical Support System website
TVOC	total VOC
TWP	Tropical West Pacific island

TXB_2	thromboxane B-2
U	uranium
UACR	urinary albumin / creatinine ratio
UAE^2	United Arab Emirates Unified Aerosol Experiment
UAP	urban ambient particle
UF	ultrafine, uncertainty factor
UFAA	ultrafine ambient air
UFC	ultrafine carbon
UfCB	ultrafine carbon black
UFDG	ultrafine diesel engine exhaust
UFID	ultrafine industrial exhaust
UFP	ultrafine particle
UFPM	ultrafine particulate matter
$UFTiO_2$	ultrafine titanium dioxide
UIO	University of Oslo
U.K.	United Kingdom
UKMO	United Kingdom Meteorological Office
ULAQ	University of lL'Aquila.
ULTRA	Exposure and Risk Assessment for Fine and Ultrafine Particles in Ambient Air
UMI	University of Michigan
UNEP	United Nations Environmental Programme
UP	urban particle
UPM	ultrafine particulate matter
UPSP	unmodified polystyrene particle(s)
URI	upper respiratory infection
URS	upper respiratory symptoms
U.S.	United States of America
U.S.C.	U.S. Code
UV	ultraviolet radiation
V	vanadium
V, mV, µV	volt, millivolt, microvolt
VAQ	visual air quality
VCAM-1	vascular adhesion molecule 1
V_d	deposition velocity
VEAPS	Vitamin E Atherosclerosis Progression Study

VEGF	vascular endothelial growth factor
VIEWS	Visibility Information Exchange Web Site
VISTAS	Visibility Improvement State and Tribal Association of the Southeast
VOC	volatile organic compound
$VOSO_4$	vanadyl sulfate
VPB	ventricular premature beat
VR	visual range
VR1	vanilloid receptor 1
VSCC	very sharp cut cyclone
VSMC	Vascular Smooth Muscle Cells
V_T	tidal volume
vWF	von Willebrand factor
W	Wilderness
WACAP	Western Airborne Contaminates Assessment Project
WBC	white blood cell(s)
WC	winter curbside particles
WHI	Women's Health Initiative
WHI OS	Women's Health Initiative Observational Study
wk	week(s)
WKY	Wistar-Kyoto rat strain
W/m^2, $W\ m^{-2}$	watts per square meter
WMO	World Meteorological Organization
Wnt	wingless gene family
WRAP	Western Regional Air Partnership
WRF	Weather Research and Forecasting model
WS	wood smoke
WSOC	water soluble organic carbon
WUB	winter urban background particles
XAD	polystyrene-divinyl benzene
XPS	X-ray photoelectron spectroscopy
Y	yttrium
yr	year
Z	radar reflectivity (measured in dBZ [decibels of Z, where Z represents the energy reflected back to the radar.])
Zn	zinc
ZnO	zinc oxide

ZnS	zinc sulfide
$ZnSO_4$	zinc sulfate
Zr	zirconium

Chapter 1. Introduction

This Integrated Science Assessment (ISA) is a review, synthesis, and evaluation of the most policy-relevant evidence, and communicates critical science judgments relevant to the National Ambient Air Quality Standards (NAAQS) review. As such, the ISA forms the scientific foundation for the review of the primary (health-based) and secondary (welfare-based) NAAQS for particulate matter (PM). The ISA accurately reflects "the latest scientific knowledge useful in indicating the kind and extent of identifiable effects on public health which may be expected from the presence of [a] pollutant in ambient air" (42 U.S.C. 7408). Key information and judgments formerly contained in an Air Quality Criteria Document (AQCD) for PM are incorporated in this assessment. Additional details of the pertinent literature published since the last review, as well as selected older studies of particular interest, are included in a series of annexes. This ISA thus serves to update and revise the evaluation of the scientific evidence available at the time of the previous review of the NAAQS for PM that was concluded in 2006.

The *Integrated Review Plan for the National Ambient Air Quality Standards for Particulate Matter* identifies a series of policy-relevant questions that provide a framework for this assessment of the scientific evidence (U.S. EPA, 2008, 157072). These questions frame the entire review of the NAAQS for PM, and thus are informed by both science and policy considerations. The ISA organizes and presents the scientific evidence such that, when considered along with findings from risk analyses and policy considerations, will help the EPA address these questions during the NAAQS review for PM. In evaluating the health evidence, the focus of this assessment will be on scientific evidence that is most relevant to the following questions that have been taken directly from the Integrated Review Plan:

- Has new information altered the body of scientific support for the occurrence of health effects following short- and/or long-term exposure to levels of fine and thoracic coarse particles found in the ambient air?

- Has new information altered conclusions from previous reviews regarding the plausibility of adverse health effects associated with exposures to $PM_{2.5}$, PM_{10}, $PM_{10-2.5}$, or alternative PM indicators that might be considered?

- What evidence is available from recent studies focused on specific size fractions, chemical components, sources, or environments (e.g., urban and non-urban areas) of PM to inform our understanding of the nature of PM exposures that are linked to various health outcomes?

- To what extent is key scientific evidence becoming available to improve our understanding of the health effects associated with various time periods of PM exposures, including not only short-term (daily or multi-day) and chronic (months to years) exposures, but also peak PM exposures (<24 hours)? To what extent is critical research becoming available that could improve our understanding of the relationship between various health endpoints and different lag periods (e.g., <1 day, single day, multi-day distributed lags)?

- What data are available to improve our understanding of spatial and/or temporal heterogeneity of PM exposures considering different size fractions and/or components?

- At what levels of PM exposure do health effects of concern occur? Is there evidence for the occurrence of adverse health effects at levels of PM lower than those observed previously? If so, at what levels and what are the important uncertainties associated with

Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISA) and the Integrated Risk Information System (IRIS).

that evidence? What is the nature of the dose-response relationships of PM for the various health effects evaluated?

- What evidence is available linking particle number concentration with adverse health effects of UF particles?

- Do risk/exposure estimates suggest that exposures of concern for PM-induced health effects will occur with current ambient levels of PM or with levels that just meet the current standards? If so, are these risks/exposures of sufficient magnitude such that the health effects might reasonably be judged to be important from a public health perspective? What are the important uncertainties associated with these risk/exposure estimates?

- To what extent is key evidence becoming available that could inform our understanding of subpopulations that are particularly sensitive or vulnerable to PM exposures? In the last review, sensitive or vulnerable subpopulations that appeared to be at greater risk for PM-related effects included individuals with pre-existing heart and lung diseases, older adults, and children. Has new evidence become available to suggest additional sensitive subpopulations should be given increased focus in this review (e.g., fetuses, neonates, genetically susceptible subpopulations)?

- To what extent is key evidence becoming available to inform our understanding of populations that are particularly vulnerable to PM exposures? Specifically, is there new or emerging evidence to inform our understanding of geographical, spatial, SES, and environmental justice considerations?

- To what extent have important uncertainties identified in the last review been reduced and/or have new uncertainties emerged?

- To what extent is new information available to inform our understanding of non-PM-exposure factors that might influence the associations between PM levels and health effects being considered (e.g., weather-related factors; behavioral factors such as heating/air conditioning use; driving patterns; and time-activity patterns)?

In evaluating evidence on welfare effects of PM, the focus will be on evidence that can help inform these questions from the Integrated Review Plan:

- What new evidence is available on the relationship between PM mass/size fraction and/or specific PM components and visibility impairment and climate-related and other welfare effects?

- To what extent has key scientific evidence now become available to improve our understanding of the nature and magnitude of visibility, climate, and ecosystem responses to PM and the variability associated with those responses (including ecosystem type, climatic conditions, environmental effects and interactions with other environmental factors and pollutants)?

- Do the evidence, the air quality assessment, and the risk/exposure assessment provide support for considering alternative averaging times?

- At what levels of ambient PM do visibility impairment and/or environmental effects of concern occur? Is there evidence for the occurrence of adverse visibility and other welfare-related effects at levels of PM lower than those observed previously? If so, at what levels and what are the important uncertainties associated with the evidence?

- Do the analyses suggest that PM-induced visibility impairment and/or other welfare-effects will occur with current ambient levels of PM or with levels that just meet the current standards? If so, are these effects of sufficient magnitude and/or frequency such

that these effects might reasonably be judged to be important from a public welfare perspective? What are the uncertainties associated with these estimates?

- What new evidence and/or techniques are available to quantify the benefits of improved visibility and/or other welfare-related effects?

- To what extent have important uncertainties identified in the last review been reduced and/or have new uncertainties emerged?

1.1. Legislative Requirements

Two sections of the United States (U.S.) Clean Air Act (CAA, the Act) govern the establishment and revision of the NAAQS. Section 108 of the Act (42 U.S.C. 7408) directs the Administrator to identify and list "air pollutants" that "in his judgment, may reasonably be anticipated to endanger public health and welfare" and whose "presence… in the ambient air results from numerous or diverse mobile or stationary sources" and to issue air quality criteria for those that are listed (42 U.S.C. 7408). Air quality criteria are intended to "accurately reflect the latest scientific knowledge useful in indicating the kind and extent of identifiable effects on public health or welfare which may be expected from the presence of [a] pollutant in ambient air…" 42 U.S.C. 7408(b).

Section 109 of the Act (42 U.S.C. 7409) directs the Administrator to propose and promulgate "primary" and "secondary" NAAQS for pollutants listed under Section 108. 42 U.S.C. 7409(a). Section 109(b)(1) defines a primary standard as one "the attainment and maintenance of which in the judgment of the Administrator, based on such criteria and allowing an adequate margin of safety, are requisite to protect the public health."[1] 42 U.S.C. 7409(b)(1). A secondary standard, as defined in Section 109(b)(2), must "specify a level of air quality the attainment and maintenance of which, in the judgment of the Administrator, based on such criteria, is required to protect the public welfare from any known or anticipated adverse effects associated with the presence of [the] pollutant in the ambient air."[2] 42 U.S.C. 7409(b)(2).

The requirement that primary standards include an adequate margin of safety was intended to address uncertainties associated with inconclusive scientific and technical information available at the time of standard setting. It was also intended to provide a reasonable degree of protection against hazards that research has not yet identified. See *Lead Industries Association v. EPA*, 647 F.2d 1130, 1154 (D.C. Cir 1980), cert. denied, 449 U.S. 1042 (1980); *American Petroleum Institute v. Costle*, 665 F.2d 1176, 1186 (D.C. Cir. 1981), cert. denied, 455 U.S. 1034 (1982); *American Farm Bureau Federation v. EPA*, 559 F. 3d 512, 533 (D.C. Cir. 2009). Both kinds of uncertainties are components of the risk associated with pollution at levels below those at which human health effects can be said to occur with reasonable scientific certainty. Thus, in selecting primary standards that include an adequate margin of safety, the Administrator is seeking not only to prevent pollution levels that have been demonstrated to be harmful, but also to prevent lower pollutant levels that may pose an unacceptable risk of harm, even if the risk is not precisely identified as to nature or degree.

In selecting a margin of safety, the EPA considers such factors as the nature and severity of the health effects involved, the size of the sensitive population(s) at risk, and the kind and degree of the uncertainties that must be addressed. The selection of any particular approach to providing an adequate margin of safety is a policy choice left specifically to the Administrator's judgment. See *Lead Industries Association v. EPA*, supra, 647 F.2d 1161-62.

In setting standards that are "requisite" to protect public health and welfare, as provided in Section 109(b), the Administrator's task is to establish standards that are neither more nor less

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[1] The legislative history of Section 109 indicates that a primary standard is to be set at "the maximum permissible ambient air level…which will protect the health of any [sensitive] group of the population," and that for this purpose "reference should be made to a representative sample of persons comprising the sensitive group rather than to a single person in such a group" [S. Rep. No. 91-1196, 91st Cong., 2d Sess. 10 (1970)].

[2] Welfare effects as defined in Section 302(h) [42 U.S.C. 7602(h)] include, but are not limited to, "effects on soils, water, crops, vegetation, man-made materials, animals, wildlife, weather, visibility and climate, damage to and deterioration of property, and hazards to transportation, as well as effects on economic values and on personal comfort and well-being."

stringent than necessary. In so doing, EPA may not consider the costs of implementing the standards. See generally *Whitman v. American Trucking Associations*, 531 U.S. 457, 465-472, 475-76 (2001).

Section 109(d)(1) requires that "not later than December 31, 1980, and at 5-yr intervals thereafter, the Administrator shall complete a thorough review of the criteria published under Section 108 and the national ambient air quality standards…and shall make such revisions in such criteria and standards and promulgate such new standards as may be appropriate…" 42 U.S.C. 7409(d)(1). Section 109(d)(2) requires that an independent scientific review…committee "shall complete a review of the criteria and the national primary and secondary ambient air quality standards…and shall recommend to the Administrator any new standards and revisions of existing criteria and standards as may be appropriate…" 42 U.S.C. 7409(d)(2). Since the early 1980s, this independent review function has been performed by the Clean Air Scientific Advisory Committee (CASAC).

1.2. History of Reviews of the NAAQS for PM

PM is the generic term for a broad class of chemically and physically diverse substances that exist as discrete particles (liquid droplets or solids) over a wide range of sizes. Particles originate from a variety of anthropogenic stationary and mobile sources, as well as from natural sources. Particles may be emitted directly or formed in the atmosphere by transformations of gaseous emissions such as sulfur oxides (SO_X), nitrogen oxides (NO_X), and volatile organic compounds (VOC). The chemical and physical properties of PM vary greatly with time, region, meteorology, and source category, thus complicating the assessment of health and welfare effects. Table 1-1 summarizes the NAAQS that have been promulgated for PM to date. These reviews are briefly described below, and further details are provided in the Integrated Review Plan (U.S. EPA, 2008, 157072).

EPA first established NAAQS for PM in 1971 (36 FR 8186, April 30, 1971), based on the original criteria document (NAPCA, 1969, 014684). The reference method specified for determining attainment of the original standards was the high-volume sampler, which collects PM up to a nominal size of 25-45 micrometers (μm) (referred to as total suspended particulates [TSP]). The primary standards (measured by the indicator TSP) were 260 μg/m^3, 24-h avg, not to be exceeded more than once per year, and 75 μg/m^3, annual geometric mean. The secondary standard was 150 μg/m^3, 24-h avg, not to be exceeded more than once per year. In October 1979 (44 FR 56730, October 2, 1979), EPA announced the first periodic review of the air quality criteria and NAAQS for PM, and significant revisions to the original standards were promulgated in 1987 (52 FR 24634, July 1, 1987). In that decision, EPA changed the indicator for particles from TSP to PM_{10}, the latter including particles with a mean aerodynamic diameter[1] ≤ 10 μm, which delineated that subset of inhalable particles small enough to penetrate to the thoracic region (including the tracheobronchial and alveolar regions) of the respiratory tract (referred to as thoracic particles). EPA also revised the level and form of the primary standards by (1) replacing the 24-h TSP standard with a 24-h PM_{10} standard of 150 μg/m^3 with no more than one expected exceedence per year; and (2) replacing the annual TSP standard with a PM_{10} standard of 50 μg/m^3, annual arithmetic mean, averaged over 3 yr.

[1] The more precise term is 50% cut point or 50% diameter (d50). This is the aerodynamic particle diameter for which the efficiency of particle collection is 50%. Larger particles are not excluded altogether, but are collected with substantially decreasing efficiency and smaller particles are collected with increasing (up to 100%) efficiency.

Table 1-1. Summary of NAAQS promulgated for PM, 1971-2006.

Year (Final Rule)	Indicator	Avg Time	Level	Form
1971 (36 FR 8186)	TSP (Total Suspended Particulates)	24 h	260 μg/m^3 (primary) 150 μg/ m^3 (secondary)	Not to be exceeded more than once per yr
		Annual	75 μg/m^3 (primary)	Annual geometric mean
1987 (52 FR 24634)	PM_{10}	24 h	150 μg/m^3	Not to be exceeded more than once per yr on average over a 3-yr period
		Annual	50 μg/m^3	Annual arithmetic mean, averaged over 3 yr
1997 (62 FR 38652)	$PM_{2.5}$	24 h	65 μg/m^3	98th percentile, averaged over 3 yr
		Annual	15 μg/m^3	Annual arithmetic mean, averaged over 3 yr[1]
	PM_{10}	24 h	150 μg/m^3	Initially promulgated 99th percentile, averaged over 3 yr; when 1997 standards were vacated in 1999, the form of 1987 standards remained in place (not to be exceeded more than once per yr on average over a 3-yr period)
		Annual	50 μg/m^3	Annual arithmetic mean, averaged over 3 yr
2006 (71 FR 61144)	$PM_{2.5}$	24 h	35 μg/m^3	98th percentile, averaged over 3 yr
		Annual	15 μg/m^3	Annual arithmetic mean, averaged over 3 yr[2]
	PM_{10}	24 h	150 μg/m^3	Not to be exceeded more than once per yr on average over a 3-yr period

Note: When not specified, primary and secondary standards are identical.

The secondary standard was revised by replacing it with 24-h and annual standards identical in all respects to the primary standards. The revisions also included a new reference method for the measurement of PM_{10} in the ambient air and rules for determining attainment of the new standards. On judicial review, the revised standards were upheld in all respects. See *Natural Resources Defense Council v. Administrator*, 902 F. 2d 962 (D.C. Cir. 1990), cert. denied, 498 U.S. 1082 (1991).

In April 1994, EPA announced its plans for the second periodic review of the air quality criteria and NAAQS for PM, and promulgated significant revisions to the NAAQS in 1997 (62 FR 38652, July 18, 1997). In that decision, EPA revised the PM NAAQS in several respects. Most significantly, EPA determined that the fine and coarse[3] fractions of PM_{10} should be considered separately. The Administrator's decision to modify the standards was based on evidence that serious health effects were associated with short- and long-term exposure to fine particles in areas that met the existing PM_{10} standards. EPA accordingly added new standards, using $PM_{2.5}$ as the indicator for fine particles (with $PM_{2.5}$ referring to particles with a nominal mean aerodynamic diameter $\leq$ 2.5 μm), and PM_{10} as the indicator for thoracic coarse particles or coarse-fraction particles (generally including particles with a nominal mean aerodynamic diameter >2.5 μm and $\leq$ 10 μm, or $PM_{10-2.5}$). The EPA established two new $PM_{2.5}$ standards: an annual standard of 15 μg/m^3, based on the 3-yr avg of annual arithmetic mean $PM_{2.5}$ concentrations from single or multiple community-oriented monitors; and a 24-h standard of 65 μg/m^3, based on the 3-yr avg of the 98th percentile of 24-h $PM_{2.5}$ concentrations at each population-oriented monitor within an area. Also, EPA established a new reference method for measuring $PM_{2.5}$ in the ambient air and adopted protocols for determining attainment of the new standards. To continue to address thoracic coarse particles, EPA retained the annual PM_{10} standard, while revising the form, but not the level, of the

[1] The level of the 1997 annual $PM_{2.5}$ standard was to be compared to measurements made at the community-oriented monitoring site recording the highest level, or, if specific constraints were met, measurements from multiple community-oriented monitoring sites could be averaged ("spatial averaging"). This approach was judged to be consistent with the short-term epidemiologic studies on which the annual $PM_{2.5}$ standard was primarily based, in which air quality data were generally averaged across multiple monitors in an area or were taken from a single monitor that was selected to represent community-wide exposures, not localized "hot spots" (62 FR 38672). These criteria and constraints were intended to ensure that spatial averaging would not result in inequities in the level of protection afforded by the $PM_{2.5}$ standards. Community-oriented monitoring sites were specified to be consistent with the intent that a spatially averaged annual standard provide protection for persons living in smaller communities, as well as those in larger population centers.

[2] In the revisions to the PM NAAQS finalized in 2006, EPA tightened the constraints on the spatial averaging criteria by further limiting the conditions under which some areas may average measurements from multiple community-oriented monitors to determine compliance (71 FR 61165-61167, October 17, 2006).

[3] See definitions of "fine" and "coarse" particles in Section 3.2.

24-h PM_{10} standard to be based on the 99th percentile of 24-h PM_{10} concentrations at each monitor in an area. The EPA revised the secondary standards by making them identical in all respects to the primary standards.

Following promulgation of the 1997 PM NAAQS, petitions for review were filed by a large number of parties, addressing a broad range of issues. In May 1999, a three-judge panel of the U.S. Court of Appeals for the District of Columbia Circuit issued an initial decision that upheld EPA's decision to establish fine particle standards, holding that "the growing empirical evidence demonstrating a relationship between fine particle pollution and adverse health effects amply justifies establishment of new fine particle standards." *American Trucking Associations v. EPA* (175 F. 3d 1027, 1055-56 (D.C. Cir. 1999); rehearing granted in part and denied in part, 195 F. 3d 4 (D.C. Cir. 1999), affirmed in part and reversed in part, *Whitman v. American Trucking Associations* 531 U.S. 457 (2001). The panel also found "ample support" for EPA's decision to regulate coarse particle pollution, but vacated the 1997 PM_{10} standards, concluding that EPA had not provided a reasonable explanation justifying use of PM_{10} as an indicator for coarse particles (175 F. 3d at 1054-55). Pursuant to the court's decision, EPA removed the vacated 1997 PM_{10} standards from the Code of Federal Regulations. The pre-existing 1987 PM_{10} standards remained in place (65 FR 80776, December 22, 2000). The Court also upheld EPA's determination not to establish more stringent secondary standards for fine particles to address effects on visibility (175 F. 3d at 1027).

More generally, the panel held (over one judge's dissent) that EPA's approach to establishing the level of the standards in 1997, both for the PM and ozone (O_3) NAAQS promulgated on the same day, effected "an unconstitutional delegation of legislative authority" (Id. at 1034-40). Although the panel stated that "the factors EPA uses in determining the degree of public health concern associated with different levels of ozone and PM are reasonable," it remanded the rule to EPA, stating that when EPA considers these factors for potential non-threshold pollutants "what EPA lacks is any determinate criterion for drawing lines" to determine where the standards should be set. Consistent with EPA's long-standing interpretation and D.C. Circuit precedent, the panel also reaffirmed its prior holdings that in setting NAAQS EPA is "not permitted to consider the cost of implementing those standards" (Id. at 1040-41).

On EPA's petition for rehearing, the panel adhered to its position on these points. *American Trucking Associations v. EPA*, 195 F. 3d 4 (D.C. Cir. 1999). The full Court of Appeals denied EPA's suggestion for rehearing en banc, with five judges dissenting (Id. at 13).

Both sides filed cross appeals on these issues to the U.S. Supreme Court, and the Court granted *certiorari*. In February 2001, the Supreme Court issued a unanimous decision upholding EPA's position on both the constitutional and cost issues. *Whitman v. American Trucking Associations*, 531 U.S. 457, 464, 475-76. On the constitutional issue, the Court held that the statutory requirement that NAAQS be "requisite" to protect public health with an adequate margin of safety sufficiently guided EPA's discretion, affirming EPA's approach of setting standards that are neither more nor less stringent than necessary. The Supreme Court remanded the case to the Court of Appeals for resolution of any remaining issues that had not been addressed in that court's earlier rulings (Id. at 475-76). In March 2002, the Court of Appeals rejected all remaining challenges to the standards, holding under the traditional standard of judicial review that $PM_{2.5}$ standards were reasonably supported by the administrative record and were not "arbitrary and capricious" *American Trucking Associations v. EPA*, 283 F. 3d 355, 369-72 (D.C. Cir. 2002).

In October 1997, EPA published its plans for the third periodic review of the air quality criteria and NAAQS for PM (62 FR 55201). After CASAC and public review, EPA finalized the 2004 PM AQCD (U.S. EPA, 2004, 056905) and 2005 Staff Paper (U.S. EPA, 2005, 090209). For the primary fine particle standards, most CASAC PM Panel members favored the option of revising the level of the 24-h $PM_{2.5}$ standard in the range of 35 to 30 $\mu g/m^3$ with a 98th percentile form, in concert with revising the level of the annual $PM_{2.5}$ standard in the range of 14 to 13 $\mu g/m^3$ (Henderson, 2005, 188316). Most of the members of the CASAC PM Panel also strongly supported establishing a new, secondary $PM_{2.5}$ standard to protect urban visibility and recommended establishing a sub-daily (4- to 8-h averaging time) $PM_{2.5}$ standard within the range of 20 to 30 $\mu g/m^3$ with a form within the range of the 92nd to 98th percentile (Henderson, 2005, 188316). For thoracic coarse particles, there was general concurrence among CASAC PM Panel members to revise the PM_{10} standards by establishing a primary standard specifically targeted to address particles in the size range of 2.5 to 10 µm ($PM_{10-2.5}$). The CASAC PM Panel was also in general agreement "that coarse particles in urban or industrial areas are likely to be enriched by anthropogenic pollutants that tend to be inherently more toxic than the windblown crustal material which typically dominates coarse particle mass in

arid rural areas." Based on its review of the Staff Paper, there was general agreement among the CASAC PM Panel members that a 24-h $PM_{10-2.5}$ standard with a level in the range of 50 to 70 $\mu g/m^3$, with a 98th percentile form, was reasonably justified and that a $PM_{10-2.5}$ standard with an annual averaging time was not warranted (Henderson, 2005, 156537). On January 17, 2006, EPA proposed to revise the NAAQS for PM (71 FR 2620). For fine particles, EPA proposed to retain $PM_{2.5}$ as the indicator, to retain standards for 24-h and annual exposures, and to revise the form of the annual standard to tighten conditions for demonstrating compliance using spatially averaged monitoring. EPA also proposed to revise the level of the 24-h $PM_{2.5}$ standard to 35 $\mu g/m^3$ to provide increased protection against health effects associated with short-term $PM_{2.5}$ exposures, including premature mortality and increased hospital admission and emergency room visits, but proposed to retain the level of the annual $PM_{2.5}$ standard at 15 $\mu g/m^3$, continuing protection against health effects associated with long-term exposure including premature mortality and development of chronic respiratory disease. With regard to the primary standards for thoracic coarse particles, EPA proposed to revise the 24-h PM_{10} standard in part by establishing a new indicator for thoracic coarse particles (particles generally between 2.5 and 10 µm in diameter), qualified so as to include any ambient mix of $PM_{10-2.5}$ that was dominated by resuspended dust from high density traffic on paved roads and PM generated by industrial sources and construction sources, and proposed to exclude any ambient mix of $PM_{10-2.5}$ that was dominated by rural windblown dust and soils and $PM_{10-2.5}$ generated by agricultural and mining sources. EPA also proposed a detailed monitoring regime in conjunction with this proposed indicator (71 FR 2710, 2731-42). The EPA proposed to set a 24-h standard (using the proposed indicator) at a level of 70 $\mu g/m^3$ to continue to provide a level of protection against health effects associated with short-term exposure (including hospital admissions for cardiopulmonary diseases, increased respiratory symptoms and possibly premature mortality) in those areas where the proposed indicator was found, generally equivalent to the level of protection provided by the existing 24-h PM_{10} standard. Also, EPA proposed to revoke, upon finalization of a primary 24-h standard for thoracic coarse particles, the 24-h PM_{10} standard as well as the annual PM_{10} standard.

EPA proposed to revise the secondary standards by making them identical to the suite of proposed primary standards for fine and coarse particles, providing protection against PM-related public welfare effects including visibility impairment, effects on vegetation and ecosystems, and materials damage and soiling. EPA also solicited comment on adding a new sub-daily $PM_{2.5}$ secondary standard to address visibility impairment in urban areas.

CASAC provided additional advice to EPA in a letter to the Administrator requesting reconsideration of CASAC's recommendations for both the primary and secondary $PM_{2.5}$ standards, as well as standards for thoracic coarse particles (Henderson, 2006, 156538).

On September 21, 2006, EPA announced its final decisions to revise the primary and secondary NAAQS for PM to provide increased protection of public health and welfare, respectively (71 FR 61144). With regard to the primary and secondary standards for fine particles, EPA revised the level of the 24-h $PM_{2.5}$ standard to 35 $\mu g/m^3$, retained the level of the annual $PM_{2.5}$ standard at 15 $\mu g/m^3$, and revised the form of the annual $PM_{2.5}$ standard by narrowing the constraints on the optional use of spatial averaging. EPA established the secondary standard for fine particles identical to the primary standards. With regard to the primary and secondary standards for thoracic coarse particles, EPA retained PM_{10} as the indicator for coarse particles, retained the level and form of the 24-h PM_{10} standard (so the standard remains 150 $\mu g/m^3$ with a one expected exceedence form) and revoked the annual standard because available evidence generally did not support a link between long-term exposure to current ambient levels of coarse particles and health or welfare effects.

Following promulgation of the revised PM NAAQS in 2006, several parties filed petitions for review with respect to: (1) selecting the level of the annual primary $PM_{2.5}$ standard; (2) setting the secondary $PM_{2.5}$ standards identical to the primary standards; (3) retaining PM_{10} as the indicator for coarse particles and retaining the level and form of the PM_{10} 24-h standard; and (4) revoking the PM_{10} annual standard. On judicial review, the D.C. Circuit remanded the annual standard for fine particles to EPA because EPA failed to adequately explain why the annual $PM_{2.5}$ standard provided the requisite protection from both short- and long-term exposures to fine particles including protection for vulnerable subpopulations. With respect to protection from short-term exposures, in 1997 EPA determined that the annual standard was the generally controlling standard for lowering both short- and long-term $PM_{2.5}$ concentrations and the 24-h standard was set to "provide an adequate margin of safety against infrequent or isolated peak concentrations that could occur in areas that attain the annual standard" (62 FR 38676-77, July 18, 1997). In the 2006 decision, the Administrator considered it appropriate to use a somewhat different evidence-based approach from

that used in 1997 to set the level of the 24-h and annual $PM_{2.5}$ standards. In that decision, the Administrator relied upon evidence from the short-term exposure $PM_{2.5}$ studies as the principal basis for selecting the proposed level of the 24-h standard and relied upon evidence from the long-term exposure $PM_{2.5}$ studies as the principal basis for selecting the level of the annual standard. The court found EPA failed to adequately explain this change in approach in light of CASAC and staff's recommendations to do otherwise. The court also found that EPA had failed to adequately explain why a short-term 24-h standard by itself would provide the protection needed from short-term exposures. *American Farm Bureau Federation v. EPA*, 559 F. 3d 512, 520-24 (D.C. Cir. 2009). With respect to protection from long-term exposure, the court found that EPA failed to adequately explain how the current standard provided "an adequate margin of safety for vulnerable subpopulations, such as children, the elderly, or those with conditions that exposure them to greater risk from fine particles". Specifically, EPA did not provide a reasonable explanation of why certain studies, including a study of children in Southern California showing lung damage from long-term exposure, did not call for a more stringent annual standard (Id. at 522-23).

The court also remanded the secondary standard for fine particles, based on EPA's failure to adequately explain why setting the secondary NAAQS equivalent to the primary standards provided the required protection for public welfare including protection from visibility impairment. The court found that EPA failed to identify a target level of visibility impairment that would be requisite to protect public welfare. This was contrary to the statute and resulted in a lack of a reasoned basis for the final decision. In addition, EPA's near exclusive reliance on a comparison of numbers of counties that would be in nonattainment under various types of standards was an inadequate basis for making a decision. It did not take into account the relative visibility protection of different standards, as well as the failure of a 24-h standard to address regional differences in humidity and its effect on visibility (Id. at 528-31).

The court upheld EPA's decision to retain the 24-h PM_{10} standard to provide protection for coarse particle exposures and to revoke the annual PM_{10} standard. The court found that EPA reasonably included all coarse PM within the standard, both urban and non-urban, to provide nationwide protection for exposure to coarse PM. It rejected arguments that the evidence showed there are no risks from exposure to non-urban coarse PM (Id. at 531-33). The court further found that EPA had a reasonable basis to not set separate standards for urban and non-urban coarse PM, namely the inability to reasonably define what ambient mixes would be included under either "urban" or "non-urban." In addition, the court found that record evidence supported EPA's cautious decision to provide "some protection from exposure to thoracic coarse particles… in all areas." The court also upheld EPA's decision to use PM_{10} as the indicator for coarse particles and to retain the level of the standard at 150 $\mu g/m^3$. EPA's final rule acknowledged that evidence of harm from urban-type coarse PM is stronger than for other types, and targeted protection at areas where urban-type coarse PM is most likely present. The targeting is done by using the indicator PM_{10} for coarse particles. PM_{10} includes both coarse PM and fine PM. Urban and industrial areas tend to have higher levels of fine PM than rural areas, so that in those areas less coarse PM is allowed – the desired targeting. Conversely, fine PM levels tend to be lower in rural areas, so more coarse particles are allowed in those areas – again the desired targeting. Likewise, the court concluded that the EPA's choice of the level for the PM_{10} standard was reasonable for many of the same reasons (Id. at 533-36). The court also upheld EPA's decision to revoke the annual PM_{10} standard (Id. at 537-38).

1.3. ISA Development

EPA initiated the current formal review of the NAAQS for PM on June 28, 2007 with a call for information from the public (72 FR 35462). In addition to the call for information, publications were identified through an ongoing literature search process that includes extensive computer database mining on specific topics. Literature searches were conducted routinely to identify studies published since the last review, focusing on publications from 2002 to May 2009. Search strategies were iteratively modified in an effort to optimize the identification of pertinent publications. Additional papers were identified for inclusion in several ways: review of pre-publication tables of contents for journals in which relevant papers may be published; independent identification of relevant literature by expert authors; and identification by the public and CASAC during the external review process. Generally, only information that had undergone scientific peer review and had been published or

accepted for publication was considered. All relevant epidemiologic, controlled human exposure, animal toxicological, and welfare effects studies published since the last review were considered, including those related to exposure-response relationships, mode(s) of action (MOA), or susceptible populations.

In general, in assessing the scientific quality and relevance of health and environmental effects studies, the following considerations have been taken into account when selecting studies for inclusion in the ISA or its annexes. The selection process for studies included in this ISA is shown in Figure 1-1.

- Are the study populations, subjects, or animal models adequately selected and are they sufficiently well defined to allow for meaningful comparisons between study or exposure groups?

- Are the statistical analyses appropriate, properly performed, and properly interpreted? Are likely covariates adequately controlled or taken into account in the study design and statistical analysis?

- Are the PM aerometric data, exposure, or dose metrics of adequate quality and sufficiently representative of information regarding ambient PM?

- Are the health or welfare effect measurements meaningful and reliable?

In selecting epidemiologic studies, EPA considered whether a given study contained information on associations with short- or long-term PM exposures at or near ambient levels of PM; evaluated health effects of PM size fractions, components or source-related indicators; considered approaches to evaluate issues related to potential confounding by other pollutants; assessed potential effect modifiers; and evaluated important methodological issues (e.g., lag or time period between exposure and effects, model specifications, thresholds, mortality displacement) related to interpretation of the health evidence. Among the epidemiologic studies selected, particular emphasis was placed on those studies most relevant to the review of the NAAQS. Specifically, studies conducted in the U.S. or Canada were discussed in more detail than those from other geographical regions. Particular emphasis was placed on: (1) recent multicity studies that employ standardized analysis methods for evaluating effects of PM and that provide overall estimates for effects based on combined analyses of information pooled across multiple cities; (2) studies that help understand quantitative relationships between exposure concentrations and effects; (3) recent studies (published since the last PM NAAQS review) that provide evidence on effects in susceptible populations; and (4) studies that consider and report PM as a component of a complex mixture of air pollutants.

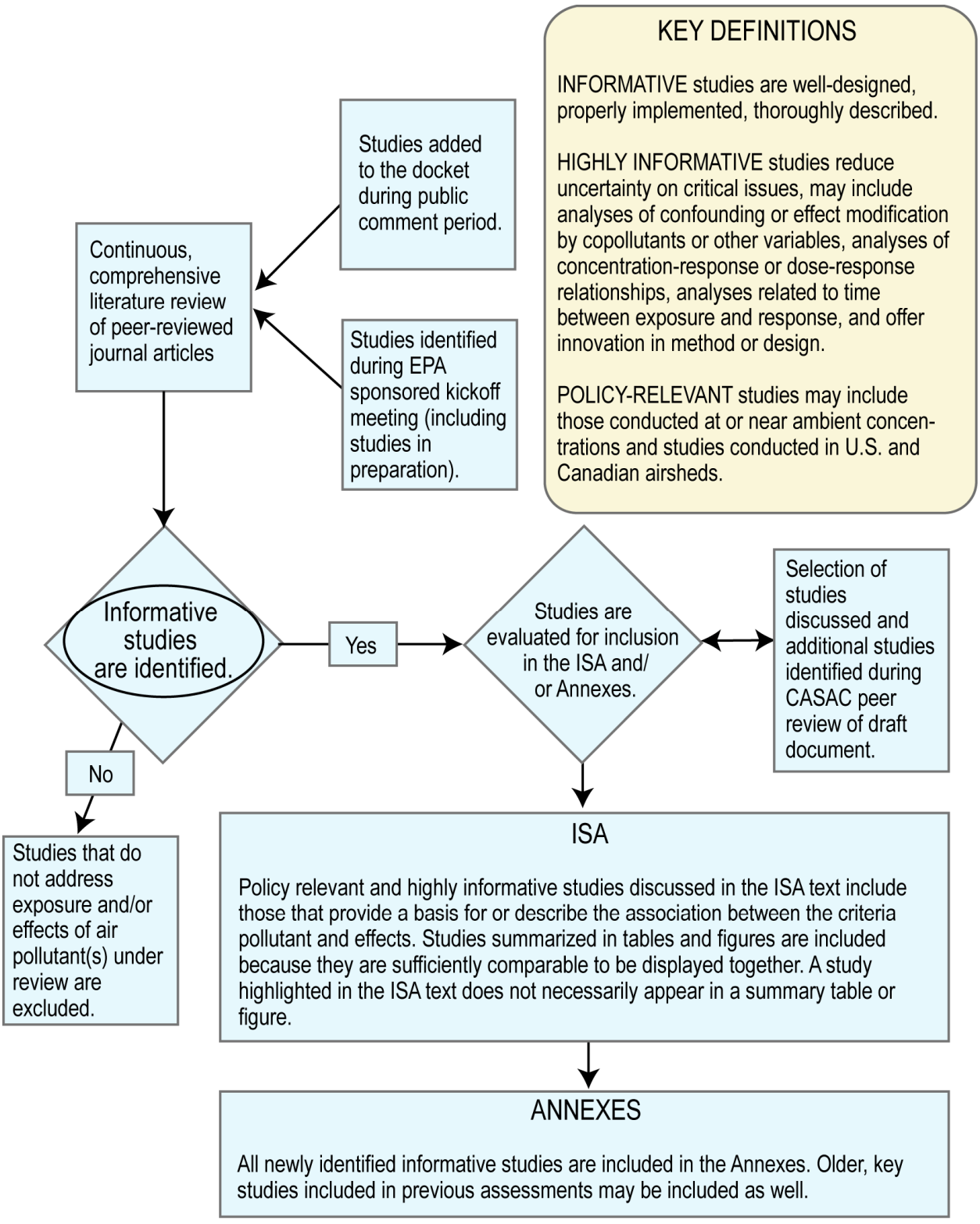

Figure 1-1. Identification of studies for inclusion in the ISA.

Criteria for the selection of research evaluating controlled human exposure or animal toxicological studies included a focus on studies conducted using relevant pollutant exposures. For both types of studies, relevant pollutant exposures are considered to be those generally within one or two orders of magnitude of ambient PM concentrations. Studies in which higher doses were used may also be considered if they provide information relevant to understanding MOAs or mechanisms, as noted below.

Evaluation of controlled human exposure studies focused on those that approximated expected human exposure conditions in terms of concentration and duration. In the selection of controlled human exposure studies, emphasis is placed on studies that: (1) investigate potentially susceptible populations such as people with cardiovascular diseases or asthmatics, particularly studies that compare responses in susceptible individuals with those in age-matched healthy controls; (2) address issues such as concentration-response or time-course of responses; (3) investigate exposure to PM separately and in combination with other pollutants such as O_3; (4) include control exposures to filtered air; and (5) have sufficient statistical power to assess findings.

For selecting toxicological studies for highlighting in the text, emphasis is placed on inhalation studies conducted at concentrations <2 mg/m^3 and those studies that approximate expected human dose conditions in terms of concentration, size distributions, and duration, which will depend on the toxicokinetics and biological sensitivity of the particular laboratory animals examined. Studies that elucidated MOAs and/or susceptibility, particularly if the studies were conducted under atmospherically relevant conditions, were emphasized whenever possible. A limited number of toxicological studies were included that employed intratracheal (IT) instillation techniques, mainly for $PM_{10-2.5}$ studies in rodents, that explored new emerging areas of investigation (e.g., vasomotor function), or that evaluated specific potential MOA or mechanisms of response. The sources, transport, and fate of fibers and unique nano-materials (viz., dots, hollow spheres, rods, fibers, tubes) are not reviewed herein because the in vivo disposition of these unique nanomaterials is not necessarily relevant to the behavior of ultrafine (UF) aerosols in the urban environment that are created by combustion sources and photochemical formation of secondary organic aerosols. In considering the potential effects of different components of PM, EPA has focused on studies that have assessed effects for a range of PM sources or components, including those using source apportionment methods or comparing effects for numerous PM components, and not on studies of individual constituents or species. Studies of ubiquitous PM sources as part of a mixture (i.e., diesel exhaust, gasoline exhaust, wood smoke) are included, provided they meet the other remaining selection criteria. Those studies of mixtures that are not a significant source of ambient PM, such as environmental tobacco smoke (ETS), are not included.

These criteria provide benchmarks for evaluating various studies and for focusing on the policy relevant studies in assessing the body of health and welfare effects evidence. Detailed critical analysis of all PM health and welfare effects studies, especially in relation to the above considerations, is beyond the scope of this document. Of most relevance for evaluation of studies is whether they provide useful qualitative or quantitative information on exposure-effect or exposure-response relationships for effects associated with current ambient air concentrations of PM that can inform decisions on whether to retain or revise the standards.

In developing the PM ISA, EPA began by reviewing and summarizing the evidence on (1) atmospheric sciences and exposure; (2) the health effects evidence from in vivo and in vitro animal toxicological, controlled human exposure, and epidemiologic studies; and (3) the welfare effects of PM, including visibility, climate, and ecological effects. In June 2008, EPA held a workshop to obtain review of the scientific content of initial draft materials or sections for the draft ISA and its annexes, that primarily contain summary information. The purpose of the initial peer review workshop was to ensure that the ISA is up to date and focused on the most policy-relevant findings, and to assist EPA with integration of evidence within and across disciplines. Following the peer review workshop, EPA addressed comments from the peer review workshop and completed the initial integration and synthesis of the evidence.

The integration of evidence on health or welfare effects involves collaboration between scientists from various disciplines. As described in the section below, the ISA organization is based on health or welfare effect categories. As an example, an evaluation of health effects evidence would include summaries of findings from epidemiologic, controlled human exposure, and toxicological studies, and integration of the results to draw conclusions based on the causal framework described below. Using the causal framework described in Section 1.5, EPA scientists consider aspects such as strength, consistency, coherence and biological plausibility of the evidence, and develop draft

causality judgments on the nature of the relationships. The draft integrative synthesis sections and conclusions are reviewed by EPA internal experts and, as appropriate, by outside expert authors. In practice, causality determinations often entail an iterative process of review and evaluation of the evidence. The draft ISA is released for review by the CASAC and the public. Comments on the characterization of the science as well as the implementation of the causal framework are carefully considered in revising and completing the ISA.

PM_{10} health studies are included in this assessment because they provide important evidence regarding the health effects of PM in general. However, the ISA draws no conclusions regarding causality for short- or long-term exposure to PM_{10}, as PM_{10} is comprised of both fine and thoracic coarse particles. As a result, causality determinations are limited to $PM_{2.5}$, $PM_{10-2.5}$, and UF particle (UFP) size fractions. In the cases where it was determined that PM_{10} is dominated by fine or thoracic coarse PM in specific study locations, these health studies are used in supporting the causality determinations for $PM_{2.5}$ or $PM_{10-2.5}$. Epidemiologic studies of short-term exposure to PM_{10} are also relied upon to examine potential effect modifiers, potential confounding by copollutants, and the influence of different modeling approaches on PM-mortality risk estimates, as well as the concentration-response relationship between PM and mortality. Therefore, to the extent possible, the findings of PM_{10} studies are considered insofar as they provide information relevant to the review of the NAAQS for fine and thoracic coarse particles.

1.4. Document Organization

This ISA is composed of nine chapters. This introductory chapter presents background information, and provides an overview of EPA's framework for making causal judgments. Key findings and conclusions for consideration in the review of the NAAQS for PM from the atmospheric sciences, ambient air data analyses, exposure assessment, dosimetry, health and welfare effects, including judgments on causality for the health and welfare effects of PM exposure, are presented in Chapter 2. More detailed summaries, evaluations and integration of the evidence are included in Chapters 3 through 9.

Chapter 3 highlights key concepts or issues relevant to understanding the atmospheric chemistry, sources, and exposure of and to PM following a "source-to-exposure" paradigm. Chapter 4 summarizes key concepts and recent findings on the dosimetry of PM, and Chapter 5 discusses possible pathways and MOA for the effects of PM. Chapters 6 and 7 evaluate and integrate epidemiologic, controlled human exposure, and animal toxicological information relevant to the review of the primary NAAQS for PM. Health effects related to short-term exposures (hours to days) to PM are the focus of Chapter 6. Chapter 7 evaluates health evidence related to long-term exposures (months to years) to PM. Chapters 6 and 7 are organized by health outcome categories, such as cardiovascular or respiratory effects, and each section includes effects of the various types of PM studied. For each health outcome category, summary sections then integrate the findings to draw conclusions on the evidence for the main size classes of PM (i.e., $PM_{2.5}$, $PM_{10-2.5}$, and UFP). Chapter 6 also includes a summary and synthesis of the recent health evidence that uses systematic approaches to assess health effects of sources and constituents of ambient PM; most such studies have evaluated effects of short-term exposure. Chapter 8 evaluates evidence related to populations potentially susceptible to PM-related effects.

Chapter 9 evaluates welfare effects evidence that is relevant to the review of the secondary NAAQS for PM. This chapter includes consideration of effects of PM on visibility impairment, materials damage, effects of PM on climate, and ecological effects of PM that were not addressed in the Integrated Science Assessment for Oxides of Nitrogen and Sulfur—Ecological Criteria (NO_XSO_X ISA) (U.S. EPA, 2008, 157074). The chapter also presents key conclusions and scientific judgments regarding causality for welfare effects of PM. In 2008, EPA completed the NO_XSO_X ISA (U.S. EPA, 2008, 157074), that focused on ecological effects related to the deposition of nitrogen (N)- and sulfur (S)-containing compounds. The 2008 NO_XSO_X ISA included ecological effects from particle-phase compounds (e.g., nitrates and sulfates), primarily effects from acidification and N-nutrient enrichment and eutrophication. In this ISA, the focus is on recent data for direct welfare effects of particle-phase NO_X and SO_X in the ambient air – primarily visibility impairment, damage to materials, and positive and negative climate interactions – not the welfare effects related to deposition of particle-phase NO_X and SO_X.

A series of annexes supplement this ISA. The annexes provide additional details of the pertinent literature published since the last review, as well as selected older studies of particular interest. These annexes contain information on:

- atmospheric chemistry of PM, sampling and analytic methods for measurement of PM, concentrations, emissions, sources and human exposure to PM (Annex A);
- studies on the dosimetry of PM (Annex B);
- controlled human exposure studies of health effects related to exposure to PM (Annex C);
- toxicological studies of health effects related to exposure to PM in laboratory animals and cell cultures (Annex D);
- epidemiologic studies of health effects from short- and long-term exposure to PM (Annex E); and
- studies that evaluate PM-induced health effects attributable to specific constituents or sources (Annex F).

Within Annexes B through F, detailed information about methods and results of health studies is summarized in tabular format, and generally includes information about: concentrations of PM and averaging times; study methods employed; results; and quantitative results for relationships between effects and exposure to PM. As noted in the section above, the most pertinent results of this body of studies are brought into the ISA.

1.5. EPA Framework for Causal Determination

The EPA has developed a consistent and transparent basis to evaluate the causal nature of air pollution-induced health or environmental effects. The framework described below establishes uniform language concerning causality and brings more specificity to the findings. It drew standardized language from across the federal government and wider scientific community, especially from the recent National Academy of Sciences (NAS) Institute of Medicine (IOM) document, *Improving the Presumptive Disability Decision-Making Process for Veterans* (IOM, 2008, 156586), the most recent comprehensive work on evaluating causality.

This introductory section focuses on the evaluation of health effects evidence; while focusing on human health outcomes, the concepts are also generally relevant to causality determination for welfare effects. This section:

- describes the kinds of scientific evidence used in establishing a general causal relationship between exposure and health effects;
- defines cause, in contrast to statistical association;
- discusses the sources of evidence necessary to reach a conclusion about the existence of a causal relationship;
- highlights the issue of multifactorial causation;
- identifies issues and approaches related to uncertainty; and
- provides a framework for classifying and characterizing the weight of evidence in support of a general causal relationship.

Approaches to assessing the separate and combined lines of evidence (e.g., epidemiologic, controlled human exposure, and animal toxicological studies) have been formulated by a number of

regulatory and science agencies, including the IOM of the NAS (IOM, 2008, 156586), International Agency for Research on Cancer (IARC, 2006, 093206), EPA Guidelines for Carcinogen Risk Assessment (U.S. EPA, 2005, 086237), Centers for Disease Control and Prevention (CDC, 2004, 056384), and National Acid Precipitation Assessment Program (NAPAP, 1991, 095894). These formalized approaches offer guidance for assessing causality. The frameworks are similar in nature, although adapted to different purposes, and have proven effective in providing a uniform structure and language for causal determinations. Moreover, these frameworks have supported decision-making under conditions of uncertainty.

1.5.1. Scientific Evidence Used in Establishing Causality

Causality determinations are based on the evaluation and synthesis of evidence from across scientific disciplines; the type of evidence that is most important for such determinations will vary by assessment. The most direct evidence of a causal relationship between pollutant exposures and human health effects comes from controlled human exposure studies. This type of study experimentally evaluates the health effects of administered exposures in human volunteers under highly-controlled laboratory conditions.

In most epidemiologic or observational studies of humans, the investigator does not control exposures or intervene with the study population. Broadly, observational studies can describe associations between exposures and effects. These studies fall into several categories: cross-sectional, prospective cohort, and time-series studies. "Natural experiments" offer the opportunity to investigate changes in health with a change in exposure; these include comparisons of health effects before and after a change in population exposures, such as the closure of a pollution source.

Experimental animal data can help characterize effects of concern, exposure-response relationships, susceptible populations, MOAs and enhance understanding of biological plausibility of observed effects. In the absence of controlled human exposure or epidemiologic data, animal data alone may be sufficient to support a likely causal determination, assuming that similar responses are expected in humans.

1.5.2. Association and Causation

"Cause" is a significant, effectual relationship between an agent and an effect on health or public welfare. "Association" is the statistical dependence among events, characteristics, or other variables. An association is *prima facie* evidence for causation; alone, however, it is insufficient proof of a causal relationship between exposure and disease or health effect. Determining whether an observed association is causal rather than spurious involves consideration of a number of factors, as described below. Much of the newly available health information evaluated in this ISA comes from epidemiologic studies that report a statistical association between ambient exposure and health outcomes.

Many of the health and environmental outcomes reported in these studies have complex etiologies. Diseases such as asthma, coronary artery disease or cancer are typically initiated by a web of multiple agents. Outcomes depend on a variety of factors, such as age, genetic susceptibility, nutritional status, immune competence, and social factors (Gee and Payne-Sturges, 2004, 093070; IOM, 2008, 156586). Effects on ecosystems are also multifactorial with a complex web of causation. Further, exposure to a combination of agents could cause synergistic or antagonistic effects. Thus, the observed risk represents the net effect of many actions and counteractions.

1.5.3. Evaluating Evidence for Inferring Causation

Moving from association to causation involves elimination of alternative explanations for the association. In estimating the causal influence of an exposure on health or environmental effects, it is recognized that scientific findings include uncertainty. Uncertainty can be defined as a state of having limited knowledge where it is impossible to exactly describe an existing state or future outcome; the lack of knowledge about the correct value for a specific measure or estimate. Uncertainty characterization and uncertainty assessment are two activities that lead to different degrees of sophistication in describing uncertainty. Uncertainty characterization generally involves a

qualitative discussion of the thought processes that lead to the selection and rejection of specific data, estimates, scenarios, etc. Uncertainty assessment is more quantitative. The process begins with simpler measures (e.g., ranges) and simpler analytical techniques and progresses, to the extent needed to support the decision for which the assessment is conducted, to more complex measures and techniques. Data will not be available for all aspects of an assessment, and those data that are available may be of questionable or unknown quality. In these situations, evaluation of uncertainty can include professional judgment or inferences based on analogy with similar situations. The net result is that the assessments will be based on a number of assumptions with varying degrees of uncertainty. Uncertainties commonly encountered in evaluating health evidence for the criteria air pollutants are outlined below for epidemiologic and experimental studies. Various approaches to characterizing uncertainty include classical statistical methods, sensitivity analysis, or probabilistic uncertainty analysis, in order of increasing complexity and data requirements. The ISA generally evaluates uncertainties qualitatively in assessing the evidence from across studies; in some situations quantitative analysis approaches, such as meta-regression may be used.

It is important to note here that, although the following discussion refers primarily to health effect studies, many parallels exist with welfare effects studies. Controlled exposure studies have been conducted in which plant species have been directly exposed to air pollutants, and the strengths and limitations of that body of studies mirror those of the controlled human exposure studies discussed below. Ecological field or natural gradient studies are similar to epidemiologic studies, for example, in the study of free-living populations and in the challenges faced in distinguishing effects of pollutants within a mixture.

Controlled human exposure studies evaluate the effects of exposures to a variety of pollutants in a highly-controlled laboratory setting. Also referred to as human clinical studies, these experiments allow investigators to expose subjects to fixed concentrations of air pollutants under carefully regulated environmental conditions and activity levels. Controlled human exposures to PM typically involve exposing subjects either at rest or while engaged in intermittent exercise in a whole-body exposure chamber, although mouthpiece and facemask systems can also be used. A variety of different types of particles are used in these studies including ambient outdoor particles, concentrated ambient particles (CAPs), diesel exhaust (DE) from a diesel engine, wood smoke generated in a wood stove, laboratory generated model particles (e.g., elemental carbon [EC] or zinc oxide [ZnO]), or particles collected on a filter, resuspended in saline, and administered either through IT instillation or inhalation. The recovery of particles on filters is variable and some components, such as organics, may be too volatile to be collected. Exposures to artificially generated particles may provide important information on the health effects of PM, but are not truly representative of ambient air pollution particles. The direct exposure of humans to ambient air pollution particles may be complicated by factors that cannot be controlled such as coexposures to other air pollutants (e.g., O_3, SO_2, and NO_2). In concentrating ambient particles, gaseous copollutants are not proportionately concentrated and interactions between PM and the copollutants cannot be investigated unless the latter are re-introduced. These limitations as well as daily variability in concentration and composition can make it difficult to compare the results from controlled human exposure studies employing particles from different sources.

In some instances, controlled human exposure studies can also be used to characterize concentration-response relationships at pollutant concentrations relevant to ambient conditions. Controlled human exposures are typically conducted using a randomized crossover design with subjects exposed both to PM and a clean air control. In this way, subjects serve as their own controls, effectively controlling for many potential confounders. However, controlled human exposure studies are limited by a number of factors including a small sample size and short exposure times. These laboratory studies are often conducted at PM concentrations much higher than those typically observed under ambient conditions, which may result in an overestimate of the acute response to exposure in the general population. Although the repetitive nature of ambient PM exposures may lead to cumulative health effects, this type of exposure is not practical to replicate in a laboratory setting. In addition, while subjects do serve as their own controls, personal exposure to pollutants in the hours and days preceding the controlled exposures may vary significantly between and within individuals. Finally, controlled human exposure studies require investigators to adhere to stringent health criteria for a subject to be included in the study, and therefore the results cannot necessarily be generalized to an entire population. Although some controlled human exposure studies have included health comprised individuals such as asthmatics or individuals with chronic obstructive pulmonary disease (COPD) or coronary artery disease, these individuals must also be relatively healthy and do

not represent the most sensitive individuals in the population. Thus, a lack of observation of effects from controlled human exposure studies does not necessarily mean that a causal relationship does not exist. While controlled human exposure studies provide important information on the biological plausibility of associations observed between air pollutant exposure and health outcomes in epidemiologic studies, observed effects in these studies may underestimate the response in certain subpopulations.

Epidemiologic studies provide important information on the associations between health effects and exposure of human populations to ambient air pollution. In the evaluation of epidemiologic evidence, one important consideration is potential confounding. Confounding is "…a confusion of effects. Specifically, the apparent effect of the exposure of interest is distorted because the effect of an extraneous factor is mistaken for or mixed with the actual exposure effect (which may be null)" (Rothman and Greenland, 1998, 086599). One approach to remove spurious associations from possible confounders is to control for characteristics that may differ between exposed and unexposed persons; this is frequently termed "adjustment." Appropriate statistical adjustment for confounders requires identifying and measuring all reasonably expected confounders. Deciding which variables to control for in a statistical analysis of the association between exposure and disease or health outcome depends on knowledge about possible mechanisms and the distributions of these factors in the population under study. In addition, scientific judgment is needed regarding likely sources and magnitude of confounding, together with consideration of how well the existing constellation of study designs, results, and analyses address this potential threat to inferential validity. One key consideration in this review is evaluation of the potential contribution of PM to health effects when it is a component of a complex air pollutant mixture. Reported PM effect estimates in epidemiologic studies may reflect independent PM effects on respiratory and cardiovascular health. Ambient PM may also be serving as an indicator of complex ambient air pollution mixtures that share the same source as PM (i.e., combustion of S-containing fuels or motor vehicle emissions). Alternatively, copollutants may mediate the effects of PM or PM may influence the toxicity of copollutants.

Another important consideration in the evaluation of epidemiologic evidence is effect modification. "Effect-measure modification differs from confounding in several ways. The main difference is that, whereas confounding is a bias that the investigator hopes to prevent or remove from the effect estimate, effect-measure modification is a property of the effect under study . . . In epidemiologic analysis one tries to eliminate confounding but one tries to detect and estimate effect-measure modification" (Rothman and Greenland, 1998, 086599). Examples of effect modifiers in some of the studies evaluated in this ISA include environmental variables (e.g., temperature or humidity), individual risk factors (e.g., education, cigarette smoking status, age), and community factors (e.g., percent of population > 65 years old). It is often possible to stratify the relationship between health outcome and exposure by one or more of these risk factor variables. Effect modifiers may be encountered (a) within single-city time-series studies; or (b) across cities in a two-stage hierarchical model or meta-analysis.

Several statistical methods are available to detect and control for potential confounders, with none of them being completely satisfactory. Multivariable regression models constitute one tool for estimating the association between exposure and outcome after adjusting for characteristics of participants that might confound the results. The use of multipollutant regression models has been the prevailing approach for controlling potential confounding by copollutants in air pollution health effects studies. Finding the pollutant likely responsible for the health outcome from multipollutant regression models is made difficult by the possibility that one or more air pollutants may be acting as a surrogate for an unmeasured or poorly-measured pollutant or for a particular mixture of pollutants. In addition, more than one pollutant may exert similar health effects, resulting in independently observed associations for multiple pollutants. Further, the correlation between the air pollutant of interest and various copollutants may make it difficult to discern associations between different pollutant exposures and health effects. Thus, results of models that attempt to distinguish gaseous and particle effects must be interpreted with caution. The number and degree of diversity of covariates, as well as their relevance to the potential confounders, remain matters of scientific judgment. Despite these limitations, the use of multipollutant models is still the prevailing approach employed in most air pollution epidemiologic studies, and provides some insight into the potential for confounding or interaction among pollutants.

Adjustment for potential confounders can be influenced by differential exposure measurement error. There are several components that contribute to exposure measurement error in epidemiologic

studies, including the difference between true and measured ambient concentrations, the difference between average personal exposure to ambient pollutants and ambient concentrations at central monitoring sites, and the use of average population exposure rather than individual exposure estimates. Previous AQCDs have examined the role of measurement error in time-series epidemiologic studies using simulated data and mathematical analyses and suggested that "transfer of effects" would only occur under unusual circumstances (i.e., "true" predictors having high positive or negative correlation; substantial measurement error; or extremely negatively correlated measurement errors) (U.S. EPA, 2004, 056905).

Confidence that unmeasured confounders are not producing the findings is increased when multiple studies are conducted in various settings using different subjects or exposures; each of which might eliminate another source of confounding from consideration. Thus, multicity studies which use a consistent method to analyze data from across locations with different levels of covariates can provide insight on potential confounding in associations. Intervention studies, because of their quasi-experimental nature, can be particularly useful in characterizing causation.

In addition to controlled human exposure and epidemiologic studies, the tools of experimental biology have been valuable for developing insights into human physiology and pathology. Animal toxicological studies explore the effects of pollutants on human health, especially through the study of model systems in other species. These studies evaluate the effects of exposures to a variety of pollutants in a highly controlled laboratory setting, and allow exploration of MOAs or mechanisms by which a pollutant may cause effects. Background knowledge of the biological mechanisms by which an exposure might or might not cause disease can prove crucial in establishing, or negating, a causal claim. There are, however, uncertainties associated with quantitative extrapolations between laboratory animals and humans on the pathophysiological effects of any pollutant. Animal species can differ from each other in fundamental aspects of physiology and anatomy (e.g., metabolism, airway branching, hormonal regulation) that may limit extrapolation. The differences between humans and rodents with regard to pollutant absorption and distribution profiles based on breathing pattern, exposure dose, and differences in lung structure and anatomy all have to be taken into consideration.

A relatively new tool available for experimental studies of PM exposure is the particle concentrator. Particle concentrators enable human subjects, animals, or cell culture systems to be exposed to atmospheric PM at concentrations greater than that observed under ambient conditions. As ambient PM is just one component of a complex mixture that interacts with gases and other aerosols, CAPs systems provide a method of exposing subjects to the particle phase. There are several instrument systems used to concentrate ambient PM in controlled human or animal exposure studies (Gordon et al., 1999, 001176; Maciejczyk and Chen, 2005, 087456; Sioutas et al., 1995, 001629; Sioutas et al., 1999, 001633). Gases (such as O_3 and SO_2) are not concentrated nor is $PM_{10-2.5}$ (except for the coarse particle concentrator) and only certain systems are capable of concentrating UFPs. In UF CAPs systems, increased number fraction of organic carbon and PAHs, along with decreased relative percentage of EC particles have been reported in concentrated PM compared to ambient PM (Su et al., 2006, 157021). These data suggest that for UF concentrators, the CAPs do not accurately reflect atmospheric UFP composition.

The ability to extrapolate between species has not generally changed since the 2004 PM AQCD but some considerations related to coarse particles merit attention. The inhalability of particles >2.5 μm in diameter is considerably lower in rats than in humans; however, once inhaled, deposition in the extrathoracic region is near 100% percent for particles >5 μm for most laboratory animal species (rat, mouse, hamster, guinea pig, and dogs). By contrast, penetration of thoracic coarse particles into the lower respiratory tract is greater in humans than rodents due to the moderately less efficient nasal deposition of humans and oronasal breathing (especially during exercise). The extent to which coarse particle deposition in the lower respiratory tract differs between the species is highly dependent on the activity level of the human exposure scenario in contrast with the resting exposure conditions common to rodent exposures. Endotracheal exposures of rodents may be needed to achieve coarse particle tissue doses in the lower respiratory tract of rodents similar to those experienced by humans. For particles <1 μm, including UFPs, deposition is expected to be relatively similar between the species.

There are also differences between species in both the rates of particle clearance from and retention in the lung. The clearance rate of particles from the ciliated airways of rats is considerably greater than humans. There is also evidence of prolonged particle retention in the smaller bronchioles of humans that does not appear to exist or has not been observed in rats. Under most

circumstances, clearance from the alveolar region of rats is also more rapid than observed in humans. Thus, these combined effects contribute to a greater particle burden in the lower respiratory tract of humans relative to rats. An important consideration in studies where are rats chronically exposed to high concentrations of insoluble particles, is the potential for "overload conditions." Rats, unlike other laboratory animals or humans, may experience a reduction in their alveolar clearance rates and an accumulation of interstitial particle burden and under these conditions, the relevance of tissue burdens and responses to humans is questionable. Considering interspecies differences in both deposition and clearance, greater exposure concentrations are required to achieve coarse particle tissue doses in the lower respiratory tract of rodents similar to those experienced by humans.

1.5.4. Application of Framework for Causal Determination

EPA uses a two-step approach to evaluate the scientific evidence on health or environmental effects of criteria pollutants. The first step determines the weight of evidence in support of causation and characterizes the strength of any resulting causal classification. The second step includes further evaluation of the quantitative evidence regarding the concentration-response relationships and the loads or levels, duration and pattern of exposures at which effects are observed.

To aid judgment, various "aspects"[1] of causality have been discussed by many philosophers and scientists. The most widely cited aspects of causality in epidemiology, and public health, in general, were articulated by Sir Austin Bradford Hill (1965, 071664) and have been widely used (CDC, 2004, 056384; IARC, 2006, 093206; IOM, 2008, 156586; NRC, 2004, 156814; U.S. EPA, 2005, 086237). Several adaptations of the Hill aspects have been used in aiding causality judgments in the ecological sciences (Adams, 2003, 156192; Collier, 2003, 155736; Fox, 1991, 156444; Gerritsen et al., 1998, 156465).

These aspects (Hill, 1965, 071664) have been modified (Table 1-2) for use in causal determinations specific to health and welfare effects or pollutant exposures.[2] Some aspects are more likely than others to be relevant for evaluating evidence on the health or environmental effects of criteria air pollutants. For example, the analogy aspect does not always apply and specificity would not be expected for multi-etiologic health outcomes such as asthma or cardiovascular disease, or ecological effects related to acidification. Aspects that usually play a larger role in determination of causality are consistency of results across studies, coherence of effects observed in different study types or disciplines, biological plausibility, exposure-response relationship, and evidence from "natural" experiments.

Although these aspects provide a framework for assessing the evidence, they do not lend themselves to being considered in terms of simple formulas or fixed rules of evidence leading to conclusions about causality (Hill, 1965, 071664). For example, one cannot simply count the number of studies reporting statistically significant results or statistically nonsignificant results and reach credible conclusions about the relative weight of the evidence and the likelihood of causality. In addition, it is important to note that the aspects in Table 1-2 cannot be used as a strict checklist, but rather to determine the weight of the evidence for inferring causality. While these aspects are particularly salient in this assessment, it is also important to recognize that no one aspect is either necessary or sufficient for drawing inferences of causality.

[1] The "aspects" described by Hill (1965, 071664) have become, in the subsequent literature, more commonly described as "criteria." The original term "aspects" is used here to avoid confusion with 'criteria' as it is used, with different meaning, in the Clean Air Act.

[2] The Hill aspects were developed for interpretation of epidemiologic results. They have been modified here for use with a broader array of data, i.e., epidemiologic, controlled human exposure, and animal toxicological studies, as well as in vitro data, and to be more consistent with EPA's Guidelines for Carcinogen Risk Assessment.

Table 1-2. Aspects to aid in judging causality.

Aspect	Description
CONSISTENCY OF THE OBSERVED ASSOCIATION	An inference of causality is strengthened when a pattern of elevated risks is observed across several independent studies, conducted in multiple locations by multiple investigators. The reproducibility of findings constitutes one of the strongest arguments for causality. If there are discordant results among investigations, possible reasons such as differences in exposure, confounding factors, and the power of the study are considered.
COHERENCE	An inference of causality from epidemiologic associations may be strengthened by other lines of evidence (e.g., controlled human exposure and animal toxicological studies) that support a cause-and-effect interpretation of the association. Causality is also supported when epidemiologic associations are reported across study designs and across related health outcomes. Evidence on ecological or welfare effects may be drawn from a variety of experimental approaches (e.g., greenhouse, laboratory, and field) and subdisciplines of ecology (e.g., community ecology, biogeochemistry and paleological/ historical reconstructions). The coherence of evidence from various fields greatly adds to the strength of an inference of causality. The absence of other lines of evidence, however, is not a reason to reject causality
BIOLOGICAL PLAUSIBILITY	An inference of causality tends to be strengthened by consistency with data from experimental studies or other sources demonstrating plausible biological mechanisms. A proposed mechanistic linking between an effect, and exposure to the agent, is an important source of support for causality, especially when data establishing the existence and functioning of those mechanistic links are available. A lack of biological understanding, however, is not a reason to reject causality.
BIOLOGICAL GRADIENT (EXPOSURE-RESPONSE RELATIONSHIP)	A well characterized exposure-response relationship (e.g., increasing effects associated with greater exposure) strongly suggests cause and effect, especially when such relationships are also observed for duration of exposure (e.g., increasing effects observed following longer exposure times). There are, however, many possible reasons that a study may fail to detect an exposure-response relationship. Thus, although the presence of a biological gradient may support causality, the absence of an exposure-response relationship does not exclude a causal relationship.
STRENGTH OF THE OBSERVED ASSOCIATION	The finding of large, precise risks increases confidence that the association is not likely due to chance, bias, or other factors. However, given a truly causal agent, a small magnitude in the effect could follow from a lower level of exposure, a lower potency, or the prevalence of other agents causing similar effects. While large effects support causality, modest effects therefore do not preclude it.
EXPERIMENTAL EVIDENCE	The strongest evidence for causality can be provided when a change in exposure brings about a change in occurrence or frequency of health or welfare effects.
TEMPORAL RELATIONSHIP OF THE OBSERVED ASSOCIATION	Evidence of a temporal sequence between the introduction of an agent and appearance of the effect constitutes another argument in favor of causality.
SPECIFICITY OF THE OBSERVED ASSOCIATION	As originally intended, this refers to increased inference of causality if one cause is associated with a single effect or disease (Hill, 1965, 071664). Based on the current understanding this is now considered one of the weaker guidelines for causality; for example, many agents cause respiratory disease and respiratory disease has multiple causes. At the scale of ecosystems, as in epidemiology, complexity is such that single agents causing single effects, and single effects following single causes, are extremely unlikely. The ability to demonstrate specificity under certain conditions remains, however, a powerful attribute of experimental studies. Thus, although the presence of specificity may support causality, its absence does not exclude it.
ANALOGY	Structure activity relationships and information on the agent's structural analogs can provide insight into whether an association is causal. Similarly, information on mode of action for a chemical, as one of many structural analogs, can inform decisions regarding likely causality.

1.5.5. First Step—Determination of Causality

In the ISA, EPA assesses the results of recent relevant publications, building upon evidence available during the previous NAAQS review, to draw conclusions on the causal relationships between relevant pollutant exposures and health or environmental effects. This ISA uses a five-level

hierarchy that classifies the weight of evidence for causation, not just association[1]. In developing this hierarchy, EPA has drawn on the work of previous evaluations, most prominently the IOM's *Improving the Presumptive Disability Decision-Making Process for Veterans* (IOM, 2008, *156586*), EPA's Guidelines for Carcinogen Risk Assessment (U.S. EPA, 2005, 086237) and the U.S. Surgeon General's smoking reports (CDC, 2004, 056384). This weight of evidence evaluation is based on various lines of evidence from across the health and environmental effects disciplines. These separate judgments are integrated into a qualitative statement about the overall weight of the evidence and causality. The five descriptors for causal determination are described in Table 1-3.

For PM, this determination of causality step involved a rather complex evaluation of evidence for different PM indices, different types of health or environmental effects, and for short- and long-term exposure periods. There were insufficient data on peak (i.e., <24 h) exposures for any PM size fraction with health effects to make causality determinations for this exposure category. Causality determinations were made for the PM measure ($PM_{2.5}$, $PM_{10-2.5}$, and UFPs, to the extent evidence was available for each measure), the overall effect category, and the exposure duration. As noted above, to the extent possible, results of PM_{10} studies are considered in causality determinations for $PM_{2.5}$ and $PM_{10-2.5}$. In the evaluation of health effects findings in Chapter 6 (for short-term exposure) and Chapter 7 (for long-term exposure), evidence was evaluated for health outcome categories, such as cardiovascular effects, and then conclusions were drawn based upon the integration of evidence from across disciplines (e.g., epidemiology, controlled human exposure, and toxicology) and also across the suite of related individual health outcomes. Chapters 6 and 7 initially summarize and evaluate findings for individual health outcomes, then integrate the results in summary sections to draw conclusions on causality for each PM indicator. The causality narratives present the weight of evidence that highlights the quality and breadth of the data, including any limitations or uncertainties. In the integrative synthesis and conclusions in Chapter 2, the ISA presents causality determinations and a summary of the underlying basis for those determinations for the PM indicator (e.g., $PM_{2.5}$), for the exposure time period (e.g., short- and long-term exposure) and for the major health effect categories.

[1] It should be noted that the CDC and IOM frameworks use a four-category hierarchy for the strength of the evidence. A five-level hierarchy is used here to be consistent with the EPA Guidelines for Carcinogen Risk Assessment and to provide a more nuanced set of categories.

Table 1-3. Weight of evidence for causal determination.

Determination	Health Effects	Ecological and Welfare Effects
CAUSAL RELATIONSHIP	Evidence is sufficient to conclude that there is a causal relationship with relevant pollutant exposures. That is, the pollutant has been shown to result in health effects in studies in which chance, bias, and confounding could be ruled out with reasonable confidence. For example: a) controlled human exposure studies that demonstrate consistent effects; or b) observational studies that cannot be explained by plausible alternatives or are supported by other lines of evidence (e.g., animal studies or mode of action information). Evidence includes replicated and consistent high-quality studies by multiple investigators.	Evidence is sufficient to conclude that there is a causal relationship with relevant pollutant exposures. That is, the pollutant has been shown to result in effects in studies in which chance, bias, and confounding could be ruled out with reasonable confidence. Controlled exposure studies (laboratory or small- to medium-scale field studies) provide the strongest evidence for causality, but the scope of inference may be limited. Generally, determination is based on multiple studies conducted by multiple research groups, and evidence that is considered sufficient to infer a causal relationship is usually obtained from the joint consideration of many lines of evidence that reinforce each other.
LIKELY TO BE A CAUSAL RELATIONSHIP	Evidence is sufficient to conclude that a causal relationship is likely to exist with relevant pollutant exposures, but important uncertainties remain. That is, the pollutant has been shown to result in health effects in studies in which chance and bias can be ruled out with reasonable confidence but potential issues remain. For example: a) observational studies show an association, but copollutant exposures are difficult to address and/or other lines of evidence (controlled human exposure, animal, or mode of action information) are limited or inconsistent; or b) animal toxicological evidence from multiple studies from different laboratories that demonstrate effects, but limited or no human data are available. Evidence generally includes replicated and high-quality studies by multiple investigators.	Evidence is sufficient to conclude that there is a likely causal association with relevant pollutant exposures. That is, an association has been observed between the pollutant and the outcome in studies in which chance, bias and confounding are minimized, but uncertainties remain. For example, field studies show a relationship, but suspected interacting factors cannot be controlled, and other lines of evidence are limited or inconsistent. Generally, determination is based on multiple studies in multiple research groups.
SUGGESTIVE OF A CAUSAL RELATIONSHIP	Evidence is suggestive of a causal relationship with relevant pollutant exposures, but is limited because chance, bias and confounding cannot be ruled out. For example, at least one high-quality epidemiologic study shows an association with a given health outcome but the results of other studies are inconsistent.	Evidence is suggestive of a causal relationship with relevant pollutant exposures, but chance, bias and confounding cannot be ruled out. For example, at least one high-quality study shows an effect, but the results of other studies are inconsistent.
INADEQUATE TO INFER A CAUSAL RELATIONSHIP	Evidence is inadequate to determine that a causal relationship exists with relevant pollutant exposures. The available studies are of insufficient quantity, quality, consistency or statistical power to permit a conclusion regarding the presence or absence of an effect.	The available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of an effect.
NOT LIKELY TO BE A CAUSAL RELATIONSHIP	Evidence is suggestive of no causal relationship with relevant pollutant exposures. Several adequate studies, covering the full range of levels of exposure that human beings are known to encounter and considering susceptible populations, are mutually consistent in not showing an effect at any level of exposure.	Several adequate studies, examining relationships with relevant exposures, are consistent in failing to show an effect at any level of exposure.

1.5.6. Second Step—Evaluation of Response

Beyond judgments regarding causality are questions relevant to quantifying health or environmental risks based on our understanding of the quantitative relationships between pollutant exposures and health or welfare effects.

1.5.6.1. Effects on Human Populations

Once a determination is made regarding the causal relationship between the pollutant and outcome category, important questions regarding quantitative relationships include:

- What is the concentration-response or dose-response relationship in the human population?
- What exposure conditions (dose or exposure, duration and pattern) are important?
- What subpopulations appear to be differentially affected (i.e., more susceptible to effects)?

To address these questions, in the second step of the EPA framework, the entirety of quantitative evidence is evaluated to best quantify those concentration-response relationships that exist. This requires evaluation of pollutant concentrations and exposure durations at which effects were observed for exposed populations including potentially susceptible populations. This integration of evidence results in identification of a study or set of studies that best approximates the concentration-response relationships between health outcomes and PM indicators for the U.S. population or subpopulations, given the current state of knowledge and the uncertainties that surrounded these estimates.

To accomplish this, evidence from multiple and diverse types of studies is considered. To the extent available, the ISA evaluates results from across epidemiologic studies that use various methods to evaluate the form of relationships between PM and health outcomes, and draws conclusions on the most well-supported shape of these relationships. Controlled human exposure studies can also provide data on the concentration-response relationship. Animal data may inform evaluation of concentration-response relationships, particularly relative to MOAs, and characteristics of susceptible populations. For some health outcomes, the probability and severity of health effects and associated uncertainties can be characterized. Chapter 2 presents the integrated findings informative for evaluation of population risks.

An important consideration in characterizing the public health impacts associated with exposure to a pollutant is whether the concentration-response relationship is linear across the full concentration range encountered, or if nonlinear relationships exist along any part of this range. Of particular interest is the shape of the concentration-response curve at and below the level of the current standards. The shape of the concentration-response curve varies, depending on the type of health outcome, underlying biological mechanisms and dose. At the human population level, however, various sources of variability and uncertainty tend to smooth and "linearize" the concentration-response function (such as the low data density in the lower concentration range, possible influence of measurement error, and individual differences in susceptibility to air pollution health effects). In addition, many chemicals and agents may act by perturbing naturally occurring background processes that lead to disease, which also linearizes population concentration-response relationships (Clewell and Crump, 2005, 156359; Crump et al., 1976, 003192; Hoel, 1980, 156555). These attributes of population dose-response may explain why the available human data at ambient concentrations for some environmental pollutants (e.g., PM, O_3, lead [Pb], ETS, radiation) do not exhibit evident thresholds for health effects, even though likely mechanisms include nonlinear processes for some key events. These attributes of human population dose-response relationships have been extensively discussed in the broader epidemiologic literature (Rothman and Greenland, 1998, 086599).

Publication bias is a source of uncertainty regarding the magnitude of health risk estimates. It is well understood that studies reporting non-null findings are more likely to be published than reports of null findings, and publication bias can also result in overestimation of effect estimate sizes (Ioannidis, 2008, 188317). For example, effect estimates from single-city epidemiologic studies have been found to be generally larger than those from multicity studies (Anderson et al., 2005, 087916).

Finally, identification of the susceptible population groups contributes to an understanding of the public health impact of pollutant exposures. Epidemiologic studies can help identify susceptible populations by evaluating health responses in the study population. Examples include stratified analyses for subsets of the population under study, or testing for interactions or effect modification by factors such as gender, age group, or health status. Experimental studies using animal models of susceptibility or disease can also inform the extent to which health risks are likely greater in specific population subgroups. Further discussion of these groups is in Chapter 8.

1.5.6.2. Effects on Public Welfare

Key questions for understanding the quantitative relationships between exposure (or concentration or deposition) to a pollutant and risk to the public welfare (e.g., ecosystems, visibility, materials, climate):

- What elements of the ecosystem (e.g., types, regions, taxonomic groups, populations, functions, etc.) appear to be affected, or are more sensitive to effects?
- Under what exposure conditions (amount deposited or concentration, duration and pattern) are effects seen?
- What is the shape of the concentration-response or exposure-response relationship?

Evaluations of causality typically consider the probability of welfare effects changing in response to exposure. A challenge to the quantification of exposure-response relationships for ecological effects is the variability across ecosystems. Ecological responses are evaluated within the range of observations, so a quantitative relationship may be determined for a given ecological system and scale. However, there is great regional and local variability in ecosystems. Thus, exposure-response relationships are often available site by site, rather than at the national or even regional scale. For example, an ecological response to deposition of a given pollutant can differ greatly between ecosystems. Where results from greenhouse or animal ecotoxicological studies are available, they may be used to aid in characterizing exposure-response relationships, particularly relative to mechanisms of action, and characteristics of sensitive biota.

1.5.7. Concepts in Evaluating Adversity of Health Effects

In evaluating the health evidence, a number of factors can be considered in determining the extent to which health effects are "adverse" for health outcomes such as changes in lung function. What constitutes an adverse health effect may vary between populations. Some changes in healthy individuals may not be considered adverse while those of a similar type and magnitude are potentially adverse in more susceptible individuals.

The American Thoracic Society (ATS) published an official statement titled *What Constitutes an Adverse Health Effect of Air Pollution?* (ATS, 2000, 011738). This statement updated the guidance for defining adverse respiratory health effects that had been published 15 years earlier (ATS, 1985, 006522), taking into account new investigative approaches used to identify the effects of air pollution and reflecting concern for impacts of air pollution on specific susceptible groups. In the 2000 update, there was an increased focus on quality of life measures as indicators of adversity and a more specific consideration of population risk. Exposure to air pollution that increases the risk of an adverse effect to the entire population is viewed as adverse, even though it may not increase the risk of any identifiable individual to an unacceptable level; estimated mean population effects do not reflect more severe effects in individuals. For example, a population of asthmatics could have a distribution of lung function such that no identifiable individual has a level associated with significant impairment. Exposure to air pollution could shift the distribution such that no identifiable individual experiences clinically-relevant effects; this shift toward decreased lung function, however, would be considered adverse because individuals within the population would have diminished reserve function and, therefore, would be at increased risk to further environmental insult.

1.6. Summary

This ISA is a review, synthesis, and evaluation of the most policy-relevant science, and communicates critical science judgments relevant to the NAAQS review. It reviews the most policy-relevant evidence from environmental effects studies and includes information on atmospheric chemistry, PM sources and emissions, exposure, and dosimetry. This ISA incorporates clarification and revisions based on advice and comments provided by EPA's CASAC (Samet, 2009, 190992; Samet, 2009, 199522). Annexes to the ISA provide additional details of the literature published since the last review. A framework for making critical judgments concerning causality

appears in this chapter. It relies on a widely accepted set of principles and standardized language to express evaluation of the evidence. This approach can bring rigor and clarity to current and future assessments. This ISA should assist EPA and others, now and in the future, to accurately represent what is presently known—and what remains unknown—concerning the effects of PM on human health and public welfare.

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Chapter 2. Integrative Health and Welfare Effects Overview

The subsequent chapters of this ISA will present the most policy-relevant information related to this review of the NAAQS for PM. This chapter integrates the key findings from the disciplines evaluated in this current assessment of the PM scientific literature, which includes the atmospheric sciences, ambient air data analyses, exposure assessment, dosimetry, health studies (e.g., toxicological, controlled human exposure, and epidemiologic), and welfare effects. The EPA framework for causal determinations described in Chapter 1 has been applied to the body of scientific evidence in order to collectively examine the health or welfare effects attributed to PM exposure in a two-step process.

As described in Chapter 1, EPA assesses the results of recent relevant publications, building upon evidence available during the previous NAAQS reviews, to draw conclusions on the causal relationships between relevant pollutant exposures and health or environmental effects. This ISA uses a five-level hierarchy that classifies the weight of evidence for causation:

- Causal relationship
- Likely to be a causal relationship
- Suggestive of a causal relationship
- Inadequate to infer a causal relationship
- Not likely to be a causal relationship

Beyond judgments regarding causality are questions relevant to quantifying health or environmental risks based on our understanding of the quantitative relationships between pollutant exposures and health or welfare effects. Once a determination is made regarding the causal relationship between the pollutant and outcome category, important questions regarding quantitative relationships include:

- What is the concentration-response or dose-response relationship?
- Under what exposure conditions (amount deposited, dose or concentration, duration and pattern) are effects observed?
- What populations appear to be differentially affected (i.e., more susceptible) to effects?
- What elements of the ecosystem (e.g., types, regions, taxonomic groups, populations, functions, etc.) appear to be affected, or are more sensitive to effects?

To address these questions, in the second step of the EPA framework, the entirety of quantitative evidence is evaluated to identify and characterize potential concentration-response relationships. This requires evaluation of levels of pollutant and exposure durations at which effects were observed for exposed populations including potentially susceptible populations.

This chapter summarizes and integrates the newly available scientific evidence that best informs consideration of the policy-relevant questions that frame this assessment, presented in Chapter 1. Section 2.1 discusses the trends in ambient concentrations and sources of PM and provides a brief summary of ambient air quality. Section 2.2 presents the evidence regarding personal exposure to ambient PM in outdoor and indoor microenvironments, and it discusses the

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relationship between ambient PM concentrations and exposure to PM from ambient sources. Section 2.3 integrates the evidence for studies that examine the health effects associated with short- and long-term exposure to PM and discusses important uncertainties identified in the interpretation of the scientific evidence. Section 2.4 provides a discussion of policy-relevant considerations, such as potentially susceptible populations, lag structure, and the PM concentration-response relationship, and PM sources and constituents linked to health effects. Section 2.5 summarizes the evidence for welfare effects related to PM exposure. Finally, Section 2.6 provides all of the causal determinations reached for each of the health outcomes and PM exposure durations evaluated in this ISA.

2.1. Concentrations and Sources of Atmospheric PM

2.1.1. Ambient PM Variability and Correlations

Recently, advances in understanding the spatiotemporal distribution of PM mass and its constituents have been made, particularly with regard to $PM_{2.5}$ and its components as well as ultrafine particles (UFPs). Emphasis in this ISA is placed on the period from 2005-2007, incorporating the most recent validated EPA Air Quality System (AQS) data. The AQS is EPA's repository for ambient monitoring data reported by the national, and state and local air monitoring networks. Measurements of $PM_{2.5}$ and PM_{10} are reported into AQS, while $PM_{10-2.5}$ concentrations are obtained as the difference between PM_{10} and $PM_{2.5}$ (after converting PM_{10} concentrations from STP to local conditions; Section 3.5). Note, however, that a majority of U.S. counties were not represented in AQS because their population fell below the regulatory monitoring threshold. Moreover, monitors reporting to AQS were not uniformly distributed across the U.S. or within counties, and conclusions drawn from AQS data may not apply equally to all parts of a geographic region. Furthermore, biases can exist for some PM constituents (and hence total mass) owing to volatilization losses of nitrates and other semi-volatile compounds, and, conversely, to retention of particle-bound water by hygroscopic species. The degree of spatial variability in PM was likely to be region-specific and strongly influenced by local sources and meteorological and topographic conditions.

2.1.1.1. Spatial Variability across the U.S.

AQS data for daily average concentrations of $PM_{2.5}$ for 2005-2007 showed considerable variability across the U.S. (Section 3.5.1.1). Counties with the highest average concentrations of $PM_{2.5}$ (>18 $\mu g/m^3$) were reported for several counties in the San Joaquin Valley and inland southern California as well as Jefferson County, AL (containing Birmingham) and Allegheny County, PA (containing Pittsburgh). Relatively few regulatory monitoring sites have the appropriate co-located monitors for computing $PM_{10-2.5}$, resulting in poor geographic coverage on a national scale (Figure 3-10). Although the general understanding of PM differential settling leads to an expectation of greater spatial heterogeneity in the $PM_{10-2.5}$ fraction, deposition of particles as a function of size depends strongly on local meteorological conditions. Better geographic coverage is available for PM_{10}, where the highest reported annual average concentrations (>50 $\mu g/m^3$) occurred in southern California, southern Arizona and central New Mexico. The size distribution of PM varied substantially by location, with a generally larger fraction of PM_{10} mass in the $PM_{10-2.5}$ size range in western cities (e.g., Phoenix and Denver) and a larger fraction of PM_{10} in the $PM_{2.5}$ size range in eastern U.S. cities (e.g., Pittsburgh and Philadelphia). UFPs are not measured as part of AQS or any other routine regulatory network in the U.S. Therefore, limited information is available regarding regional variability in the spatiotemporal distribution of UFPs.

Spatial variability in $PM_{2.5}$ components obtained from the Chemical Speciation Network (CSN) varied considerably by species from 2005-2007 (Figures 3-12 through 3-18). The highest annual average organic carbon (OC) concentrations were observed in the western and southeastern U.S. OC concentrations in the western U.S. peaked in the fall and winter, while OC concentrations in the Southeast peaked anytime between spring and fall. Elemental carbon (EC) exhibited less seasonality than OC and showed lowest seasonal variability in the eastern half of the U.S. The

highest annual average EC concentrations were present in Los Angeles, Pittsburgh, New York, and El Paso. Concentrations of sulfate (SO_4^{2-}) were higher in the eastern U.S. as a result of higher SO_2 emissions in the East compared with the West. There is also considerable seasonal variability with higher SO_4^{2-} concentrations in the summer months when the oxidation of SO_2 proceeds at a faster rate than during the winter. Nitrate (NO_3^-) concentrations were highest in California and during the winter in the Upper Midwest. In general, NO_3^- was higher in the winter across the country, in part as a result of temperature-driven partitioning and volatilization. Exceptions existed in Los Angeles and Riverside, CA, where high NO_3^- concentrations appeared year-round. There is variation in both $PM_{2.5}$ mass and composition among cities, some of which might be due to regional differences in meteorology, sources, and topography.

2.1.1.2. Spatial Variability on the Urban and Neighborhood Scales

In general, $PM_{2.5}$ has a longer atmospheric lifetime than $PM_{10-2.5}$. As a result, $PM_{2.5}$ is more homogeneously distributed than $PM_{10-2.5}$, whose concentrations more closely reflect proximity to local sources (Section 3.5.1.2). Because PM_{10} encompasses $PM_{10-2.5}$ in addition to $PM_{2.5}$, it also exhibits more spatial heterogeneity than $PM_{2.5}$. Urban- and neighborhood-scale variability in PM mass and composition was examined by focusing on 15 metropolitan areas, which were chosen based on their geographic distribution and coverage in recent health effects studies. The urban areas selected were Atlanta, Birmingham, Boston, Chicago, Denver, Detroit, Houston, Los Angeles, New York, Philadelphia, Phoenix, Pittsburgh, Riverside, Seattle and St. Louis. Inter-monitor correlation remained higher over long distances for $PM_{2.5}$ as compared with PM_{10} in these 15 urban areas. To a large extent, greater variation in $PM_{2.5}$ and PM_{10} concentrations within cities was observed in areas with lower ratios of $PM_{2.5}$ to PM_{10}. When the data was limited to only sampler pairs with less than 4 km separation (i.e., on a neighborhood scale), inter-sampler correlations remained higher for $PM_{2.5}$ than for PM_{10}. The average inter-sampler correlation was 0.93 for $PM_{2.5}$, while it dropped to 0.70 for PM_{10} (Section 3.5.1.3). Insufficient data were available in the 15 metropolitan areas to perform similar analyses for $PM_{10-2.5}$ using co-located, low volume FRM monitors.

As previously mentioned, UFPs are not measured as part of AQS or any other routine regulatory network in the U.S. Therefore, information about the spatial variability of UFPs is sparse; however, their number concentrations are expected to be highly spatially and temporally variable. This has been shown on the urban scale in studies in which UFP number concentrations drop off quickly with distance from roads compared to accumulation mode particle numbers.

2.1.2. Trends and Temporal Variability

Overall, $PM_{2.5}$ concentrations decreased from 1999 (the beginning of nationwide monitoring for $PM_{2.5}$) to 2007 in all ten EPA Regions, with the 3-yr avg of the 98th percentile of 24-h $PM_{2.5}$ concentrations dropping 10% over this time period. However from 2002-2007, concentrations of $PM_{2.5}$ were nearly constant with decreases observed in only some EPA Regions (Section 3.5.2.1). Concentrations of $PM_{2.5}$ components were only available for 2002-2007 using CSN data and showed little decline over this time period. This trend in $PM_{2.5}$ components is consistent with trends in $PM_{2.5}$ mass concentration observed after 2002 (shown in Figures 3-44 through 3-47). Concentrations of PM_{10} also declined from 1988 to 2007 in all ten EPA Regions.

Using hourly PM observations in the 15 metropolitan areas, diel variation showed average hourly peaks that differ by size fraction and region (Section 3.5.2.3). For both $PM_{2.5}$ and PM_{10}, a morning peak was typically observed starting at approximately 6:00 a.m., corresponding with the start of morning rush hour. There was also an evening concentration peak that was broader than the morning peak and extended into the overnight period, reflecting the concentration increase caused by the usual collapse of the mixing layer after sundown. The magnitude and duration of these peaks varied considerably by metropolitan area investigated.

UFPs were found to exhibit similar two-peaked diel patterns in Los Angeles and the San Joaquin Valley of CA and Rochester, NY as well as in Kawasaki City, Japan, and Copenhagen, Denmark. The morning peak in UFPs likely represents primary source emissions, such as rush-hour traffic, while the afternoon peak likely represents the combination of primary source emissions and nucleation of new particles.

2.1.3. Correlations between Copollutants

Correlations between PM and gaseous copollutants, including SO_2, NO_2, carbon monoxide (CO) and O_3, varied both seasonally and spatially between and within metropolitan areas (Section 3.5.3). On average, $PM_{2.5}$ and PM_{10} were correlated with each other better than with the gaseous copollutants. Although data are limited for $PM_{10-2.5}$, the available data suggest a stronger correlation between PM_{10} and $PM_{10-2.5}$ than between $PM_{2.5}$ and $PM_{10-2.5}$ on a national basis.There was relatively little seasonal variability in the mean correlation between PM in both size fractions and SO_2 and NO_2. CO, however, showed higher correlations with $PM_{2.5}$ and PM_{10} on average in the winter compared with the other seasons. This seasonality results in part because a larger fraction of PM is primary in origin during the winter. To the extent that this primary component of PM is associated with common combustion sources of NO_2 and CO, then higher correlations with these gaseous copollutants are to be expected. Increased atmospheric stability in colder months also results in higher correlations between primary pollutants (Section 3.5).

The correlation between daily maximum 8-h avg O_3 and 24-h avg $PM_{2.5}$ showed the highest degree of seasonal variability with positive correlations on average in summer (avg = 0.56) and negative correlations on average in the winter (avg = -0.30). During the transition seasons, spring and fall, correlations were mixed but on average were still positive. $PM_{2.5}$ is both primary and secondary in origin, whereas O_3 is only secondary. Photochemical production of O_3 and secondary PM in the planetary boundary layer (PBL) is much slower during the winter than during other seasons. Primary pollutant concentrations (e.g., primary $PM_{2.5}$ components, NO and NO_2) in many urban areas are elevated in winter as the result of heating emissions, cold starts and low mixing heights. O_3 in the PBL during winter is mainly associated with air subsiding from above the boundary layer following the passage of cold fronts, and this subsiding air has much lower PM concentrations than are present in the PBL. Therefore, a negative association between O_3 and $PM_{2.5}$ is frequently observed in the winter. During summer, both O_3 and secondary $PM_{2.5}$ are produced in the PBL and in the lower free troposphere at faster rates compared to winter, and so they tend to be positively correlated.

2.1.4. Measurement Techniques

The federal reference methods (FRMs) for $PM_{2.5}$ and PM_{10} are based on criteria outlined in the Code of Federal Regulations. They are, however, subject to several limitations that should be kept in mind when using compliance monitoring data for health studies. For example, FRM techniques are subject to the loss of semi-volatile species such as organic compounds and ammonium nitrate (especially in the West). Since FRMs based on gravimetry use 24-h integrated filter samples to collect PM mass, no information is available for variations over shorter averaging times from these instruments. However, methods have been developed to measure real-time PM mass concentrations. Real-time (or continuous and semi-continuous) measurement techniques are also available for PM species, such as particle into liquid sampler (PILS) for multiple ions analysis and aerosol mass spectrometer (AMS) for multiple components analysis (Section 3.4.1). Advances have also been achieved in PM organic speciation. New 24-h FRMs and Federal Equivalent Methods (FEMs) based on gravimetry and continuous FEMs for $PM_{10-2.5}$ are available. FRMs for $PM_{10-2.5}$ rely on calculating the difference between co-located PM_{10} and $PM_{2.5}$ measurements while a dichotomous sampler is designated as an FEM.

2.1.5. PM Formation in the Atmosphere and Removal

PM in the atmosphere contains both primary (i.e., emitted directly by sources) and secondary components, which can be anthropogenic or natural in origin. Secondary PM components can be produced by the oxidation of precursor gases such as SO_2 and NO_X to acids followed by neutralization with ammonia (NH_3) and the partial oxidation of organic compounds. In addition to being emitted as primary particles, UFPs are produced by the nucleation of H_2SO_4 vapor, H_2O vapor, and perhaps NH_3 and certain organic compounds. Over most of the earth's surface, nucleation is probably the major mechanism forming new UFPs. New UFP formation has been observed in environments ranging from relatively unpolluted marine and continental environments to polluted

urban areas as an ongoing background process and during nucleation events. However, as noted above, a large percentage of UFPs come from combustion-related sources such as motor vehicles.

Developments in the chemistry of formation of secondary organic aerosol (SOA) indicate that oligomers are likely a major component of OC in aerosol samples. Recent observations also suggest that small but significant quantities of SOA are formed from the oxidation of isoprene in addition to the oxidation of terpenes and organic hydrocarbons with six or more carbon atoms. Gasoline engines have been found to emit a mix of nucleation-mode heavy and large polycyclic aromatic hydrocarbons on which unspent fuel and trace metals can condense, while diesel particles are composed of a soot nucleus on which sulfates and hydrocarbons can condense. To the extent that the primary component of organic aerosol is overestimated in emissions from combustion sources, the semi-volatile components are underestimated. This situation results from the lack of capture of evaporated semi-volatile components upon dilution in common emissions tests. As a result, near-traffic sources of precursors to SOA would be underestimated. The oxidation of these precursors results in more oxidized forms of SOA than previously considered, in both near source urban environments and further downwind. Primary organic aerosol can also be further oxidized to forms that have many characteristics in common with oxidized SOA formed from gaseous precursors. Organic peroxides constitute a significant fraction of SOA and represent an important class of reactive oxygen species (ROS) that have high oxidizing potential. More information on sources, emissions and deposition of PM are included in Section 3.3.

Wet and dry deposition are important processes for removing PM and other pollutants from the atmosphere on urban, regional, and global scales. Wet deposition includes incorporation of particles into cloud droplets that fall as rain (rainout) and collisions with falling rain (washout). Other hydrometeors (snow, ice) can also serve the same purpose. Dry deposition involves transfer of particles through gravitational settling and/or by impaction on surfaces by turbulent motions. The effects of deposition of PM on ecosystems and materials are discussed in Section 2.5 and in Chapter 9.

2.1.6. Source Contributions to PM

Results of receptor modeling calculations indicate that $PM_{2.5}$ is produced mainly by combustion of fossil fuel, either by stationary sources or by transportation. A relatively small number of broadly defined source categories, compared to the total number of chemical species that typically are measured in ambient monitoring source receptor studies, account for the majority of the observed PM mass. Some ambiguity is inherent in identifying source categories. For example, quite different mobile sources such as trucks, farm equipment, and locomotives rely on diesel engines and ancillary data is often required to resolve these sources. A compilation of study results shows that secondary SO_4^{2-} (derived mainly from SO_2 emitted by Electricity Generating Units [EGUs]), NO_3^- (from the oxidation of NO_x emitted mainly from transportation sources and EGUs), and primary mobile source categories, constitute most of $PM_{2.5}$ (and PM_{10}) in the East. $PM_{10-2.5}$ is mainly primary in origin, having been emitted as fully formed particles derived from abrasion and crushing processes, soil disturbances, plant and insect fragments, pollens and other microorganisms, desiccation of marine aerosol emitted from bursting bubbles, and hygroscopic fine PM expanding with humidity to coarse mode. Gases such as HNO_3 can also condense directly onto preexisting coarse particles. Suspended primary coarse PM can contain Fe, Si, Al, and base cations from soil, plant and insect fragments, pollen, fungal spores, bacteria, and viruses, as well as fly ash, brake lining particles, debris, and automobile tire fragments. Quoted uncertainties in the source apportionment of constituents in ambient aerosol samples typically range from 10 to 50%. An intercomparison of source apportionment techniques indicated that the same major source categories of $PM_{2.5}$ were consistently identified by several independent groups working with the same data sets. Soil-, sulfate-, residual oil-, and salt-associated mass were most clearly identified by the groups. Other sources with more ambiguous signatures, such as vegetative burning and traffic-related emissions were less consistently identified.

Spatial variability in source contributions across urban areas is an important consideration in assessing the likelihood of exposure error in epidemiologic studies relating health outcomes to sources. Concepts similar to those for using ambient concentrations as surrogates for personal exposures apply here. Some source attribution studies for $PM_{2.5}$ indicate that intra-urban variability increases in the following order: regional sources (e.g., secondary SO_4^{2-} originating from EGUs) < area sources (e.g., on-road mobile sources) < point sources (e.g., metals from stacks of smelters).

Although limited information was available for $PM_{10-2.5}$, it does indicate a similar ordering, but without a regional component (resulting from the short lifetime of $PM_{10-2.5}$ compared to transport times on the regional scale). More discussion on source contributions to PM is available in Section 3.6.

2.1.7. Policy-Relevant Background

The background concentrations of PM that are useful for risk and policy assessments, which inform decisions about the NAAQS are referred to as policy-relevant background (PRB) concentrations. PRB concentrations have historically been defined by EPA as those concentrations that would occur in the U.S. in the absence of anthropogenic emissions in continental North America defined here as the U.S., Canada, and Mexico. For this document, PRB concentrations include contributions from natural sources everywhere in the world and from anthropogenic sources outside continental North America. Background concentrations so defined facilitated separation of pollution that can be controlled by U.S. regulations or through international agreements with neighboring countries from those that were judged to be generally uncontrollable by the U.S. Over time, consideration of potential broader ranging international agreements may lead to alternative determinations of which PM source contributions should be considered by EPA as part of PRB.

Contributions to PRB concentrations of PM include both primary and secondary natural and anthropogenic components. For this document, PRB concentrations of $PM_{2.5}$ for the continental U.S. were estimated using EPA's Community Multi-scale Air Quality (CMAQ) modeling system, a deterministic, chemical-transport model (CTM), using output from GEOS-Chem a global-scale model for CMAQ boundary conditions. PRB concentrations of $PM_{2.5}$ were estimated to be less than 1 $\mu g/m^3$ on an annual basis, with maximum daily average values in a range from 3.1 to 20 $\mu g/m^3$ and having a peak of 63 $\mu g/m^3$ at the nine national park sites across the U.S. used to evaluate model performance for this analysis. A description of the models and evaluation of their performance is given in Section 3.6 and further details about the calculations of PRB concentrations are given in Section 3.7.

2.2. Human Exposure

This section summarizes the findings from the recent exposure assessment literature. This summary is intended to support the interpretation of the findings from epidemiologic studies and reflects the material presented in Section 3.8. Attention is given to how concentration metrics can be used in exposure assessment and what errors and uncertainties are incurred for different approaches. Understanding of exposure errors is important because exposure error can potentially bias an estimate of a health effect or increase the size of confidence intervals around a health effect estimate.

2.2.1. Spatial Scales of PM Exposure Assessment

Assessing population-level exposure at the urban scale is particularly relevant for time-series epidemiologic studies, which provide information on the relationship between health effects and community-average exposure, rather than an individual's exposure. PM concentrations measured at a central-site ambient monitor are used as surrogates for personal PM exposure. However, the correlation between the PM concentration measured at central-site ambient monitor(s) and the unknown true community average concentration depends on the spatial distribution of PM, the location of the monitoring site(s) chosen to represent the community average, and division of the community by terrain features or local sources into several sub-communities that differ in the temporal pattern of pollution. Concentrations of SO_4^{2-} and some components of SOA measured at central-site monitors are expected to be uniform in urban areas because of the regional nature of their sources. However, this is not true for primary components like EC whose sources are strongly spatially variable in urban areas.

At micro-to-neighborhood scales, heterogeneity of sources and topography contribute to variability in exposure. This is particularly true for $PM_{10-2.5}$ and for UFPs, which have spatially

variable urban sources and loss processes (mainly gravitational settling for $PM_{10-2.5}$ and coagulation for UFPs) that also limit their transport from sources more readily than for $PM_{2.5}$. Personal activity patterns also vary across urban areas and across regions. Some studies, conducted mainly in Europe, have found personal $PM_{2.5}$ and PM_{10} exposures for pedestrians in street canyons to be higher than ambient concentrations measured by urban central site ambient monitors. Likewise, microenvironmental UFP concentrations were observed to be substantially higher in near-road environments, street canyons, and tunnels when compared with urban background concentrations. In-vehicle UFP and $PM_{2.5}$ exposures can also be important. As a result, concentrations measured by ambient monitors likely do not reflect the contributions of UFP or $PM_{2.5}$ exposures to individuals while commuting.

There is significant variability within and across regions of the country with respect to indoor exposures to ambient PM. Infiltrated ambient PM concentrations depend in part on the ventilation properties of the building or vehicle in which the person is exposed. PM infiltration factors depend on particle size, chemical composition, season, and region of the country. Infiltration can best be modeled dynamically rather than being represented by a single value. Season is important to PM infiltration because it affects the ventilation practices (e.g., open windows) used. In addition, ambient temperature and humidity conditions affect the transport, dispersion, and size distribution of PM. Residential air exchange rates have been observed to be higher in the summer for regions with low air conditioning usage. Regional differences in air exchange rates (Southwest < Southeast < Northeast < Northwest) also reflect ventilation practices. Differential infiltration occurs as a function of PM size and composition (the latter of which is described below). PM infiltration is larger for accumulation mode particles than for UFPs and $PM_{10-2.5}$. Differential infiltration by size fraction can affect exposure estimates if not accurately characterized.

2.2.2. Exposure to PM Components and Copollutants

Emission inventories and source apportionment studies suggest that sources of PM exposure vary by region. Comparison of studies performed in the eastern U.S. with studies performed in the western U.S. suggest that the contribution of SO_4^{2-} to exposure is higher for the East (16-46%) compared with the West (~4%) and that motor vehicle emissions and secondary NO_3^- are larger sources of exposure for the West (~9%) as compared with the East (~4%). Results of source apportionment studies of exposure to SO_4^{2-} indicate that SO_4^{2-} exposures are mainly attributable to ambient sources. Source apportionment for OC and EC is difficult because they originate from both indoor and outdoor sources. Exposure to OC of indoor and outdoor origin can be distinguished by the presence of aliphatic C-H groups generated indoors, since outdoor concentrations of aliphatic C-H are low. Studies of personal exposure to ambient trace metal have shown significant variation among cities and over seasons. This is in response to geographic and seasonal variability in sources including incinerator operation, fossil fuel combustion, biomass combustion (wildfires), and the resuspension of crustal materials in the built environment. Differential infiltration is also affected by variations in particle composition and volatility. For example, EC infiltrates more readily than OC. This can lead to outdoor-indoor differentials in PM composition.

Some studies have explored the relationship between PM and copollutant gases and suggested that certain gases can serve as surrogates for describing exposure to other air pollutants. The findings indicate that ambient concentrations of gaseous copollutants can act as surrogates for personal exposure to ambient PM. Several studies have concluded that ambient concentrations of O_3, NO_2, and SO_2 are associated with the ambient component of personal exposure to total $PM_{2.5}$. If associations between ambient gases and personal exposure to $PM_{2.5}$ of ambient origin exist, such associations are complex and vary by season and location.

2.2.3. Implications for Epidemiologic Studies

In epidemiologic studies, exposure may be estimated using various approaches, most of which rely on measurements obtained using central site monitors. The magnitude and direction of the biases introduced through error in exposure measurement depend on the extent to which the error is associated with the measured PM concentration. In general, when exposure error is not strongly correlated with the measured PM concentration, bias is toward the null and effect estimates are

underestimated. Moreover, lack of information regarding exposure measurement error can also add uncertainty to the health effects estimate.

One important factor to be considered is the spatial variation in PM concentrations. The degree of urban-scale spatial variability in PM concentrations varies across the country and by size fraction. $PM_{2.5}$ concentrations are relatively well-correlated across monitors in the urban areas examined for this assessment. The limited available evidence indicates that there is greater spatial variability in $PM_{10-2.5}$ concentrations than $PM_{2.5}$ concentrations, resulting in increased exposure error for the larger size fraction. Likewise, studies have shown UFPs to be more spatially variable across urban areas compared to $PM_{2.5}$. Even if $PM_{2.5}$, $PM_{10-2.5}$, or UFP concentrations measured at sites within an urban area are generally highly correlated, significant spatial variation in their concentrations can occur on any given day. In addition, there can be differential exposure errors for PM components (e.g., SO_4^{2-}, OC, EC). Current information suggests that UFPs, $PM_{10-2.5,}$ and some PM components are more spatially variable than $PM_{2.5}$. Spatial variability of these PM indicators adds uncertainty to exposure estimates.

Overall, recent studies generally confirm and build upon the key conclusions of the 2004 PM AQCD: separation of total PM exposures into ambient and nonambient components reduces potential uncertainties in the analysis and interpretation of PM health effects data; and ambient PM concentration can be used as a surrogate for ambient PM exposure in community time-series epidemiologic studies because the change in ambient PM concentration should be reflected in the change in the health risk coefficient. The use of the community average ambient $PM_{2.5}$ concentration as a surrogate for the community average personal exposure to ambient $PM_{2.5}$ is not expected to change the principal conclusions from time-series and most panel epidemiologic studies that use community average health and pollution data. Several recent studies support this by showing how the ambient component of personal exposure to $PM_{2.5}$ could be estimated using various tracer and source apportionment techniques and by showing that the ambient component is highly correlated with ambient concentrations of $PM_{2.5}$. These studies show that the non-ambient component of personal exposure to $PM_{2.5}$ is largely uncorrelated with ambient $PM_{2.5}$ concentrations. A few panel epidemiologic studies have included personal as well as ambient monitoring data, and generally reported associations with all types of PM measurements. Epidemiologic studies of long-term exposure typically exploit the differences in PM concentration across space, as well as time, to estimate the effect of PM on the health outcome of interest. Long-term exposure estimates are most accurate for pollutants that do not vary substantially within the geographic area studied.

2.3. Health Effects

This section evaluates the evidence from toxicological, controlled human exposure, and epidemiologic studies that examined the health effects associated with short- and long-term exposure to PM (i.e., $PM_{2.5}$, $PM_{10-2.5}$ and UFPs). The results from the health studies evaluated in combination with the evidence from atmospheric chemistry and exposure assessment studies contribute to the causal determinations made for the health outcomes discussed in this assessment (a description of the causal framework can be found in Section 1.5.4). In the following sections a discussion of the causal determinations will be presented by PM size fraction and exposure duration (i.e., short- or long-term exposure) for the health effects for which sufficient evidence was available to conclude a causal, likely to be causal or suggestive relationship. Although not presented in depth in this chapter, a detailed discussion of the underlying evidence used to formulate each causal determination can be found in Chapters 6 and 7.

2.3.1. Exposure to $PM_{2.5}$

2.3.1.1. Effects of Short-Term Exposure to $PM_{2.5}$

Table 2-1. Summary of causal determinations for short-term exposure to $PM_{2.5}$.

Size Fraction	Outcome	Causality Determination
$PM_{2.5}$	Cardiovascular Effects	Causal
	Respiratory Effects	Likely to be causal
	Mortality	Causal

Cardiovascular Effects

Epidemiologic studies that examined the effect of $PM_{2.5}$ on cardiovascular emergency department (ED) visits and hospital admissions reported consistent positive associations (predominantly for ischemic heart disease [IHD] and congestive heart failure [CHF]), with the majority of studies reporting increases ranging from 0.5 to 3.4% per 10 $\mu g/m^3$ increase in $PM_{2.5}$. These effects were observed in study locations with mean[1] 24-h avg $PM_{2.5}$ concentrations ranging from 7-18 $\mu g/m^3$ (Section 6.2.10). The largest U.S.-based multicity study evaluated, Medicare Air Pollution Study (MCAPS), provided evidence of regional heterogeneity (e.g., the largest excess risks occurred in the Northeast [1.08%]) and seasonal variation (e.g., the largest excess risks occurred during the winter season [1.49%]) in $PM_{2.5}$ cardiovascular disease (CVD) risk estimates, which is consistent with the null findings of several single-city studies conducted in the western U.S. These associations are supported by multicity epidemiologic studies that observed consistent positive associations between short-term exposure to $PM_{2.5}$ and cardiovascular mortality and also reported regional and seasonal variability in risk estimates. The multicity studies evaluated reported consistent increases in cardiovascular mortality ranging from 0.47 to 0.85% in study locations with mean 24-h avg $PM_{2.5}$ concentrations above 12.8 $\mu g/m^3$ (Table 6-15).

Controlled human exposure studies have demonstrated $PM_{2.5}$-induced changes in various measures of cardiovascular function among healthy and health-compromised adults. The most consistent evidence is for altered vasomotor function following exposure to diesel exhaust (DE) or CAPs with O_3 (Section 6.2.4.2). Although these findings provide biological plausibility for the observations from epidemiologic studies, the fresh DE used in the controlled human exposure studies evaluated contains gaseous components (e.g., CO, NO_x), and therefore, the possibility that some of the changes in vasomotor function might be due to gaseous components cannot be ruled out. Furthermore, the prevalence of UFPs in fresh DE limits the ability to conclusively attribute the observed effects to either the UF fraction or $PM_{2.5}$ as a whole. An evaluation of toxicological studies found evidence for altered vessel tone and microvascular reactivity, which provide coherence and biological plausibility for the vasomotor effects that have been observed in both the controlled human exposure and epidemiologic studies (Section 6.2.4.3). However, most of these toxicological studies exposed animals via intratracheal (IT) instillation or using relatively high inhalation concentrations.

In addition to the effects observed on vasomotor function, myocardial ischemia has been observed across disciplines through $PM_{2.5}$ effects on ST-segment depression, with toxicological studies providing biological plausibility by demonstrating reduced blood flow during ischemia (Section 6.2.3). There is also a growing body of evidence from controlled human exposure and toxicological studies demonstrating $PM_{2.5}$-induced changes on heart rate variability (HRV) and

[1] In this context mean represents the arithmetic mean of 24-h avg PM concentrations.

markers of systemic oxidative stress (Sections 6.2.1 and 6.2.9, respectively). Additional but inconsistent effects of $PM_{2.5}$ on blood pressure (BP), blood coagulation markers, and markers of systemic inflammation have also been reported across disciplines. Toxicological studies have provided biologically plausible mechanisms (e.g., increased right ventricular pressure and diminished cardiac contractility) for the associations observed between $PM_{2.5}$ and CHF in epidemiologic studies.

Together, the collective evidence from epidemiologic, controlled human exposure, and toxicological studies is sufficient to conclude that **a causal relationship exists between short-term exposures to $PM_{2.5}$ and cardiovascular effects.**

Respiratory Effects

The recent epidemiologic studies evaluated report consistent positive associations between short-term exposure to $PM_{2.5}$ and respiratory ED visits and hospital admissions for chronic obstructive pulmonary disease (COPD) and respiratory infections (Section 6.3). Positive associations were also observed for asthma ED visits and hospital admissions for adults and children combined, but effect estimates are imprecise and not consistently positive for children alone. Most studies reported effects in the range of ~1% to 4% increase in respiratory hospital admissions and ED visits and were observed in study locations with mean 24-h avg $PM_{2.5}$ concentrations ranging from 6.1-22 $\mu g/m^3$. Additionally, multicity epidemiologic studies reported consistent positive associations between short-term exposure to $PM_{2.5}$ and respiratory mortality as well as regional and seasonal variability in risk estimates. The multicity studies evaluated reported consistent, precise increases in respiratory mortality ranging from 1.67 to 2.20% in study locations with mean 24-h avg $PM_{2.5}$ concentrations above 12.8 $\mu g/m^3$ (Table 6-15). Evidence for $PM_{2.5}$-related respiratory effects was also observed in panel studies, which indicate associations with respiratory symptoms, pulmonary function, and pulmonary inflammation among asthmatic children. Although not consistently observed, some controlled human exposure studies have reported small decrements in various measures of pulmonary function following controlled exposures to $PM_{2.5}$ (Section 6.3.2.2).

Controlled human exposure studies using adult volunteers have demonstrated increased markers of pulmonary inflammation following exposure to a variety of different particle types; oxidative responses to DE and wood smoke; and exacerbations of allergic responses and allergic sensitization following exposure to DE particles (Section 6.3). Toxicological studies have provided additional support for $PM_{2.5}$-related respiratory effects through inhalation exposures of animals to CAPs, DE, other traffic-related PM and wood smoke. These studies reported an array of respiratory effects including altered pulmonary function, mild pulmonary inflammation and injury, oxidative responses, airway hyperresponsiveness (AHR) in allergic and non-allergic animals, exacerbations of allergic responses, and increased susceptibility to infections (Section 6.3).

Overall, the evidence for an effect of $PM_{2.5}$ on respiratory outcomes is somewhat restricted by limited coherence between some of the findings from epidemiologic and controlled human exposure studies for the specific health outcomes reported and the sub-populations in which those health outcomes occur. Epidemiologic studies have reported variable results among specific respiratory outcomes, specifically in asthmatics (e.g., increased respiratory symptoms in asthmatic children, but not increased asthma hospital admissions and ED visits) (Section 6.3.8). Additionally, respiratory effects have not been consistently demonstrated following controlled exposures to $PM_{2.5}$ among asthmatics or individuals with COPD. Collectively, the epidemiologic, controlled human exposure, and toxicological studies evaluated demonstrate a wide range of respiratory responses, and although results are not fully consistent and coherent across studies the evidence is sufficient to conclude that **a causal relationship is likely to exist between short-term exposures to $PM_{2.5}$ and respiratory effects.**

Mortality

An evaluation of the epidemiologic literature indicates consistent positive associations between short-term exposure to $PM_{2.5}$ and all-cause, cardiovascular-, and respiratory-related mortality (Section 6.5.2.2.). The evaluation of multicity studies found that consistent and precise risk estimates for all-cause (nonaccidental) mortality that ranged from 0.29 to 1.21% per 10 $\mu g/m^3$

increase in $PM_{2.5}$ at lags of 1 and 0-1 days. In these study locations, mean 24-h avg $PM_{2.5}$ concentrations were 12.8 $\mu g/m^3$ and above (Table 6-15). Cardiovascular-related mortality risk estimates were found to be similar to those for all-cause mortality; whereas, the risk estimates for respiratory-related mortality were consistently larger (i.e., 1.01-2.2%) using the same lag periods and averaging indices. The studies evaluated that examined the relationship between short-term exposure to $PM_{2.5}$ and cardiovascular effects (Section 6.2) provide coherence and biological plausibility for $PM_{2.5}$-induced cardiovascular mortality, which represents the largest component of total (nonaccidental) mortality (~ 35%) (American Heart Association, 2009, 198920). However, as noted in Section 6.3, there is limited coherence between some of the respiratory morbidity findings from epidemiologic and controlled human exposure studies for the specific health outcomes reported and the subpopultions in which those health outcomes occur, complicating the interpretation of the $PM_{2.5}$ respiratory mortality effects observed. Regional and seasonal patterns in $PM_{2.5}$ risk estimates were observed with the greatest effect estimates occurring in the eastern U.S. and during the spring. Of the studies evaluated only Burnett et al. (2004, 086247), a Canadian multicity study, analyzed gaseous pollutants and found mixed results, with possible confounding of $PM_{2.5}$ risk estimates by NO_2. Although the recently evaluated U.S.-based multicity studies did not analyze potential confounding of $PM_{2.5}$ risk estimates by gaseous pollutants, evidence from the limited number of single-city studies evaluated in the 2004 PM AQCD (U.S. EPA, 2004, 056905) suggest that gaseous copollutants do not confound the $PM_{2.5}$-mortality association. This is further supported by studies that examined the PM_{10}-mortality relationship. An examination of effect modifiers (e.g., demographic and socioeconomic factors), specifically air conditioning use as an indicator for decreased pollutant penetration indoors, has suggested that $PM_{2.5}$ risk estimates increase as the percent of the population with access to air conditioning decreases. Collectively, the epidemiologic literature provides evidence that **a causal relationship exists between short-term exposures to $PM_{2.5}$ and mortality.**

2.3.1.2. Effects of Long-Term Exposure to $PM_{2.5}$

Table 2-2. Summary of causal determinations for long-term exposure to $PM_{2.5}$.

Size Fraction	Outcome	Causality Determination
$PM_{2.5}$	Cardiovascular Effects	Causal
	Respiratory Effects	Likely to be causal
	Mortality	Causal
	Reproductive and Developmental	Suggestive
	Cancer, Mutagenicity, and Genotoxicity	Suggestive

Cardiovascular Effects

The strongest evidence for cardiovascular health effects related to long-term exposure to $PM_{2.5}$ comes from large, multicity U.S.-based studies, which provide consistent evidence of an association between long-term exposure to $PM_{2.5}$ and cardiovascular mortality (Section 7.2.10). These associations are supported by a large U.S.-based epidemiologic study (i.e., Women's Health Initiative [WHI] study) that reports associations between $PM_{2.5}$ and CVDs among post-menopausal women using a 1-yr avg $PM_{2.5}$ concentration (mean = 13.5 $\mu g/m^3$) (Section 7.2). However, epidemiologic studies that examined subclinical markers of CVD report inconsistent findings. Epidemiologic studies have also provided some evidence for potential modification of the $PM_{2.5}$-CVD association when examining individual-level data, specifically smoking status and the use of anti-

hyperlipidemics. Although epidemiologic studies have not consistently detected effects on markers of atherosclerosis due to long-term exposure to $PM_{2.5}$, toxicological studies have provided strong evidence for accelerated development of atherosclerosis in $ApoE^{-/-}$ mice exposed to CAPs and have shown effects on coagulation, experimentally-induced hypertension, and vascular reactivity (Section 7.2.1.2). Evidence from toxicological studies provides biological plausibility and coherence with studies of short-term exposure and cardiovascular morbidity and mortality, as well as with studies that examined long-term exposure to $PM_{2.5}$ and cardiovascular mortality. Taken together, the evidence from epidemiologic and toxicological studies is sufficient to conclude that **a causal relationship exists between long-term exposures to $PM_{2.5}$ and cardiovascular effects.**

Respiratory Effects

Recent epidemiologic studies conducted in the U.S. and abroad provide evidence of associations between long-term exposure to $PM_{2.5}$ and decrements in lung function growth, increased respiratory symptoms, and asthma development in study locations with mean $PM_{2.5}$ concentrations ranging from 13.8 to 30 $\mu g/m^3$ during the study periods (Section 7.3.1.1 and Section 7.3.2.1). These results are supported by studies that observed associations between long-term exposure to PM_{10} and an increase in respiratory symptoms and reductions in lung function growth in areas where PM_{10} is dominated by $PM_{2.5}$. However, the evidence to support an association with long-term exposure to $PM_{2.5}$ and respiratory mortality is limited (Figure 7-7). Subchronic and chronic toxicological studies of CAPs, DE, roadway air and woodsmoke provide coherence and biological plausibility for the effects observed in the epidemiologic studies. These toxicological studies have presented some evidence for altered pulmonary function, mild inflammation, oxidative responses, immune suppression, and histopathological changes including mucus cell hyperplasia (Section 7.3). Exacerbated allergic responses have been demonstrated in animals exposed to DE and wood smoke. In addition, pre- and postnatal exposure to ambient levels of urban particles was found to affect lung development in an animal model. This finding is important because impaired lung development is one mechanism by which PM exposure may decrease lung function growth in children. Collectively, the evidence from epidemiologic and toxicological studies is sufficient to conclude that **a causal relationship is likely to exist between long-term exposures to $PM_{2.5}$ and respiratory effects.**

Mortality

The recent epidemiologic literature reports associations between long-term $PM_{2.5}$ exposure and increased risk of mortality. Mean $PM_{2.5}$ concentrations ranged from 13.2 to 29 $\mu g/m^3$ during the study period in these areas (Section 7.6). When evaluating cause-specific mortality, the strongest evidence can be found when examining associations between $PM_{2.5}$ and cardiovascular mortality, and positive associations were also reported between $PM_{2.5}$ and lung cancer mortality (Figure 7-7). The cardiovascular mortality association has been confirmed further by the extended Harvard Six Cities and American Cancer Society studies, which both report strong associations between long-term exposure to $PM_{2.5}$ and cardiopulmonary and IHD mortality (Figure 7-7). Additional new evidence from a study that used the WHI cohort found a particularly strong association between long-term exposure to $PM_{2.5}$ and CVD mortality in post-menopausal women. Fewer studies have evaluated the respiratory component of cardiopulmonary mortality, and, as a result, the evidence to support an association with long-term exposure to $PM_{2.5}$ and respiratory mortality is limited (Figure 7-7). The evidence for cardiovascular and respiratory morbidity due to short- and long-term exposure to $PM_{2.5}$ provides biological plausibility for cardiovascular- and respiratory-related mortality. Collectively, the evidence is sufficient to conclude that **a causal relationship exists between long-term exposures to $PM_{2.5}$ and mortality.**

Reproductive and Developmental Effects

Evidence is accumulating for $PM_{2.5}$ effects on low birth weight and infant mortality, especially due to respiratory causes during the post-neonatal period. The mean $PM_{2.5}$ concentrations during the study periods ranged from 5.3-27.4 $\mu g/m^3$ (Section 7.4), with effects becoming more precise and consistently positive in locations with mean $PM_{2.5}$ concentrations of 15 $\mu g/m^3$ and above (Section 7.4). Exposure to $PM_{2.5}$ was usually associated with greater reductions in birth weight than exposure to PM_{10}. The evidence from a few U.S. studies that investigated PM_{10} effects on fetal growth, which reported similar decrements in birth weight, provide consistency for the $PM_{2.5}$ associations observed and strengthen the interpretation that particle exposure may be causally related to reductions in birth weight. The epidemiologic literature does not consistently report associations between long-term exposure to PM and preterm birth, growth restriction, birth defects or decreased sperm quality. Toxicological evidence supports an association between $PM_{2.5}$ and PM_{10} exposure and adverse reproductive and developmental outcomes, but provide little mechanistic information or biological plausibility for an association between long-term PM exposure and adverse birth outcomes (e.g., low birth weight or infant mortality). New evidence from animal toxicological studies on heritable mutations is of great interest, and warrants further investigation. Overall, the epidemiologic and toxicological evidence is **suggestive of a causal relationship between long-term exposures to $PM_{2.5}$ and reproductive and developmental outcomes.**

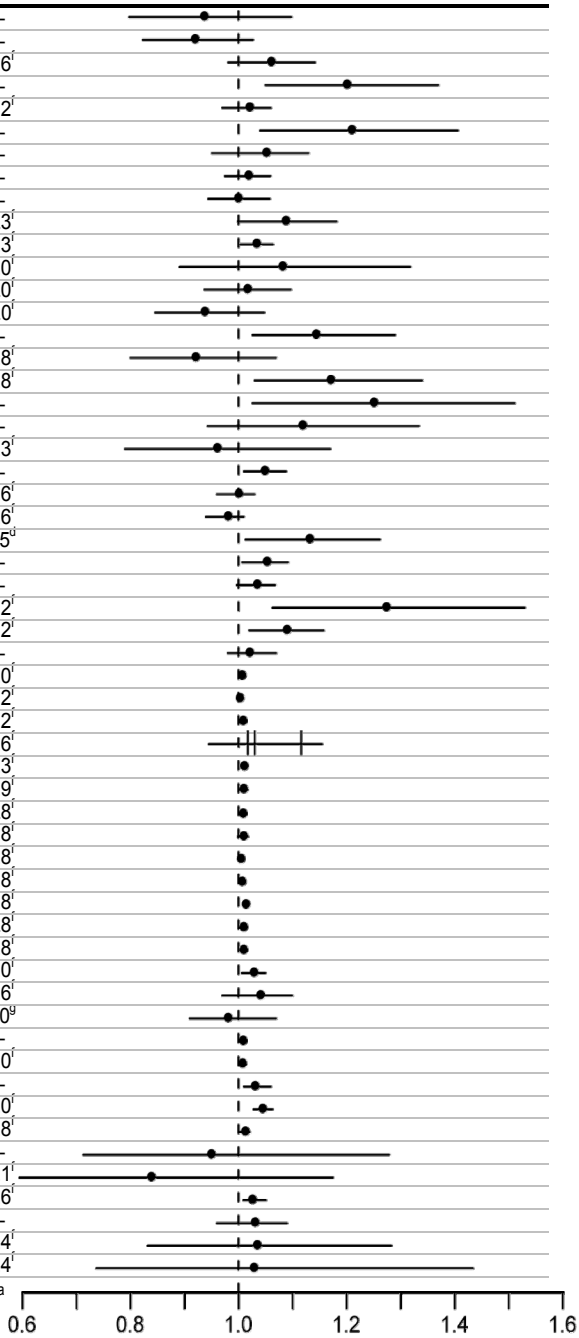
Cancer, Mutagenicity, and Genotoxicity

Multiple epidemiologic studies have shown a consistent positive association between $PM_{2.5}$ and lung cancer mortality, but studies have generally not reported associations between $PM_{2.5}$ and lung cancer incidence (Section 7.5). Animal toxicological studies have examined the potential relationship between PM and cancer, but have not focused on specific size fractions of PM. Instead they have examined ambient PM, wood smoke, and DEP. A number of studies indicate that ambient urban PM, emissions from wood/biomass burning, emissions from coal combustion, and gasoline and DE are mutagenic, and that PAHs are genotoxic. These findings are consistent with earlier studies that concluded that ambient PM and PM from specific combustion sources are mutagenic and genotoxic and provide biological plausibility for the results observed in the epidemiologic studies. A limited number of epidemiologic and toxicological studies examined epigenetic effects, and demonstrate that PM induces some changes in methylation. However, it has yet to be determined how these alterations in the genome could influence the initiation and promotion of cancer. Additionally, inflammation and immune suppression induced by exposure to PM may confer susceptibility to cancer. Collectively, the evidence from epidemiologic studies, primarily those of lung cancer mortality, along with the toxicological studies that show some evidence of the mutagenic and genotoxic effects of PM is **suggestive of a causal relationship between long-term exposures to $PM_{2.5}$ and cancer.**

2.3.2. Integration of $PM_{2.5}$ Health Effects

In epidemiologic studies, short-term exposure to $PM_{2.5}$ is associated with a broad range of respiratory and cardiovascular effects, as well as mortality. For cardiovascular effects and mortality, the evidence supports the existence of a causal relationship with short-term $PM_{2.5}$ exposure; while the evidence indicates that a causal relationship is likely to exist between short-term $PM_{2.5}$ exposure and respiratory effects. The effect estimates from recent and older U.S. and Canadian-based epidemiologic studies that examined the relationship between short-term exposure to $PM_{2.5}$ and health outcomes with mean 24-h avg $PM_{2.5}$ concentrations <17 $\mu g/m^3$ are shown in Figure 2-1. A number of different health effects are included in Figure 2-1 to provide an integration of the range of effects by mean concentration, with a focus on cardiovascular and respiratory effects and all-cause (nonaccidental) mortality (i.e., health effects categories with at least a suggestive causal determination). A pattern of consistent positive associations with mortality and morbidity effects can be seen in this figure. Mean $PM_{2.5}$ concentrations ranged from 6.1 to 16.8 $\mu g/m^3$.in these study locations.

Study	Outcome	Mean[a]	98th[a]
Chimonas & Gessner (2007, 093261)	Asthma HA	6.1	---
	LRI HA	6.1	---
Lisabeth et al. (2008, 155939)	Ischemic Stroke/TIA HA	7.0[e]	23.6[f]
Slaughter et al. (2005, 073854)	Asthma Exacerbation	7.3[e]	---
Rabinovitch et al. (2006, 088031)	Asthma Medication Use	7.4	17.2[f]
Chen et al. (2004, 087262)	COPD HA	7.7	---
Chen et al. (2005, 087555)	Respiratory HA	7.7	---
Fung et al. (2006, 089789)	Respiratory HA	7.7	---
Villeneuve et al. (2003, 055051)	Nonaccidental Mortality	7.9	---
Stieb et al. (2000, 011675)	CVD ED Visits	8.5	27.3[f]
	Respiratory ED Visits	8.5	27.3[f]
Villeneuve et al. (2006, 090191)	Hemhrgc Stroke HA	8.5	24.0[f]
	Ischemic Stroke HA	8.5	24.0[f]
	TIA HA	8.5	24.0[f]
Lin et al. (2005, 087828)	RTI HA	9.6	---
Mar et al. (2004, 057309)	Respiratory Symptoms (any)	9.8[c]	25.8[f]
	Respiratory Symptoms (any)	9.8[c]	25.8[f]
Rich et al. (2005, 079620)	Ventricular Arrhythmia	9.8[e]	---
Dockery et al. (2005, 078995)	Ventricular Arrhythmia	10.3[e]	---
Rabinovitch et al. (2004, 096753)	Asthma Exacerbation	10.6[d]	29.3[f]
Pope et al. (2006, 091246)	IHD HA	10.7[c]	---
Slaughter et al. (2005, 073854)	CVD HA	10.8	29.6[f]
	Respiratory ED Visits	10.8	29.6[f]
Pope et al. (2008, 191969)	CHF HA	10.8	44.5[d]
Zanobetti and Schwartz (2006, 090195)	MI HA	11.1[e]	---
	Pneumonia HA	11.1[e]	---
Peters et al. (2001, 016546)	MI	12.1	28.2[f]
Delfino et al. (1997, 082687)	Respiratory HA (summer)	12.1	31.2[f]
Sullivan et al. (2005, 050854)	MI	12.8	---
Burnett et al. (2004, 086247)	Nonaccidental Mortality	12.8	38.0[f]
Bell et al. (2008, 156266)	Respiratory HA	12.9[d]	34.2[f]
	CVD HA	12.9[d]	34.2[f]
Wilson et al. (2007, 157149)[m]	CVD Mortality	13.0	31.6[f]
Zanobetti & Schwartz (2009, 188462)	Nonaccidental Mortality	13.2[d]	34.3[f]
Burnett and Goldberg (2003, 042798)	Nonaccidental Mortality	13.3	38.9[f]
Dominici et al. (2006, 088398)	CBVD HA	13.3	34.8[f]
	PVD HA	13.3	34.8[f]
	IHD HA	13.3	34.8[f]
	Dysrhythmia HA	13.3	34.8[f]
	CHF HA	13.3	34.8[f]
	COPD HA	13.3	34.8[f]
	RTI HA	13.3	34.8[f]
Fairley (2003, 042850)	Nonaccidental Mortality	13.6	59.0[f]
Zhang et al. (2009, 191970)	ST Segment Depression	13.9[j]	37.6[f]
O'Connor et al. (2008, 156818)	Wheeze/Cough	14.0[c]	39.0[g]
Klemm and Mason (2003, 042801)	Nonaccidental Mortality	14.7[e,j]	---
Franklin et al. (2008, 097426)	Nonaccidental mortality	14.8	43.0[f]
NYDOH (2006, 090132)	Asthma ED Visits	15.0[k]	---
Ito et al. (2007, 156594)	Asthma HA	15.1	39.0[f]
Franklin et al. (2007, 091257)	Non-accidental Mortality	15.6	45.8[f]
Rich et al. (2006, 089814)	Ventricular Arrhythmia	16.2[e]	---
Symons et al. (2006, 091258)	CHF HA	16.5[d]	50.1[f]
Sheppard (2003, 042826)	Asthma HA	16.7	46.6[f]
NYDOH (2006, 090132)	Asthma ED Visits	16.7[l]	---
Burnett et al. (1997, 084194)	Respiratory HA (summer)	16.8	47.4[f]
	CVD HA (summer)	16.8	47.4[f]



[a] µg/m^3

[b] Study did not present mean; median presented.

[c] Mean estimated from data in study.

[d] Mean value slightly different from those reported in the published study or not reported in the published study; mean was either provided by study authors or calculated from data provided by study authors.

[e] Mean value not reported in study; median presented.

[f] 98th percentile of $PM_{2.5}$ distribution was either provided by study authors or calculated from data provided by study authors.

[g] 98th estimated from data in study.

[h] Averaged annual values for years in study from data provided by study author.

[i] Air quality data obtained from original study by Schwartz et al. (1996, 077325)

[j] Mean $PM_{2.5}$ concentration reported is for lag 0-2.

[k] Bronx; TEOM data.

[l] Manhattan; TEOM data.

[m] Study does not present an overall effect estimate; the vertical lines represent the effect estimate for each of the areas of Phoenix examined.

Figure 2-1. Summary of effect estimates (per 10 µg/m^3) by increasing concentration from U.S. studies examining the association between short-term exposure to $PM_{2.5}$ and cardiovascular and respiratory effects, and mortality, conducted in locations where the reported mean 24-h avg $PM_{2.5}$ concentrations were <17 µg/m^3.

Long-term exposure to $PM_{2.5}$ has been associated with health outcomes similar to those found in the short-term exposure studies, specifically for respiratory and cardiovascular effects and mortality. As found for short-term $PM_{2.5}$ exposure, the evidence indicates that a causal relationship exists between long-term $PM_{2.5}$ exposure and cardiovascular effects and mortality, and that a causal relationship is likely to exist between long-term $PM_{2.5}$ exposure and effects on the respiratory system.

Figure 2-2 highlights the findings of epidemiologic studies where the long-term mean $PM_{2.5}$ concentrations were ≤ 29 µg/m^3. A range of health outcomes are displayed (including cardiovascular mortality, all-cause mortality, infant mortaltiy, and bronchitis) ordered by mean concentration. The range of mean $PM_{2.5}$ concentrations in these studies was 10.7-29 µg/m^3 during the study periods. Additional studies not included in this figure that focus on subclinical outcomes, such as changes in lung function or atherosclerotic markers also report effects in areas with similar concentrations (Sections 7.2 and 7.3). Although not highlighted in the summary figure, long-term $PM_{2.5}$ exposure studies also provide evidence for reproductive and developmental effects (i.e., low birth weight) and cancer (i.e., lung cancer mortality) in response to to exposure to $PM_{2.5}$.

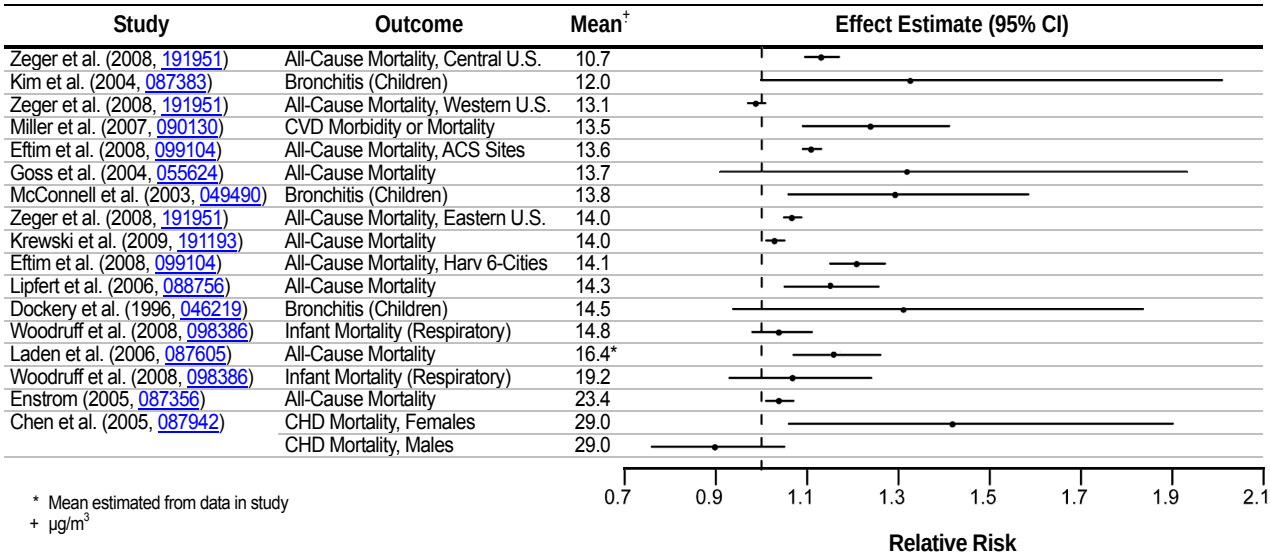


Figure 2-2. Summary of effect estimates (per 10 µg/m^3) by increasing concentration from U.S. studies examining the association between long-term exposure to $PM_{2.5}$ and cardiovascular and respiratory effects, and mortality.

The observations from both the short- and long-term exposure studies are supported by experimental findings of $PM_{2.5}$-induced subclinical and clinical cardiovascular effects. Epidemiologic studies have shown an increase in ED visits and hospital admissions for IHD upon exposure to $PM_{2.5}$. These effects are coherent with the changes in vasomotor function and ST-segment depression observed in both toxicological and controlled human exposure studies. It has been postulated that exposure to $PM_{2.5}$ can lead to myocardial ischemia through an effect on the autonomic nervous system or by altering vasomotor function. PM-induced systemic inflammation, oxidative stress and/or endothelial dysfunction may contribute to altered vasomotor function. These effects have been demonstrated in recent animal toxicological studies, along with altered microvascular reactivity, altered vessel tone, and reduced blood flow during ischemia. Toxicological studies demonstrating increased right ventricular pressure and diminished cardiac contractility also provide biological plausibility for the associations observed between $PM_{2.5}$ and CHF in epidemiologic studies.

Thus, the overall evidence from the short-term epidemiologic, controlled human exposure, and toxicological studies evaluated provide coherence and biological plausibility for cardiovascular effects related to myocardial ischemia and CHF. Coherence in the cardiovascular effects observed

can be found in long-term exposure studies, especially for CVDs among post-menopausal women. Additional studies provide limited evidence for subclinical measures of atherosclerosis in epidemiologic studies with stronger evidence from toxicological studies that have demonstrated accelerated development of atherosclerosis in $ApoE^{-/-}$ mice exposed to $PM_{2.5}$ CAPs along with effects on coagulation, experimentally-induced hypertension, and vascular reactivity. Repeated acute responses to PM may lead to cumulative effects that manifest as chronic disease, such as atherosclerosis. Contributing factors to atherosclerosis development include systemic inflammation, endothelial dysfunction, and oxidative stress all of which are associated with $PM_{2.5}$ exposure. However, it has not yet been determined whether PM initiates or promotes atherosclerosis. The evidence from both short- and long-term exposure studies on cardiovascular morbidity provide coherence and biological plausibility for the cardiovascular mortality effects observed when examining both exposure durations. In addition, cardiovascular hospital admission and mortality studies that examined the PM_{10} concentration-response relationship found evidence of a log-linear no-threshold relationship between PM exposure and cardiovascular-related morbidity (Section 6.2) and mortality (Section 6.5).

Epidemiologic studies have also reported respiratory effects related to short-term exposure to $PM_{2.5}$, which include increased ED visits and hospital admissions, as well as alterations in lung function and respiratory symptoms in asthmatic children. These respiratory effects were found to be generally robust to the inclusion of gaseous pollutants in copollutant models with the strongest evidence from the higher powered studies (Figure 6-9 and Figure 6-15). Consistent positive associations were also reported between short-term exposure to $PM_{2.5}$ and respiratory mortality in epidemiologic studies. However, uncertainties exist in the $PM_{2.5}$-respiratory mortality associations reported due to the limited number of studies that examined potential confounders of the $PM_{2.5}$-respiratory mortality relationship, and the limited information regarding the biological plausibility of the clinical and subclinical respiratory outcomes observed in the epidemiologic and controlled human exposure studies (Section 6.3) resulting in the progression to $PM_{2.5}$-induced respiratory mortality. Important new findings, which support the $PM_{2.5}$-induced respiratory effects mentioned above, include associations with post-neonatal (between 1 mo and 1 yr of age) respiratory mortality. Controlled human exposure studies provide some support for the respiratory findings from epidemiologic studies, with demonstrated increases in pulmonary inflammation following short-term exposure. However, there is limited and inconsistent evidence of effects in response to controlled exposures to $PM_{2.5}$ on respiratory symptoms or pulmonary function among healthy adults or adults with respiratory disease. Long-term exposure epidemiologic studies provide additional evidence for $PM_{2.5}$-induced respiratory morbidity, but little evidence for an association with respiratory mortality. These epidemiologic morbidity studies have found decrements in lung function growth, as well as increased respiratory symptoms, and asthma. Toxicological studies provide coherence and biological plausibility for the respiratory effects observed in response to short and long-term exposures to PM by demonstrating a wide array of biological responses including: altered pulmonary function, mild pulmonary inflammation and injury, oxidative responses, and histopathological changes in animals exposed by inhalation to $PM_{2.5}$ derived from a wide variety of sources. In some cases, prolonged exposures led to adaptive responses. Important evidence was also found in an animal model for altered lung development following pre- and post-natal exposure to urban air, which may provide a mechanism to explain the reduction in lung function growth observed in children in response to long-term exposure to PM.

Additional respiratory-related effects have been tied to allergic responses. Epidemiologic studies have provided evidence for increased hospital admissions for allergic symptoms (e.g., allergic rhinitis) in response to short- and long-term exposure to $PM_{2.5}$. Panel studies also positively associate long-term exposure to $PM_{2.5}$ and PM_{10} with indicators of allergic sensitization. Controlled human exposure and toxicological studies provide coherence for the exacerbation of allergic symptoms, by showing that $PM_{2.5}$ can promote allergic responses and intensify existing allergies. Allergic responses require repeated exposures to antigen over time and co-exposure to an adjuvant (possibly DE particles or UF CAPs) can enhance this response. Allergic sensitization often underlies allergic asthma, characterized by inflammation and AHR. In this way, repeated or chronic exposures involving multifactorial responses (immune system activation, oxidative stress, inflammation) can lead to irreversible outcomes. Epidemiologic studies have also reported evidence for increased hospital admissions for respiratory infections in response to both short- and long-term exposures to $PM_{2.5}$. Toxicological studies suggest that PM impairs innate immunity, which is the first line of

defense against infection, providing coherence for the respiratory infection effects observed in epidemiologic studies.

The difference in effects observed across studies and between cities may be attributed, at least in part, to the differences in PM composition across the U.S. Differences in PM toxicity may result from regionally varying PM composition and size distribution, which in turn reflects differences in sources and PM volatility. A person's exposure to ambient PM will also vary due to regional differences in personal activity patterns, microenvironmental characteristics and the spatial variability of PM concentrations in urban areas. Regional differences in $PM_{2.5}$ composition are outlined briefly in Section 2.1 above and in more detail in Section 3.5. An examination of data from the CSN indicates that East-West gradients exist for a number of PM components. Specifically, SO_4^{2-} concentrations are higher in the East, OC constitutes a larger fraction of PM in the West, and NO_3^- concentrations are highest in the valleys of central California and during the winter in the Midwest. However, the available evidence and the limited amount of city-specific speciated $PM_{2.5}$ data does not allow conclusions to be drawn that specifically differentiate effects of PM in different locations.

It remains a challenge to determine relationships between specific constituents, combinations of constituents, or sources of $PM_{2.5}$ and the various health effects observed. Source apportionment studies of $PM_{2.5}$ have attempted to decipher some of these relationships and in the process have identified associations between multiple sources and various respiratory and cardiovascular health effects, as well as mortality. Although different source apportionment methods have been used across these studies, the methods used have been evaluated and found generally to identify the same sources and associations between sources and health effects (Section 6.6). While uncertainty remains, it has been recognized that many sources and components of $PM_{2.5}$ contribute to health effects. Overall, the results displayed in Table 6-18 indicate that many constituents of $PM_{2.5}$ can be linked with multiple health effects, and the evidence is not yet sufficient to allow differentiation of those constituents or sources that are more closely related to specific health outcomes.

Variability in the associations observed across $PM_{2.5}$ epidemiologic studies may be due in part to exposure error related to the use of county-level air quality data. Because western U.S. counties tend to be much larger and more topographically diverse than eastern U.S. counties, the day-to-day variations in concentration at one site, or even for the average of several sites, may not correlate well with the day-to-day variations in all parts of the county. For example, site-to-site correlations as a function of distance between sites (Section 3.5.1.2) fall off rapidly with distance in Los Angeles, but high correlations extend to larger distances in eastern cities such as Boston and Pittsburgh. These differences may be attributed to a number of factors including topography, the built environment, climate, source characteristics, ventilation usage, and personal activity patterns. For instance, regional differences in climate and infrastructure can affect time spent outdoors or indoors, air conditioning usage, and personal activity patterns. Characteristics of housing stock may also cause regional differences in effect estimates because new homes tend to have lower infiltration factors than older homes. Biases and uncertainties in exposure estimates resulting from these aspects can, in turn, cause bias and uncertainty in associated health effects estimates.

The new evidence reviewed in this ISA greatly expands upon the evidence available in the 2004 PM AQCD particularly in providing greater understanding of the underlying mechanisms for $PM_{2.5}$ induced cardiovascular and respiratory effects for both short- and long-term exposures. Recent studies have provided new evidence linking long-term exposure to $PM_{2.5}$ with cardiovascular outcomes that has expanded upon the continuum of effects ranging from the more subtle subclinical measures to cardiopulmonary mortality.

2.3.3. Exposure to $PM_{10-2.5}$

2.3.3.1. Effects of Short-Term Exposure to $PM_{10-2.5}$

Table 2-3. Summary of causal determinations for short-term exposure to $PM_{10-2.5}$.

Size Fraction	Outcome	Causality Determination
$PM_{10-2.5}$	Cardiovascular Effects	Suggestive
	Respiratory Effects	Suggestive
	Mortality	Suggestive

Cardiovascular Effects

Generally positive associations were reported between short-term exposure to $PM_{10-2.5}$ and hospital admissions or ED visits for cardiovascular causes. These results are supported by a large U.S. multicity study of older adults that reported $PM_{10-2.5}$ associations with CVD hospital admissions, and only a slight reduction in the $PM_{10-2.5}$ risk estimate when included in a copollutant model with $PM_{2.5}$ (Section 6.2.10). The $PM_{10-2.5}$ associations with cardiovascular hospital admissions and ED visits were observed in study locations with mean 24-h avg $PM_{10-2.5}$ concentrations ranging from 7.4 to 13 $\mu g/m^3$. These results are supported by the associations observed between $PM_{10-2.5}$ and cardiovascular mortality in areas with 24-h avg $PM_{10-2.5}$ concentrations ranging from 6.1-16.4 $\mu g/m^3$ (Section 6.2.11). The results of the epidemiologic studies were further confirmed by studies that examined dust storm events, which contain high concentrations of crustal material, and found an increase in cardiovascular-related ED visits and hospital admissions. Additional epidemiologic studies have reported $PM_{10-2.5}$ associations with other cardiovascular health effects including supraventricular ectopy and changes in HRV (Section 6.2.1.1). Although limited in number, studies of controlled human exposures provide some evidence to support the alterations in HRV observed in the epidemiologic studies (Section 6.2.1.2). The few toxicological studies that examined the effect of $PM_{10-2.5}$ on cardiovascular health effects used IT instillation due to the technical challenges in exposing rodents via inhalation to $PM_{10-2.5}$, and, as a result, provide only limited evidence on the biological plausibility of $PM_{10-2.5}$ induced cardiovascular effects. The potential for $PM_{10-2.5}$ to elicit an effect is supported by dosimetry studies, which show that a large proportion of inhaled particles in the 3-6 micron (d_{ae}) range can reach and deposit in the lower respiratory tract, particularly the tracheobronchial (TB) airways (Figures 4-3 and 4-4). Collectively, the evidence from epidemiologic studies, along with the more limited evidence from controlled human exposure and toxicological studies **is suggestive of a causal relationship between short-term exposures to $PM_{10-2.5}$ and cardiovascular effects.**

Respiratory Effects

A number of recent epidemiologic studies conducted in Canada and France found consistent, positive associations between respiratory ED visits and hospital admissions and short-term exposure to $PM_{10-2.5}$ in studies with mean 24-h avg concentrations ranging from 5.6-16.2 $\mu g/m^3$ (Section 6.3.8). In these studies, the strongest relationships were observed among children, with less consistent evidence for adults and older adults (i.e., $\geq$ 65). In a large multicity study of older adults, $PM_{10-2.5}$ was positively associated with respiratory hospital admissions in both single and copollutant models with $PM_{2.5}$. In addition, a U.S.-based multicity study found evidence for an increase in respiratory mortality upon short-term exposure to $PM_{10-2.5}$, but these associations have not been consistently

observed in single-city studies (Section 6.3.9). A limited number of epidemiologic studies have focused on specific respiratory morbidity outcomes, and found no evidence of an association with lower respiratory symptoms, wheeze, and medication use (Section 6.3.1.1). While controlled human exposure studies have not observed an effect on lung function or respiratory symptoms in healthy or asthmatic adults in response to short-term exposure to $PM_{10-2.5}$, healthy volunteers have exhibited an increase in markers of pulmonary inflammation. Toxicological studies using inhalation exposures are still lacking, but pulmonary injury has been observed in animals after IT instillation exposure (Section 6.3.5.3). In some cases, $PM_{10-2.5}$ was found to be more potent than $PM_{2.5}$ and effects were not attributable to endotoxin. Both rural and urban $PM_{10-2.5}$ have induced inflammation and injury responses in rats or mice exposed via IT instillation, making it difficult to distinguish the health effects of $PM_{10-2.5}$ from different environments. Overall, epidemiologic studies, along with the limited number of controlled human exposure and toxicological studies that examined $PM_{10-2.5}$ respiratory effects provide evidence that **is suggestive of a causal relationship between short-term exposures to $PM_{10-2.5}$ and respiratory effects.**

Mortality

The majority of studies evaluated in this review provide some evidence for mortality associations with $PM_{10-2.5}$ in areas with mean 24-h avg concentrations ranging from 6.1-16.4 $\mu g/m^3$. However, uncertainty surrounds the $PM_{10-2.5}$ associations reported in the studies evaluated due to the different methods used to estimate $PM_{10-2.5}$ concentrations across studies (e.g., direct measurement of $PM_{10-2.5}$ using dichotomous samplers, calculating the difference between PM_{10} and $PM_{2.5}$ concentrations). In addition, only a limited number of $PM_{10-2.5}$ studies have investigated potential confounding by gaseous copollutants or the influence of model specification on $PM_{10-2.5}$ risk estimates.

A new U.S.-based multicity study, which estimated $PM_{10-2.5}$ concentrations by calculating the difference between the county-average PM_{10} and $PM_{2.5}$, found associations between $PM_{10-2.5}$ and mortality across the U.S., including evidence for regional variability in $PM_{10-2.5}$ risk estimates (Section 6.5.2.3). Additionally, the U.S.-based multicity study provides preliminary evidence for greater effects occurring during the warmer months (i.e., spring and summer). A multicity Canadian study provides additional evidence for an association between short-term exposure to $PM_{10-2.5}$ and mortality (Section 6.5.2.3). Although consistent positive associations have been observed across both multi- and single-city studies, more data are needed to adequately characterize the chemical and biological components that may modify the potential toxicity of $PM_{10-2.5}$ and compare the different methods used to estimate exposure. Overall, the evidence evaluated **is suggestive of a causal relationship between short-term exposures to $PM_{10-2.5}$ and mortality.**

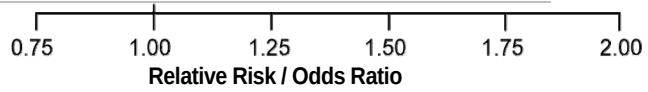
2.3.4. Integration of $PM_{10-2.5}$ Effects

Epidemiologic, controlled human exposure, and toxicological studies have provided evidence that is suggestive for relationships between short-term exposure to $PM_{10-2.5}$ and cardiovascular effects, respiratory effects, and mortality. Conclusions regarding causation for the various health effects and outcomes were made for $PM_{10-2.5}$ as a whole regardless of origin, since $PM_{10-2.5}$-related effects have been demonstrated for a number of different environments (e.g., cities reflecting a wide range of environmental conditions). Associations between short-term exposure to $PM_{10-2.5}$ and cardiovascular and respiratory effects, and mortality have been observed in locations with mean $PM_{10-2.5}$ concentrations ranging from 5.6 to 33.2 $\mu g/m^3$, and maximum $PM_{10-2.5}$ concentrations ranging from 24.6 to 418.0 $\mu g/m^3$) (Figure 2-3). A number of different health effects are included in Figure 2-3 to provide an integration of the range of effects by mean concentration, with a focus on cardiovascular and respiratory effects, and mortality (i.e., health effects categories with at least a suggestive causal determination). To date, a sufficient amount of evidence does not exist in order to draw conclusions regarding the health effects and outcomes associated with long-term exposure to $PM_{10-2.5}$.

In epidemiologic studies, associations between short-term exposure to $PM_{10-2.5}$ and cardiovascular outcomes (i.e., IHD hospital admissions, supraventricular ectopy, and changes in HRV) have been found that are similar in magnitude to those observed in $PM_{2.5}$ studies. Controlled human exposure studies have also observed alterations in HRV, providing consistency and coherence

for the effects observed in the epidemiologic studies. To date, only a limited number of toxicological studies have been conducted to examine the effects of $PM_{10-2.5}$ on cardiovascular effects. All of these studies involved IT instillation due to the technical challenges of using $PM_{10-2.5}$ for rodent inhalation studies. As a result, the toxicological studies evaluated provide limited biological plausibility for the $PM_{10-2.5}$ effects observed in the epidemiologic and controlled human exposure studies.

Study	Outcome	Mean[a]	Max[a]
Chen et al. (2004, 087262)	COPD HA	5.6	24.6
Fung et al. (2006, 089789)	RD HA	5.6	27.1
Chen et al. (2005, 087942)	RD HA	5.6	24.6
Villeneuve et al. (2003, 055051)	Nonaccidental Mortality	6.1	72.0
Lipfert et al. (2000, 004088)	CVD Mortality	6.9[d]	28.3
Peters et al. (2001, 016546)	MI	7.4	- - -
Tolbert et al. (2007, 090316)	CVD ED Visits	9.0	50.3
	RD ED Visits	9.0	50.3
Klemm et al. (2003, 042801)	Nonaccidental Mortality	9.0[b]	30.0
Metzger et al. (2007, 092856)	Ventricular Arrhythmia	9.6	50.3
Peel et al. (2005, 056305)	Asthma ED Visits	9.7	34.2[e]
	COPD ED Visits	9.7	34.2[e]
	RD ED Visits	9.7	34.2[e]
	Pneumonia ED Visits	9.7	34.2[e]
	URI ED Visits	9.7	34.2[e]
Metzger et al. (2004, 044222)	CHF ED Visits	9.7[d]	34.2[e]
	IHD ED Visits	9.7[d]	34.2[e]
Klemm et al. (2004, 056585)	Nonaccidental Mortality	9.9	25.2
Mar et al. (2004, 057309)	Symptoms (any)	10.8[c]	50.9[e]
	Asthma Symptoms	10.8[c]	50.9[e]
Lin et al. (2005, 087828)	RTI HA	10.9	45.0
Burnett et al. (2004, 086247)	Non-accidental Mortality	11.4	151.0
Burnett et al. (1997, 084194)	CVD HA	11.5[d]	56.1
	Respiratory HA	11.5[d]	56.1
Fairley (2003, 042850)	Nonaccidental Mortality	11.7[d]	55.2
Zanobetti & Schwartz (2009, 188462)	Nonaccidental Mortality	11.8	88.3[e]
Lin et al. (2002, 026067)	Asthma HA (boys)	12.2	68.0
Lin et al. (2002, 026067; 2004, 056067)	Asthma HA (girls)	12.2	68.0
Peng et al. (2008, 156850)	RD HA	12.3[d]	81.3[e]
	CVD HA	12.3[d]	81.3[e]
Burnett and Goldberg (2003, 042798)	Nonaccidental Mortality	12.6	99.0
Ito (2003, 042856)	Nonaccidental Mortality	13.3[d]	50.0
	CHF HA	13.3[d]	50.0
	IHD HA	13.3[d]	50.0
	COPD HA	13.3[d]	50.0
	Pneumonia HA	13.3[d]	50.0
Thurston et al. (1994, 043921)	Respiratory HA	14.4[c]	33.0
Sheppard (2003, 042826)	Asthma HA	16.2	88.0
Ostro et al. (2003, 042824)	CVD Mortality	30.5	418.0
Mar et al. (2003, 042841)	CVD Mortality	33.2	158.6



[a] µg/m^3
[b] Study did not present mean; median presented.
[c] Mean estimated from data in study.
[d] Mean value slightly different from those reported in the published study; mean was either provided by study authors or calculated from data provided by study authors.
[e] Maximum $PM_{10-2.5}$ concentration provided by study authors or calculated from data provided by study authors.

Figure 2-3. Summary of U.S. studies examining the association between short-term exposure to $PM_{10-2.5}$ and cardiovascular morbidity/mortality and respiratory morbidity/mortality. All effect estimates have been standardized to reflect a 10 µg/m^3 increase in mean 24-h avg $PM_{10-2.5}$ concentration and ordered by increasing concentration.

Limited evidence is available from epidemiologic studies for respiratory health effects and outcomes in response to short-term exposure to $PM_{10-2.5}$. An increase in respiratory hospital admissions and ED visits has been observed, but primarily in studies conducted in Canada and Europe. In addition, associations are not reported for lower respiratory symptoms, wheeze, or medication use. Controlled human exposure studies have not observed an effect on lung function or respiratory symptoms in healthy or asthmatic adults, but healthy volunteers have exhibited pulmonary inflammation. The toxicological studies (all IT instillation) provide evidence of

pulmonary injury and inflammation. In some cases, $PM_{10-2.5}$ was found to be more potent than $PM_{2.5}$ and effects were not solely attributable to endotoxin.

Currently, a national network is not in place to monitor $PM_{10-2.5}$ concentrations. As a result, uncertainties surround the concentration at which the observed associations occur. Ambient concentrations of $PM_{10-2.5}$ are generally determined by the subtraction of PM_{10} and $PM_{2.5}$ measurements, using various methods. For example, some epidemiologic studies estimate $PM_{10-2.5}$ by taking the difference between collocated PM_{10} and $PM_{2.5}$ monitors while other studies have taken the difference between county average PM_{10} and $PM_{2.5}$ concentrations. Moreover, there are potential differences among operational flow rates and temperatures for PM_{10} and $PM_{2.5}$ monitors used to calculate $PM_{10-2.5}$. Therefore, there is greater error in ambient exposure to $PM_{10-2.5}$ compared to $PM_{2.5}$. This would tend to increase uncertainty and make it more difficult to detect effects of $PM_{10-2.5}$ in epidemiologic studies. In addition, the various differences between eastern and western U.S. counties can lead to exposure misclassification, and the potential underestimation of effects in western counties (as discussed for $PM_{2.5}$ in Section 2.3.2).

It is also important to note that the chemical composition of $PM_{10-2.5}$ can vary considerably by location, but city-specific speciated $PM_{10-2.5}$ data are limited. $PM_{10-2.5}$ may contain Fe, Si, Al, and base cations from soil, plant and insect fragments, pollen, fungal spores, bacteria, and viruses, as well as fly ash, brake lining particles, debris, and automobile tire fragments.

The 2004 PM AQCD presented the limited amount of evidence available that examined the potential association between exposure to $PM_{10-2.5}$ and health effects and outcomes. The current evidence, primarily from epidemiologic studies, builds upon the results from the 2004 PM AQCD and indicates that short-term exposure to $PM_{10-2.5}$ is associated with effects on both the cardiovascular and respiratory systems. However, variability in the chemical and biological composition of $PM_{10-2.5}$, limited evidence regarding effects of the various components of $PM_{10-2.5}$, and lack of clearly defined biological mechanisms for $PM_{10-2.5}$-related effects are important sources of uncertainty.

2.3.5. Exposure to UFPs

2.3.5.1. Effects of Short-Term Exposure to UFPs

Table 2-4. Summary of causal determinations for short-term exposure to UFPs.

Size Fraction	Outcome	Causality Determination
UFPs	Cardiovascular Effects	Suggestive
	Respiratory Effects	Suggestive

Cardiovascular Effects

Controlled human exposure studies provide the majority of the evidence for cardiovascular health effects in response to short-term exposure to UFPs. While there are a limited number of studies that have examined the association between UFPs and cardiovascular morbidity, there is a larger body of evidence from studies that exposed subjects to fresh DE, which is typically dominated by UFPs. These studies have consistently demonstrated changes in vasomotor function following exposure to atmospheres containing relatively high concentrations of particles (Section 6.2.4.2). Markers of systemic oxidative stress have also been observed to increase after exposure to various particle types that are predominantly in the UFP size range. In addition, alterations in HRV parameters have been observed in response to controlled human exposure to UF CAPs, with inconsistent evidence for changes in markers of blood coagulation following exposure to UF CAPs

and DE (Sections 6.2.1.2 and 6.2.8.2). A few toxicological studies have also found consistent changes in vasomotor function, which provides coherence with the effects demonstrated in the controlled human exposure studies (Section 6.2.4.3). Additional UFP-induced effects observed in toxicological studies include alterations in HRV, with less consistent effects observed for systemic inflammation and blood coagulation. Only a few epidemiologic studies have examined the effect of UFPs on cardiovascular morbidity and collectively they found inconsistent evidence for an association between UFPs and CVD hospital admissions, but some positive associations for subclinical cardiovascular measures (i.e., arrhythmias and supraventricular beats) (Section 6.2.2.1). These studies were conducted in the U.S. and Europe in areas with mean particle number concentration ranging from ~8,500 to 36,000 particles/cm^3. However, UFP number concentrations are highly variable (i.e., concentrations drop off quickly from the road compared to accumulation mode particles), and therefore, more subject to exposure error than accumulation mode particles. In conclusion, the evidence from the studies evaluated **is suggestive of a causal relationship between short-term exposures to UFPs and cardiovascular effects.**

Respiratory Effects

A limited number of epidemiologic studies have examined the potential association between short-term exposure to UFPs and respiratory morbidity. Of the studies evaluated, there is limited, and inconsistent evidence for an association between short-term exposure to UFPs and respiratory symptoms, as well as asthma hospital admissions in locations a median particle number concentration of ~6,200 to a mean of 38,000 particles/cm^3 (Section 6.3.10). The spatial and temporal variability of UFPs also affects these associations. Toxicological studies have reported respiratory effects including oxidative, inflammatory, and allergic responses using a number of different UFP types (Section 6.3). Although controlled human exposure studies have not extensively examined the effect of UFPs on respiratory outcomes, a few studies have observed small UFP-induced asymptomatic decreases in pulmonary function. Markers of pulmonary inflammation have been observed to increase in healthy adults following controlled exposures to UFPs, particularly in studies using fresh DE. However, it is important to note that for both controlled human exposure and animal toxicological studies of exposures to fresh DE, the relative contributions of gaseous copollutants to the respiratory effects observed remain unresolved. Thus, the current collective evidence **is suggestive of a causal relationship between short-term exposures to UFPs and respiratory effects.**

2.3.6. Integration of UFP Effects

The controlled human exposure studies evaluated have consistently demonstrated effects on vasomotor function and systemic oxidative stress with additional evidence for alterations in HRV parameters in response to exposure to UF CAPs. The toxicological studies provide coherence for the changes in vasomotor function observed in the controlled human exposure studies. Epidemiologic studies are limited because a national network is not in place to measure UFP in the U.S. UFP concentrations are spatially and temporally variable, which would increase uncertainty and make it difficult to detect associations between health effects and UFPs in epidemiologic studies. In addition, data on the composition of UFPs, the spatial and temporal evolution of UFP size distribution and chemical composition, and potential effects of UFP constituents are sparse.

More limited evidence is available regarding the effect of UFPs on respiratory effects. Controlled human exposure studies have not extensively examined the effect of UFPs on respiratory measurements, but a few studies have observed small decrements in pulmonary function and increases in pulmonary inflammation. Additional effects including oxidative, inflammatory, and pro-allergic outcomes have been demonstrated in toxicological studies. Epidemiologic studies have found limited and inconsistent evidence for associations between UFPs and respiratory effects.

Overall, a limited number of studies have examined the association between exposure to UFPs and morbidity and mortality. Of the studies evaluated, controlled human exposure and toxicological studies provide the most evidence for UFP-induced cardiovascular and respiratory effects; however, many studies focus on exposure to DE. As a result, it is unclear if the effects observed are due to UFP, larger particles (i.e., $PM_{2.5}$), or the gaseous components of DE. Additionally, UF CAPs systems

are limited as the atmospheric UFP composition is modified when concentrated, which adds uncertainty to the health effects observed in controlled human exposure studies (Section 1.5.3).

2.4. Policy Relevant Considerations

2.4.1. Potentially Susceptible Populations

Upon evaluating the association between short- and long-term exposure to PM and various health outcomes, studies also attempted to identify populations that are more susceptible to PM (i.e., populations that have a greater likelihood of experiencing health effects related to exposure to an air pollutant (e.g., PM) due to a variety of factors including, but not limited to: genetic or developmental factors, race, gender, life stage, lifestyle (e.g., smoking status and nutrition) or preexisting disease; as well as, population-level factors that can increase an individual's exposure to an air pollutant (e.g., PM) such as socioeconomic status [SES], which encompasses reduced access to health care, low educational attainment, residential location, and other factors). These studies did so by conducting stratified analyses; by examining effects in individuals with an underlying health condition; or by developing animal models that mimic the pathophysiologic conditions associated with an adverse health effect. In addition, numerous studies that focus on only one potentially susceptible population provide supporting evidence on whether a population is susceptible to PM exposure. These studies identified a multitude of factors that could potentially contribute to whether an individual is susceptible to PM (Table 8-2). Although studies have primarily used exposures to $PM_{2.5}$ or PM_{10}, the available evidence suggests that the identified factors may also enhance susceptibility to $PM_{10-2.5}$. The examination of susceptible populations to PM exposure allows for the NAAQS to provide an adequate margin of safety for both the general population and for susceptible populations.

During specific periods of life (i.e., childhood and advanced age), individuals may be more susceptible to environmental exposures, which in turn can render them more susceptible to PM-related health effects. An evaluation of age-related health effects suggests that older adults have heightened responses for cardiovascular morbidity with PM exposure. In addition, epidemiologic and toxicological studies provide evidence that indicates children are at an increased risk of PM-related respiratory effects. It should be noted that the health effects observed in children could be initiated by exposures to PM that occurred during key windows of development, such as in utero. Epidemiologic studies that focus on exposures during development have reported inconsistent findings (Section 7.4), but a recent toxicological study suggests that inflammatory responses in pregnant women due to exposure to PM could result in health effects in the developing fetus.

Epidemiologic studies have also examined whether additional factors, such as gender, race, or ethnicity modify the association between PM and morbidity and mortality outcomes. Although gender and race do not seem to modify PM risk estimates, limited evidence from two studies conducted in California suggest that Hispanic ethnicity may modify the association between PM and mortality.

Recent epidemiologic and toxicological studies provided evidence that individuals with null alleles or polymorphisms in genes that mediate the antioxidant response to oxidative stress (i.e., GSTM1), regulate enzyme activity (i.e., MTHFR and cSHMT), or regulate levels of procoagulants (i.e., fibrinogen) are more susceptible to PM exposure. However, some studies have shown that polymorphisms in genes (e.g., HFE) can have a protective effect against effects of PM exposure. Additionally, preliminary evidence suggests that PM exposure can impart epigenetic effects (i.e., DNA methylation); however, this requires further investigation.

Collectively, the evidence from epidemiologic and toxicological, and to a lesser extent, controlled human exposure studies, indicate increased susceptibility of individuals with underlying CVDs and respiratory illnesses (i.e., asthma) to PM exposure. Controlled human exposure and toxicological studies provide additional evidence for increased PM-related cardiovascular effects in individuals with underlying respiratory health conditions.

Recently studies have begun to examine the influence of preexisting chronic inflammatory conditions, such as diabetes and obesity, on PM-related health effects. These studies have found some evidence for increased associations for cardiovascular outcomes along with pathophysiologic alterations in markers of inflammation, oxidative stress, and acute phase response. However, more

research is needed to thoroughly examine the affect of PM exposure on obese individuals and to identify the biological pathway(s) that could increase the susceptibility of diabetic and obese individuals to PM.

There is also evidence that SES, measured using surrogates such as educational attainment or residential location, modifies the association between PM and morbidity and mortality outcomes. In addition, nutritional status, another surrogate measure of SES, has been shown to have protective effects against PM exposure in individuals that have a higher intake of some vitamins and nutrients.

Overall, the epidemiologic, controlled human exposure, and toxicological studies evaluated in this review provide evidence for increased susceptibility for various populations, including children and older adults, people with pre-existing cardiopulmonary diseases, and people with lower SES.

2.4.2. Lag Structure of PM-Morbidity and PM-Mortality Associations

Epidemiologic studies have evaluated the time-frame in which exposure to PM can impart a health effect. PM exposure-response relationships can potentially be influenced by a multitude of factors, such as the underlying susceptibility of an individual (e.g., age, pre-existing diseases), which could increase or decrease the lag times observed.

An attempt has been made to identify whether certain lag periods are more strongly associated with specific health outcomes. The epidemiologic evidence evaluated in the 2004 PM AQCD supported the use of lags of 0-1 days for cardiovascular effects and longer moving averages or distributed lags for respiratory diseases (U.S. EPA, 2004, 056905). However, currently, little consensus exists as to the most appropriate a priori lag times to use when examining morbidity and mortality outcomes. As a result, many investigators have chosen to examine the lag structure of associations between PM concentration and health outcome instead of focusing on a priori lag times. This approach is informative because if effects are cumulative, higher overall risks may exist than would be observed for any given single-day lag.

2.4.2.1. PM-Cardiovascular Morbidity Associations

Most of the studies evaluated that examined the association between cardiovascular hospital admissions and ED visits report associations with short-term PM exposure at lags 0- to 2-days, with more limited evidence for shorter durations (i.e., hours) between exposure and response for some health effects (e.g., onset of MI) (Section 6.2.10). However, these studies have rarely examined alternative lag structures. Controlled human exposure and toxicological studies provide biological plausibility for the health effects observed in the epidemiologic studies at immediate or concurrent day lags. Although the majority of the evidence supports shorter lag times for cardiovascular health effects, a recent study has provided preliminary evidence suggesting that longer lag times (i.e., 14-day distributed lag model) may be plausible for non-ischemic cardiovascular conditions (Section 6.2.10). Panel studies of short-term exposure to PM and cardiovascular endpoints have also examined the time frame from exposure to health effect using a wide range of lag times. Studies of ECG changes indicating ischemia show effects at lags from several hours to 2 days, while lag times ranging from hours to several week moving averages have been observed in studies of arrhythmias, vasomotor function and blood markers of inflammation, coagulation and oxidative stress (Section 6.2). The longer lags observed in these panel studies may be explained if the effects of PM are cumulative. Although few studies of cumulative effects have been conducted, toxicological studies have demonstrated PM-dependent progression of atherosclerosis. It should be noted that PM exposure could also lead to an acute event (e.g., infarction or stroke) in individuals with atherosclerosis that may have progressed in response to cumulative PM exposure. Therefore, effects have been observed at a range of lag periods from a few hours to several days with no clear evidence for any lag period having stronger associations then another.

2.4.2.2. PM-Respiratory Morbidity Associations

Generally, recent studies of respiratory hospital admissions that evaluate multiple lags, have found effect sizes to be larger when using longer moving averages or distributed lag models. For example, when examining hospital admissions for all respiratory diseases among older adults, the strongest associations were observed when using PM concentrations 2 days prior to the hospital

admission (Section 6.3.8). Longer lag periods were also found to be most strongly associated with asthma hospital admissions and ED visits in children (3-5 days) with some evidence for more immediate effects in older adults (lags of 0 and 1 day), but these observations were not consistent across studies (Section 6.3.8). These variable results could be due to the biological complexity of asthma, which inhibits the identification of a specific lag period. The longer lag times identified in the epidemiologic studies evaluated are biologically plausible considering that PM effects on allergic sensitization and lung immune defenses have been observed in controlled human exposure and toxicological studies. These effects could lead to respiratory illnesses over a longer time course (e.g., within several days respiratory infection may become evident, resulting in respiratory symptoms or a hospital admission). However, inflammatory responses, which contribute to some forms of asthma, may result in symptoms requiring medical care within a shorter time frame (e.g., 0-1 days).

2.4.2.3. PM-Mortality Associations

Epidemiologic studies that focused on the association between short-term PM exposure and mortality (i.e., all-cause, cardiovascular, and respiratory) mostly examined a priori lag structures of either 1 or 0-1 days. Although mortality studies do not often examine alternative lag structures, the selection of the aforementioned a priori lag days has been confirmed in additional studies, with the strongest PM-mortality associations consistently being observed at lag 1 and 0-1-days (Section 6.5). However, of note is recent evidence for larger effect estimates when using a distributed lag model.

Epidemiologic studies that examined the association between long-term exposure to PM and mortality have also attempted to identify the latency period from PM exposure to death (Section 7.6.4). Results of the lag comparisons from several cohort studies indicate that the effects of changes in exposure on mortality are seen within five years, with the strongest evidence for effects observed within the first two years. Additionally, there is evidence, albeit from one study, that the mortality effect had larger cumulative effects spread over the follow-up year and three preceding years.

2.4.3. PM Concentration-Response Relationship

An important consideration in characterizing the PM-morbidity and mortality association is whether the concentration-response relationship is linear across the full concentration range that is encountered or if there are concentration ranges where there are departures from linearity (i.e., nonlinearity). In this ISA studies have been identified that attempt to characterize the shape of the concentration-response curve along with possible PM "thresholds" (i.e., levels which PM concentrations must exceed in order to elicit a health response). The epidemiologic studies evaluated that examined the shape of the concentration-response curve and the potential presence of a threshold have focused on cardiovascular hospital admissions and ED visits and mortality associated with short-term exposure to PM_{10} and mortality associated with long-term exposure to $PM_{2.5}$.

A limited number of studies have been identified that examined the shape of the PM-cardiovascular hospital admission and ED visit concentration-response relationship. Of these studies, some conducted an exploratory analysis during model selection to determine if a linear curve most adequately represented the concentration-response relationship; whereas, only one study conducted an extensive analysis to examine the shape of the concentration-response curve at different concentrations (Section 6.2.10.10). Overall, the limited evidence from the studies evaluated supports the use of a no-threshold, log-linear model, which is consistent with the observations made in studies that examined the PM-mortality relationship.

Although multiple studies have previously examined the PM-mortality concentration-response relationship and whether a threshold exists, more complex statistical analyses continue to be developed to analyze this association. Using a variety of methods and models, most of the studies evaluated support the use of a no-threshold, log-linear model; however, one study did observe heterogeneity in the shape of the concentration-response curve across cities (Section 6.5). Overall, the studies evaluated further support the use of a no-threshold log-linear model, but additional issues such as the influence of heterogeneity in estimates between cities, and the effect of seasonal and regional differences in PM on the concentration-response relationship still require further investigation.

In addition to examining the concentration-response relationship between short-term exposure to PM and mortality, Schwartz et al. (2008, 156963) conducted an analysis of the shape of the concentration-response relationship associated with long-term exposure to PM. Using a variety of statistical methods, the concentration-response curve was found to be indistinguishable from linear, and, therefore, little evidence was observed to suggest that a threshold exists in the association between long-term exposure to $PM_{2.5}$ and the risk of death (Section 7.6).

2.4.4. PM Sources and Constituents Linked to Health Effects

Recent epidemiologic, toxicological, and controlled human exposure studies have evaluated the health effects associated with ambient PM constituents and sources, using a variety of quantitative methods applied to a broad set of PM constituents, rather than selecting a few constituents a priori (Section 6.6). There is some evidence for trends and patterns that link particular ambient PM constituents or sources with specific health outcomes, but there is insufficient evidence to determine whether these patterns are consistent or robust.

For cardiovascular effects, multiple outcomes have been linked to a $PM_{2.5}$ crustal/soil/road dust source, including cardiovascular mortality and ST-segment changes. Additional studies have reported associations between other sources (i.e., traffic and wood smoke/vegetative burning) and cardiovascular outcomes (i.e., mortality and ED visits). Studies that only examined the effects of individual $PM_{2.5}$ constituents found evidence for an association between EC and cardiovascular hospital admissions and cardiovascular mortality. Many studies have also observed associations between other sources (i.e., salt, secondary SO_4^{2-}/long-range transport, other metals) and cardiovascular effects, but at this time, there does not appear to be a consistent trend or pattern of effects for those factors.

There is less consistent evidence for associations between PM sources and respiratory health effects, which may be partially due to the fact that fewer source apportionment studies have been conducted that examined respiratory-related outcomes (e.g., hospital admissions) and measures (e.g., lung function). However, there is some evidence for associations between respiratory ED visits and decrements in lung function with secondary SO_4^{2-} $PM_{2.5}$. In addition, crustal/soil/road dust and traffic sources of PM have been found to be associated with increased respiratory symptoms in asthmatic children and decreased PEF in asthmatic adults. Inconsistent results were observed in those $PM_{2.5}$ studies that used individual constituents to examine associations with respiratory morbidity and mortality, although Cu, Pb, OC, and Zn were related to respiratory health effects in two or more studies.

A few studies have identified $PM_{2.5}$ sources associated with total mortality. These studies found an association between mortality and the $PM_{2.5}$ sources: secondary SO_4^{2-}/long-range transport, traffic, and salt. In addition, studies have evaluated whether the variation in associations between $PM_{2.5}$ and mortality or PM_{10} and mortality reflects differences in $PM_{2.5}$ constituents. PM_{10}-mortality effect estimates were greater in areas with a higher proportion of Ni in $PM_{2.5}$, but the overall PM_{10}-mortality association was diminished when New York City was excluded in sensitivity analyses in two of the studies. V was also found to modify PM_{10}-mortality effect estimates. When examining the effect of species-to-$PM_{2.5}$ mass proportion on $PM_{2.5}$-mortality effect estimates, Ni, but not V, was also found to modify the association.

Overall, the results indicate that many constituents of PM can be linked with differing health effects and the evidence is not yet sufficient to allow differentiation of those constituents or sources that are more closely related to specific health outcomes. These findings are consistent with the conclusions of the 2004 PM AQCD (U.S. EPA, 2004, 056905) (i.e., that a number of source types, including motor vehicle emissions, coal combustion, oil burning, and vegetative burning, are associated with health effects). Although the crustal factor of fine particles was not associated with mortality in the 2004 PM AQCD (U.S. EPA, 2004, 056905), recent studies have suggested that PM (both $PM_{2.5}$ and $PM_{10-2.5}$) from crustal, soil or road dust sources or PM tracers linked to these sources are associated with cardiovascular effects. In addition, $PM_{2.5}$ secondary SO_4^{2-} has been associated with both cardiovascular and respiratory effects.

2.5. Welfare Effects

This section presents key conclusions and scientific judgments regarding causality for welfare effects of PM as discussed in Chapter 9. The effects of particulate NO_X and SO_X have recently been evaluated in the ISA for Oxides of Nitrogen and Sulfur – Ecological Criteria (U.S. EPA, 2008, 157074). That ISA focused on the effects from deposition of gas- and particle-phase pollutants related to ambient NO_X and SO_X concentrations that can lead to acidification and nutrient enrichment. Thus, emphasis in Chapter 9 is placed on the effects of airborne PM, including NO_X and SO_X, on visibility and climate, and on the effects of deposition of PM constituents other than NO_X and SO_X, primarily metals and carbonaceous compounds. EPA's framework for causality, described in Chapter 1, was applied and the causal determinations are highlighted.

Table 2-5. Summary of causality determination for welfare effects.

Welfare Effects	Causality Determination
Effects on Visibility	Causal
Effects on Climate	Causal
Ecological Effects	Likely to be causal
Effects on Materials	Causal

2.5.1. Summary of Effects on Visibility

Visibility impairment is caused by light scattering and absorption by suspended particles and gases. There is strong and consistent evidence that PM is the overwhelming source of visibility impairment in both urban and remote areas. EC and some crustal minerals are the only commonly occurring airborne particle components that absorb light. All particles scatter light, and generally light scattering by particles is the largest of the four light extinction components (i.e., absorption and scattering by gases and particles). Although a larger particle scatters more light than a similarly shaped smaller particle of the same composition, the light scattered per unit of mass is greatest for particles with diameters from ~0.3-1.0 μm.

For studies where detailed data on particle composition by size are available, accurate calculations of light extinction can be made. However, routinely available PM speciation data can be used to make reasonable estimates of light extinction using relatively simple algorithms that multiply the concentrations of each of the major PM species by its dry extinction efficiency and by a water growth term that accounts for particle size change as a function of relative humidity for hygroscopic species (e.g., sulfate, nitrate, and sea salt). This permits the visibility impairment associated with each of the major PM components to be separately approximated from PM speciation monitoring data.

Direct optical measurement of light extinction measured by transmissometer, or by combining the PM light scattering measured by integrating nephelometers with the PM light absorption measured by an aethalometer, offer a number of advantages compared to algorithm estimates of light extinction based on PM composition and relative humidity data. The direct measurements are not subject to the uncertainties associated with assumed scattering and absorption efficiencies used in the PM algorithm approach. The direct measurements have higher time resolution (i.e., minutes to hours), which is more commensurate with visibility effects compared with calculated light extinction using routinely available PM speciation data (i.e., 24-h duration).

Particulate sulfate and nitrate have comparable light extinction efficiencies (haze impacts per unit mass concentration) at any relative humidity value. Their light scattering per unit mass concentration increases with increasing relative humidity, and at sufficiently high humidity values (RH>85%) they are the most efficient particulate species contributing to haze. Particulate sulfate is

the dominant source of regional haze in the eastern U.S. (>50% of the particulate light extinction) and an important contributor to haze elsewhere in the country (>20% of particulate light extinction). Particulate nitrate is a minor component of remote-area regional haze in the non-California western and eastern U.S., but an important contributor in much of California and in the upper Midwestern U.S., especially during winter when it is the dominant contributor to particulate light extinction.

EC and OC have the highest dry extinction efficiencies of the major PM species and are responsible for a large fraction of the haze, especially in the northwestern U.S., though absolute concentrations are as high in the eastern U.S. Smoke plume impacts from large wildfires dominate many of the worst haze periods in the western U.S. Carbonaceous PM is generally the largest component of urban excess $PM_{2.5}$ (i.e., the difference between urban and regional background concentration). Western urban areas have more than twice the average concentrations of carbonaceous PM than remote areas sites in the same region. In eastern urban areas $PM_{2.5}$ is dominated by about equal concentrations of carbonaceous and sulfate components, though the usually high relative humidity in the East causes the hydrated sulfate particles to be responsible for about twice as much of the urban haze as that caused by the carbonaceous PM.

$PM_{2.5}$ crustal material (referred to as fine soil) and $PM_{10-2.5}$ are significant contributors to haze for remote areas sites in the arid southwestern U.S. where they contribute a quarter to a third of the haze, with $PM_{10-2.5}$ usually contributing twice that of fine soil. Coarse mass concentrations are as high in the Central Great Plains as in the deserts though there are no corresponding high concentrations of fine soil as in the Southwest. Also the relative contribution to haze by the high coarse mass in the Great Plains is much smaller because of the generally higher haze values caused by the high concentrations of sulfate and nitrate PM in that region.

Visibility has direct significance to people's enjoyment of daily activities and their overall sense of wellbeing. For example, psychological research has demonstrated that people are emotionally affected by poor VAQ such that their overall sense of wellbeing is diminished. Urban visibility has been examined in two types of studies directly relevant to the NAAQS review process: urban visibility preference studies and urban visibility valuation studies. Both types of studies are designed to evaluate individuals' desire for good VAQ where they live, using different metrics. Urban visibility preference studies examine individuals' preferences by investigating the amount of visibility degradation considered unacceptable, while economic studies examine the value an individual places on improving VAQ by eliciting how much the individual would be willing to pay for different amounts of VAQ improvement.

There are three urban visibility preference studies and two additional pilot studies that have been conducted to date that provide useful information on individuals' preferences for good VAQ in the urban setting. The completed studies were conducted in Denver, Colorado, two cities in British Columbia, Canada, and Phoenix, AZ. The additional studies were conducted in Washington, DC. The range of median preference values for an acceptable amount of visibility degradation from the 4 urban areas was approximately 19-33 dv. Measured in terms of visual range (VR), these median acceptable values were between approximately 59 and 20 km.

The economic importance of urban visibility has been examined by a number of studies designed to quantify the benefits (or willingness to pay) associated with potential improvements in urban visibility. Urban visibility valuation research was described in the 2004 PM AQCD (U.S. EPA, 2004, 056905) and the 2005 PM Staff Paper (U.S. EPA, 2005, 090209). Since the mid-1990s, little new information has become available regarding urban visibility valuation (Section 9.2.4).

Collectively, the evidence is sufficient to conclude that **a causal relationship exists between PM and visibility impairment.**

2.5.2. Summary of Effects on Climate

Aerosols affect climate through direct and indirect effects. The direct effect is primarily realized as planet brightening when seen from space because most aerosols scatter most of the visible spectrum light that reaches them. The Intergovernmental Panel on Climate Change (IPCC) Fourth Assessment Report (AR4) (IPCC, 2007, 092765), hereafter IPCC AR4, reported that the radiative forcing from this direct effect was -0.5 (±0.4) W/m^2 and identified the level of scientific understanding of this effect as 'Medium-low'. The global mean direct radiative forcing effect from individual components of aerosols was estimated for the first time in the IPCC AR4 where they were reported to be (all in W/m^2 units): -0.4 (±0.2) for sulfate, -0.05 (±0.05) for fossil fuel-derived organic

carbon, +0.2 (±0.15) for fossil fuel-derived black carbon (BC), +0.03 (±0.12) for biomass burning, -0.1 (±0.1) for nitrates, and -0.1 (±0.2) for mineral dust. Global loadings of anthropogenic dust and nitrates remain very troublesome to estimate, making the radiative forcing estimates for these constituents particularly uncertain.

Numerical modeling of aerosol effects on climate has sustained remarkable progress since the time of the 2004 PM AQCD (U.S. EPA, 2004, 056905), PM AQCD, though model solutions still display large heterogeneity in their estimates of the direct radiative forcing effect from anthropogenic aerosols. The clear-sky direct radiative forcing over ocean due to anthropogenic aerosols is estimated from satellite instruments to be on the order of -1.1 (±0.37) W/m^2 while model estimates are -0.6 W/m^2. The models' low bias over ocean is carried through for the global average: global average direct radiative forcing from anthropogenic aerosols is estimated from measurements to range from -0.9 to -1.9 W/m^2, larger than the estimate of -0.8 W/m^2 from the models.

Aerosol indirect effects on climate are primarily realized as an increase in cloud brightness (termed the 'first indirect' or Twomey effect), changes in precipitation, and possible changes in cloud lifetime. The IPCC AR4 reported that the radiative forcing from the Twomey effect was -0.7 (range: -1.1 to +4) and identified the level of scientific understanding of this effect as “Low” in part owing to the very large unknowns concerning aerosol size distributions and important interactions with clouds. Other indirect effects from aerosols are not considered to be radiative forcing.

Taken together, direct and indirect effects from aerosols increase Earth's shortwave albedo or reflectance thereby reducing the radiative flux reaching the surface from the Sun. This produces net climate cooling from aerosols. The current scientific consensus reported by IPCC AR4 is that the direct and indirect radiative forcing from anthropogenic aerosols computed at the top of the atmosphere, on a global average, is about -1.3 (range: -2.2 to -0.5) W/m^2. While the overall global average effect of aerosols at the top of the atmosphere and at the surface is negative, absorption and scattering by aerosols within the atmospheric column warms the atmosphere between the Earth's surface and top of the atmosphere. In part, this is owing to differences in the distribution of aerosol type and size within the vertical atmospheric column since aerosol type and size distributions strongly affect the aerosol scattering and reradiation efficiencies at different altitudes and atmospheric temperatures. And, although the magnitude of the overall negative radiative forcing at the top of the atmosphere appears large in comparison to the analogous IPCC AR4 estimate of positive radiative forcing from anthropogenic GHG of about +2.9 (± 0.3) W/m^2, the horizontal, vertical, and temporal distributions and the physical lifetimes of these two very different radiative forcing agents are not similar; therefore, the effects do not simply off-set one another.

Overall, the evidence is sufficient to conclude that **a causal relationship exists between PM and effects on climate, including both direct effects on radiative forcing and indirect effects that involve cloud feedbacks that influence precipitation formation and cloud lifetimes.**

2.5.3. Summary of Ecological Effects of PM

Ecological effects of PM include direct effects to metabolic processes of plant foliage; contribution to total metal loading resulting in alteration of soil biogeochemistry and microbiology, plant growth and animal growth and reproduction; and contribution to total organics loading resulting in bioaccumulation and biomagnification across trophic levels. These effects were well-characterized in the 2004 PM AQCD (U.S. EPA, 2004, 056905). Thus, the summary below builds upon the conclusions provided in that review.

PM deposition comprises a heterogeneous mixture of particles differing in origin, size, and chemical composition. Exposure to a given concentration of PM may, depending on the mix of deposited particles, lead to a variety of phytotoxic responses and ecosystem effects. Moreover, many of the ecological effects of PM are due to the chemical constituents (e.g., metals, organics, and ions) and their contribution to total loading within an ecosystem.

Investigations of the direct effects of PM deposition on foliage have suggested little or no effects on foliar processes, unless deposition levels were higher than is typically found in the ambient environment. However, consistent and coherent evidence of direct effects of PM has been found in heavily polluted areas adjacent to industrial point sources such as limestone quarries, cement kilns, and metal smelters (Sections 9.4.3 and 9.4.5.7). Where toxic responses have been

documented, they generally have been associated with the acidity, trace metal content, surfactant properties, or salinity of the deposited materials.

An important characteristic of fine particles is their ability to affect the flux of solar radiation passing through the atmosphere, which can be considered in both its direct and diffuse components. Foliar interception by canopy elements occurs for both up- and down-welling radiation. Therefore, the effect of atmospheric PM on atmospheric turbidity influences canopy processes both by radiation attenuation and by changing the efficiency of radiation interception in the canopy through conversion of direct to diffuse radiation. Crop yields can be sensitive to the amount of radiation received, and crop losses have been attributed to increased regional haze in some areas of the world such as China (Section 9.4.4). On the other hand, diffuse radiation is more uniformly distributed throughout the canopy and may increase canopy photosynthetic productivity by distributing radiation to lower leaves. The enrichment in photosynthetically active radiation (PAR) present in diffuse radiation may offset a portion of the effect of an increased atmospheric albedo due to atmospheric particles. Further research is needed to determine the effects of PM alteration of radiative flux on the growth of vegetation in the U.S.

The deposition of PM onto vegetation and soil, depending on its chemical composition, can produce responses within an ecosystem. The ecosystem response to pollutant deposition is a direct function of the level of sensitivity of the ecosystem and its ability to ameliorate resulting change. Many of the most important ecosystem effects of PM deposition occur in the soil. Upon entering the soil environment, PM pollutants can alter ecological processes of energy flow and nutrient cycling, inhibit nutrient uptake, change ecosystem structure, and affect ecosystem biodiversity. The soil environment is one of the most dynamic sites of biological interaction in nature. It is inhabited by microbial communities of bacteria, fungi, and actinomycetes, in addition to plant roots and soil macro-fauna. These organisms are essential participants in the nutrient cycles that make elements available for plant uptake. Changes in the soil environment can be important in determining plant and ultimately ecosystem response to PM inputs.

There is strong and consistent evidence from field and laboratory experiments that metal components of PM alter numerous aspects of ecosystem structure and function. Changes in the soil chemistry, microbial communities and nutrient cycling, can result from the deposition of trace metals. Exposures to trace metals are highly variable, depending on whether deposition is by wet or dry processes. Although metals can cause phytotoxicity at high concentrations, few heavy metals (e.g., Cu, Ni, Zn) have been documented to cause direct phytotoxicity under field conditions. Exposure to coarse particles and elements such as Fe and Mg are more likely to occur via dry deposition, while fine particles, which are more often deposited by wet deposition, are more likely to contain elements such as Ca, Cr, Pb, Ni, and V. Ecosystems immediately downwind of major emissions sources can receive locally heavy deposition inputs. Phytochelatins produced by plants as a response to sublethal concentrations of heavy metals are indicators of metal stress to plants. Increased concentrations of phytochelatins across regions and at greater elevation have been associated with increased amounts of forest injury in the northeastern U.S.

Overall, the ecological evidence is sufficient to conclude that **a causal relationship is likely to exist between deposition of PM and a variety of effects on individual organisms and ecosystems, based on information from the previous review and limited new findings in this review.** However, in many cases, it is difficult to characterize the nature and magnitude of effects and to quantify relationships between ambient concentrations of PM and ecosystem response due to significant data gaps and uncertainties as well as considerable variability that exists in the components of PM and their various ecological effects.

2.5.4. Summary of Effects on Materials

Building materials (metals, stones, cements, and paints) undergo natural weathering processes from exposure to environmental elements (wind, moisture, temperature fluctuations, sunlight, etc.). Metals form a protective film of oxidized metal (e.g., rust) that slows environmentally induced corrosion. However, the natural process of metal corrosion is enhanced by exposure to anthropogenic pollutants. For example, formation of hygroscopic salts increases the duration of surface wetness and enhances corrosion.

A significant detrimental effect of particle pollution is the soiling of painted surfaces and other building materials. Soiling changes the reflectance of opaque materials and reduces the transmission

of light through transparent materials. Soiling is a degradation process that requires remediation by cleaning or washing, and, depending on the soiled surface, repainting. Particulate deposition can result in increased cleaning frequency of the exposed surface and may reduce the usefulness of the soiled material.

Attempts have been made to quantify the pollutant exposure levels at which materials damage and soiling have been perceived. However, to date, insufficient data are available to advance the knowledge regarding perception thresholds with respect to pollutant concentration, particle size, and chemical composition. Nevertheless, the evidence is sufficient to conclude that **a causal relationship exists between PM and effects on materials.**

2.6. Summary of Health Effects and Welfare Effects Causal Determinations

This chapter has provided an overview of the underlying evidence used in making the causal determinations for the health and welfare effects and PM size fractions evaluated. This review builds upon the main conclusions of the last PM AQCD (U.S. EPA, 2004, **056905**):

- "A growing body of evidence both from epidemiological and toxicological studies… supports the general conclusion that $PM_{2.5}$ (or one or more $PM_{2.5}$ components), acting alone and/or in combination with gaseous copollutants, are likely causally related to cardiovascular and respiratory mortality and morbidity." (pg 9-79)

- "A much more limited body of evidence is suggestive of associations between short-term (but not long-term) exposures to ambient coarse-fraction thoracic particles… and various mortality and morbidity effects observed at times in some locations. This suggests that $PM_{10-2.5}$, or some constituent component(s) of $PM_{10-2.5}$, may contribute under some circumstances to increased human health risks… with somewhat stronger evidence for… associations with morbidity (especially respiratory) endpoints than for mortality." (pg 9-79 and 9-80)

- "Impairment of visibility in rural and urban areas is directly related to ambient concentrations of fine particles, as modulated by particle composition, size, and hygroscopic characteristics, and by relative humidity." (pg 9-99)

- "Available evidence, ranging from satellite to in situ measurements of aerosol effects on incoming solar radiation and cloud properties, is strongly indicative of an important role in climate for aerosols, but this role is still poorly quantified." (pg 9-111)

The evaluation of the epidemiologic, toxicological, and controlled human exposure studies published since the completion of the 2004 PM AQCD have provided additional evidence for PM-related health effects. Table 2-6 provides an overview of the causal determinations for all PM size fractions and health effects. Causal determinations for PM and welfare effects, including visibility, climate, ecological effects, and materials are included in Table 2-7. Detailed discussions of the scientific evidence and rationale for these causal determinations are provided in the subsequent chapters of this ISA.

Table 2-6. Summary of PM causal determinations by exposure duration and health outcome.

Size Fraction	Exposure	Outcome	Causality Determination
$PM_{2.5}$	Short-term	Cardiovascular Effects	Causal
		Respiratory Effects	Likely to be causal
		Central Nervous System	Inadequate
		Mortality	Causal
	Long-term	Cardiovascular Effects	Causal
		Respiratory Effects	Likely to be Causal
		Mortality	Causal
		Reproductive and Developmental	Suggestive
		Cancer, Mutagenicity, Genotoxicity	Suggestive
$PM_{10-2.5}$	Short-term	Cardiovascular Effects	Suggestive
		Respiratory Effects	Suggestive
		Central Nervous System	Inadequate
		Mortality	Suggestive
	Long-term	Cardiovascular Effects	Inadequate
		Respiratory Effects	Inadequate
		Mortality	Inadequate
		Reproductive and Developmental	Inadequate
		Cancer, Mutagenicity, Genotoxicity	Inadequate
UFPs	Short-term	Cardiovascular Effects	Suggestive
		Respiratory Effects	Suggestive
		Central Nervous System	Inadequate
		Mortality	Inadequate
	Long-term	Cardiovascular Effects	Inadequate
		Respiratory Effects	Inadequate
		Mortality	Inadequate
		Reproductive and Developmental	Inadequate
		Cancer, Mutagenicity, Genotoxicity	Inadequate

Table 2-7. Summary of PM causal determinations for welfare effects

Welfare Effects	Causality Determination
Effects on Visibility	Causal
Effects on Climate	Causal
Ecological Effects	Likely to be causal
Effects on Materials	Causal

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Chapter 3. Source to Human Exposure

3.1. Introduction

This chapter describes basic concepts and new and established findings in atmospheric sciences and human exposure assessment relevant to PM to establish a foundation for the health and ecological effects discussed in subsequent chapters. Information in this chapter builds on previous AQCDs for PM using new data and re-interpretations of extant studies as well. This includes new knowledge of PM chemistry, the latest developments in monitoring methodologies, recent national and local measurements and trends in PM concentrations as a function of size range and composition, advances in receptor and chemistry-transport modeling, revised estimates of policy-relevant background PM, and recent work on exposure assessment.

The chapter and its associated annex material are organized as follows: Section 3.2 presents an overview of basic information related to the size distribution and composition of airborne particles. Section 3.3 provides a brief description of the sources, emissions, and deposition of PM, including discussions of possible mechanisms of secondary PM formation from gaseous precursors and of the atmospheric processes that deposit PM to the earth's surface. Issues related to the measurement of PM and its chemical components and to monitors and networks in the U.S. are covered in Section 3.4; supplementary material on these topics is contained in Annex A, Section A.1. Analyses of data for ambient concentrations of PM and its components are characterized in Section 3.5, and supplementary information can be found in Annex A, Section A.2. Section 3.6 describes methods for determining source contributions to ambient samples by receptor models and presents results from recent receptor modeling studies. In addition, the construction of chemistry-transport models (CTMs) to determine pollutant concentrations is described in Section 3.6. Supplementary information about receptor model methods and results is given in Annex A, Section A.3. Policy relevant background concentrations of PM, i.e., those concentrations defined to result from natural sources everywhere in the world together with anthropogenic sources outside of Canada, the United States, and Mexico, are presented in Section 3.7. Issues related to human exposure assessment including sources of exposure and implications for epidemiologic studies are discussed in Section 3.8. Supplementary information on exposure studies is included in Annex A, Section A.4. Finally, the summary and conclusions from Chapter 3 are presented in Section 3.9.

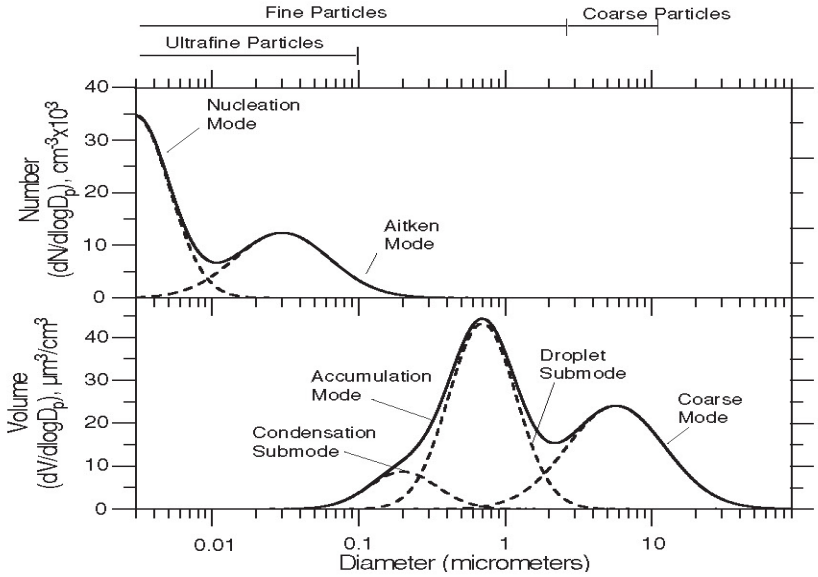
3.2. Overview of Basic Aerosol Properties

Unlike gas-phase pollutants such as SO_2, CO, H_2CO and O_3, which are well-defined chemical entities, atmospheric PM varies in size, shape, and chemical composition. Atmospheric chemical and microphysical processing of direct emissions of PM and its precursors together with mechanical generation of particles tend to produce distinct lognormal modes (Whitby, 1978, 071181) as shown in Figure 3-1. To the extent that information is available, discussions in this and subsequent chapters will focus on particles in specific size ranges (i.e., $PM_{2.5}$, $PM_{10-2.5}$ and PM_{10}). The subscripts after PM

Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISA) and the Integrated Risk Information System (IRIS).

refer to the aerodynamic diameter[1] (d_{ae}) in micrometers (µm) of 50% cut points of sampling devices. For example, EPA defines PM_{10} as particles collected by a sampler with an upper 50% cut point of 10 µm d_{ae} and a specific, fairly sharp, penetration curve, as defined in the Code of Federal Regulations (40 CFR Part 58). $PM_{2.5}$ is defined in an analogous way. Ultrafine particles (UFPs), defined here as particles with a diameter ≤ 0.1 µm (typically based on physical size, thermal diffusivity, or electrical mobility), will also be discussed.

The terms "fine particles" and "coarse particles" have lost the precise meaning as defined in Whitby (1978, 071181), where "fine particles" refers to all particles in the nucleation, Aitken, and accumulation modes; and "coarse particles" characterizes all particles larger than these. UFPs correspond loosely to the nucleation plus Aitken modes (in earlier literature, these modes were not separated and the combination, unresolved by older instruments, was called the Aitken mode). Now, the term "fine particles" is most often associated with the $PM_{2.5}$ fraction, which includes the nucleation, Aitken and accumulation modes and some particles from the lower-size tail of the coarse particle mode between about 1 and 2.5 µm aerodynamic diameter. "Thoracic coarse" is frequently used in reference to $PM_{10\text{-}2.5}$, which does not include the low-end tail of the coarse particle mode. With high relative humidity, larger particles in the accumulation mode could also extend into the 1 to 3 µm size range. These relationships can be seen in Figure 3-1, which shows the number distribution for UPFs and the volume distribution (or mass distribution if particle density is constant across the size range) for fine and (thoracic) coarse particles. The figure is arranged this way because particle number is most highly concentrated in the ultrafine (UF) size range but volume (or mass) is most concentrated in the larger size ranges.



Source:Reprinted with Permission of Cambridge University Press from Pandis (2004, 156838).

Figure 3-1. Particle size distributions by number and volume. Dashed lines refer to values in individual modes and solid lines to their sum. Note that ultrafine particles are a subset of fine particles.

[1] Aerodynamic diameter is the diameter of a unit density (1 g/cm^3) sphere that has the same gravitational settling velocity as the particle of interest and is a useful metric for characterizing particles >~ 1 µm. For sub-micron particles, forces other than gravity increase in importance in determining a particle's motion and air can no longer be considered a continuum. Aerodynamic diameter is frequently reported down to ~ 0.1 µm where the assumptions used in its derivation no longer hold. A useful metric for characterizing particles <~ 0.5 µm is the mobility diameter defined as the diameter of a particle having the same diffusivity or electrical mobility in air as the particle of interest. In the region between ~ 0.5–1.0 µm, aerodynamic and mobility diameters are not necessarily the same. The question of how best to merge these diameters is unresolved and depends on the particle properties of interest.

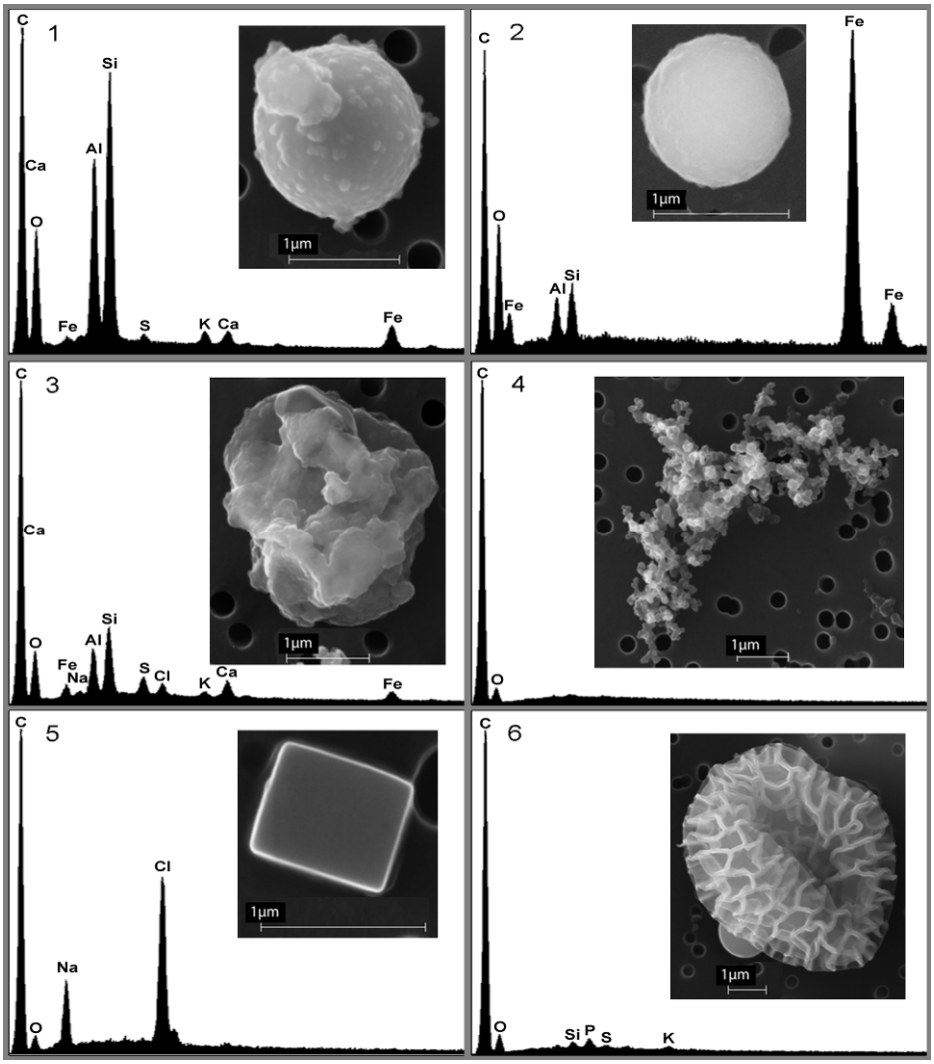
Characterizing particle size is important because different size particles penetrate to different regions of the human respiratory tract. Thoracic particles refer to particles that travel past the larynx to reach the lung airways and the gas-exchange region of the lung, and respirable particles are those that reach the gas-exchange region. The selection of PM_{10} as an indicator of thoracic particles was based in large part on dosimetry (U.S. EPA, 1996, 079380). However, the selection of $PM_{2.5}$ to characterize respirable particles was driven mainly by considerations related to measurement techniques available at the time rather than dosimetry. Currently, cut points other than 2.5 μm are attainable and frequently put into use. For example, the American Conference of Governmental Industrial Hygienists (ACGIH, 2005, 156188), the International Standards Organization, and the European Standardization Committee have adopted a 50% cut point of 4 μm as an indicator of respirable particles. Most commonly, however, $PM_{2.5}$ is used as an indicator of respirable particles, $PM_{10-2.5}$ is used as an indicator of the thoracic component of coarse particles that is sometimes referred to as thoracic coarse (noting that it excludes some coarse particles below 2.5 μm and above 10 μm), and PM_{10} is used as an indicator of thoracic particles.

As can be seen from Table 3-1, particles in individual size modes are characterized by rather distinct sources, composition, chemical properties, lifetimes in the atmosphere (τ) and distances over which they can travel. Whereas particles in the smaller size modes are formed mainly by combustion processes and by nucleation and condensation of gases, coarse particles are generated mainly by mechanical activity, such as by the action of wind on either the ground or the sea surface or by construction or by resuspension by traffic. Particles in the UF size range are either emitted directly to the atmosphere or are formed by nucleation of gaseous constituents in the atmosphere. The properties of fibers and engineered nano-objects and nanometer scale products (e.g., dots, hollow spheres, rods, fibers, and tubes) are not reviewed in this chapter because these classes of objects are found mainly in certain occupational settings rather than in ambient air.

Table 3-1. Characteristics of ambient fine (ultrafine plus accumulation-mode) and coarse particles.

	Fine		Coarse
	Ultrafine	Accumulation	
Formation Processes	Combustion, high-temperature processes, and atmospheric reactions		Break-up of large solids/droplets
Formed by	Nucleation of atmospheric gases including H_2SO_4, NH_3 and some organic compounds Condensation of gases	Condensation of gases Coagulation of smaller particles Reactions of gases in or on particles Evaporation of fog and cloud droplets in which gases have dissolved and reacted	Mechanical disruption (crushing, grinding, abrasion of surfaces) Evaporation of sprays Suspension of dusts Reactions of gases in or on particles
Composed of	Sulfate EC Metal compounds Organic compounds with very low saturation vapor pressure at ambient temperature	Sulfate, nitrate, ammonium, and hydrogen ions EC Large variety of organic compounds Metals: compounds of Pb, Cd, V, Ni, Cu, Zn, Mn, Fe, etc. Particle-bound water Bacteria, viruses	Nitrates/chlorides/sulfates from HNO_3/HCl/SO_2 reactions with coarse particles Oxides of crustal elements (Si, Al, Ti, Fe) $CaCO_3$, $CaSO_4$, NaCl, sea salt Bacteria, pollen, mold, fungal spores, plant and animal debris
Solubility	Not well characterized	Largely soluble, hygroscopic, and deliquescent	Largely insoluble and nonhygroscopic
Sources	High temperature combustion Atmospheric reactions of primary, gaseous compounds.	Combustion of fossil and biomass fuels, and high temperature industrial processes, smelters, refineries, steel mills etc. Atmospheric oxidation of NO_2, SO_2, and organic compounds, including biogenic organic species (e.g., terpenes)	Resuspension of particles deposited onto roads Tire, brake pad, and road wear debris Suspension from disturbed soil (e.g., farming, mining, unpaved roads) Construction and demolition Fly ash from uncontrolled combustion of coal, oil, and wood Ocean spray
Atmospheric half-life	Minutes to hours	Days to weeks	Minutes to hours
Removal Processes	Grows into accumulation mode Diffuses to raindrops and other surfaces	Forms cloud droplets and rains out Dry deposition	Dry deposition by fallout Scavenging by falling rain drops
Travel distance	<1 to 10s of km	100s to 1000s of km	<1 to 10s of km (100s to 1,000s of km in dust storms for the small size tail)

Source: Adapted with Permission of the Air & Waste Management Association from Wilson and Suh (1997, 077408)



Source: National Exposure Research Laboratory.

Figure 3-2. X-ray spectra and scanning electron microscopy images of individual particles. These include: (1) an aluminum-silicate fly ash sphere emitted from a coal-fired power plant; (2) an iron oxide sphere emitted from a steel manufacturing facility; (3) an aluminum-silicate particle, probably of crustal origin; (4) a carbon soot aggregate from a diesel engine consisting of many sub-micron size carbon particles; (5) a sodium chloride crystal, potentially of marine origin; and (6) a partially collapsed pollen particle. The polycarbonate filter substrate used to collect the particles is visible in the background of each image and contributes to the carbon peak in each spectrum.

Particles appear in a wide variety of shapes such as spheres, ellipsoids, cubes, and irregular or fractal geometries. This is one reason why a standard metric such as aerodynamic diameter is useful for describing the mechanical properties of the particles. The shape of particles is important for determining the optical properties of the particles. The directionality of sunlight scattered by certain shapes of particles, such as plates, also depends strongly on their physical orientation while suspended. The shape of particles also affects the surface area of the particles in contact with the surface it is deposited on, including cell membranes.

Images of six types of individual particles obtained using scanning electron microscope (SEM) and their corresponding x-ray spectra showing their major elemental composition are shown

in Figure 3-2. The images show particles sitting on a thin polycarbonate film with pores and a 1 μm scale bar for size reference. Air is pulled through the filter pores with a vacuum pump and the particles are left behind on the surface. The metal dominated spherical particles (image 2) were formed at high temperatures and were quickly cooled. Particles which are liquid such as sulfate are also spherical. Sodium chloride (NaCl) crystals are cubic (image 5); this particular particle could be marine sea salt due to the proximity to the ocean where the sample was collected. Other particles, such as the carbon chain agglomerates from diesel engines have much more irregular and complex shapes (image 4). Note that these particles were placed under vacuum resulting in volatilization of water and other volatile components and partial collapse of the pollen grain (image 6). Changes in composition and possibly morphology could occur during the sampling, collection and analysis of aerosol samples. For example, particles may be coated with semi-volatile material that evolves off the particles under vacuum and under the electron beam. Similarly, particles in ambient air are generally mixtures or agglomerates of particles coming from multiple sources and have a diverse chemical make-up.

3.3. Sources, Emissions and Deposition of Primary and Secondary PM

PM is composed of both primary (derived directly from emissions) or secondary (derived from atmospheric reactions involving gaseous precursors) components. Table 3-4 summarizes anthropogenic and natural sources for the major primary and secondary aerosol constituents of fine and coarse particles. Anthropogenic sources can be further divided into stationary and mobile sources. Stationary sources include fuel combustion for electrical utilities, residential space heating and cooking; industrial processes; construction and demolition; metal, mineral, and petrochemical processing; wood products processing; mills and elevators used in agriculture; erosion from tilled lands; waste disposal and recycling; and biomass combustion. Biomass combustion encompasses many emission activities including burning of wood for fuel, burning of vegetation to clear land for agriculture and construction, to dispose of agricultural and domestic waste, to control the growth of animal or plant pests, and to manage forest resources (prescribed burning). Wildlands also burn due to lightning strikes and arson. Mobile or transportation-related sources include direct emissions of primary PM and secondary PM precursors from highway vehicles and non-road sources as well as fugitive dust from paved and unpaved roads. Also shown in Table 3-2 are sources for several precursor gases, the oxidation of which can form secondary PM. An overview of estimates of emissions of primary PM and precursors to secondary PM from major sources is given in Section 3.3.1. The transformations from gaseous precursors shown in Table 3-2 to secondary PM are described in Section 3.3.2.

In general, the sources of fine PM are very different from those of coarse PM. Some of the mass in the fine size fraction forms during combustion from material that has volatilized in combustion chambers and then recondensed before emission to the atmosphere. Some ambient $PM_{2.5}$ forms in the atmosphere from photochemical reactions involving precursor gases. Included in this category is the formation of new UFPs by (1) homogeneous nucleation of precursor gases and (2) the condensation of gases on pre-existing particles. Biological material also exists in the fine fraction including many types of microorganisms, especially viruses and bacteria and fragments of pollens and fungal spores. $PM_{10-2.5}$ is mainly primary in origin, as it is produced by surface abrasion or by suspension of biological material and fragments of living things (e.g., plant and insect debris). In addition, atmospheric reaction products condense on coarse particles. Because precursor gases undergo mixing during transport from their sources and chemical reactions, and the oxidation of different gases can produce the same reaction products, it is difficult to identify individual sources of secondary PM. Transport and transformation of precursors can occur over distances of hundreds of kilometers. $PM_{10-2.5}$ has a shorter lifetime in the atmosphere, so its effects tend to be more localized. However, intercontinental transport of dust from African and Asian deserts occurs and some of this material is in the $PM_{10-2.5}$ size range. Major intercontinental dust events are highly episodic but small contributions can be present at other times (see Section 3.7).

Table 3-2. Constituents of atmospheric particles and their major sources.

	Primary (PM <2.5 μm)		Primary (PM >2.5 μm)		Secondary PM Precursors (PM <2.5 μm)	
Aerosol species	**Natural**	**Anthropogenic**	**Natural**	**Anthropogenic**	**Natural**	**Anthropogenic**
Sulfate (SO_4^{2-})	Sea spray	Fossil fuel combustion	Sea spray	—	Oxidation of reduced sulfur gases emitted by the oceans and wetlands and SO_2 and H_2S emitted by volcanism and forest fires	Oxidation of SO_2 emitted from fossil fuel combustion
Nitrate (NO_3^-)	—	Mobile source exhaust	—	—	Oxidation of NO_X produced by soils, forest fires, and lightning	Oxidation of NO_X emitted from fossil fuel combustion and in motor vehicle exhaust
Minerals	Erosion and re-entrainment	Fugitive dust from paved and unpaved roads, agriculture, forestry, construction, and demolition	Erosion and re-entrainment	Fugitive dust, paved and unpaved road dust, agriculture, forestry, construction, and demolition	—	—
Ammonium (NH_4^+)	—	Mobile source exhaust	—	—	Emissions of NH_3 from wild animals, and undisturbed soil	Emissions of NH_3 from motor vehicles, animal husbandry, sewage, and fertilized land
Organic carbon (OC)	Wildfires	Prescribed burning, wood burning, mobile source exhaust, cooking, tire wear and industrial processes	Soil humic matter	Tire and asphalt wear, paved and unpaved road dust	Oxidation of hydrocarbons emitted by vegetation (terpenes, waxes) and wild fires	Oxidation of hydrocarbons emitted by motor vehicles, prescribed burning, wood burning, solvent use and industrial processes
EC	Wildfires	Mobile source exhaust (mainly diesel), wood biomass burning, and cooking	—	Tire and asphalt wear, paved and unpaved road dust	—	—
Metals	Volcanic activity	Fossil fuel combustion, smelting and other metallurgical processes, and brake wear	Erosion, re-entrainment, and organic debris	—	. —	—
Bioaerosols	Viruses and bacteria	—	Plant and insect fragments, pollen, fungal spores, and bacterial agglomerates	—	—	—

Dash (—) indicates either very minor source or no known source of component.

Source: U.S. EPA (2004, 056905).

Only major sources for each constituent within each broad category shown at the top of Table 3-2 are listed. Not all sources are equal in magnitude. Chemical characterizations of primary particulate emissions for a wide variety of natural and anthropogenic sources (as shown in Table 3-2) were given in Chapter 5 of the 1996 PM AQCD (U.S. EPA, 1996, 079380). Summary tables of the composition of source emissions presented in the 1996 PM AQCD (U.S. EPA, 1996, 079380) and updates to that information are provided in Appendix 3D to the 2004 PM AQCD (U.S. EPA, 2004, 056905). Source composition profiles are archived by the EPA at http://www.epa.gov/ttn/chief/software/speciate/. The profiles of source composition were based in large measure on the results of studies that collected source signatures for use in source apportionment studies.

Natural sources of primary PM include windblown dust from undisturbed land, sea spray, and biological material. The oxidation of a fraction of terpenes emitted by vegetation and reduced sulfur species from anaerobic environments leads to secondary PM formation. Ammonium (NH_4^+) ions, which play a major role in regulating the pH of particles, are derived from emissions of NH_3 gas. Source categories for NH_3 have been divided into emissions from undisturbed soils (natural) and emissions that are related to human activities (e.g., fertilized lands, domestic and farm animal waste). There is ongoing debate about characterizing emissions from wildfires as either natural or anthropogenic. Wildfires have been listed in Table 3-2 as natural in origin, but land management practices and other human actions affect the occurrence and scope of wildfires. For example, fire suppression practices allow the buildup of combustible fuels and increase the susceptibility of forests to more severe and infrequent fires from whatever cause, including lightning strikes. Similarly, prescribed burning is listed as anthropogenic, but can be viewed as a substitute for wildfires that would otherwise occur eventually on the same land.

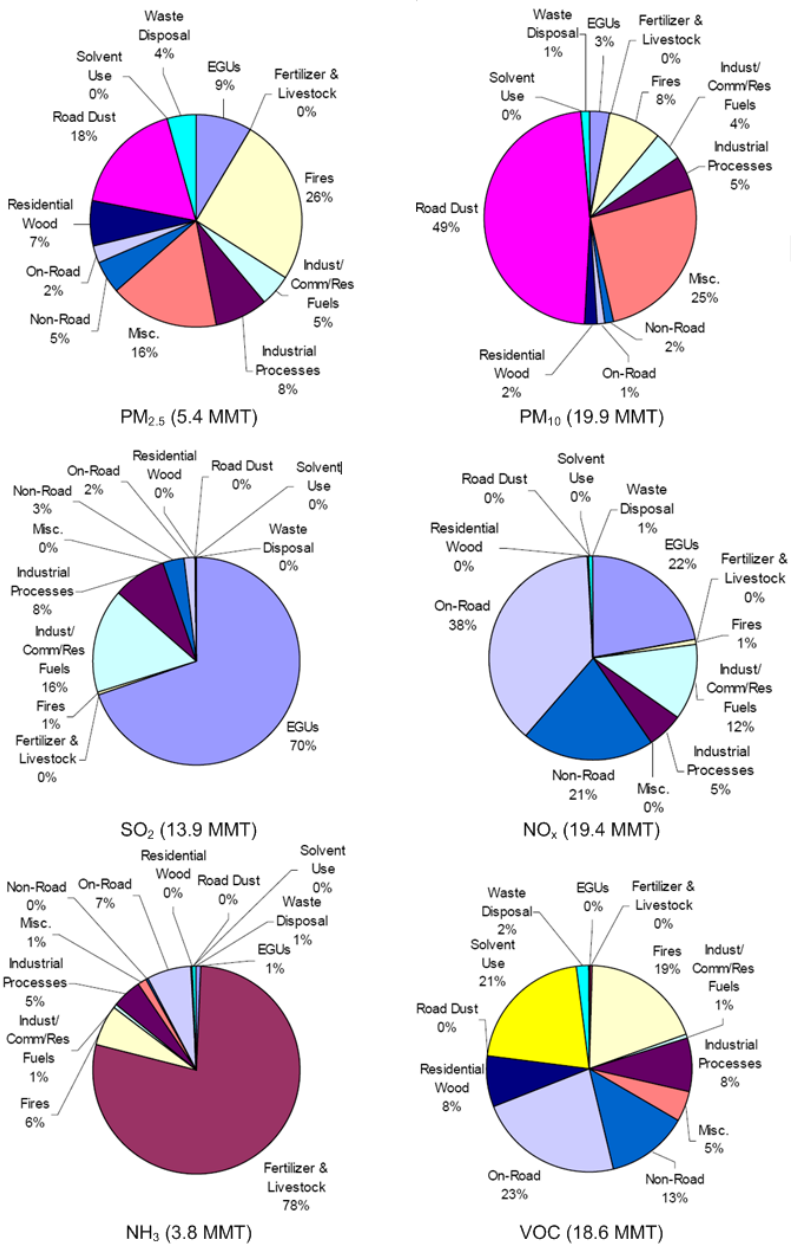
3.3.1. Emissions of Primary PM and Precursors to Secondary PM

U.S. national average emissions of primary $PM_{2.5}$, PM_{10} and gaseous precursor species (SO_2, NO_X, NH_3 and VOCs) from different source categories are shown in Figure 3-3. Note that the entries refer mainly to anthropogenic sources, with little information about natural sources. However, for categories such as VOCs, the contribution from biogenic emissions of isoprene and terpenes can be quite large. The entries are continually undergoing revision and are subject to varying degrees of uncertainty. For example, almost all of the sulfur in fuel is released as volatile components (SO_2 or SO_3) during combustion. Hence, sulfur emissions can be calculated on the basis of sulfur content in fuels to a greater accuracy than can be done for other pollutants like nitrogen oxides or primary PM. There have been notable downward revisions to the inventories since 2002 in the emissions of dust from roads. These have resulted in large measure from incorporation of emissions test data with updated methods for measuring dust emissions. Also, the spatial and temporal characterization of wildfire emissions has improved since 2002 by integrating satellite-derived fire detection and state-of-the-art fuels characterization and consumption models (Pouliot et al., 2008, 156883). Emission measurements from high-temperature combustion sources are sensitive to the dilution, temperature, and pre-treatment of dilution air (England et al., 2007, 156420; England et al., 2007, 156421; Sheya et al., 2008, 156977).

To a large extent, especially with regard to the contribution of road dust to PM, refinements in emission estimates have been guided by the use of receptor modeling. See Section 3.6.1 for a description of receptor modeling techniques and the 2004 PM AQCD (U.S. EPA, 2004, 056905) for the role of receptor models in refining emissions estimates. Note that since the estimates given in Figure 3-3 are U.S. national averages, they may not accurately reflect the contribution of specific local sources determining a person's exposures to PM at any given time and location.

As can be seen from a comparison of the total U.S. emissions (in million metric tons) shown in Figure 3-3, estimates of total emissions of potential precursors to secondary PM formation including SO_2, NO_X, NH_3 and VOCs are considerably larger than those for primary PM sources. However, translating the emissions of precursors into production rates of secondary PM or using these emissions as a guide to estimate PM composition is highly problematic. A significant fraction of gaseous precursors are lost before they could be converted to PM. Dry deposition and precipitation scavenging of some of these gaseous precursors and their intermediate oxidation products occur before they are transformed in the atmosphere, and most VOCs emitted are oxidized to carbon dioxide (CO_2) rather than to PM. Some of these precursors are also transported outside the United States. Even if gaseous precursors are converted to PM components, the effects of atmospheric transformations must also be considered (discussed in Section 3.3.2 below). As a result of these transformations, ratios of masses of particle phase products to each other will not be the same as those in the emissions inventories for their precursors. For example, SO_2, NO_X and NH_3 are converted to secondary PM as SO_4^{2-}, NO_3^- and NH_4^+. The ratios of molecular weights of PM products (SO_4^{2-}, NO_3^- and NH_4^+) to gaseous precursors (SO_2, NO_X and NH_3) are 1.5, 1.35, and 1.07, respectively. Estimating a conversion factor for carbon in VOCs is less straightforward. The oxidation of VOCs leads to the formation of secondary OC in PM. As the result of atmospheric transformations, nitrogen and oxygen are added to the carbon originally present in VOCs. Turpin and Lim (2001, 017093) recommend adjustment factors ranging from 1.4 to 2.0 to account for the presence of oxygen and nitrogen in organic compounds in OC in the aerosol phase. Because of all

the above issues, the resultant mass and composition of ambient PM is quite different from what might be inferred from examining the emissions inventories alone.



Source: U.S. EPA (2006, 157070)

Figure 3-3. Detailed source categorization of anthropogenic emissions of primary $PM_{2.5}$, PM_{10} and gaseous precursor species SO_2, NO_X, NH_3 and VOCs for 2002 in units of million metric tons (MMT). EGUs = Electricity Generating Units.

3.3.2. Formation of Secondary PM

Precursors to secondary PM have natural and anthropogenic sources, just as primary PM has natural and anthropogenic sources. A substantial fraction of the fine particle mass, especially during the warmer months of the year, is secondary in nature, formed as the result of atmospheric reactions involving both inorganic and organic gaseous precursors. The major atmospheric chemical transformations leading to the formation of particulate nitrate (pNO_3) and particulate sulfate (pSO_4) are relatively well understood; whereas those involving the formation of secondary organic aerosol (SOA) are less well understood and are subject to much current investigation. A large number of organic precursors are involved and many of the kinetic details still need to be determined. Also, many of the products of the oxidation of hydrocarbons have yet to be identified. However, there has been substantial progress made in understanding the chemistry of SOA formation in the past few years.

3.3.2.1. Formation of Nitrate and Sulfate

The basic mechanism of the gas and aqueous phase oxidation of NO_2 and SO_2 has long been studied and can be found in numerous texts on atmospheric chemistry, e.g., Seinfeld and Pandis (1998, 018352), Finlayson-Pitts and Pitts (2000, 055565), Jacob (1999, 091122), and Jacobson (2002, 090667). The reader is referred to the 2004 PM AQCD (U.S. EPA, 2004, 056905) as well as the 2008 NO_X and SO_X ISAs (U.S. EPA, 2008, 157073; U.S. EPA, 2008, 157074; U.S. EPA, 2008, 157075) where these processes are described in great detail.

3.3.2.2. Formation of Secondary Organic Aerosol

Some key new findings have altered perceptions of SOA formation since the 2004 PM AQCD (see especially the reviews by Kroll and Seinfeld (2008, 155910) and Rudich et al. (2007, 156059)). New measurement techniques for estimating the speciation and water solubility of organic aerosols have noted the dominant contribution of oxygenated species in atmospheric particles. Recent measurements show that the abundance of oxidized SOA exceeds that of more reduced hydrocarbon like organic aerosol in Pittsburgh (Zhang et al., 2005, 157185) and in about 30 other cities across the Northern Hemisphere (Zhang et al., 2007, 101119). Based on aircraft and ship-based sampling of organic aerosols in coastal waters downwind of northeastern U.S. cities, de Gouw et al. (2008, 191757) reported that 40-70% of measured organic mass was water soluble and estimated that approximately 37% of SOA is attributable to aromatic precursors, based on PM yields estimated for NO_X-limited conditions. However, the remaining mass of estimated SOA (63%) was unexplained, possibly due to oxidation of semivolatile precursors not measured by standard gas chromatography. Aerosol yields from the oxidation of aromatic compounds have been reported to be higher when reactions with NO_X are not dominant, suggesting that transport of less reactive compounds (e.g., benzene) out of source regions with high NO_X levels could result in greater overall SOA yields than previously estimated (Ng et al., 2007, 199528). Furthermore, Zhang et al. (2007, 189998) noted that the most common mass spectrum of oxygenated OA measured in ambient air resembles mass spectra measured in irradiated diesel exhaust reported by Robinson et al. (2007, 156053) and Sage et al. (2008, 191758).

Typical dilution sampling of combustion sources employ dilution rate, temperature, pressure, and background aerosol concentrations that can differ substantially from ambient conditions. Lipsky and Robinson (2006, 189891) and Robinson et al. (2007, 156053) showed that under higher dilution conditions, the fraction of diesel engine organic emissions that volatilizes is higher than that measured using common test methods.

Murphy and Pandis (2009, 190095) pointed out the importance of characterizing the volatility distribution of emissions of organic species from combustion sources for more accurately predicting the abundance and oxidation state of SOA in both urban and surrounding regional background environments. They note that in urban areas, volatile emissions can be photochemically oxidized to more non-volatile compounds which then condense, forming oxidized SOA. Braun (2009, 189997) suggested that the weathering of diesel exhaust particles involves the desorption of semi-volatile organic compounds followed by the decomposition and reaction of the amorphous non-volatile carbon. These reactions would result in the formation of a number of functional groups on the

surface of the carbon core including quinones, carbohydroxide and carboxyl groups as well as sulfate. In general, all the above studies underscore the importance of accurately describing the phase distribution of semivolatile organic compounds emitted by combustion sources under atmospheric conditions, and of atmospheric photochemical reactions in modifying the composition of emissions.

Until a few years ago, the oxidation of terpenes and aromatic compounds were considered as sources of SOA, and the oxidation of isoprene was not considered a source of SOA. However, observations of 2-methyl tetrols in ambient samples from a number of different environments suggest that small but not insignificant quantities of SOA are formed from isoprene oxidation (Claeys et al., 2004, 058608). Laboratory studies also indicate the formation of 2-methyl tetrols from isoprene oxidation (Edney et al., 2005, 155760; Kleindienst et al., 2006, 156650). Xia and Hopke (2006, 179947) observed the seasonal variations for the two major diastereoisomers produced during the oxidation of isoprene with highest concentrations occurring during summer and lowest concentrations occurring during winter. During summer, the maximum contribution of these two diastereoisomers to OC was 2.8%, however it is not clear if more SOA could have been produced from isoprene oxidation.

Kroll and Seinfeld (2008, 155910) and Rudich et al. (2007, 156059) noted that the composition of SOA evolves from repeated cycles of volatilization and condensation of chemical reaction products in both the particle and gas phases. Rudich et al. (2007, 156059) focused on the oxidation of particle phase species by reaction with gas phase oxidants. Kroll and Seinfeld (2008, 155910) identified three factors that determine the SOA forming potential of organic compounds in the atmosphere:

1. Oxidation reactions of gas-phase organic species. These species include alkanes, alkenes, aromatics, cyclic olefins, isoprene and terpenes. Note that oxidation reactions can either lower volatility by addition of functional groups or increase volatility by cleavage of carbon-carbon bonds;
2. Reactions in the particle, or condensed, phase that can change volatility either by oxidation or formation of high-molecular-weight species. These reactions can lead to the formation of oligomers, thereby decreasing volatility or to the formation of more volatile products; and
3. Ongoing reactions that result from the varied volatility of oxidation products.

Other detailed work has focused on the formation of higher molecular weight particle-phase oligomers (Gao et al., 2004, 156460; Kalberer et al., 2004, 156619; Tolocka et al., 2004, 087578), the importance of cloud processing in the evolution of SOA (Blando and Turpin, 2000, 155692; Gelencser and Varga, 2005, 156463), and the role of acid seeds in oligomer formation (Tolocka et al., 2004, 087578). These results imply that ambient samples could contain mixtures of SOA from different sources at different stages of processing, some with common reaction products making source identification of SOA problematic. Figure 3-4 shows a schematic of processes involved in the formation of SOA.

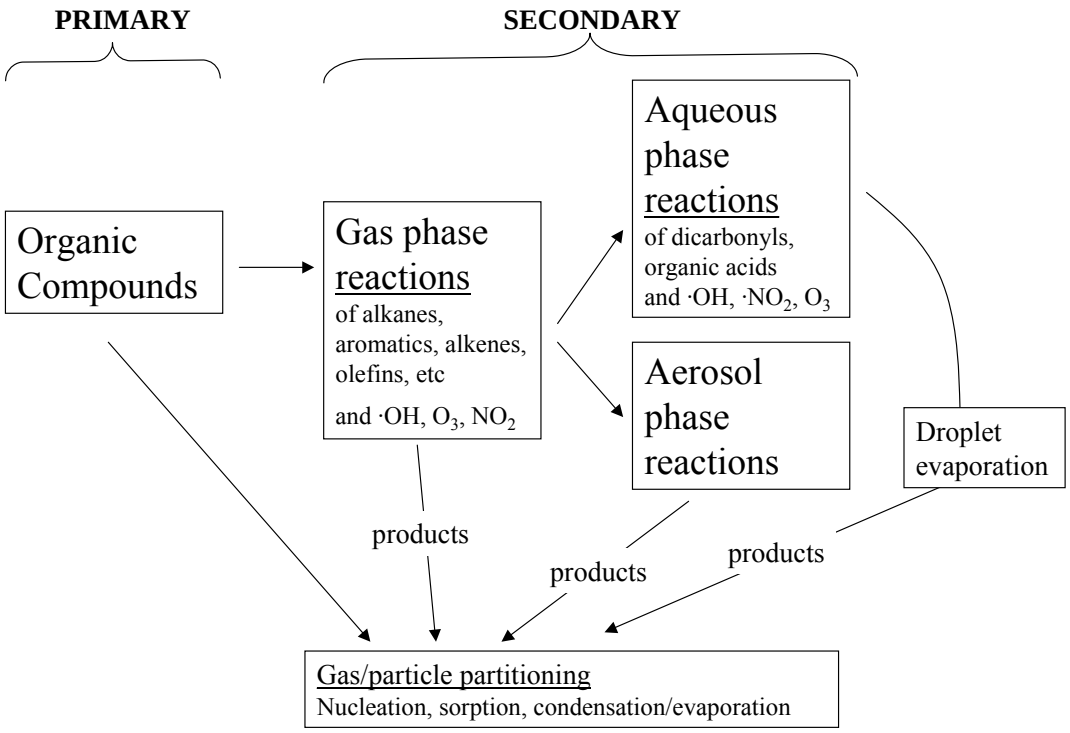


Figure 3-4. Primary emissions and formation of SOA through gas, cloud and condensed phase reactions.

It should be noted that many of the products of terpene oxidation are oxidative in nature, and are not merely nonreactive oxidation products. Organic peroxides represent an important class of reactive oxygen species (ROS) that have high oxidizing potential and could cause oxidative stress in cells on which these species deposit. For example, Docherty (2005, 087613) found evidence for the substantial production of organic hydroperoxides in secondary organic aerosol (SOA) resulting from the reaction of monoterpenes with O_3. Analysis of the SOA formed in their environmental chamber indicated that the SOA was mainly organic hydroperoxides. In particular, they obtained yields of 47% and 85% of organic peroxides from the oxidation of α- and β-pinene. The hydroperoxides then react with aldehydes in particles to form peroxyhemiacetals, which can either rearrange to form other compounds such as alcohols and acids or revert back to the hydroperoxides. The aldehydes are also produced in large measure during the ozonolysis of the monoterpenes. Monoterpenes also react with OH radicals resulting, however, in the production of more lower molecular weight products than in their reaction with O_3. Various terpenoid compounds are used in a number of household products and can be oxidized by ozone that has infiltrated from outdoors. The oxidation of terpenoid compounds indoors produces UFPs as described in the 2006 O_3 AQCD (U.S. EPA, 2006, 088089).

3.3.2.3. Formation of New Particles

In addition to being emitted by high temperature combustion sources, new particles can form by nucleation of atmospheric gases. New particle formation has been observed in environments ranging from relatively unpolluted marine and continental environments to polluted urban areas (Kulmala et al., 2004, 089159). These new, nucleation mode particles are formed from molecular clusters. Competition between condensation of gases and clusters onto existing particles and coagulation of clusters determines which process will dominate (McMurry et al., 2005, 191759). Because of this competition, it is expected that particle number concentrations are dominated by primary anthropogenic emissions in highly polluted settings and by nucleation in remote continental sites. However, nucleation still occurs in urban environments and can still be the major source under certain conditions. The composition of UFPs will differ depending on the nature of their sources.

Nucleation is observed in the morning and extending into the afternoon, and occurs at higher rates during summer than during winter, consistent with a photochemical process. New particle formation events have been observed to occur over distances of several hundred kilometers in what have been called regional nucleation events (Shi et al., 2007, 191760).

The major gas phase nucleating species involved are sulfuric acid vapor and water vapor. Kuang et al. (2008, 191196) suggested that the rate of nucleation is second order with respect to H_2SO_4 vapor depending on mechanism. However, other studies (e.g., Kulmala et al., 2007, 097838) have suggested that the nucleation rate is first order with respect to H_2SO_4 vapor. These differences imply that a number of mechanistic details still remain to be determined, including the interactions with other species. However, this disparity is small compared to classical thermodynamic binary nucleation theory involving H_2SO_4 and water vapor, in which the nucleation rate is given by H_2SO_4 vapor to at least the 10th power (Kulmala et al., 1998, 129411). H_2SO_4 vapor is produced by the gas phase oxidation of SO_2 by OH radicals (U.S. EPA, 2008, 157075). Ammonia (Gaydos et al., 2005, 191762) and organic acids and bases (amines) are also involved to some extent (Smith et al., 2008, 199529). The formation of UFPs indoors from the oxidation of terpenoids by O_3 as mentioned above also indicates that nucleation occurs indoors as well (U.S. EPA, 2006, 088089).

3.3.3. Mobile Source Emissions

3.3.3.1. Emissions from Gasoline Fueled Engines

PM emitted from gasoline fueled engines is a mix of OC, EC and small quantities of trace metals and sulfates, with OC constituting anywhere from 26-88% of PM (Cadle et al., 1999, 007636; Geller et al., 2006, 139644; Schauer et al., 2002, 035332). Most of the compounds in OC have yet to be characterized. High molecular weight and large PAHs have been identified in gasoline fueled vehicle emissions (Phuleria et al., 2006, 156867; Riddle et al., 2007, 115272). EPA exhaust emission standards do not control PM from gasoline vehicles as stringently as diesel vehicles. PM emissions from gasoline fueled vehicles decreased greatly as other exhaust emissions (primarily hydrocarbons and carbon monoxide) were controlled by improvements in the catalytic converter and better control of air-to-fuel mixture ratios for the engine intake. When leaded gasoline was used in pre-1975 model year vehicles, gasoline engine PM emissions were relatively large (about 300 mg/mile) and consisted largely of lead salts from combustion of the lead additive. A current gasoline fueled vehicle emits far lower PM, about 1-10 mg/mile. Emissions of gasoline PM increase at colder ambient temperatures and recent rulemaking for air toxics will result in significant reduction of gasoline PM at colder temperatures. Further details about the composition of motor vehicle emissions in the context of source apportionment modeling can be found in Section 3.6.1.

3.3.3.2. Emissions from Diesel Fueled Engines

Matti Maricq (2007, 155973) presents a conceptual model of diesel PM as a mix of nucleation-mode SO_4^{2-} and hydrocarbons from unspent fuel and soot embedded with trace metals on which SO_4^{2-} and hydrocarbons condense. PM emissions from pre-2007 diesels consist largely of EC (about 70% by mass) and OC (high molecular weight compounds derived from both diesel fuel and lubricating oil) which is responsible for about 25% of the PM (Maricq, 2007, 155973). The EC is non-volatile, while the organic material present exhibits temperature-dependent evaporation in similar fashion to a mixture of C24-C32 alkanes (Sakurai et al., 2003, 113924). Sulfates constitute about 5% of the PM. A small fraction of the diesel fuel sulfur (typically about 1-2%) is oxidized to sulfate. Trace elements (such as Zn and halogens, mainly from lubricating oil; and others) are also present. Mass spectra of organic diesel particles from pre-2007 engines appear to be largely similar to engine lube oil with minor contributions from unburned diesel fuel.

Effective with the 2007 model year for on-road diesel heavy-duty highway truck engines, the new EPA PM standard (0.01 g per brake horsepower-hour [g/bhp-h]) reduced PM emission limits by 90% from the prior standard (0.10 g/bhp-h). By comparison, uncontrolled heavy-duty diesels (pre-1988 model years) emitted about 1-2 g/bhp-h of PM. The 2007 standard resulted in the introduction of new emission control technology, mainly the diesel particulate filter (DPF). Other elements of the

new control technology also include water-cooled exhaust gas recirculation (mostly for control of NO_X), a diesel oxidation catalyst (DOC) used in some vehicles and improved fuel injection systems.

Besides the large reduction in diesel PM on a mass basis, the composition of diesel PM changed greatly. EPA regulations required that diesel fuel for on-road vehicles contain no more than 15 ppm sulfur as of January 2007 (Lim et al., 2007, 155931). Prior to that, the limit on diesel fuel sulfur established in 1995 for on-road vehicles was 500 ppm. The HEI-ACES study characterizes emissions from four engines and shows that PM emissions are about 0.001 g/bhp-h or 90% below the level of the current (2007) emission standard (Shimpi et al., 2009, 189888). This study also characterizes the composition of the much lower mass of PM emitted with this new technology. PM samples collected over a composite type test consisted of 53% sulfate, 30% OC, 13% EC and 4% other components, including metals. A substantial fraction of sulfur is converted to sulfate over the diesel particulate filter resulting in the higher fractional content of sulfate emissions. However, due to the much lower mass of PM being emitted (over a 90% reduction compared to earlier diesels) as well as the low sulfur content of the fuel, the total mass of sulfate emitted is somewhat less than that from earlier diesels. This work also shows that UFP number emissions are lower (about 90% lower) and that a number of other emissions are also controlled, including PAHs, nitro-PAHs, carbonyls (such as aldehdyes), and metals.

Pre-2007 engines can be retrofitted with exhaust aftertreatment devices, including DPFs, DOCs, and selective catalytic reduction (SCR) systems to reduce emissions (U.S. EPA, 2009, 189885). Hu et al. (2009, 189886) examined emissions of various metals (V, Pt) from various diesel retrofit systems including those using V-SCR and a zeolite-based SCR with a DPF. Pakbin et al. (2009, 189893) shows significant reductions in emissions of various PAHs for diesels with SCR retrofit systems for NO_X control. Biswas et al. (2008, 189969) examined PM size distribution and composition (including semi-volatiles and non-volatiles) from several advanced technology diesels including those with SCR. They showed major reductions in PM number in most driving conditions but did not show a reduction in PM number under cruise conditions. Biswas et al. (2009, 189880) examined four heavy-duty diesel vehicles with various retrofits showing, in general, large reductions in PM but, in some cases, somewhat higher emissions (or smaller decreases than expected) for EC and OC.

In general, under light load conditions such as idle, diesel PM has a higher percentage of OC emissions than at high load conditions. Under lighter loads, organic compounds are not oxidized as effectively as under high loads. Under higher loads, PM contains more EC than under light loads. Also, newer model year diesels through the 2006 model year tend to have a higher fraction of PM that is EC than older models.

Emissions have been measured with the new technology engines under a number of driving cycles besides the Federal Test Procedure. The HEI ACES study examined emissions during a range of test procedures. In general, the low-load test cycle resulted in lower exhaust temperatures and higher emission than did the high-load cycles. Regeneration events also produced short-term increases in particle emissions. However, particle emission measurements on the ACES engines were consistently lower than those on a typical 2004 engine (Shimpi et al., 2009, 189888).

EPA standards will result in non-road diesels also having technology like catalyzed diesel particulate filters starting in 2012. Similar standards have also been promulgated for locomotives powered by diesel engines. Some work has been done with prototype SCR systems for diesel NO_X control such as would be used for the 2010 diesel NO_X standard. This standard will also result in reductions for NO_X similar to those seen for PM in the 2007 standard.

There is no information on emissions from diesel engines with this new technology at temperatures of $\leq 10°$ C. In general, the ratio of emissions under cold start conditions at low temperatures to emissions at 24° C is significantly higher for diesel engines with new technology compared to emissions from non-catalyst systems. Note that the engines with the newer technology require time to allow the catalyst to reach normal operating temperatures for full emission reductions. During the period of catalyst heating, particles will be trapped in the DPF, but volatile components can pass through. As a result of this particle-trapping, post-2007 model year engines still emit less than the older engines, even under cold start conditions.

3.3.4. Deposition of PM

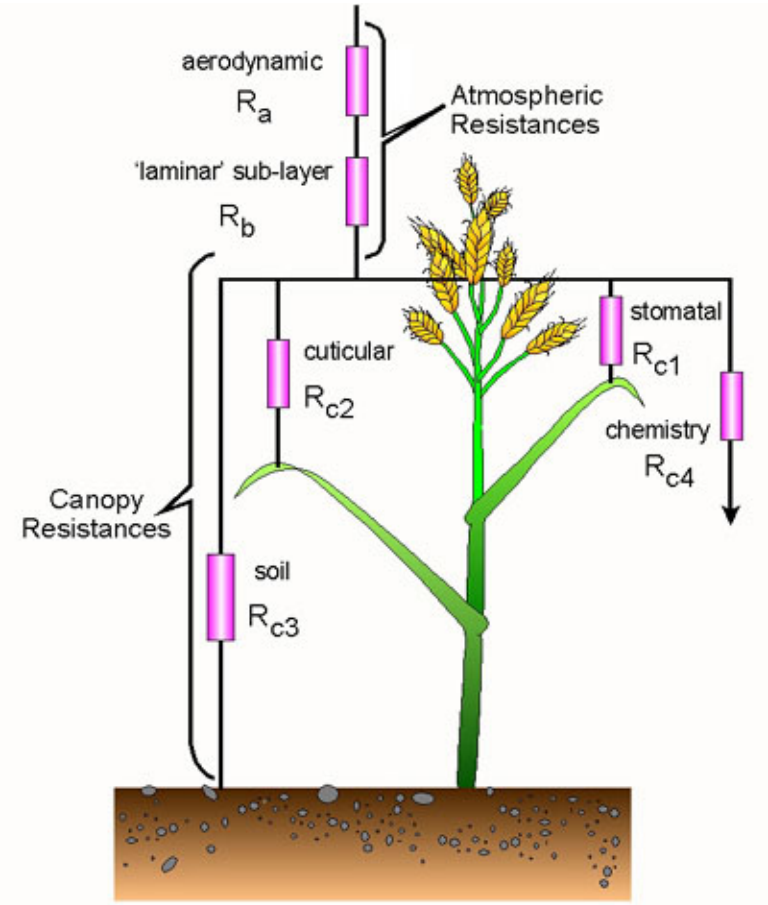
Wet and dry deposition are important processes for removing PM and other pollutants from the atmosphere on urban, regional, and global scales. The conceptual model for dry deposition is to view

the flux deposited on a surface as the product of a concentration (mass or moles of a pollutant/m^3) times a deposition velocity (V_d) (m/s). Therefore, deposition has the units of mass per unit time per unit area, or flux. The general approach used to estimate V_d for gases or very small particles is the resistance-in-series method represented by Equation 3-1:

$$V_d = 1/(R_a + R_b + R_c)$$

Equation 3-1

where R_a, R_b, and R_c represent the resistance due to atmospheric turbulence, transport in the fluid sublayer very near the elements of the surface, such as leaves or soil, and the resistance to uptake of the surface itself, respectively. Typically, these resistances are empirically derived and can vary as a function of wind speed, solar radiation, plant characteristics, precipitation/moisture, and soil/air temperature. These processes are shown schematically in Figure 3-5. This approach works for a range of substances, although it is inappropriate for species with substantial re-emissions from the surface or for species where deposition to the surface depends on concentrations at the surface itself. The approach is also modified somewhat for aerosols where R_b and R_c are replaced with a surface V_d to account for gravitational settling.



Resistance analogy for the deposition of atmospheric pollutants

Source: Courtesy of T. Pierce, USEPA / ORD / NERL / Atmospheric Modeling Division.

Figure 3-5. Schematic of the resistance-in-series analogy for atmospheric deposition.

Wesley and Hicks (2000, 025018) listed several shortcomings of the then-current knowledge of dry deposition. Among those shortcomings were difficulties in representing dry deposition over

varying terrain where horizontal advection plays a significant role in determining the magnitude of R_a and difficulties in adequately determining V_d for extremely stable conditions such as those occurring at night; see the discussion by Mahrt (1998, 048210). Under optimal conditions, when a model is exercised over a relatively small area where dry deposition measurements have been made, models still generally showed uncertainties on the order of ± 30% (e.g., Brook et al., 1996, 024023; Massman et al., 1994, 043681; Padro, 1996, 052446; Wesely and Hicks, 2000, 025018). Wesley and Hicks (2000, 025018) concluded that an important result of those comparisons was that the level of sophistication of most dry deposition models was relatively low, and that deposition estimates, therefore, must rely heavily on empirical data. Still larger uncertainties exist when the surface features in the built environment are not well known or when the surface comprises a patchwork of different surface types, as is common in the eastern U.S.

3.3.4.1. Deposition Forms

Wet Deposition

Wet deposition results from the incorporation of atmospheric particles and gases into cloud droplets and their subsequent precipitation as rain or snow, or from the scavenging of particles and gases by raindrops or snowflakes as they fall (Lovett, 1994, 024049). Wet deposition depends on precipitation amount and ambient pollutant concentrations. Vegetation surface properties have little effect on wet deposition, although leaves can retain liquid and solubilized PM.

Landscape characteristics can affect wet deposition via orographic effects and by the closer aerodynamic coupling to the atmosphere of tall forest canopies as compared to the shorter shrub and herbaceous canopies. Following wet deposition, humidity and temperature conditions further affect the extent of drying versus concentrating of solutions on foliar surfaces, which influence the rate of metabolic uptake of surface solutes (Swietlik and Faust, 1984, 046678). The net consequence of these factors on direct physical effects of wet deposited PM on leaves is not known (U.S. EPA, 2004, 056905).

Rainfall introduces new wet deposition and also redistributes throughout the canopy previously dry-deposited particles (Peters and Eiden, 1992, 045277). The concentrations of suspended and dissolved materials are typically highest at the onset of precipitation and decline with duration of individual precipitation events (Hansen et al., 1994, 046634). Sustained rainfall removes much of the accumulation of dry-deposited particles from foliar surfaces, reducing direct foliar effects and combining the associated chemical burden with the wet-deposited material (Lovett, 1994, 024049) for transfer to the soil. Intense rainfall may contribute substantial total particulate inputs to the soil, but it also removes bioavailable or injurious pollutants from foliar surfaces. This washing effect, combined with differential foliar uptake and foliar leaching of different chemical constituents from particles, alters the composition of the rainwater that reaches the soil and the pollutant burden that is taken-up by plants. Once in the soil, these particle constituents may affect biogeochemical cycles of major, minor, and trace elements. Low intensity precipitation events, in contrast, may deposit significantly more particulate pollutants to foliar-surfaces than high intensity precipitation events. Additionally, low-intensity events may enhance foliar uptake through the hydrating of some previously dry-deposited particles (U.S. EPA, 2004, 056905)

Dry Deposition

Dry particulate deposition, especially of heavy metals, base cations, and organic contaminants, is a complex and poorly characterized process. It appears to be controlled primarily by such variables as atmospheric stability, macro- and micro-surface roughness, particle diameter, and surface characteristics (Hosker and Lindberg, 1982, 019118). The range of particle sizes, the diversity of canopy surfaces, and the variety of chemical constituents in airborne particles have made it difficult to predict and to estimate dry particulate deposition (U.S. EPA, 2004, 056905).

Dry deposition of atmospheric particles to plant and soil surfaces affects all exposed surfaces. Larger particles >5 μm diameter are dry-deposited mainly by gravitational sedimentation and inertial impaction. Smaller particles, especially those with diameters between 0.2 and 2.0 μm, are not readily

dry-deposited and may travel long distances in the atmosphere until their eventual deposition, most often via precipitation. Plant parts of all types, along with exposed soil and water surfaces, receive steady deposits of dry dusts, EC, and heterogeneous secondary particles formed from gaseous precursors (U.S. EPA, 1982, 017610).

Estimates of regional particulate dry deposition infer fluxes from the product of variable and uncertain measured or modeled particulate concentrations in the atmosphere and even more variable and uncertain estimates of V_d parameterized for a variety of specific surfaces (e.g., Brook et al., 1996, 024023). Even for specific sites and well-defined particles, uncertainties are large. Modeling the dry deposition of particles to vegetation is at a relatively early stage of development, and it is not currently possible to identify a best or most generally applicable modeling approach (U.S. EPA, 2004, 056905).

Deposition from Clouds and Fog

The occurrence of cloud and fog deposition tends to be geographically restricted to coastal and high mountain areas. Several factors make it particularly effective for the delivery of dissolved and suspended particles to vegetation. Concentrations of particulate-derived materials are often many-fold higher in cloud or fog water than in precipitation or ambient air due to orographic effects and gas-liquid partitioning. In addition, fog and cloud water deliver particulate chemical species in a bioavailable-hydrated form to foliar surfaces. This enhances deposition by sedimentation and impaction of submicron aerosol particles that exhibit low V_d before fog droplet formation (Fowler et al., 1989, 002515). Deposition to vegetation in fog droplets is proportional to wind speed, droplet size, concentration, and fog density. In some areas, typically along foggy coastlines or at high elevations, this deposition represents a substantial fraction of total deposition to foliar surfaces (Fowler et al., 1991, 046630).

3.3.4.2. Methods for Estimating Dry Deposition

Methods for estimating dry deposition of particles are more restricted than for gaseous species and fall into two major categories: surface analysis methods, which include all types of estimates of contaminant accumulation on surfaces of interest, and atmospheric deposition rate methods, which use measurements of contaminant concentrations in the atmosphere and descriptions of surrounding surface elements to estimate deposition rates (Davidson and Wu, 1990, 036799). Surface extraction or washing methods characterize the accumulation of particles on natural surfaces of interest or on experimental surrogate surfaces. These techniques rely on methods designed specifically to remove only surface-deposited material. Total surface rinsate may be equated to accumulated deposition or to the difference in concentrations in rinsate between exposed and control (sheltered) surfaces and may be used to refine estimates of deposition. Foliar extraction techniques may underestimate deposition to leaves because of uptake and translocation processes that remove pollutants from the leaf surface (Garten and Hanson, 1990, 036803; Taylor et al., 1988, 019289). Foliar extraction methods also cannot distinguish gas from particle-phase sources (Bytnerowicz et al., 1987, 036493; Dasch, 1987, 036496; Kelly, 1988, 037379; Lindberg and Lovett, 1985, 036530; Van Aalst, 1982, 036481).

The National Dry Deposition Network was established in 1986 to document the magnitude, spatial variability, and trends in dry deposition across the United States. Currently, the network operates as a component of the CASTNet (Clarke et al., 1997, 025022). A significant limitation on current capacity to estimate regional effects of NO_X and SO_X deposition is inadequate knowledge of the mechanisms and factors governing particle dry deposition to diverse surfaces (U.S. EPA, 2004, 056905).

Collection and analysis of stem flow and throughfall can also provide useful estimates of particulate deposition when compared to directly sampled precipitation. The method is most precise for particle deposition when gaseous deposition is a small component of the total dry deposition and when leaching or uptake of compounds of interest out of or into the foliage is not a significant fraction of the deposition because these lead to positive and negative artifacts in the calculated totals.

Foliar washing, whether using precipitation or experimental lavage, is one of the best available methods to determine dry deposition to vegetated ecosystems. Major limitations include the site specificity of the measurements and the restriction to elements that are largely conserved within the

vegetative system. Surrogate surfaces have not been found that can adequately replicate essential features of natural surfaces, and therefore do not produce reliable estimates of particle deposition to the landscape.

Micrometeorological methods employ eddy covariance, eddy accumulation, or flux gradient protocols for quantifying dry deposition. These techniques require measurements of particulate concentrations and of atmospheric transport processes. They are currently well developed for ideal conditions of flat, homogeneous, and extensive landscapes and for chemical species for which accurate and rapid sensors are available. Additional studies are needed to extend these techniques to more complex terrain and more chemical species.

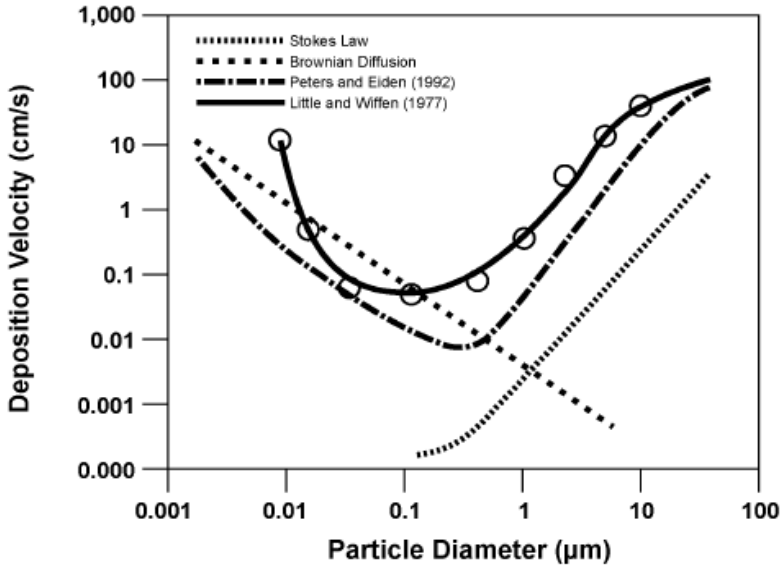
The eddy covariance technique measures vertical fluxes of gases and fine particles from calculations of the mean covariance between the vertical component of wind velocity and pollutant concentration (Wesely et al., 1982, 036564) using sensors acquiring concentration data at 5-20 Hz. For the flux gradient or profile techniques, vertical fluxes are calculated from a concentration difference and an eddy exchange coefficient determined at discrete heights (Erisman et al., 1988, 036510; Huebert et al., 1988, 036569). Most measurements of eddy transport of PM have used chemical sensors (rather than mass or particle counting) to focus on specific PM components. These techniques have not been well developed for generalized particles and may be less suitable for coarse particles that are transported efficiently in high frequency eddies (Gallagher et al., 1988, 046631).

3.3.4.3. Factors Affecting Dry Deposition Rates and Totals

In the size range of ~0.1-1.0 μm where V_d is relatively independent of particle diameter as shown in Figure 3-6, particulate deposition is controlled by roughness of the surface and by the stability and turbulence of the atmospheric surface layer. Impaction and interception dominate over diffusion as dry deposition processes, and the V_d is considerably lower than for particles that are either smaller than ~0.1 μm or larger than ~1.0 μm.

Deposition of particles between 1 and 10 μm diameter is strongly dependent on particle size as shown in Figure 3-6. Larger particles within this size range are collected more efficiently at typical wind speeds than are smaller particles (Clough, 1975, 070850), suggesting the importance of impaction. Impaction is related to wind speed, the square of the particle diameter, and the inverse of the deposition surface cross-section. As a depositing particle's trajectory deviates from the streamlines of the air in which it is suspended, increasing either wind speed or the ratio of particle size to the deposition surface cross-section increases the probability of collision.

Empirical estimates of V_d for fine particles under wind tunnel and field conditions are often several-fold greater than predicted by theory (Unsworth and Wilshaw, 1989, 046682). A large number of transport phenomena, including streamlining of foliar obstacles, turbulence structure near surfaces, and various phoretic transport mechanisms are not well characterized (U.S. EPA, 2004, 056905). The discrepancy between estimated and predicted values of V_d may reflect model limitations or experimental limitations in the specification of the effective size and number of deposition obstacles. Previous reviews (e.g., U.S. EPA, 1996, 079380; U.S. EPA, 2004, 056905) suggest the following generalizations: (1) particles >10 μm exhibit variable V_d between 0.5 and 1.1 cm/s depending on friction velocities, whereas a minimum particle V_d of 0.03 cm/s exists for particles in the size range 0.1 to 1.0 μm; (2) the V_d of particles is approximately a linear function of friction velocity; and (3) deposition of particles from the atmosphere to a forest canopy is from 2 to 16 times greater than deposition in adjacent open terrain like grasslands or other low vegetation.



Source: U.S. EPA (2004, 056905).

Figure 3-6. The relationship between particle diameter and V_d for particles. Values measured in wind tunnels by Little and Wiffen (1977, 070869) over short grass with wind speed of 2.5 mi/s closely approximate the theoretical distribution determined by Peters and Eiden (1992, 045277) for a tall spruce forest. These distributions reflect the interaction of Brownian diffusivity (descending dashed line), which decreases with particle size and sedimentation velocity (ascending dotted line derived from Stokes Law), which increases with particle size. Intermediate-sized particles (0.1-1.0 µm) are influenced strongly by both particle size and sedimentation velocity, and deposition is relatively independent of size.

Leaf Surface Effects on V_d

The chemical composition of a particle is not usually considered to be a primary determinant of its V_d. Rather, the plant leaf surface has an important influence on the V_d of particles, and therefore on the flux of dry deposition to the terrestrial environment. Relevant leaf surface properties include stickiness, microscale roughness, and cross-sectional area. These properties affect the probability of impaction and particle bounce. The efficiency of deposition to vegetation also varies with leaf shape. Particles impact more frequently on the adaxial (upper) surface than on the abaxial (lower) surface. Most particles accumulate in the midvein, central portion of leaves. The greatest particle loading on dicotyledonous leaves is frequently on the adaxial surface at the base of the blade, just above the petiole junction. Precipitation washing probably plays an important role in this distribution pattern (U.S. EPA, 2004, 056905).

Lead particles have been shown to accumulate to a greater extent on older as compared with younger needles and twigs of white pine, suggesting that wind and rain may be insufficient to fully wash the foliage. Fungal mycelia (derived from windborne spores) were frequently observed in intimate contact with other particles on leaves, which may reflect minimal re-entrainment of the spore due to shelter by the particles, mycelia development near sources of soluble nutrients provided by the particles, or simply co-deposition (Smith and Staskawicz, 1977, 046675).

Leaves with complex shapes tend to collect more particles than do those with shapes that are more regular. For example, conifer needles are more efficient than broad leaves in collecting particles by impaction as a result of the small cross-section of the needles relative to the larger leaf laminae of broadleaves allowing for greater penetration of wind into conifer canopies than broadleaf ones (U.S. EPA, 2004, 056905).

Canopy Surface Effects on V_d

Surface roughness increases particulate deposition, and V_d is usually greater for a forest than for a nonforested area and greater for a field than for a water surface. Different size particles have different transport properties and V_d. The upwind leading edges of forests, hedgerows, and individual plants are primary sites of coarse particle deposition. Impaction at high wind speed and the sedimentation that follows the reduction in wind speed and carrying capacity of the air in these areas lead to preferential deposition of larger particles (U.S. EPA, 2004, 056905).

Air movement is slowed in proximity to vegetated surfaces. Canopies of uneven age or with a diversity of species are typically aerodynamically rougher and receive larger inputs of dry-deposited pollutants than do smooth, low, or monoculture vegetation (Garner et al., 1989, 042085; U.S. EPA, 2004, 056905). Canopies on slopes facing the prevailing winds receive larger inputs of pollutants than more sheltered, interior canopy regions.

All foliar surfaces within a forest canopy are not equally exposed to particle deposition. Upper canopy foliage tends to receive maximum exposure to coarse and fine particles, but foliage within the canopy tends to receive primarily fine aerosol exposures. The dry deposition of fine-mode particles and unreactive gases tends to be more evenly distributed throughout the canopy.

Both uptake and release of PM constituents can occur within the canopy. The leaf surface is a region of leaching and uptake. Exchange also occurs with epiphytic organisms and bark and through solubilization of previously dry-deposited PM. Vegetation emits a variety of particles and particulate precursor materials.

3.4. Monitoring of PM

3.4.1. Ambient Measurement Techniques

3.4.1.1. PM Mass

Federal reference methods (FRMs) and federal equivelance methods (FEMs) for PM were discussed in detail in the 2004 PM AQCD (U.S. EPA, 2004, 056905). Issues discussed there include the definition or description of FRMs and FEMs for $PM_{2.5}$ and PM_{10}, and measurement methods for $PM_{10-2.5}$. Also included are detailed descriptions of the WINS impactor, virtual and cascade multistage impactors for $PM_{10-2.5}$ measurement, high-volume and low-volume PM_{10} samplers, and real-time or continuous methods for $PM_{2.5}$ and PM_{10} including:

- Tapered Element Oscillating Microbalance (TEOM) operated at various temperatures;
- Sample Equilibration System (SES)-TEOM;
- Differential TEOM;
- β-Gauge Techniques (BGT);
- Piezoelectric Microbalance;
- Real-Time Total Ambient Mass Sampler (RAMS);
- Continuous Ambient Mass Monitor (CAMM);
- Continuous Coarse Particle Monitor (CCPM);
- Micro-orifice Uniform Deposit Impactor (MOUDI);

- Multichannel diffusion denuder sampling system (BOSS); and
- Light scattering photometric instruments.

In this section, FRMs and FEMs for $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10} will be revisited and evaluated based on the cumulative understanding of these methods with a focus on evaluations performed following the 2004 PM AQCD (U.S. EPA, 2004, 056905), followed by the discussion of new techniques under development or evaluation.

Federal Reference Method and Federal Equivalent Method

FRM and FEM PM samplers are designed to measure the mass concentrations of ambient particulate matter. The FRMs for measuring $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10} are specified in CFR 40 Part 50, Appendices L, O and J, respectively. The FRM for $PM_{2.5}$ is a hybrid-based method that specifies certain aspects of the method (e.g., component dimensions and tolerances, sample handling and analysis) by design specifications and other aspects (e.g., flow control) by performance specifications (U.S. EPA, 2004, 056905). The PM_{10} FRM is performance-based; particles are inertially separated with a penetration efficiency of 50% at 10 ± 0.5 μm aerodynamic diameter. The required collection efficiency as a function of particle size larger and smaller than 10 μm aerodynamic diameter is explicitly specified by a penetration curve in the CFR. Particles larger than 10 μm in aerodynamic diameter are collected on the filter with diminishing collection efficiency as particle size increases. Likewise, particles smaller than 10 μm in aerodynamic diameter are collected on the filter with increasing collection efficiency as particle size decreases. The FRM for $PM_{10-2.5}$ concentration is computed as the numeric difference between concurrent and co-located PM_{10} and $PM_{2.5}$ concentrations obtained from low-volume FRM samplers of the same make and model. It should be noted that while the FRM for $PM_{2.5}$ and $PM_{10-2.5}$ reports data under local conditions, the FRM for PM_{10} reports data corrected to standard temperature (298 K) and pressure (101.3 kPa) (STP).

A very sharp cut cyclone (VSCC) was approved in 2004 as a Class II $PM_{2.5}$ FEM method (Kenny et al., 2004, 155895). The VSCC provides superior performance over long sampling periods under heavy loading and was also incorporated as an optional second-stage separator for the $PM_{2.5}$ FRM (71 FR 61214, October 17, 2006). In 2006, EPA finalized new performance criteria (40 CFR Part 53) for the approval of FEMs as Class II equivalent methods when based on integrated filter sampling and as Class III equivalent methods when based on continuous technologies that can provide at least hourly data reporting. The performance criteria include evaluating additive bias (intercept) and multiplicative bias (slope) as well as correlation with co-located candidate and FRM methods at field studies covering multiple seasons and sampling locations. As a result of these new performance criteria, EPA has recently approved two filter-based $PM_{2.5}$ and two filter-based $PM_{10-2.5}$ Class II FEMs based on the virtual impactor techniques (dichotomous sampler), and five $PM_{2.5}$ and one $PM_{10-2.5}$ Class III continuous FEMs based on BGT or TEOM techniques. The most recent list of FRMs and FEMs can be found in Annex A, Table A-2 and on the following EPA web site: http://www.epa.gov/ttn/amtic/files/ambient/criteria/reference-equivalent-methods-list.pdf.

Evaluations of FRMs and FEMs were conducted both in supersite studies and in other research studies (Ayers, 2004, 097440; Brown et al., 2006, 097665; Butler et al., 2003, 156313; Cabada et al., 2004, 148859; Chang and Tsai, 2003, 155718; Charron et al., 2004, 053849; Grover et al., 2005, 090044; Hains et al., 2007, 091039; Hering et al., 2004, 155837; Jaques et al., 2004, 155878; Krieger et al., 2007, 129657; Lee et al., 2005, 155925; Lee et al., 2005, 128139; Price et al., 2003, 098082; Rees et al., 2004, 097164; Russell et al., 2004, 082453; Salminen and Karlsson, 2003, 156070; Schwab et al., 2004, 098450; Schwab et al., 2006, 098449; Solomon et al., 2003, 156994; Tsai et al., 2006, 098312; Vega et al., 2003, 105974; Wilson et al., 2006, 091142; Yi et al., 2004, 156169; Zhu et al., 2007, 098367) (see Annex A, Tables A-3, A-5 and A-11). In general, the co-located FRMs showed very good precision with coefficient of variation (CV) <5%. For different co-located FRMs, the regression slope of one sampler on another is commonly close to unity with R^2 >0.95. The $PM_{2.5}$ and PM_{10} concentrations measured by dichotomous samplers were within 10% of the FRM methods, and the differences can be attributed to the sampling artifacts of semi-volatile components; see Section 3.4.1.2 for details. The precision of various TEOMs ranges from 10-30%. The concentration measured by the TEOM operated at 50°C was consistently lower than those measured by the TEOM operated at 30°C. The differences between these monitors were also found to be a function of season

and location. BGTs were highly correlated with FRMs but BGT mass could be higher than the FRM mass (30% higher at the Fresno supersite) (Chow et al., 2008, 156355). Additionally, a number of techniques have been developed to reduce positive and negative sampling artifacts. These are described in the ISA for NO_X and SO_X – Ecological Criteria (U.S. EPA, 2008, 157074).

Several papers (Buser et al., 2007, 156310; Buser et al., 2007, 156311; Buser et al., 2007, 156312) published since the 2004 PM AQCD (U.S. EPA, 2004, 056905) claim that the EPA FRM samplers for PM_{10} "oversample certain agricultural and other source emissions." These claims are based on the erroneous assumption that the "true" PM_{10} concentration is what would be given by a PM_{10} sampler that excluded all particles greater than 10 µm aerodynamic diameter and included all particles less than 10 µm aerodynamic diameter. The legal definitions for $PM_{2.5}$ and PM_{10}, as defined in the CFR (40 CFR Part 58), include both a 50% cut-point and a penetration curve. For PM_{10}, the 50% cut-point of 10 ± 0.5 µm aerodynamic diameter means that 50% of particles with aerodynamic diameter of 10 ± 0.5 µm are removed by the inlet and 50% pass through the inlet where they are collected on the filter. The penetration curve specifies, as a function of particle size, the fraction of particles larger than 10 µm that pass through the inlet and the fraction of particles less than 10 µm that are intercepted by the inlet. No effort was made in the development of the FRM to have the PM_{10} sampler collect all particles less than 10 µm and no particles greater than 10 µm since the sampler was designed to collect a fraction of atmospheric particles similar to the "inhalable" or thoracic fraction, i.e., those particles that would pass through the nose and throat and reach the lungs (Miller et al., 1979, 070577; U.S. EPA, 2004, 056905). Thus, the FRM PM_{10} sampler correctly and intentionally collects particles greater than 10 µm.

For $PM_{2.5}$ and PM_{10}, it has long been known that FRMs are subject to sampling artifacts including particle bounce on heavily-loaded impaction substrates and the loss of semi-volatile components of PM (e.g., NH_4NO_3, and some organics). Although there are no standard reference materials that provide a test of accuracy of the sampling method for airborne PM mass, in comparison with other sampling techniques that can measure both semi-volatile and nonvolatile PM, FRMs reported $PM_{2.5}$ or PM_{10} mass concentrations biased low by as much as 10-30% (Chow et al., 2008, 156355). The bias of the FRMs depends on the composition of ambient PM and the sampling conditions (e.g., ambient temperature and relative humidity), which vary from day to day and from season to season. Another limitation of the current FRM sampling protocol is that filter samples are typically collected every 3 or 6 days (only ~150 of the 900+ $PM_{2.5}$ FRMs operating in 2007 were scheduled to sample every day). Under this operating condition, the concentration-response relationship in air pollution health studies (especially in time-series studies) cannot be fully evaluated in terms of lag structures and distributed lags between ambient concentration and health outcome (Lippmann, 2009, 190083; Solomon and Hopke, 2008, 156997).

Development and Evaluation of New Techniques

Several new innovations have recently emerged to measure both fine and coarse PM fractions in the ambient air. These techniques include the Filter Dynamics Measurement System-TEOM (FDMS-TEOM) (Grover et al., 2006, 138080) for real-time measurement of $PM_{2.5}$ or PM_{10} and several new methods for measurement of $PM_{10-2.5}$. In addition, several new techniques exist for measuring UFPs (discussed later in Section 3.4.1.4) and for estimating PM mass concentration indirectly using particle size (discussed later in Section 3.4.1.5).

Real-time Measurement of $PM_{2.5}$ or PM_{10} using the FDMS-TEOM

The FDMS-TEOM incorporates self-referencing capability to the traditional TEOM by alternating measurement of ambient air and chilled clean air (particles and semivolatile gases are removed by filtration at 4°C after which the clean air is reheated to 30°C) in 6-min intervals. As clean air flows over the sample filter, the semivolatile PM on the sample filter is evaporated. Thus, the instrument provides direct measurements of the nonvolatile particle mass and incorporates an adjustment for the semivolatile NH_4NO_3 and organic material. In a comparison between the TEOM, FDMS-TEOM, and FRM mass, the $PM_{2.5}$ concentration measured by the TEOM operated at 50°C was consistently lower than those measured by the TEOM operated at 30°C. The TEOM operated at 30°C provided concentrations 50% lower than the FDMS-TEOM, and the FDMS-TEOM provided concentrations 10-30% higher than the FRM mass (Chow et al., 2008, 156355; Schwab et al., 2006, 098449).

Techniques for Measurement of $PM_{10-2.5}$

Methods developed to measure $PM_{10-2.5}$ are based on three measurement techniques: (1) virtual impactors using low-volume, high-volume, and real-time techniques; (2) cascade impactors; and (3) passive samplers.

A low-volume dichotomous sampler (operated at 16.7 L/min), based on virtual impaction, was described in the 2004 PM AQCD (U.S. EPA, 2004, 056905). Since then, a high-volume dichotomous sampler was developed to operate at 1,000 L/min (Sardar et al., 2006, 156071). The sampler was evaluated in the field by comparison with a MOUDI sampler, and the measured $PM_{10-2.5}$ mass concentrations were within 10%. The high-volume dichotomous sampler provides sufficient mass collection for comprehensive standard chemical analyses over short sampling intervals. Using the virtual impactor technique in conjunction with a TEOM or BGT as the detector, continuous $PM_{10-2.5}$ measurement techniques were developed (Misra et al., 2001, 018998; Misra et al., 2003, 195001; Solomon and Sioutas, 2008, 190139). The TEOM method was highly correlated with the $PM_{10-2.5}$ FRM, but mass concentrations measured by the TEOM were 20-30% lower (Solomon and Sioutas, 2008, 190139). The BGT method also agreed well with the $PM_{10-2.5}$ FRM (slopes = 0.88-1.17, and R^2>0.95) (Solomon and Sioutas, 2008, 190139).

Case et al. (2008, 155149) evaluated a cascade PM sampler designed to collect $PM_{10-2.5}$ on a foam impactor. Particle bouncing on impactors has long been a concern for PM collection. Porous foam was used to serve as the impactor substrate to reduce particle bounce and to collect relatively large amounts of particles (Demokritou et al., 2004, 186901; Demokritou et al., 2004, 190115; Huang et al., 2005, 186991; Kuo et al., 2005, 186997). The sampler was operated at 5 L/min, and it agreed with a low-volume dichotomous sampler within ±20%. The precision of the sampler was 20% as determined by the CV.

An inexpensive passive sampler for $PM_{10-2.5}$ was also developed (Leith et al., 2007, 098241; Ott et al., 2008, 195004; Wagner and Leith, 2001, 190153; Wagner and Leith, 2001, 190154). The passive sampler collects particles by gravity, diffusion, and convective diffusion onto a glass coverslip, and then an image analysis is conducted on the collected particles to estimate mass flux as a function of aerodynamic diameter. Leith et al. (2007, 098241) conducted a field evaluation of the passive sampler, and the difference between a FRM and the co-located passive sampler was within 1σ of concentrations measured with $PM_{10-2.5}$ FRM samplers. Ott et al. (2008, 119394) reported the precision of the sampler was 11.6% (CV), and the detection limit was 2.3 μg/m^3 for a 5-day sample.

3.4.1.2. PM Speciation

The following sections describe recent developments regarding measurement techniques to ascertain quantities of particle-bound water, cations and anions, elemental composition, carbon, and organic species.

Particle-Bound Water

Particle-bound water is an important component of ambient PM (U.S. EPA, 2004, 056905). Recently, a differential method was developed to measure particle-bound water (Santarpia et al., 2004, 156944; Stanier et al., 2004, 095955). The dry ambient aerosol size spectrometer (DAASS) can measure particle-bound water in the particle size range from 3 nm-10 μm (Stanier et al., 2004, 095955), by alternatively measuring ambient PM size distribution at low relative humidity (RH) and ambient RH. A comparison of the two size distributions provides information on the water absorption and change in particle size due to RH. Khlystov et al. (2005, 156635) reported that the particle-bound water, measured by DAASS, was underestimated for particles <200 nm and overestimated for particles >200 nm compared with thermodynamic models. The loss of semi-volatile components during measurement may bias the particle-bound water measurement results. Methods and analytical specifications for particle-bound water are listed in Annex A, Table A-12.

Cations and Anions

The measurement of cations and anions including SO_4^{2-}, NO_3^-, NH_4^+, Cl^-, Na^+, and K^+ still relies primarily on filter-based collection, water based extraction and ion chromatography (IC) based chemical speciation and quantification. In addition, denuders are frequently used in the sampling system to adjust for sampling artifacts. These methods have been reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905). Filter-denuder based integrated sampling methods for SO_4^{2-}, NO_3^-, and NH_4^+ have been detailed in the 2008 SO_X - Health ISA (U.S. EPA, 2008, 157075) and the 2008 NO_X and SO_X - Ecological ISA (U.S. EPA, 2008, 157074).

Recent developments in multiple ion measurements have focused on the coupling of IC and a sample dissolution system, represented by the Particle into Liquid Sampler-Ion Chromatography (PILS-IC) and the Ambient Ion Monitor (AIM) (Orsini et al., 2003, 156008; Weber et al., 2001, 024640). When ambient PM passes through the PILS-IC system, water droplets are generated by mixing ambient PM with saturated water vapor and collected by impaction. The resulting liquid stream is then introduced into the IC system for ion speciation and quantification. Hourly concentrations of multiple ions can be obtained with the system, with a CV of 10%. For the AIM system, a parallel plate denuder is used to remove the interfering gases, and then particles enter a super-saturation chamber to form droplets. The collected droplets are then introduced into the IC for analysis. The AIM system can provide hourly concentrations for multiple ions. The particle mass spectrometer is another advance in multiple PM component measurements, but most of these types of measurements are semi-quantitative and will be detailed later in Section 3.4.1.3. Note that measurement and analytical specifications for ions other than SO_4^{2-} and NO_3^- are listed in Annex A, Table A-9.

Sulfate

Methods used for continuous (sampling interval of minutes) measurements of SO_4^{2-} include Aerosol Mass Spectrometry (AMS) (Drewnick et al., 2003, 099160; Hogrefe et al., 2004, 099003), PILS-IC (Weber et al., 2001, 024640), flash volatilization techniques (Bae, 2007, 155669; Stolzenburg and Hering, 2000, 013289) and the Harvard School of Public Health (HSPH) tube furnace to convert SO_4^{2-} to SO_2 for detection by a SO_2 analyzer (Allen et al., 2001, 156205). These methods are described in detail by Drewnick et al. (2003, 099160), along with an inter-sampler comparison that found overall agreement within 2.9% for all continuous instruments with R^2 of 0.87 or better. When compared with filter samples, Drewnick et al. (2003, 099160) showed differences were less than 25% for the AMS, PILS, flash vaporization, and HSPH continuous SO_4^{2-} monitors. The Thermo 5020 particulate sulfate analyzer (based on the HSPH technique) compared within 80% of 24-h filter-based measurement at a rural site in New York (Schwab et al., 2006, 098449). Annex A, Tables A-8 and A-14, list detailed methods and analytical specifications for sampling SO_4^{2-}.

Nitrate

In addition to the nylon filter-based method and the new developments mentioned for SO_4^{2-}, methods based on flash volatilization-chemiluminescence analysis and catalytic conversion-chemiluminescence analysis have also been developed for continuous NO_3^- measurement (averaging time 30 s-10 min). For the flash volatilization system (Fine et al., 2003, 155775; Stolzenburg and Hering, 2000, 013289; Stolzenburg et al., 2003, 156102), particles are collected by a humidified impaction process and analyzed in place by flash vaporization and chemiluminescent detection of the evolved NO_X. For the catalytic conversion-chemiluminescence analysis system (Weber et al., 2003, 157129), NO_3^- was measured by conversion of particle NO_3^- into NO, and then detected with the chemiluminescence method. Field and lab comparisons were conducted to compare the different instruments mentioned above. Although the R&P 8400N ambient particulate NO_3^- monitor, which is based on the Stolzenburg flash vaporization technique, could provide 10-min resolution data and showed excellent precision (with a CV <10%) (Harrison et al., 2004, 136787; Hogrefe et al., 2004, 099003; Long and McClenny, 2006, 098214; Rattigan et al., 2006, 115897), it consistently reported NO_3^- concentrations ~30% lower than the denuder-filter systems in both the Baltimore supersite and the multiyear field study in New York (Harrison et al., 2004, 136787; Hogrefe et al., 2004, 099003; Rattigan et al., 2006, 115897). In the New York measurement campaign, an AMS was also co-located with other instruments to obtain the real-time NO_3^- information. AMS did not always agree well with the denuder-filter system for reasons not

entirely apparent. However, Bae et al. (2007, 156244) reported that some organic compounds can also produce signals at mass-to-charge ratio $m/z = 30$, which is one of the characteristic m/z for NO_3^-. Therefore, the disagreement between the AMS and the filter-based method could be a result of the interference of organic compounds using the AMS. Annex A, Tables A-7 and A-13, list methods and analytical specifications for sampling NO_3^-.

Ammonium

Several continuous and semi-continuous instruments can be used to monitor ambient ammonium concentrations (Al-Horr et al., 2003, 153951; Bae, 2007, 155669) including many listed above for SO_4^{2-} and NO_3^-. Bae et al. (2007, 155669) conducted an inter-comparison of three semi-continuous instruments during the New York multiyear air sampling campaign: a PILS-IC, an AMS, and a wet scrubbing-long path absorption photometer. Bae et al. (2007, 155669) reported the inter-sampler coefficients of determination (R^2) between these instruments were above 0.75, and the slopes (with zero intercept) were between 0.71 and 1.04. Annex A, Table A-9 describes measurement of ions other than NO_3^- and SO_4^{2-}, including NH_4^+.

Elemental Composition

Techniques for measuring the elemental composition of PM samples were reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905). These methods include:

- Energy dispersive X-ray fluorescence (ED-XRF);
- Synchrotron X-ray fluorescence (SXRF);
- Particle-induced X-ray emission (PIXE);
- Particle elastic scattering analysis (PESA);
- Total reflection X-ray fluorescence (TR-XRF);
- Instrumental neutron activation analysis (INAA);
- Atomic absorption spectrophotometry (AAS);
- Inductively-coupled plasma-atomic emission spectroscopy (ICP-AES);
- Inductively-coupled plasma-mass spectrometry (ICP-MS); and
- Scanning electron microscopy (SEM).

Recent development in this area focused on the semi-continuous measurement methods, in which elements were analyzed in the lab using the methods mentioned above on time-resolved and/or size resolved samples (Kidwell and Ondov, 2004, 155898). The concentrated slurry/graphite furnace atomic absorption spectrometry (GFAAS) method collects ambient PM as a slurry using impactors, and then the collected PM is analyzed by AAS in the lab. Laser induced breakdown spectroscopy (LIBS) was used to measure seven metals at the Pittsburgh supersite. LIBS concentrates ambient PM using a virtual impactor into a sample cell, and then a Nd:YAG laser-spectrometer is used to identify and quantify different elements. A full listing of measurement techniques and analytical specifications for trace elements is provided in Annex A, Table A-6.

Elemental and Organic Carbon

The large variety of aspects of carbon analyses were reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905). Measurement and analytical specifications for carbon measurements are listed in Annex A, Tables A-10 and A-15. Aspects of the measurements include sampling artifacts

associated with the integrated filter-based OC and EC sampling methods, the IMPROVE vs. CSN thermal optical protocols (i.e., different thermal optical methods) and optical techniques to measure light-absorption or BC. One significant change taking place in the CSN is that the method for carbon measurements is being changed from the CSN method to a method designed to be consistent with the IMPROVE carbon analysis protocol. This is a phased process that began in May of 2007 with the conversion of 56 stations. Phase 2 of the carbon sampler conversion occurred in April of 2009 with another 62 stations. The balance of the CSN is scheduled to be converted to IMPROVE-like sampling and IMPROVE analysis in late 2009 (Henderson, 2005, 156537). The CSN network was implemented to support the $PM_{2.5}$ NAAQS and provides data for $PM_{2.5}$ mass, SO_4^{2-}, NO_3^-, NH_4^+, Na, K, EC, OC, and select trace elements (Al through Pb) at many sites across the U.S. This conversion will increase consistency between these two networks. Also, since the release of the 2004 PM AQCD (U.S. EPA, 2004, 056905), more studies have been conducted to extend the understanding of sampling artifact issues (Chow et al., 2008, 156355; Watson et al., 2005, 157125), evaluate different thermal and optical procedures (Chen et al., 2004, 199501; Chow et al., 2004, 156347; Chow et al., 2005, 155728; Chow et al., 2007, 156354; Conny et al., 2003, 145948; Han et al., 2007, 155823; Subramanian et al., 2004, 081203; Watson et al., 2005, 157125), develop reference materials (Klouda et al., 2005, 130382; Lee, 2007, 155926), create water soluble organic carbon (WSOC) measurement techniques (Andracchio et al., 2002, 155657; Yang et al., 2003, 156167), develop semi-continuous/continuous/real-time carbon measurement techniques (Chow et al., 2008, 156355; Watson et al., 2005, 157125), and introduce isotope identification into the OC/EC measurement (Huang et al., 2006, 097654).

OC sampling artifact issues were further addressed in various studies (Arhami et al., 2006, 156224; Bae et al., 2004, 156243; Chow et al., 2005, 155728; Fan et al., 2003, 058628; Fan et al., 2004, 155770; Grover et al., 2008, 156502; Lim et al., 2003, 037037; Mader et al., 2003, 155955; Matsumoto et al., 2003, 124293; Muller et al., 2004, 097109; Offenberg et al., 2007, 098101; Olson and Norris, 2005, 156005; Park et al., 2006, 098104; Rice, 2004, 156049; Subramanian et al., 2004, 081203; ten Brink et al., 2004, 097110; ten Brink et al., 2005, 156115; Viana et al., 2006, 179987), and were well summarized by Watson et al. (2005, 157125) and Chow et al. (2008, 156355). There are two commonly used methods to correct OC sampling artifacts: the filter with backup filter system (TBQ: placing a backup quartz-fiber filter behind the front Teflon-membrane filter; QBQ: placing a backup quartz-fiber filter behind the front quartz-fiber filter); and the denuder-filter-adsorbent system. Subramanian et al. (2004, 081203) and Chow et al. (2006, 099031) reported that during the Pittsburgh and Fresno supersite studies the positive artifact (organic gases condensed on filters) from TBQ (24-34%, up to 4 $\mu g/m^3$ OC) was nearly twice that from QBQ (13-17%). With the denuder-filter-adsorbent system, the negative artifact (OC evaporating from the filter) was 5-10%. Watson and Chow (2002, 037873) reported that the XAD-coated denuder could function as efficiently as a parallel plate denuder using carbon-impregnated charcoal filters (CIF) with frequent denuder changes. Huebert and Charlson (2000, 156577) reported that using tandem filter packs may hinder a quantitative analysis of the artifacts.

Different temperature protocols and optical correction methods in thermal-optical analyses were further evaluated by Watson et al. (2005, 157125), Chow et al. (2004, 156347; 2005, 155728; 2007, 156354), Subramanian et al. (2006, 156107), Conny et al. (2003, 145948), Han et al. (2007, 155823), Chen et al. (2004, 199501) and (Conny et al., 2009, 191999). Solomon et al. (2003, 156994) reported a 20-50% difference for OC and a 20-200% difference for EC using 11 filter samples and 4 different analytical protocols. In an assessment of the different thermal-optical analysis protocols used around the world, Watson et al. (2005, 157125) reported that differences of a factor of 2 to 7 in EC between different methods could be observed, and a factor of 2 was common, while the relative differences in OC between different methods were small. As Watson et al. (2005, 157125) stated, there are 12 major differences among the thermal methods: (1) analysis atmosphere; (2) temperature ramping rates; (3) temperature plateaus; (4) residence time at each plateau; (5) optical pyrolysis monitoring configuration and wavelength; (6) standardization; (7) oxidation and reduction catalysts; (8) sample aliquot and size; (9) evolved carbon detection method; (10) carrier gas flow through or across the sample; (11) location of the temperature monitor relative to the sample; and (12) oven flushing conditions. Chow et al. (2004, 156347) and Chen et al. (2004, 199501) addressed the difference between optical transmission and optical reflectance methods for charring correction, and they reported that the charring OC on the surface of or inside a filter dominated the differences between these two correction methods. The differences between different sampling and measurement methods are also applied to the in-situ/semi-continuous methods, since

most of these methods are also based on thermal-optical analysis of collected filters. Most of these methods agree with integrated filter methods within 30%.

The differences observed between methods for OC and EC come largely from how OC and EC are defined. They are defined on an operational basis, as there are no standard reference materials. Initial efforts have been made to produce OC/EC reference materials at the National Institute of Science and Technology (NIST) (Klouda et al., 2005, 130382; Lee, 2007, 155926). Klouda et al. (2005, 130382) described the development of Reference Material 8785: Air Particulate Matter on Filter Media. Each reference filter is uniquely identified by its air PM number and its gravimetrically determined mass of fine Standard Reference Material (SRM) 1649a, and each filter has values assigned for total carbon, EC, and organic carbon mass fractions measured according to both IMPROVE and NIOSH protocols. Lee et al. (2007, 155926) reported a method to create a reference filter with a known amount of OC (as potassium hydrogen phthalate), and EC (as carbon black hydrosol).

Measurement methods for WSOC have been developed recently (Miyazaki et al., 2006, 156767; Sullivan and Weber, 2006, 157031; Sullivan et al., 2004, 157029; Sullivan et al., 2006, 157030; Sullivan et al., 2007, 100083; Yu et al., 2004, 156172). WSOC can be measured on integrated filter samples, or in-situ measurement can be conducted by coupling with the PILS-IC (Sullivan et al., 2004, 157029). For integrated filter samples, filters are extracted with deionized water and followed by oxidation of total WSOC to CO_2. CO_2 can then be detected by either infrared spectroscopy (IR) (Decesari et al., 2000, 155748; Kiss et al., 2002, 156646; Yang et al., 2003, 156167), FID (Yang et al., 2003, 156167), or pyrolysis gas chromatography/mass spectrometry (GC/MS) (Gelencsér et al., 2000, 155785). A correlation coefficient of 0.84 was reported by Sullivan et al. (Sullivan et al., 2004, 157029) between in-situ and filter based measurement of WSOC.

Further development and evaluation has been conducted on the measurement of BC with light absorption instruments (Andreae and Gelencsér, 2006, 156215; Arnott et al., 2003, 037711; Bae et al., 2004, 156243; Borak et al., 2003, 156284; Cyrys et al., 2003, 049634; Kurniawan and Schmidt-Ott, 2006, 098823; Park et al., 2006, 098104; Saathoff et al., 2003, 156066; Sadezky et al., 2005, 097499; Slowik et al., 2007, 096177; Taha et al., 2007, 096277; Virkkula et al., 2007, 157098; Wallace, 2000, 000803; Weingartner et al., 2003, 156149; Williams et al., 2006, 157148; Wu et al., 2005, 157155). These instruments include the aethalometer, particle absorption photometer, and photoacoustic analyzer. However, these instruments are subject to interferences by particle scattering, interactions with the filter substrate, particle loading on filters, and other pollutants (e.g., NO_2). Uncertainties of up to 50% were observed in the studies mentioned above by comparing these methods with integrated filter methods and thermal analysis methods.

Huang et al. (2006, 097654) reported the measurement of a stable isotope, ^{13}C, in OC and EC with a thermal optical transmission analyzer coupled with gas chromatography-isotope ratio mass spectrometer (TOT-GC-IRMS). The ratio of $^{13}C/^{12}C$ in OC and EC can provide useful information on OC/EC source categories and origin. The method was applied to Pacific2001 aerosol samples from the greater Vancouver area in Canada and produced a precision of ~0.03%. Gustafsson et al. (2009, 192000) applied the radiocarbon measurement technique and quantified the source contributions of carbonaceous aerosols to the Indian Ocean "brown cloud," with particular relevance for understanding and mitigating the climate effects of EC/BC.

Organic Speciation

Organic matter makes up a substantial fraction of PM in all regions of the U.S. (U.S. EPA, 2004, 056905), and 10-40% of the total organic matter is currently quantifiable at the individual compound level (Pöschl, 2005, 156882). Recent advancements in traditional solvent extraction GC/MS and high pressure liquid chromatography (HPLC) as well as application of thermal desorption (TD) techniques are helping to expand the understanding of the composition of organic matter as well as improving detection limits for quantification of organic molecular marker (OMM) compounds (Robinson et al., 2006, 156918; Schnelle-Kreis et al., 2005, 112944; Sheesley et al., 2007, 112017; Shrivastava et al., 2007, 111594). In addition, information about organic functional groups can be obtained with Fourier transform infrared spectrometry (FTIR) (Tsai and Kuo, 2006, 156127).

Recent advancements in GC/MS technology including inert electron ionization sources and improved instrument sensitivity and scan rates for better OMM quantification, have increased its

application in organic aerosol characterization studies (Cass, 1998, 155716; Dutton et al., 2009, 194887; Fraser et al., 2003, 042231; Graham et al., 2003, 156489; Hays et al., 2002, 026104; Robinson et al., 2006, 156918; Schauer et al., 1996, 051162; Sheesley et al., 2007, 112017; Subramanian et al., 2006, 156107; Watson et al., 1998, 012257; Zheng et al., 2002, 026100; Zheng et al., 2006, 157189). Incorporation of high volume injection using programmable temperature vaporization (PTV) (Engewald et al., 1999, 155765) has further lowered detection limits for trace level OMM compounds. High volume injection has the added benefit of preventing the loss of semivolatile compounds (Swartz et al., 2003, 157035), and has been applied for analysis of PAHs using low volume samplers (down to 5 L/min), allowing for smaller required mass loadings (Bruno et al., 2007, 155706; Crimmins and Baker, 2006, 097008). Since last review, HPLC analysis with fluorescence detection has also been used frequently for quantification of semivolatile organic compounds in both the particle and gas phase (Albinet et al., 2007, 154426; Barreto et al., 2007, 155676; Chow, 2007, 157209; Eiguren-Fernandez et al., 2003, 142609; Goriaux et al., 2006, 156484; Murahashi, 2003, 096539; Rynö et al., 2006, 156065; Stracquadanio et al., 2005, 156104; Temime-Roussel et al., 2004, 098530; Temime-Roussel et al., 2004, 098521). Lengthy extraction and analysis times remain a limiting factor for these methods.

TD techniques bypass one of the time consuming steps in traditional solvent extraction analysis for nonpolar organic compounds (n-alkanes, branched alkanes, cyclohexanes, hopanes, steranes, alkenes, phthalates and PAHs). This is achieved by vaporizing and analyzing organic constituents directly from the collection substrate, thereby bypassing the extraction step (Chow, 2007, 157209). Methods exist for both off-line TD analysis of previously collected filter samples and semi-continuous TD analysis. Annex A, Table A-17 is adapted from Chow et al. (2007, 157209) and summarizes recent TD-GC/MS studies. The most common off-line method is TD-GC/MS (Hays and Lavrich, 2007, 155831). Continuous or semi-continuous methods have been developed for direct analysis of individual organic constituents by coupling TD with various forms of mass spectrometry (Smith et al., 2004, 156090; Tobias and Ziemann, 1999, 157053; Tobias et al., 2000, 156121; Voisin et al., 2003, 156141; Williams et al., 2006, 156157). A comparison of measurement and analytical specifications for filter analysis using solvent extraction and TD methods for organic speciation are summarized in Annex A, Table A-17.

3.4.1.3. Multiple-Component Measurements on Individual Particles

The 2004 PM AQCD (U.S. EPA, 2004, 056905) discussed the aerosol time-of-flight mass spectrometry (ATOFMS). Recently, the ATOFMS and several other aerosol mass spectrometry methods have been further developed. Both lab and field comparisons have been conducted to evaluate the reliability of these types of instruments.

There are four types of commonly used aerosol mass spectrometry: (1) particle analysis by laser MS (PALMS; National Oceanic and Atmospheric Administration [NOAA]); (2) rapid single particle mass spectrometer (RSMS; University of Delaware); (3) aerosol time-of-flight MS (ATOFMS; TSI, Inc.); and (4) AMS (Aerodyne) (Chow et al., 2008, 156355; Nash et al., 2006, 199502). The differences between these instruments primarily come from the particle sizing methods of mass spectrometers, as shown in Annex A, Table A-16. Although the technique varies, the underlying principle is to fragment each particle into ions, using either a high-power laser or a heated surface, and then a mass spectrometer to measure the mass to charge ratio of each ion fragment in a vacuum.

These instruments were evaluated at the Atlanta, Houston, Fresno, Pittsburgh, New York, and Baltimore supersites (Bein et al., 2005, 156265; Drewnick et al., 2004, 155755; Drewnick et al., 2004, 155754; Hogrefe et al., 2004, 099003; Jimenez et al., 2003, 156611; Lake et al., 2003, 156669; Lake et al., 2004, 088411; Middlebrook et al., 2003, 042932; Phares et al., 2003, 156866; Qin and Prather, 2006, 156895; Wenzel et al., 2003, 157139). Measurements of the gross composition and abundance of particles by these instruments were generally semi-quantitative, with the exception of AMS. Particles of similar composition (e.g., OC/SO_4^{2-}, $Na/K/SO_4^{2-}$, soot/hydrocarbon, and mineral particle types) were characterized by these instruments during the studies mentioned above. NO_3^- and SO_4^{2-} concentrations measured with AMS were comparable with other continuous and filter-based methods, as mentioned in Section 3.4.1.2. In addition, concentrations of different particle types can be obtained by the co-location of these aerosol mass spectrometers and other particle sizing instruments, such as particle counters or the Micro-Orifice Uniform Deposit Impactor (MOUDI).

3.4.1.4. UFPs: Mass, Surface Area, and Number

Instruments for measuring UPFs developed during the past decade permit measurement of size distributions of particles down to 3 nm in diameter with mobility particle sizers. Concentrations down to this size range can be obtained by a MOUDI. The recently developed low pressure-drop UFP impactor coupled with a β Attenuation Monitor (nano-BAM) can also provide UFP (<150 nm) mass concentrations (Chakrabarti et al., 2004, 157426). A high correlation coefficient was observed between MOUDIs and nano-BAMs, with a correlation of 0.96. A 50% cut point (d_{50}) of 13-200 nm can be achieved by a high-volume slot-type UFP virtual impactor (Middha and Wexler, 2006, 155982).

Methods are also being developed to measure the surface area of UFPs. Particle surface area is usually measured by attaching labeled (radioactive or electrical labeling) molecules to particles and detecting the radioactive or electrical properties of the attached molecules. Wilson et al. (2007, 098398) suggested that the electrical aerosol detector (EAD, based on diffusion charging) measurement might be a useful indicator of the particle surface area deposited in the lung. This method can be potentially useful for examining the association between health effects and particle surface areas.

Developments involving the condensation particle counter include use of de-ionized water as a condensation medium in lieu of butanol or n-propanol in condensation particle counters (Hering et al., 2005, 155838; Hermann et al., 2007, 155840; Petäjä et al., 2006, 156021). This development makes the condensation particle counter (CPC) easier to use in field studies because water does not have some of the same chemical properties (with respect to hazard and odor) as butanol or n-propanol. The performance of this CPC was reported to be similar to the conventional butanol based CPC (Hering et al., 2005, 155838). Use of a battery of water and butanol-based CPCs was demonstrated to detect a range of solubilities in nucleation-mode particles (Kulmala et al., 2007, 155911). Additionally, CPCs have been used to measure particles in the smaller end of the UF scale through adjustment of CPC cut-off diameters through tuning the temperature difference between the CPC saturator and condenser (Kulmala et al., 2007, 155911) and improved charge reduction techniques (Winkler et al., 2008, 156160). The latter method was effective in reducing the size of particles detected by a CPC to <2 nm. These studies include assessment of errors related to these developments with the CPC and generally show that counting efficiencies with these devices is upwards of 95% (Hermann et al., 2007, 155840). Additionally, recent advancements have been made in development of fast scanning methods for UFP size distributions, including diffusion screens (DS) (Feldpausch et al., 2006, 155773) and fast integrated mobility scanners (FIMS) (Olfert et al., 2008, 156004).

3.4.1.5. PM Size Distribution

Along with particle density and shape (U.S. EPA, 2004, 056905), the particle size distribution can be used to estimate PM mass concentrations. For particles >0.1 µm, several instruments, including DRUM, MOUDIs, and aerodynamic particle sizer (APS), are available to measure mass-based or count-based particle size distribution. An APS incorporating very sharp cut points between 0.1 and 10 µm is now available (Peters, 2006, 156860; Zeng, 2006, 098375). For particles in this range, inertial forces are used to separate particles based on impaction. For particles <0.1 µm, particles can be separated by their electrical mobility, and as a result, electrical mobility diameter is often used to describe UFP size distribution in lieu of aerodynamic diameter. It has been necessary to develop techniques to convert mobility diameters, measured by the scanning mobility particle sizer (SMPS) or the Engine Exhaust Particle Sizer (EEPS), to aerodynamic diameters, measured by the APS, or vice versa, in order to merge the distributions spanning the UF, accumulation, and coarse modes. A variety of techniques for combining SMPS and APS diameters have been reported in the literature (Hand and Kreidenweis, 2002, 155824; Khlystov et al., 2004, 155897; Morawska et al., 1999, 007609; Morawska et al., 2007, 155990; Shen et al., 2002, 156086; TSI, 2005, 157196). However, each of these techniques incurs some uncertainty of which the user must be aware.

3.4.1.6. Satellite Measurement

Instruments sensing back scattered solar radiation on satellites have made it possible to derive information about tropospheric aerosol properties on the global scale. The satellite borne instruments

vary in their complexity and in the aerosol properties they can measure. Satellite instruments measure radiance (or brightness temperature) that can then be used to provide information on the aerosol column amount, or the aerosol optical depth (AOD). Depending on the wavelengths sampled and the spectral resolution of the instruments, information about the composition of particles of diameter <2 μm and particles of diameter >2μm can be obtained. Data from two main instruments, the moderate resolution imaging spectroradiometer (MODIS) and the multiangle imaging spectroradiometer (MISR) have been used to estimate surface PM in the U.S. MODIS measures the intensity of back scattered sunlight at seven wavelengths through the visible to the near infrared at one viewing direction; and MISR measures the intensity at four wavelengths (from the visible to the near IR) and the same ground pixel at nine viewing angles. The spatial resolution of reported AOD is 17.6×17.6 km for MISR and either 10×10 or 1×1 km for MODIS, depending on retrieval algorithm. Since both instruments are located on the same satellite, their times of overpass are the same, about 1330 local time. Due to precession of the satellite's orbit, the satellite does not pass over the same path every day, and instruments cannot sense aerosol properties beneath cloud tops.

The problem of using satellite data to retrieve properties of the atmospheric aerosol is complex because the surface contribution to satellite measured reflectance must be separated from the aerosol signal. Difficulties can arise when attempting to derive aerosol information over land surfaces because of uncertainties in surface reflectivity, similarities between aerosol and surface composition, and high signal-to-noise ratio when viewing AOD over reflective surfaces such as desert and snow. To overcome this difficulty, data from MODIS have been applied over dark land surfaces and ongoing improvements in retrieval algorithms are being developed. Instruments such as the MISR that sense at multiple viewing angles can better cope with the problems over land surfaces because they can use the information on the angular dependence of reflection from the surface and the atmosphere to distinguish between their signals. Not only can total AODs be derived, but fractional AODs that reflect external mixtures characterized by particle shape, effective radius, and single scattering albedo can also be derived. These properties can then be used to infer particle composition. Retrievals over the oceans have had less difficulty because the optical properties of sunlight reflected from the sea surface are much better known, and reflectivities are low over most zenith angles at less than gazing incidence.

Kokhanovsky et al. (2007, 190009) examined the errors associated with MODIS, MISR, and a number of other satellite instruments with respect to associated retrieval algorithms for retrievals over Central Europe. They found a correlation coefficient between MODIS and MISR AOD of 0.62. Both MODIS and MISR AOD tended to underestimate ground-based AOD measurements from AERONET (NASA's AErosol RObotic NETwork) slightly with MODIS generally retrieving higher AODs than MISR. Chu et al. (2003, 190049) found correlations between MODIS and AERONET AODs ranging from 0.82-0.91; and Kahn et al. (2005, 189961) found correlations of 0.7-0.9 between MISR and AERONET AODs.

Further complexity is added when attempting to relate surface $PM_{2.5}$ to aerosol optical depths. The detailed comparisons of surface measurement and satellite measurements are given in Chapter 9.

3.4.2. Ambient Network Design

3.4.2.1. Monitor Siting Requirements

The EPA Air Quality System database (AQS) contains measurements of air pollutant concentrations in the 50 states, plus the District of Columbia, Puerto Rico, and the Virgin Islands, for the 6 criteria air pollutants as well as a more limited dataset of hazardous air pollutants. In 2007, there were 4,693 PM_{10} monitors and 2,194 $PM_{2.5}$ monitors reporting values to the AQS. Where SLAMS PM_{10} and $PM_{2.5}$ monitoring is required, at least one of the sites must be a maximum concentration site for that specific area. The appropriate spatial scales for $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10} monitoring differ given the contrasting spatial gradients of coarse PM relative to fine. The relevant scales for each size classification are provided in Annex A, Table A-18.

Criteria for siting ambient monitors for PM at national monitoring networks are summarized below by PM size, and details are given in the CFR 40 Part 58 Appendix D, and SLAMS/NAMS/PAMS Network Review Guidance (U.S. EPA, 1998, 093211). Table A-19 in Annex A provides a summary of the number of sites and operating specifications of these networks. Probing

and monitoring path siting criteria for any specific monitoring site are given in CFR 40 Part 58 Appendix E, including horizontal and vertical placement, spacing from minor source, spacing from obstructions, spacing from trees, and spacing from roadways.

$PM_{2.5}$

The minimum number of $PM_{2.5}$ monitors required in a metropolitan statistical area is determined by the population and the air quality in the area, as specified in Appendix D of 40 CFR Part 58. The required minimum number of $PM_{2.5}$ monitors ranges from 0 to 3 in any given metropolitan statistical area. Continuous $PM_{2.5}$ monitors must be operated in no fewer than one-half of the minimum required sites in each area. Most $PM_{2.5}$ monitoring in urban areas should be representative of a neighborhood scale (for trends and compliance with standards). Urban or regional scale sites are located to characterize regional transport of $PM_{2.5}$. In certain instances where population-oriented micro- or middle-scale $PM_{2.5}$ monitoring are determined by the Regional Administrator to represent many such locations throughout a metropolitan area, these smaller scales can be considered to represent community-wide air quality. $PM_{2.5}$ measurements are obtained at local temperature and pressure across the NAMS/SLAMS networks (40 CFR Part 58).

$PM_{2.5}$ chemical speciation monitoring is currently conducted at 197 CSN sites (http://www.epa.gov/ttn/amtic/specgen.html). Within the CSN network, 53 locations are recognized as the Speciation Trends Network (STN) operating on a sample schedule of one in every three days, while the rest of the CSN typically operates every sixth day.

$PM_{10-2.5}$

$PM_{10-2.5}$ monitoring has not been required at SLAMS sites, but will be required at NCore[1] Stations (which is a sub-set of the SLAMS) by January 1, 2011. Middle and neighborhood scale measurements are the most important station classifications for $PM_{10-2.5}$ to assess the variation in coarse particle concentrations that would be expected across populated areas that are in proximity to large emissions sources. $PM_{10-2.5}$ chemical speciation monitoring and analyses will also be required at NCore sites by January 1, 2011. EPA has already approved FRMs and FEMs for $PM_{10-2.5}$ mass; however, methods for $PM_{10-2.5}$ speciation are still being developed (Henderson, 2009, 192001). $PM_{10-2.5}$ measurements are obtained at local temperature and pressure by recalculating the co-located PM_{10} for local conditions.

PM_{10}

As for $PM_{2.5}$, the minimum number of PM_{10} monitors required in a metropolitan statistical area is determined by the population and the air quality in the area, as specified in Appendix D of 40 CFR Part 58. The required minimum number of PM_{10} monitors ranges from 0 to 8 in any given metropolitan statistical area. Except for some circumstances where microscale (<100 m, for maximum PM_{10} exposure) monitoring may be appropriate, the most important scales to characterize the emissions of PM_{10} effectively from both mobile and stationary sources are the middle scale (for short-term public exposure) and neighborhood scale (for trends and compliance with standards). PM_{10} measurements are obtained at standard temperature and pressure across the NAMS/SLAMS networks (40 CFR Part 58).

3.4.2.2. Spatial and Temporal Coverage

Locations of $PM_{2.5}$ and PM_{10} Monitors in Selected Metropolitan Areas in the U.S.

Fifteen metropolitan regions were chosen for closer investigation of monitor siting based on their distribution across the nation and relevance to health studies analyzed in subsequent chapters of this ISA. These regions were: Atlanta, Birmingham, Boston, Chicago, Denver, Detroit, Houston, Los Angeles, New York City, Philadelphia, Phoenix, Pittsburgh, Riverside, Seattle, and St. Louis. Core-

[1] For more information on NCore, see the NCore web site at: http://www.epa.gov/ttn/amtic/ncore/index.html.

Based Statistical Areas (CBSAs) and Combined Statistical Areas (CSAs), as defined by the U.S. Census Bureau (http://www.census.gov/), were used to determine which counties, and hence which monitors, to include for each metropolitan region.[1] Figure 3-7 and Figure 3-8 display $PM_{2.5}$ and PM_{10} monitor density, respectively, with respect to population density in Boston. Annex A includes similar information for all fifteen metropolitan regions (Figure A-1 through Figure A-30).

[1] A CBSA represents a county-based region surrounding an urban center of at least 10,000 people determined using 2000 census data and replaces the older Metropolitan Statistical Area (MSA) definition from 1990. The CSA represents an aggregate of adjacent CBSAs tied by specific commuting behaviors. The broader CSA definition was used when selecting monitors for the cities listed above with the exception of Los Angeles, Riverside and Phoenix. Los Angeles and Riverside are contained within the same CSA, so the smaller CBSA definition was used to delineate these two cities. Phoenix is not contained within a CSA, so the smaller CBSA definition was used for this city as well.

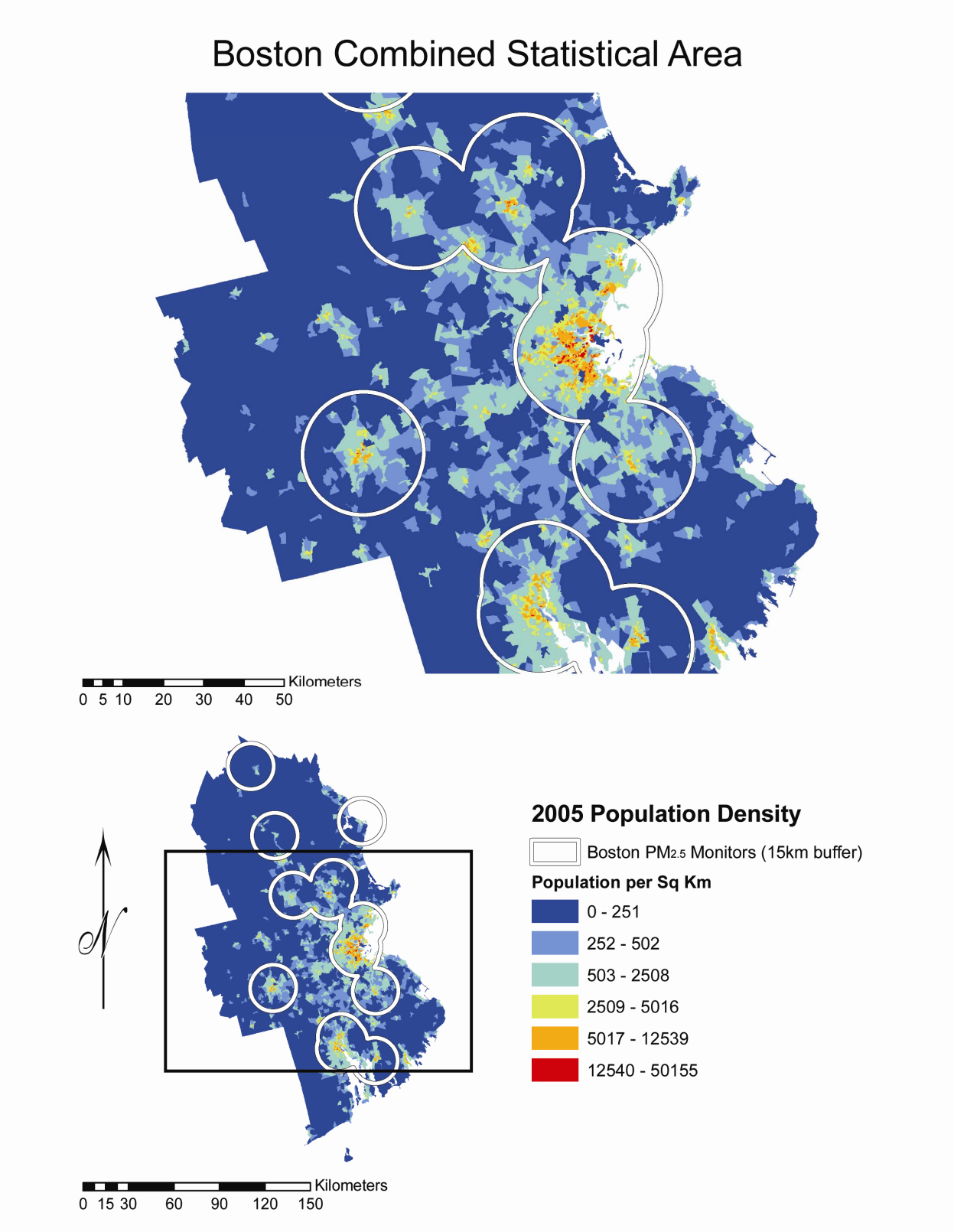


Figure 3-7. $PM_{2.5}$ monitor distribution in comparison with population density, Boston CSA.

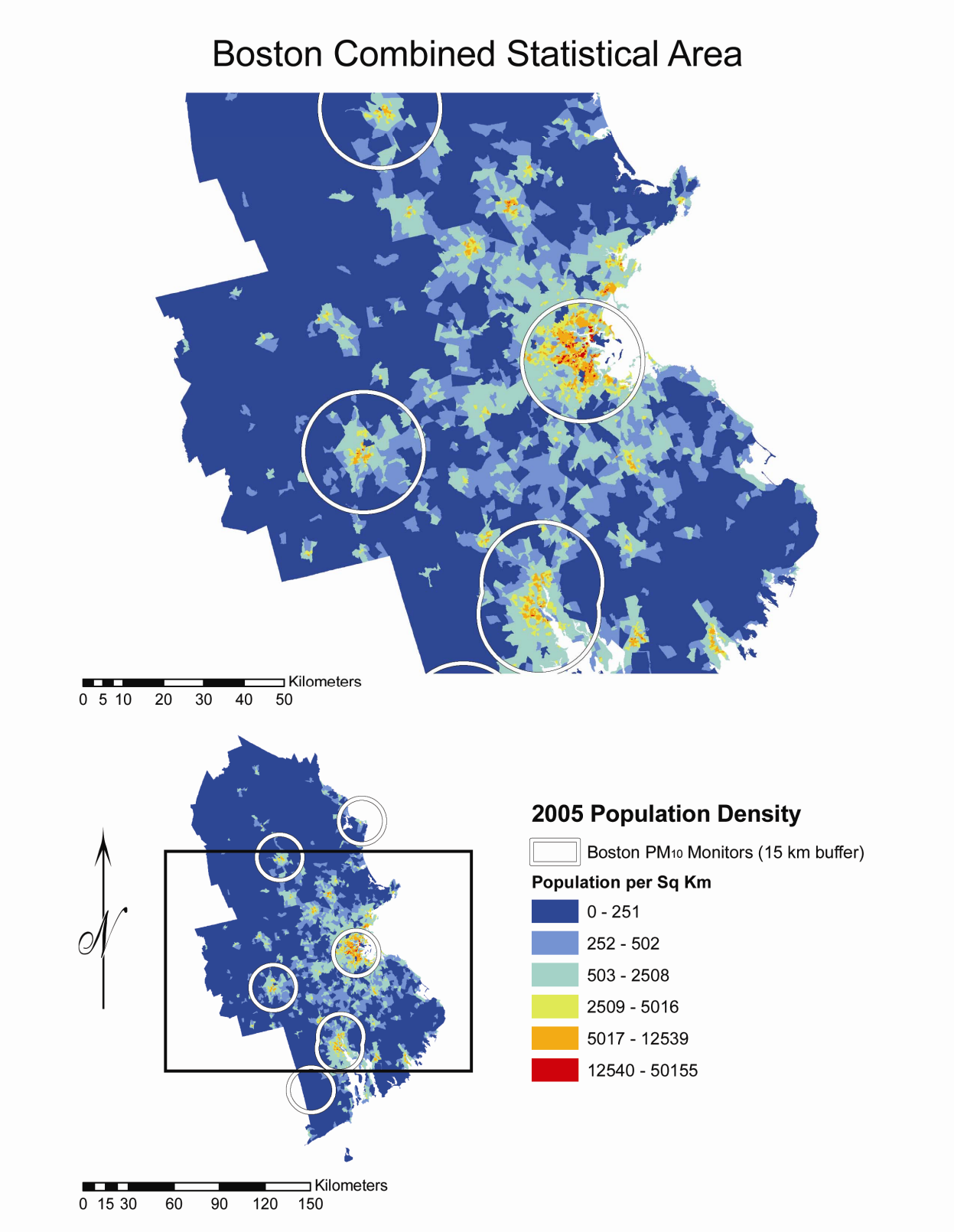


Figure 3-8. PM_{10} monitor distribution in comparison with population density, Boston CSA.

Table 3-3. Proximity to $PM_{2.5}$ and PM_{10} monitors for total population[a] by city.

Region	Proximity to PM Monitors[b]							
	Total CSA/CBSA	≤ 1 km		≤ 5 km		≤ 10 km		≤ 15 km	
	N	N	%	N	%	N	%	N	%
PROXIMITY TO $PM_{2.5}$ MONITORS									
Atlanta	5,316,742	23,461	0.44	581,461	10.94	1,990,477	37.44	3,179,844	59.81
Birmingham	1,166,100	12,925	1.11	240,383	20.61	666,926	57.19	848,447	72.76
Boston	7,502,707	185,457	2.47	1,877,180	25.02	3,356,019	44.73	4,641,175	61.86
Chicago	9,754,262	177,076	1.82	3,091,573	31.69	6,473,463	66.37	8,185,010	83.91
Denver	2,952,039	40,601	1.38	649,953	22.02	1,548,976	52.47	2,252,657	76.31
Detroit	5,553,465	54,997	0.99	1,174,733	21.15	2,791,555	50.27	3,845,190	69.24
Houston	5,503,320	11,586	0.21	213,708	3.88	905,007	16.44	1,599,079	29.06
Los Angeles	13,061,361	115,477	0.88	2,579,809	19.75	7,544,466	57.76	10,792,727	82.63
New York	22,050,940	717,094	3.25	8,107,764	36.77	13,493,867	61.19	16,571,764	75.15
Philadelphia	6,388,913	117,389	1.84	1,878,373	29.40	3,517,321	55.05	4,393,136	68.76
Phoenix	3,818,147	37,133	0.97	490,072	12.84	1,099,069	28.79	1,739,542	45.56
Pittsburgh	2,515,383	40,574	1.61	587,148	23.34	1,331,230	52.92	1,883,301	74.87
Riverside	3,781,063	43,739	1.16	723,829	19.14	1,855,296	49.07	2,344,394	62.00
Seattle	3,962,434	13,723	0.35	287,373	7.25	931,630	23.51	1,561,792	39.41
St. Louis	2,869,955	37,329	1.30	563,176	19.62	1,338,349	46.63	1,760,985	61.36
PROXIMITY TO PM_{10} MONITORS									
Atlanta	5,316,742	30,973	0.58	416,440	7.83	1,090,497	20.51	1,837,983	34.57
Birmingham	1,166,100	23,943	2.05	251,310	21.55	473,054	40.57	638,472	54.75
Boston	7,502,707	63,614	0.85	1,090,172	14.53	2,087,770	27.83	2,939,870	39.18
Chicago	9,754,262	55,642	0.57	844,714	8.66	2,374,972	24.35	3,844,297	39.41
Denver	2,952,039	38,449	1.30	521,201	17.66	1,146,286	38.83	1,799,187	60.95
Detroit	5,553,465	14,050	0.25	309,623	5.58	748,971	13.49	1,300,995	23.43
Houston	5,503,320	36,795	0.67	832,767	15.13	2,227,314	40.47	3,141,150	57.08
Los Angeles	13,061,361	52,052	0.40	1,404,389	10.75	4,899,254	37.51	9,075,863	69.49
New York	22,050,940	19,842	0.09	292,105	1.32	592,631	2.69	773,962	3.51
Philadelphia	6,388,913	23,988	0.38	376,966	5.90	1,091,532	17.08	2,238,309	35.03
Phoenix	3,818,147	99,520	2.61	1,255,430	32.88	2,615,738	68.51	3,416,682	89.49
Pittsburgh	2,515,383	65,906	2.62	706,413	28.08	1,291,700	51.35	1,705,451	67.80
Riverside	3,781,063	61,356	1.62	895,615	23.69	2,360,272	62.42	2,922,799	77.30
Seattle	3,962,434	4,851	0.12	220,539	5.57	709,887	17.92	1,211,430	30.57
St. Louis	2,869,955	27,872	0.97	380,411	13.25	891,695	31.07	1,212,543	42.25

[a]Based on 2005 population totals.
[b]Percentages are given with respect to the total population per city provided.

Table 3-3 shows the population density around $PM_{2.5}$ and PM_{10} monitors for the total population for each CSA/CBSA individually. Population totals within various distances of PM monitors were calculated assuming equal internal population distribution for individual census blocks. Between-city disparities in population density were large and were dependent primarily on the location and number of PM monitoring sites per CSA/CBSA. For $PM_{2.5}$, Los Angeles (83%) and Denver (76%) had the largest proportion of the total population within 15 km of a monitor. Houston (29%) had the least population coverage with their $PM_{2.5}$ monitors. For PM_{10}, Phoenix (89%) had the largest proportion of the total population within 15 km of a monitor. Detroit (23%), Boston (39%), Seattle (31%), and Philadelphia (35%) had the smallest proportions of the population within 15 km of a PM_{10} monitor. Proximity to monitoring stations is considered further in Section 3.5 and Section 3.8 regarding spatial variability within cities. Figure 3-7 shows that the $PM_{2.5}$ network more closely samples near population centers in the Boston CSA compared with the PM_{10} network shown in Figure 3-8, although both $PM_{2.5}$ and PM_{10} networks place at least one monitor in the city center.

3.4.2.3. Network Application for Exposure Assessment with Respect to Susceptible Populations

Subject Age

Table 3-4 breaks down the population density around $PM_{2.5}$ and PM_{10} monitors for sub-populations of children age 0-4 yr, children age 5-17 yr, and elderly adults age 65 yr and over cumulatively for the 15 CSAs/CBSAs examined. Table 3-5 shows the distribution for adults age 65 years and over for each CSA/CBSA individually. This detail of information is not provided for the 0- to 4-yr and 5- to 17-yr age groups because variation in percentage within a certain radius of the monitor was generally fairly low for each city across the child age groups when compared to total population. In the cases of Denver, Detroit, Phoenix, Riverside, and St. Louis for $PM_{2.5}$ and Birmingham, Denver, Riverside, and St. Louis for PM_{10}, the elderly population's distribution around the samplers varied more from the total population compared to other age groups. When all CSAs/CBSAs were considered cumulatively, the percentage of the population within 15 km of a monitor was similar for all age groups for both $PM_{2.5}$ and PM_{10}. Between-city disparities in elderly population density within a sampler radius were larger. For $PM_{2.5}$, Chicago (87%) and Denver (84%) had the largest proportion of the elderly population within 15 km of a monitor. Houston (31%) had the least population coverage with their $PM_{2.5}$ monitors. For PM_{10}, Phoenix (90%) had the largest proportion of the total population within 15 km of a monitor. New York (4%), Detroit (27%), Seattle (32%), and Philadelphia (39%) had the smallest proportions of the population within 15 km of a PM_{10} monitor. These differences may reflect overall density of the samplers within a given city, with $PM_{2.5}$ monitors more numerous than PM_{10} monitors in most of the CSAs/CBSAs, and retirement and settlement trends among elderly adults.

Table 3-4. Proximity to $PM_{2.5}$ and PM_{10} monitors for children age 0-4 yr, children age 5-17 yr, and adults age 65 yr and older.[a] The figures presented here are cumulative for the 15 CSAs/CBSAs examined in Chapter 3.

Age Grouping	Proximity to PM Monitors[b]								
	Total CSA/CBSA	≤ 1 km		≤ 5 km		≤ 10 km		≤ 15 km	
	N	N	%	N	%	N	%	N	%
PROXIMITY TO $PM_{2.5}$ MONITORS									
0-4	6,400,785	109,466	1.71	1,603,000	25.04	3,361,922	52.52	4,462,403	69.72
5-17	17,212,825	275,427	1.60	4,164,132	24.19	8,814,179	51.21	11,813,997	68.63
≥ 65	10,391,023	175,113	1.69	2,570,909	24.74	5,483,776	52.77	7,288,049	70.14
PROXIMITY TO PM_{10} MONITORS									
0-4	6,400,785	44,384	0.69	695,120	10.86	1,725,419	26.96	2,636,782	41.19
5-17	17,212,825	110,882	0.64	1,756,246	10.20	4,441,239	25.80	6,942,001	40.33
≥ 65	10,391,023	68,367	0.66	1,056,375	10.17	2,631,243	25.32	4,041,802	38.90

[a] Based on 2000 population totals.
[b] Percentages are given with respect to the total population per city provided.

Race and Hispanic Origin

Table 3-6 shows the percent of the population self-identified as white or black and having a Hispanic or non-Hispanic origin within 1, 5, 10, or 15 km distances from $PM_{2.5}$ and PM_{10} monitors cumulatively across the fifteen CSAs/CBSAs. For $PM_{2.5}$, blacks and Hispanics had similar percentages of the population within 15 km of a monitor (86% and 82%, respectively), while a smaller proportion of whites and non-Hispanics were within that same distance (63% and 67%, respectively), across the fifteen CSAs/CBSAs studied. For $PM_{10,}$ Hispanics (54%) represented the subpopulation with the largest percentage of total population within 15 km of a monitor across the fifteen CSAs/CBSAs studied. The percentage of blacks within that same distance was marginally lower (48%), whereas the percentage of whites and non-Hispanics within 15 km of a monitor was approximately two-thirds that of Hispanics (35% and 37%, respectively). Higher percentages of individual ethnic subpopulations within 15 km of a $PM_{2.5}$ monitor most likely represents the fact that more $PM_{2.5}$ monitors are currently deployed compared with PM_{10} monitors. While no ethnic subpopulation appears to be well represented at the neighborhood scale, greater percentages of the black and Hispanic populations (1% each) are within 1 km of a PM_{10} monitor than the corresponding white and non-Hispanic populations (0.5% each). Likewise, 2.5% of the black population and 2.8% of the Hispanic population reside within 1 km of a $PM_{2.5}$ monitor compared to 1.4% of the white population and 1.5% of the non-Hispanic population. Furthermore, it is notable that at any scale shown in Table 3-6 for both $PM_{2.5}$ and PM_{10} monitors, those self-identified as black or Hispanic actually have greater representation by the monitors than those identified as white or non-Hispanic.

Table 3-5. Proximity to $PM_{2.5}$ and PM_{10} monitors for adults age 65 yr and older[a] by city.

Age Grouping	Proximity to PM Monitors[b]								
	Total CSA/CBSA	**≤ 1 km**		**≤ 5 km**		**≤ 10 km**		**≤ 15 km**	
	N	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
PROXIMITY TO $PM_{2.5}$ MONITORS									
Atlanta	362,201	1,757	0.49	36,772	10.15	136,179	37.60	207,122	57.18
Birmingham	145,905	1,619	1.11	29,952	20.53	84,223	57.72	106,488	72.98
Boston	945,790	18,821	1.99	224,628	23.75	438,920	46.41	606,231	64.10
Chicago	1,018,983	18,539	1.82	348,656	34.22	713,194	69.99	883,112	86.67
Denver	232,974	3,891	1.67	59,625	25.59	140,523	60.32	196,361	84.28
Detroit	626,216	5,765	0.92	138,672	22.14	345,808	55.22	469,462	74.97
Houston	377,586	1,010	0.27	14,911	3.95	66,741	17.68	117,661	31.16
Los Angeles	1,207,436	9,653	0.80	229,893	19.04	688,844	57.05	984,889	81.57
New York	2,710,675	78,918	2.91	921,599	34.00	1,619,177	59.73	2,048,842	75.58
Philadelphia	834,110	13,323	1.60	251,459	30.15	487,003	58.39	605,663	72.61
Phoenix	388,150	2,738	0.71	39,833	10.26	90,304	23.27	142,084	36.61
Pittsburgh	449,544	8,933	1.99	111,050	24.70	249,269	55.45	347,711	77.35
Riverside	342,334	3,024	0.88	50,901	14.87	129,836	37.93	170,933	49.93
Seattle	390,372	1,721	0.44	29,429	7.54	101,223	25.93	156,562	40.11
St. Louis	358,747	5,401	1.51	83,528	23.28	192,532	53.67	244,929	68.27
PROXIMITY TO PM_{10} MONITORS									
Atlanta	362,201	2,115	0.58	35,448	9.79	93,903	25.93	139,240	38.44
Birmingham	145,905	3,663	2.51	35,628	24.42	66,839	45.81	86,299	59.15
Boston	945,790	6,852	0.72	124,911	13.21	262,854	27.79	385,046	40.71
Chicago	1,018,983	7,619	0.75	107,540	10.55	291,705	28.63	441,771	43.35
Denver	232,974	3,675	1.58	43,658	18.74	107,548	46.16	168,447	72.30
Detroit	626,216	1,555	0.25	41,833	6.68	99,680	15.92	167,760	26.79
Houston	377,586	2,085	0.55	57,413	15.21	166,715	44.15	219,615	58.16
Los Angeles	1,207,436	4,693	0.39	126,696	10.49	422,725	35.01	810,078	67.09
New York	2,710,675	2,463	0.09	37,580	1.39	80,222	2.96	104,951	3.87
Philadelphia	834,110	2,740	0.33	49,413	5.92	154,535	18.53	322,700	38.69
Phoenix	388,150	8,605	2.22	119,306	30.74	267,456	68.91	348,464	89.78
Pittsburgh	449,544	13,302	2.96	133,285	29.65	243,723	54.22	314,941	70.06
Riverside	342,334	4,181	1.22	65,499	19.13	182,615	53.34	236,900	69.20
Seattle	390,372	503	0.13	22,333	5.72	72,979	18.69	123,054	31.52
St. Louis	358,747	4,316	1.20	55,833	15.56	117,743	32.82	172,535	48.09

[+]Based on 2000 population totals.
[b]Percentages are given with respect to the total population per city provided.

Table 3-6. Proximity to $PM_{2.5}$ and PM_{10} monitors based on the population identified as white, black, Hispanic, or non-Hispanic [a]. The figures presented here are cumulative for the 15 CSAs/CBSAs examined in Chapter 3.

Race or Hispanic Origin	Total CSA/CBSA	Proximity to PM Monitors[b] ≤ 1 km		≤ 5 km		≤ 10 km		≤ 15 km	
	N	N	%	N	%	N	%	N	%
PROXIMITY TO $PM_{2.5}$ MONITORS									
White	61,936,855	863,823	1.39	12,257,978	19.79	27,553,900	44.49	39,030,037	63.02
Black	12,668,004	320,447	2.53	4,780,620	37.74	9,241,172	72.95	10,906,346	86.09
Hispanic	15,916,208	445,126	2.80	5,782,482	36.33	10,661,947	66.99	13,094,618	82.27
Non-Hispanic	74,611,962	1,135,999	1.52	16,553,574	22.19	36,318,474	48.68	49,629,054	66.52
PROXIMITY TO PM_{10} MONITORS									
White	61,936,855	325,771	0.53	5,554,906	8.97	14,041,215	22.67	21,913,907	35.38
Black	12,668,004	134,174	1.06	1,611,263	12.72	3,867,436	30.53	6,020,348	47.52
Hispanic	15,916,208	169,305	1.06	2,496,959	15.69	5,905,322	37.10	8,589,819	53.97
Non-Hispanic	74,611,962	421,917	0.57	6,767,187	9.07	17,261,734	23.14	27,254,421	36.53

[a]Based on 2000 population totals
[b]Percentages are given with respect to the total population per city provided.

Socioeconomic Status

Table 3-7 shows the percent of the population below and above the poverty level and the percent of the population over age 25 years stratified by education level that reside within 1 km, 5 km, 10 km, and 15 km of a $PM_{2.5}$ and PM_{10} monitor cumulatively across the 15 CSAs/CBSAs. For $PM_{2.5}$, 80% of the population below poverty level and 77% of the population with less than high school education are within 15 km of a monitor for the 15 CSAs/CBSAs studied. Populations of those above the poverty line, those with a high school or more education, and those with a college education within 15 km of a monitor were less than the low SES groups (67% for each). For PM_{10}, 47% of the population below the poverty level and 45% of the population with less than a high school education are within 15 km of a monitor, whereas the percentage of those above the poverty line (39%), those with a high school or more education (38%), and those with a college education (35%) were slightly less. Higher percentages of individual SES subpopulations within a given distance of $PM_{2.5}$ monitors relative to PM_{10} monitors likely reflect the fact that more $PM_{2.5}$ monitors are currently deployed within the 15 CSAs/CBSAs studied compared with PM_{10} monitors. Lower SES groups are not shown to be well-represented at the neighborhood scale, with 1.2% of the population below the poverty level and 1.0% of the population with less than a high school education residing within 1 km of a PM_{10} monitor. Likewise, 3.1% of the population below the poverty level and 2.4% of the population with less than high school education reside within 1 km of a $PM_{2.5}$ monitor. However, the populations of low SES groups are more represented at the neighborhood scale than those for higher SES groups. For example, only about 1.5-1.7% of those above the poverty line, those with a high school or more education, or those with a college education are within 1 km of a $PM_{2.5}$ monitor. Moreover, it is notable that at any scale shown in Table 3-7 and for both $PM_{2.5}$ and PM_{10}, those living under the poverty line and those age 25 years and older with less than high school education have greater representation by the monitors than those above the poverty line or those age 25 and older with high school or college education.

Table 3-7. Proximity to $PM_{2.5}$ and PM_{10} monitors based on the population below or above the poverty line, population over age 25 with less than high school education, population over 25 with high school education, and population over 25 with college education or more[a]. The figures presented here are cumulative for the 15 CSAs/CBSAs examined in Chapter 3.

SES	Total CSA/CBSA	Proximity to PM Monitors[b]							
		≤ 1 km		≤ 5 km		≤ 10 km		≤ 15 km	
	N	N	%	N	%	N	%	N	%
PROXIMITY TO $PM_{2.5}$ MONITORS									
Below poverty line	10,645,411	330,970	3.11	3,951,549	37.12	7,107,192	66.76	8,528,731	80.12
Above poverty line	85,551,420	1,297,591	1.52	19,094,985	22.32	41,736,460	48.79	57,070,312	66.71
Less than HS education	11,606,042	276,942	2.39	3,806,208	32.80	7,225,291	62.25	8,930,174	76.94
HS education	30,583,598	444,262	1.45	6,940,261	22.69	15,152,047	49.54	20,489,904	67.00
College education	16,433,811	280,810	1.71	3,451,717	21.00	7,776,218	47.32	11,000,917	66.94
PROXIMITY TO PM_{10} MONITORS									
Below poverty line	10,645,411	132,979	1.25	1,626,694	15.28	3,504,957	32.92	5,024,714	47.20
Above poverty line	85,551,420	485,874	0.57	8,171,398	9.55	21,096,615	24.66	33,034,279	38.61
Less than HS education	11,606,042	112,901	0.97	1,544,594	13.31	3,537,414	30.48	5,186,441	44.69
HS education	30,583,598	185,439	0.61	2,975,200	9.73	7,580,000	24.78	11,747,653	38.41
College education	16,433,811	59,892	0.36	1,229,885	7.48	3,447,148	20.98	5,722,347	34.82

[a]Based on 2000 population totals
[b]Percentages are given with respect to the total population per city provided.

3.5. Ambient PM Concentrations

This section describes measurements of ambient PM mass and composition made since the 2004 PM AQCD (U.S. EPA, 2004, 056905) including analyses using AQS data as well as published findings. Emphasis is placed on the period from 2005-2007 which incorporates the most recent validated AQS data available at the time this document was prepared.

When the 2004 PM AQCD (U.S. EPA, 2004, 056905) was written, the full nationwide $PM_{2.5}$ compliance monitoring network had only recently been deployed, providing three years (1999-2001) of completed measurements. Based on observations from these first three years, the 2004 PM AQCD (U.S. EPA, 2004, 056905) found that $PM_{2.5}$ in eastern cities was generally more highly correlated across monitoring sites than in western cities. The higher spatial correlations in the eastern cities resulted from the more regionally dispersed sources of $PM_{2.5}$ in the East. Although $PM_{2.5}$ concentrations at sites within an urban area can be highly correlated, significant differences in concentrations can occur on any given day. The ratio of $PM_{2.5}$ to PM_{10} was found to be higher in the East than in the West in general, and values for this ratio are consistent with those found in numerous earlier studies presented in the 1996 PM AQCD (U.S. EPA, 1996, 079380). Differences in the composition of $PM_{2.5}$ between eastern and western cities were also found to be consistent with differences found in the 1996 PM AQCD (U.S. EPA, 1996, 079380). Much more limited data were

available for describing the spatial variability of coarse particulate mass measured as $PM_{10-2.5}$, UFPs, and PM composition. The 2004 PM AQCD (U.S. EPA, 2004, 056905) noted that components produced by area (e.g., traffic) and point sources are more spatially variable than regionally dispersed components (e.g., secondary SO_4^{2-}). Spatial variability will affect estimates of community-scale human exposure and caution should be exercised in extrapolating conclusions from one area to another, particularly on a regional scale.

For this PM ISA, the $PM_{2.5}$ monitoring network has been active for 8 or 9 years depending on location. Observations and analyses based on $PM_{2.5}$ measurements reported to AQS are included in this chapter. Furthermore, by selecting locations where PM_{10} and $PM_{2.5}$ measurements are co-located, information about the spatiotemporal distribution of the $PM_{10-2.5}$ size fraction is investigated. Given the form of the current standard and the relative abundance of PM_{10} monitors in the AQS network, PM_{10} mass concentrations are also included in this section with the understanding that PM_{10} includes mass contributions from the smaller size fractions and therefore overlaps with $PM_{2.5}$, $PM_{10-2.5}$ and UFP mass concentrations. Although compliance monitoring does not apply for UFPs because there is no ambient standard for them, new observational information is available from detailed studies in several cities. Similarly, advancements have been made in understanding PM composition from the CSN and IMPROVE networks. Descriptions of UFPs and speciated PM are covered throughout this section where information is available.

Unless otherwise specified, the $PM_{2.5}$, $PM_{10-2.5}$ and PM_{10} data utilized in this section comes from the AQS. Based on the population and exposure requirements for monitor siting in 40 CFR Part 58 described in Section 3.4.2, monitors reporting to the AQS are not uniformly distributed across the U.S. Monitors are far more abundant in urban areas than rural ones, so actual rural spatiotemporal distributions may differ considerably from those reported here. Furthermore, biases exist for some PM constituents (and hence, total mass) owing to volatilization losses of NO_3^- and other semi-volatile compounds and, conversely, retention of particle-bound water with hygroscopic species. The magnitude of these effects is likely to be region-specific.

Spatial distributions of PM across a range of geographic scales are covered in Section 3.5.1. Temporal behavior including trends, seasonality and hourly variability are covered in Section 3.5.2. Finally, statistical associations between different size fractions of PM and copollutants including CO, NO_2, O_3 and SO_2 are covered in Section 3.5.3.

3.5.1. Spatial Distribution

Spatial scales of interest for PM range from global and continental scales (>1000 km) down to micro scale (~5-100 m). Variation in PM concentration depends on the spatial scale and magnitude of PM sources, formation and removal mechanisms, and transport and dispersion of PM. These different sources and processes can cause substantial variation in particle size distribution and chemistry. This section addresses the spatial variability of PM by focusing primarily on AQS data across three different scales: variability across the U.S., urban-scale variability and neighborhood-scale variability. These sections are further subdivided to the extent possible into PM size fractions and composition.

3.5.1.1. Variability across the U.S.

$PM_{2.5}$

Figure 3-9 shows the 3-yr mean of the 24-h $PM_{2.5}$ concentrations by county across the U.S. for 2005-2007. The data used in generating this map are from FRM or FRM-like[1] data obtained fromthe AQS database after applying a completeness criterion of 75% per quarter (i.e., 11 out of 15 quarterly measurements for a 1-in-6 day sampling schedule). Counties shown in white did not contain sufficient $PM_{2.5}$ data between 2005-2007 to meet the completeness criterion as a result of either a lack of monitoring sites or a lack of adequate or complete data from existing monitoring sites within the county. Of the 3,225 U.S. counties, 540 (17%) had $PM_{2.5}$ data meeting the completeness criterion in all three years (2005-2007). These 540 counties represent roughly 63% of the U.S. population. The fraction of the population residing within each county-average concentration range is shown on the left-hand margin of Figure 3-9. Given the number of counties with no data, the varying size of counties, and the non-uniform spacing of the monitors and population within each reporting county, this should only be taken as a rough estimate of the relationship between population and average ambient concentrations. As seen in Figure 3-9,Kern County, CA reported the highest 3-yr avg 24-h $PM_{2.5}$ concentration in excess of 20 $\mu g/m^3$. Average concentrations between 18 and 20 $\mu g/m^3$ were reported for several counties in the San Joaquin Valley and inland southern California as well as Jefferson County, AL containing Birmingham and Allegheny County, PA containing Pittsburgh.

[1] FRM-like refers to $PM_{2.5}$ concehntration data associated with the parameter code "88502 - Acceptable $PM_{2.5}$ AQI and Speciation Mass" in the AQS. These data were collected by continuous instruments which are not approved as FRM or FEM, and consequently EPA does not use these data for regulatory purposes. These data are denoted as "FRM-like" because state and local monitoring agencies have individually decided that the continuous instruments reporting these data have a degree of agreement with FRM/FEM methods that is sufficient in their opinion for the data to be used in public advisories regarding current air quality. In some cases, these data include statistical adjustments by the state/local monitoring agency based on one-time or ongoing correlation analysis with co-located FRM/FEM monitors, intended to improve the "FRM-likeness" of the continuous concentration data (e.g., Bortnick et al., 2002, 156285). State/local monitoring agency decisions about whether to adjust continuous $PM_{2.5}$ data and whether their raw or adjusted continuous $PM_{2.5}$ data should be associated with parameter code 88502 were informed by non-binding EPA guidance issued in 2006 (Technical Note on Reporting $PM_{2.5}$ Continuous Monitoring and Speciation Data to AQS http://www.epa.gov/ttn/amtic/files/ambient/pm25/datamang/contrept.pdf).

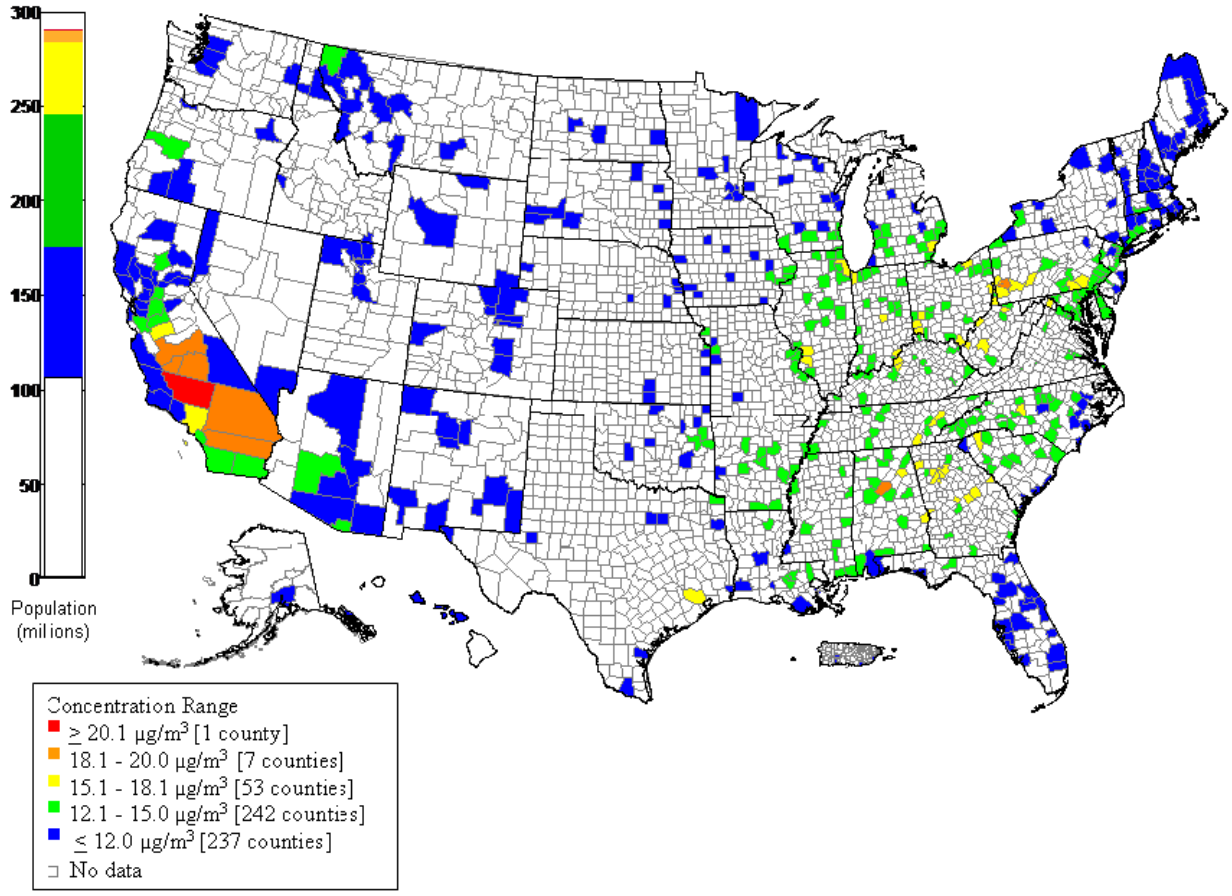


Figure 3-9. Three-yr avg 24-h $PM_{2.5}$ concentration by county derived from FRM or FRM-like data, 2005-2007. The population bar shows the number of people residing within counties that reported county-wide average concentrations within the specified ranges.

Table 3-8 contains summary statistics for $PM_{2.5}$ reported to AQS for the period 2005-2007. All 24-h FRM and 1-h FRM-like data reported to AQS and meeting the completeness criterion outlined above are included in the table. The table provides a distributional comparison between annual, 24-h and 1-h averaging times, calendar years (2005, 2006 and 2007) and seasons: winter (December-February), spring (March-May), summer (June-August), and fall (September-November). In addition, 15 CSAs/CBSAs were chosen for their importance in recent PM health studies, as described in Section 3.4, and have been included individually in the table.

The distribution of $PM_{2.5}$ annual averages (calculated without seasonal weighting and presented in Table 3-8) was generated from 2,382 individual annual means reported by 794 24-h FRM monitors reporting to AQS between 2005 and 2007. The mean of the annual averages was 12 µg/m^3, equivalent to the mean of the individual 24-h avg. The maximum annual average $PM_{2.5}$ concentration calculated from 24-h FRM data over these 3 yr was 23 µg/m^3 in Bakersfield, CA (AQS monitor ID: 060290010) during 2007. This site is located in the heavily populated portion of the San Joaquin Valley where air pollution frequently becomes trapped at ground level due to local topography. The distribution of the 24-h and 1-h avg, both generated from the same 1-h FRM-like data, are comparable up to the 90th percentile. The 1-h avg is 3 µg/m^3 higher than the 24-h avg at the 95th percentile and 7 µg/m^3 higher at the 99th percentile. This deviation between 1-h and 24-h averaging times is a result of short duration spikes in $PM_{2.5}$ mass lasting long enough to influence the upper percentiles of the 1-h distribution but not necessarily the 24-h avg distribution. Exceptional events were not removed from this data set and are responsible for at least some of the higher

concentrations observed. For example, the maximum 1-h reading of 828 µg/m^3 was reported by a monitor in Boise, ID (AQS monitor ID: 160010011) on July 4, 2007. Nine of the top 12 1-h $PM_{2.5}$ concentrations reported across the country also occurred on July 4th, implicating fireworks as the common source for these high values.

Table 3-8. $PM_{2.5}$ distributions derived from AQS data (concentration in µg/m^3).

	n	Mean	Percentiles									Max
			1	5	10	25	50	75	90	95	99	
2005-2007 $PM_{2.5}$ FOR DIFFERENT AVERAGING PERIODS												
Annual avg[a] (24-h FRM)	2,382	12	5	7	8	10	12	14	16	17	19	23
24-h avg (24-h FRM)	349,028	12	2	4	4	7	10	16	23	28	39	193
24-h avg (1-h FRM-like)	183,057	10	1	2	3	5	8	13	19	24	35	126
1-h avg (1-h FRM-like)	4,403,817	10	0	1	2	4	8	13	21	27	42	828
$PM_{2.5}$ ANNUAL AND SEASONAL STRATIFICATION USING 24-H AVG FRM DATA												
2005	114,346	13	2	4	5	7	11	17	24	30	42	133
2006	113,197	12	2	4	4	7	10	15	21	26	36	193
2007	121,485	12	2	4	4	7	10	16	22	27	40	145
Winter (December-February)	86,286	12	2	4	5	7	10	15	22	27	44	193
Spring (March-May)	88,489	11	2	3	4	6	9	14	20	24	33	145
Summer (June-August)	86,830	14	2	4	5	8	12	19	26	31	40	133
Fall (September-November)	87,423	12	2	3	4	6	10	15	22	26	39	126
2005-2007 $PM_{2.5}$ IN INDIVIDUAL CSAS/CBSAS USING 24-H AVG FRM DATA												
Atlanta	4,939	15	4	6	7	10	14	19	25	29	37	145
Birmingham	4,869	16	4	6	7	10	15	21	29	34	47	64
Boston	8,464	10	2	3	4	5	9	13	20	24	32	50
Chicago	10,308	14	3	4	6	8	13	18	25	31	42	65
Denver	4,192	9	2	3	4	6	8	10	14	18	31	61
Detroit	5,223	14	2	3	5	7	12	19	26	31	45	82
Houston	1,342	15	4	6	8	10	14	18	23	26	34	44
Los Angeles	6,600	15	3	5	6	9	13	18	25	32	50	133
New York	15,826	13	2	4	4	6	10	17	24	29	39	58
Philadelphia	7,541	14	3	4	5	8	12	18	25	30	38	63
Phoenix	1,634	10	2	3	4	6	9	12	17	21	32	77
Pittsburgh	5,783	16	3	5	6	9	13	20	29	36	52	101
Riverside	2,751	17	3	5	6	10	14	21	31	40	58	106
Seattle	1,297	9	2	3	3	4	7	10	20	29	43	68
St. Louis	6,887	14	3	5	6	9	13	18	24	29	40	50
All 15 CSAs/CBSAs	87,656	14	2	4	5	7	12	17	25	30	42	145
Not in the 15 CSAs/CBSAs	261,372	12	2	3	4	6	10	15	22	27	38	193

[a]Straight annual average without quarterly weighting.

The distribution of the 24-h FRM $PM_{2.5}$ data was similar across the 3 years (2005-2007) investigated. Summer (June-August) had the highest mean and median relative to other seasons, but only by a small margin. For the 99th percentile, winter (December-February) was slightly higher than the other seasons. This is consistent with wintertime stagnation events resulting in short-term elevated $PM_{2.5}$ concentrations. Of the 15 CSAs/CBSAs investigated, the highest mean of 24-h $PM_{2.5}$ concentrations was reported for Riverside (17 $\mu g/m^3$), Birmingham (16 $\mu g/m^3$) and Pittsburgh (16 $\mu g/m^3$); the lowest was reported for Denver (9 $\mu g/m^3$) and Seattle (9 $\mu g/m^3$).

$PM_{10-2.5}$

Since $PM_{10-2.5}$ is not routinely measured and reported to AQS, co-located PM_{10} and $PM_{2.5}$ measurements from the AQS network were used to investigate the spatial distribution in $PM_{10-2.5}$. Only low-volume FRM or FRM-like samplers were considered in calculating $PM_{10-2.5}$ to avoid complications with vastly different sampling protocols (e.g., flow rates) between the independent PM_{10} and $PM_{2.5}$ measurements. The same 11+ days per quarter completeness criterion discussed above was applied to the PM_{10} and $PM_{2.5}$ measurements. The $PM_{2.5}$ concentrations are reported to AQS at local conditions whereas the PM_{10} concentrations are reported at standard conditions. Therefore, prior to calculating $PM_{10-2.5}$ by subtraction, the PM_{10} AQS data were adjusted to local conditions on a daily basis using temperature and pressure measurements from the nearest National Weather Service station. Figure 3-10 shows the 3-yr mean of the 24-h $PM_{10-2.5}$ concentration by county across the U.S. for 2005-2007. There is considerably less coverage for $PM_{10-2.5}$ than for $PM_{2.5}$ or PM_{10} alone since only a small subset of PM monitors are co-located and low-volume. The 40 counties included in Figure 3-10 incorporate less than 5% of the U.S. population. Of the 3,225 U.S. counties, only 40 (1%) met the completeness and co-location criteria in all 3 yr (2005-2007), and therefore the available measurements do not provide sufficient information to adequately characterize regional-scale coarse PM spatial concentration distributions.

Table 3-9 contains summary statistics for $PM_{10-2.5}$ for the period 2005-2007 similar to those reported in Table 3-8 for $PM_{2.5}$. Only six of the 15 CSAs/CBSAs had sufficient data for inclusion in Table 3-9. Although fewer monitoring sites within these CSAs/CBSAs were used for $PM_{10-2.5}$ than for $PM_{2.5}$, Table 3-8 and Table 3-9 provide a rough comparison of the PM present in the fine and thoracic coarse modes for these six cities. The eastern cities including Atlanta, Boston, Chicago and New York all had a higher fraction in the fine mode with the greatest ratio of fine to thoracic coarse in Chicago (14 $\mu g/m^3$ $PM_{2.5,}$ 5 $\mu g/m^3$ $PM_{10-2.5,}$ ratio = 2.8). In contrast, Denver (9 $\mu g/m^3$ $PM_{2.5}$, 20 $\mu g/m^3$ $PM_{10-2.5}$, ratio = 0.45) and Phoenix (10 $\mu g/m^3$ $PM_{2.5}$, 22 $\mu g/m^3$ $PM_{10-2.5}$, ratio = 0.45) had a higher fraction in the thoracic coarse mode. Given the limited information available from AQS for $PM_{10-2.5}$ and the current NAAQS for PM_{10}, the next section characterizes the more prevalent PM_{10} data, acknowledging that PM_{10} incorporates both thoracic coarse and fine particles.

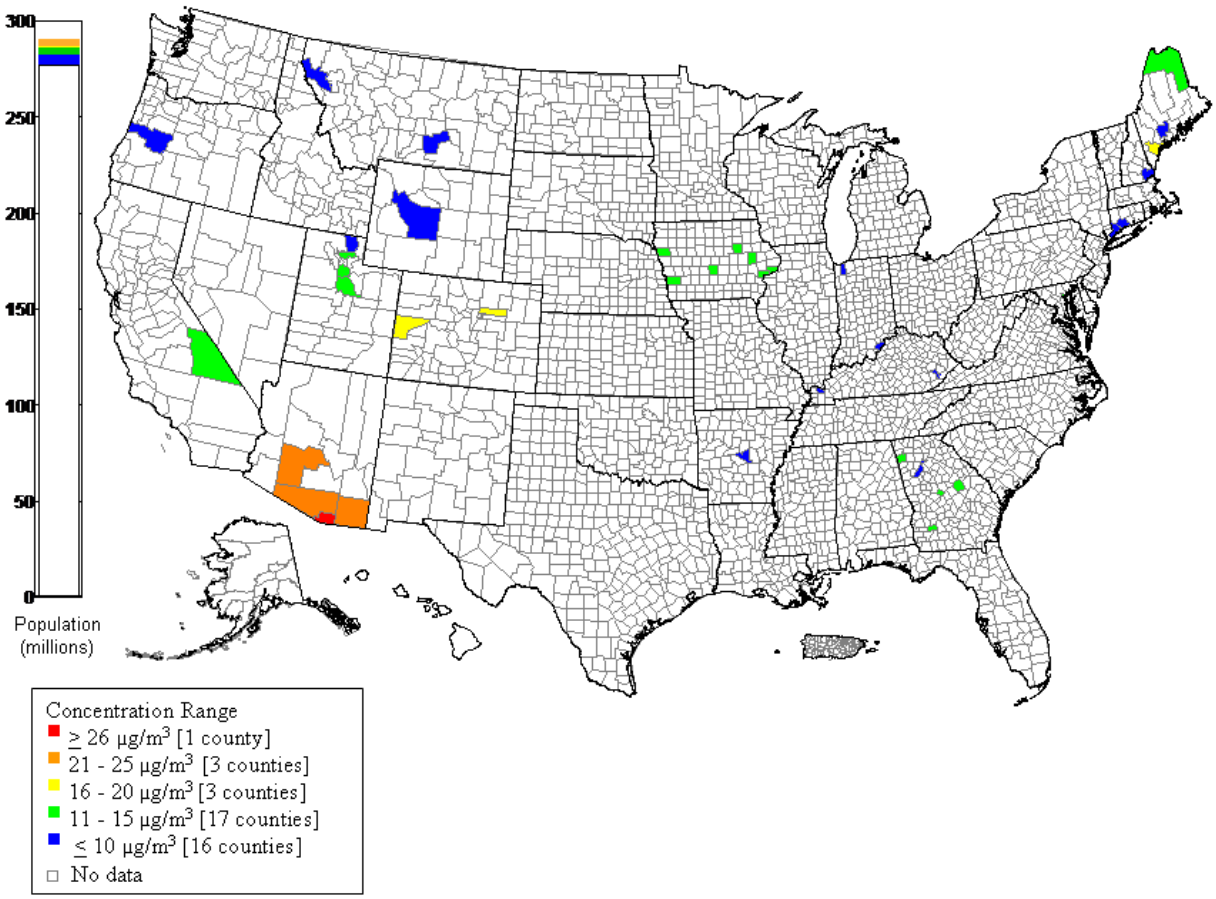


Figure 3-10. Three-yr avg 24-h $PM_{10-2.5}$ concentration by county derived from co-located low volume FRM PM_{10} and $PM_{2.5}$ monitors, 2005-2007. The population bar shows the number of people residing within counties that reported county-wide average concentrations within the specified ranges.

Table 3-9. $PM_{10-2.5}$ distributions derived from AQS data (concentration in µg/m^3).

	n	Mean	Percentiles									Max
			1	5	10	25	50	75	90	95	99	
2005-2007 $PM_{10-2.5}$ FOR DIFFERENT AVERAGING PERIODS												
Annual avg[a] (low volume FRM)	130	12	3	5	6	9	11	14	19	23	39	43
24-h avg (low volume FRM)	12,027	13	-3	1	2	6	10	17	26	33	54	246
$PM_{10-2.5}$ ANNUAL AND SEASONAL STRATIFICATION USING 24-H AVG LOW VOLUME FRM DATA												
2005	3,990	12	-5	0	2	5	10	16	26	33	52	246
2006	4,037	13	-2	1	2	6	10	17	27	34	56	182
2007	4,000	13	-2	1	3	6	11	18	26	33	56	148
Winter (December-February)	2,942	11	-5	-1	1	4	8	15	27	34	56	246
Spring (March-May)	3,088	13	-2	1	2	5	10	17	26	33	62	151
Summer (June-August)	2,968	14	-2	3	5	8	12	18	25	31	44	93
Fall (September-November)	3,029	14	-2	1	3	6	11	18	28	34	60	148
2005-2007 $PM_{10-2.5}$ IN INDIVIDUAL CSAS/CBSAS USING 24-H AVG LOW VOLUME FRM DATA[b]												
Atlanta	167	10	-4	1	2	5	9	13	18	21	30	46
Boston	340	7	-2	1	2	4	6	9	12	16	25	27
Chicago	161	5	-8	-4	-3	1	4	8	14	19	37	37
Denver	353	20	0	4	6	11	19	28	36	42	59	78
New York	338	9	-16	-2	1	5	8	12	17	23	34	56
Phoenix	163	22	-3	8	11	16	20	29	35	46	67	70
All 6 CSAs/CBSAs	1,522	12	-6	0	2	5	10	17	27	34	51	78
Not in the 6 CSAs/CBSAs	10,505	13	-2	1	2	6	10	17	26	33	56	246

[a]Straight annual average without quarterly weighting.
[b]No co-located low-volume FRM PM_{10} and FRM-like $PM_{2.5}$ monitors available for Birmingham, Detroit, Houston, Los Angeles, Philadelphia, Pittsburgh, Riverside, Seattle or St. Louis.

PM_{10}

Figure 3-11 shows the 3-yr mean of the 24-h PM_{10} concentrations by county across the U.S. for 2005-2007. Both FRM and FEM PM_{10} data reported to AQS were included and the same 11+ days per quarter completeness criterion described above for $PM_{2.5}$ was applied. The highest 3-yr avg for PM_{10} (>50 µg/m^3) occurred in inland southern California and the populous counties of southern Arizona and central New Mexico. Of the 3,225 U.S. counties, 676 (12%) contained PM_{10} data meeting the completeness criterion in all three years; these 676 counties incorporate approximately 43% of the U.S. population.

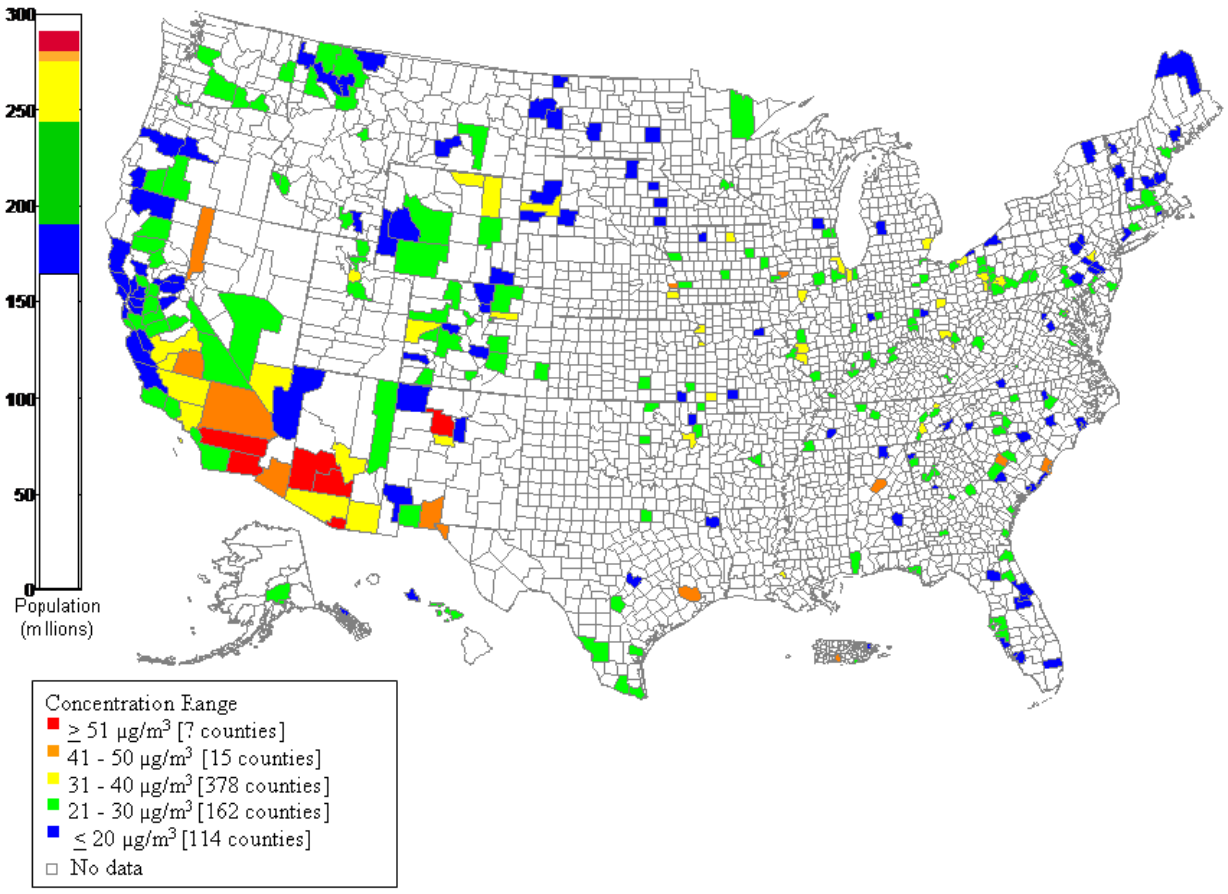


Figure 3-11. Three-yr avg 24-h PM_{10} concentration by county derived from FRM or FEM monitors, 2005-2007. The population bar shows the number of people residing within counties that reported county-wide average concentrations within the specified ranges.

Table 3-10 contains summary statistics for PM_{10} reported to AQS for the period 2005-2007. Both 24-h FRM and 1-h FEM data are included in the table. To facilitate a distributional comparison between averaging times, annual, 24-h and 1-h averaging times using the FRM and FEM data have been included separately in Table 3-10. As in the earlier tables, the data is also stratified by year and season and includes the 15 CSAs/CBSAs individually.

Table 3-10. PM_{10} distributions derived from AQS data (concentration in $\mu g/m^3$).

	n	Mean	Percentiles									Max
			1	5	10	25	50	75	90	95	99	
2005-2007 PM_{10} FOR DIFFERENT AVERAGING PERIODS												
Annual avg[a] (24-h FRM and 1-h FEM)	2022	25	10	14	16	19	23	28	35	44	60	85
24-h avg (24-h FRM and 1-h FEM)	326,675	26	3	6	9	14	21	32	46	59	97	8299
24-h avg (24-h FRM)	167,310	25	2	6	9	14	21	31	45	57	91	8299
24-h avg (1-h FEM)	156,931	26	4	7	9	14	21	32	48	62	105	979
1-h avg (1-h FEM)	3,767,533	27	1	4	6	11	19	32	51	69	145	8540
PM_{10} ANNUAL AND SEASONAL STRATIFICATION USING 24-H AVG FRM AND FEM DATA												
2005	107,524	25	2	6	9	13	21	31	46	58	93	1441
2006	109,505	26	3	6	9	13	21	32	46	59	101	8299
2007	109,646	26	4	7	9	14	21	32	47	60	99	2253
Winter (December-February)	80,959	23	2	5	7	11	17	27	42	57	99	8299
Spring (March-May)	82,772	25	2	6	8	13	20	31	45	58	96	2253
Summer (June-August)	81,351	29	6	10	12	18	25	35	49	60	92	1839
Fall (September-November)	81,593	26	3	7	9	14	21	32	48	62	102	1212
2005-2007 PM_{10} IN INDIVIDUAL CSAS/CBSAS USING 24-H AVG FRM AND FEM DATA												
Atlanta	1,868	24	6	9	11	16	23	31	39	44	57	108
Birmingham	5,478	34	6	9	12	19	28	43	64	82	120	241
Boston	1,412	17	2	5	7	10	15	22	30	36	50	58
Chicago	6,165	26	6	9	11	16	23	32	45	55	78	214
Denver	4,706	28	5	10	12	18	25	35	47	54	75	118
Detroit	1,407	30	7	10	12	18	26	38	53	64	81	182
Houston	1,397	31	7	10	12	17	23	34	56	80	137	248
Los Angeles	2,020	27	4	8	11	18	25	33	42	51	74	489
New York	514	19	2	6	7	11	17	25	35	40	51	83
Philadelphia	4,207	19	4	7	9	12	17	24	34	40	52	84
Phoenix	12,005	52	7	14	19	29	44	65	91	112	166	2253
Pittsburgh	12,677	24	4	7	9	13	19	31	45	57	83	157
Riverside	4,327	35	4	8	11	19	30	45	64	75	111	1212
Seattle	2,136	19	5	7	9	12	17	23	31	37	52	79
St. Louis	2,464	33	6	10	12	18	28	42	59	74	114	315
All 15 CSAs/CBSAs	62,783	32	5	8	10	16	25	39	60	77	120	2253
Not in the 15 CSAs/CBSAs	263,892	24	2	6	8	13	20	30	43	54	88	8299

[a]Straight annual average without quarterly weighting

The maximum annual average PM_{10} concentration calculated from 24-h FRM data over these three years was 85 $\mu g/m^3$ in Stanfield, AZ (AQS monitor ID: 040213008) during 2007. Stanfield is a small agricultural town (2007 population = 1074) approximately 64 km south of Phoenix and is in a region heavily influenced by windblown dust. Many of the maximum 24-h and 1-h avg PM_{10} concentrations in Table 3-10 exceed 1,000 $\mu g/m^3$, but these represent rare events given the much lower 99th percentiles. Exceptional events were not removed from this data set and are responsible for at least some of the higher concentrations observed.

The distribution of the 24-h FRM and FEM PM_{10} data was similar across the three years (2005-2007) investigated. Summer (June-August) had the highest mean and median relative to other seasons, consistent with $PM_{2.5}$ observations. Of the 15 CSAs/CBSAs investigated, the highest mean of 24-h PM_{10} concentrations was reported for Phoenix (52 $\mu g/m^3$), considerably higher than the means for the other CSAs/CBSAs investigated. The lowest was reported for Boston (17 $\mu g/m^3$) with New York, Philadelphia and Seattle only slightly higher (19 $\mu g/m^3$).

On average using the 2005-2007 data for $PM_{2.5}$ in Table 3-8 and PM_{10} in Table 3-10, the distribution between fine and coarse PM varies substantially by location. A larger fraction of PM mass is present in the thoracic coarse mode in Phoenix and Denver (3-yr mean $PM_{2.5}/PM_{10}$ ratios of 0.19 and 0.32, respectively). In contrast, a larger fraction is present in the fine mode in Philadelphia (0.74), New York (0.68) and Pittsburgh (0.67). Comparisons of $PM_{2.5}$ to PM_{10} as reported to AQS should be used with caution, however, since $PM_{2.5}$ concentrations are reported for local conditions while PM_{10} concentrations are converted to STP before reporting. Nevertheless, these findings are consistent with those in Table 3-9 for $PM_{10-2.5}$ in the subset of 6 cities with available co-located low-volume PM data that have been properly adjusted for temperature and pressure. These findings are also consistent with those reported in the 2004 PM AQCD (U.S. EPA, 2004, 056905) where ratios of $PM_{2.5}$ to PM_{10} were observed to be highest in the northeast (0.70), southeast (0.70), and industrial Midwest (0.70) and lower in the upper Midwest (0.53), northwest (0.50), southern California (0.47) and southwest (0.38).

UFPs

Little is known about the spatiotemporal distribution or composition of UFPs on a regional scale. New particle formation has been observed in environments ranging from relatively unpolluted marine and continental environments to polluted urban areas as an ongoing background process and during nucleation events (Kulmala et al., 2004, 089159). During nucleation events, which may last for several hours, UFP number concentrations can exceed 10^4 per cm^3 over distances of several hundred kilometers (Kulmala et al., 2004, 089159; Qian et al., 2007, 116435). These events occur throughout the year on 5-40% of days, depending on location (Qian et al., 2007, 116435). Cloud condensation nuclei, with diameters between ~10 and ~100 nm have been monitored for several years at a number of nonurban sites in the U.S. (http://cmdl.noaa.gov/aero/data/). Average particle number counts at these sites in the U.S. range from several hundred to several thousand per cm^3. The particles are formed by nucleation of atmospheric gases with additional contribution from primary emissions in these environments (Pierce and Adams, 2009, 191189).

In an urban setting, a large percentage of UFPs come from combustion-related emissions from mobile sources (Sioutas et al., 2005, 088428). UFP number concentrations drop off quickly with distance from the roadway (Levy et al., 2003, 052661; Reponen et al., 2003, 088425; Zhu et al., 2005, 157191), and therefore concentrations can be highly heterogeneous in the near-road environment depending on traffic, meteorological and topographic conditions (Baldauf et al., 2008, 190239). Studies characterizing spatial variability in UFPs are currently limited to a handful of close proximity locations and therefore are discussed in Sections 3.5.1.2 and 3.5.1.3 in the context of urban- and neighborhood-scale variability. Further elaboration on the composition of UFPs is included below.

PM Constituents

Only $PM_{2.5}$ is collected routinely at CSN network sites so the majority of this section on PM constituents is devoted to $PM_{2.5}$ composition. $PM_{10-2.5}$ and UFP composition is discussed to the extent possible below. Figure 3-12 through Figure 3-16 contain U.S. concentration maps for OC, EC, SO_4^{2-}, NO_3^-, and NH_4^+ mass from $PM_{2.5}$ measurements taken as part of the CSN network for the period 2005-2007. Data used in these figures are as reported to AQS: no correction was applied to OC for non-carbon mass and NO_3^- represents total particulate nitrate. Figure 3-12 shows regions of

high $PM_{2.5}$ OC mass concentration with annual average concentrations greater than 5 $\mu g/m^3$ in the western and the southeastern U.S. Concentrations at the western monitors peak in the fall and winter while those in the Southeast peak anywhere from spring through fall. The central and northeastern portions of the U.S. generally contain lower measured OC. Bell et al. (2007, 155683) present a similar map for estimated organic carbon mass (OCM) from 2000-2005 calculated by multiplying the blank corrected OC measurement by 1.4 to account for non-carbon mass. There are a range of estimates in the literature for suggested scaling factors (Turpin and Lim, 2001, 017093), depending predominantly on how highly oxygenated the aerosol is (Pang et al., 2006, 156012). Fresh PM, more common in urban regions, has undergone limited chemical transformation. As the aerosol is transported to rural regions, it becomes more oxygenated. Turpin and Lim (2001, 017093) recommended ratios of 1.6 ± 0.2 for urban and 2.1 ± 0.2 for non-urban aerosols. Estimates range from 1.6 to 2.6 for rural IMPROVE monitors (El-Zanan et al., 2005, 155764). Therefore, applying one correction factor of 1.4 across the entire U.S. will lead to an underestimate of the OCM in rural regions. Therefore, the OC data in Figure 3-12 is presented as measured with a national blank correction, but no adjustment to OCM.

Figure 3-13 contains a similar map for $PM_{2.5}$ EC mass concentration that exhibits smaller seasonal variability than OC, particularly in the eastern half of the U.S. There are isolated monitors spread throughout the country that measure high annual average EC concentrations. These EC 'hot spots' are primarily associated with larger metropolitan areas such as Los Angeles, Pittsburgh, and New York, but El Paso, TX, also reported high annual average EC concentrations (driven by a wintertime average concentration greater than 2 $\mu g/m^3$). In a similar analysis for EC by Bell et al. (2007, 155683) for 2000-2005 data, there were also high wintertime EC concentrations in eastern Kentucky and western Montana. These particular locations do not stand out in the 2005-2007 data in Figure 3-13.

Figure 3-14 contains a map for $PM_{2.5}$ SO_4^{2-} mass concentration which shows that SO_4^{2-} is more prevalent in the eastern U.S. owing to the strong west-to-east gradient in SO_2 emissions. This gradient is magnified in the summer months when more sunlight is available for photochemical formation of SO_4^{2-}. In contrast, $PM_{2.5}$ NO_3^- mass concentration in Figure 3-15 is highest in the west, particularly in California. There are also elevated concentrations of NO_3^- in the upper Midwest. The seasonal plots show generally higher NO_3^- in the wintertime as a result of temperature driven partitioning. Exceptions exist in Los Angeles and Riverside where high NO_3^- readings appear year-round. The $PM_{2.5}$ NH_4^+ mass concentration maps in Figure 3-16 shows spatial patterns related to both SO_4^{2-} and NO_3^- resulting from its presence in both $(NH_4)_2SO_4$ and NH_4NO_3. Figure A-31 through Figure A-36 in Annex A show similar U.S. concentration maps for $PM_{2.5}$ Cu, Fe, Ni, Pb, Se and V mass concentrations as measured by XRF. There is considerably less seasonal variation in the concentration profile for these metals than OC or the ions.

For the 15 metropolitan areas identified earlier, the contribution of the major component classes to total $PM_{2.5}$ mass was derived using the measured sulfate, adjusted NO_3^-, derived water, inferred carbonaceous mass approach (SANDWICH) (Frank, 2006, 098909). This approach uses the measured FRM $PM_{2.5}$ mass and co-located CSN chemical constituents to perform a mass balance-based estimation of the $PM_{2.5}$ mass fraction attributed to SO_4^{2-}, NO_3^-, EC, OCM, and crustal material. SO_4^{2-} and NO_3^- include associated NH_4^+ mass and estimated particle-bound water. Furthermore, NO_3^- is assumed to be fully neutralized as NH_4NO_3 and has been adjusted to represent the amount retained by the FRM monitor. EC is taken as measured, and the crustal component is derived from common oxides contained in the Earth's crust (Pettijohn, 1957, 156862), but can also include significant anthropogenic contributions, such as coal fly ash that are unrelated to soil resuspension. Finally, OCM is estimated using mass balance by subtracting the sum of all other constituents from the FRM $PM_{2.5}$ mass. The SANDWICH method takes into account passive collection of semi-volatile or handling-related mass on the FRM filters in the mass balance calculation. The magnitude of this artifact is assigned a nominal value of 0.5 $\mu g/m^3$, which is derived from limited analysis of FRM field blanks. Other constituents such as salt and other metallic oxides, however, are not included in these calculations and therefore the OCM fraction estimated by mass balance represents an upper bound on the FRM retained OCM. The calculations and assumptions that go into the SANDWICH method are discussed in detail in Frank (2006, 098909)with further information available on EPA's AirExplorer web site
http://www.epa.gov/cgi-bin/htmSQL/mxplorer/query_spe.hsql

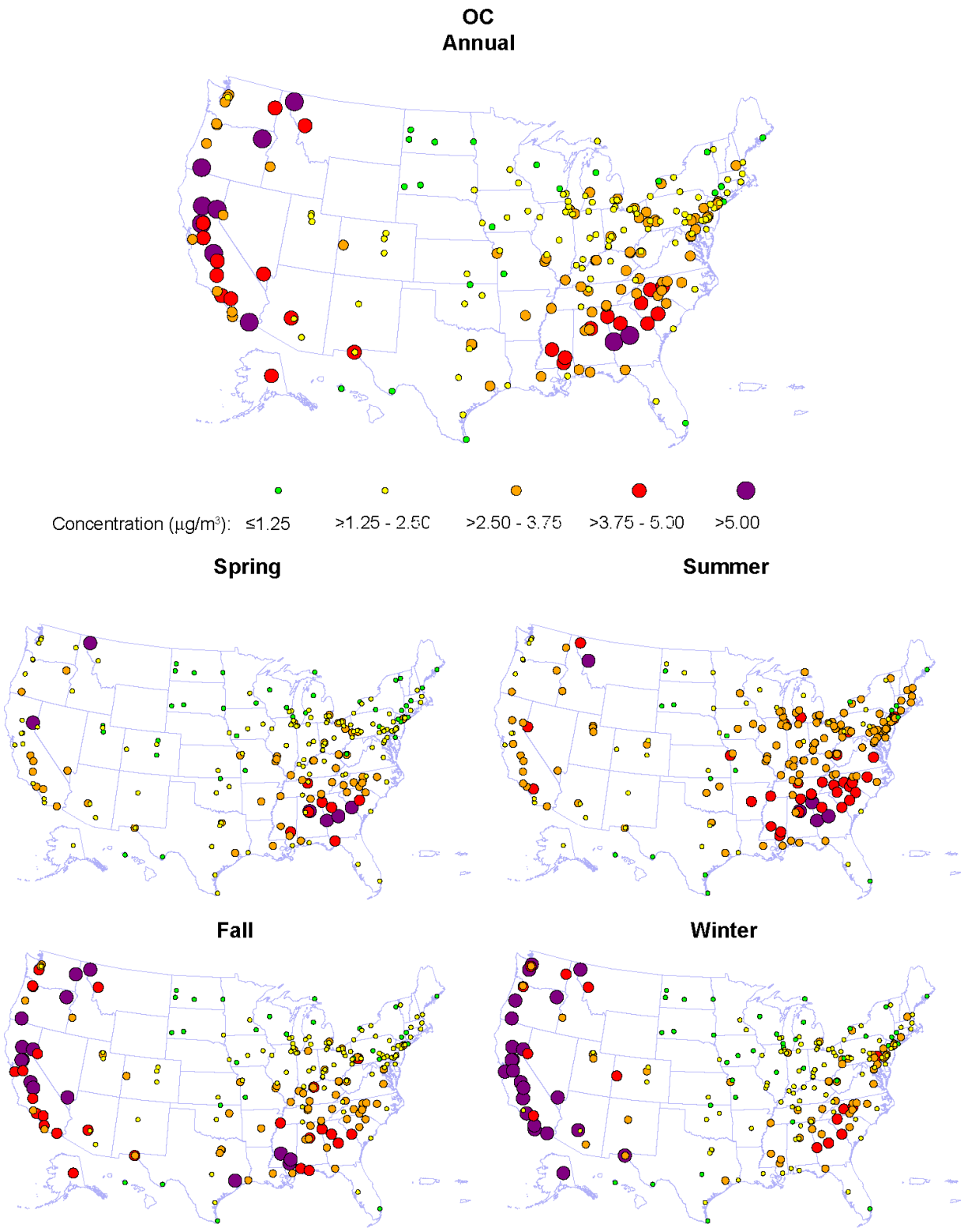


Figure 3-12. Three-yr avg 24-h $PM_{2.5}$ OC concentrations measured at CSN sites across the U.S., 2005-2007.

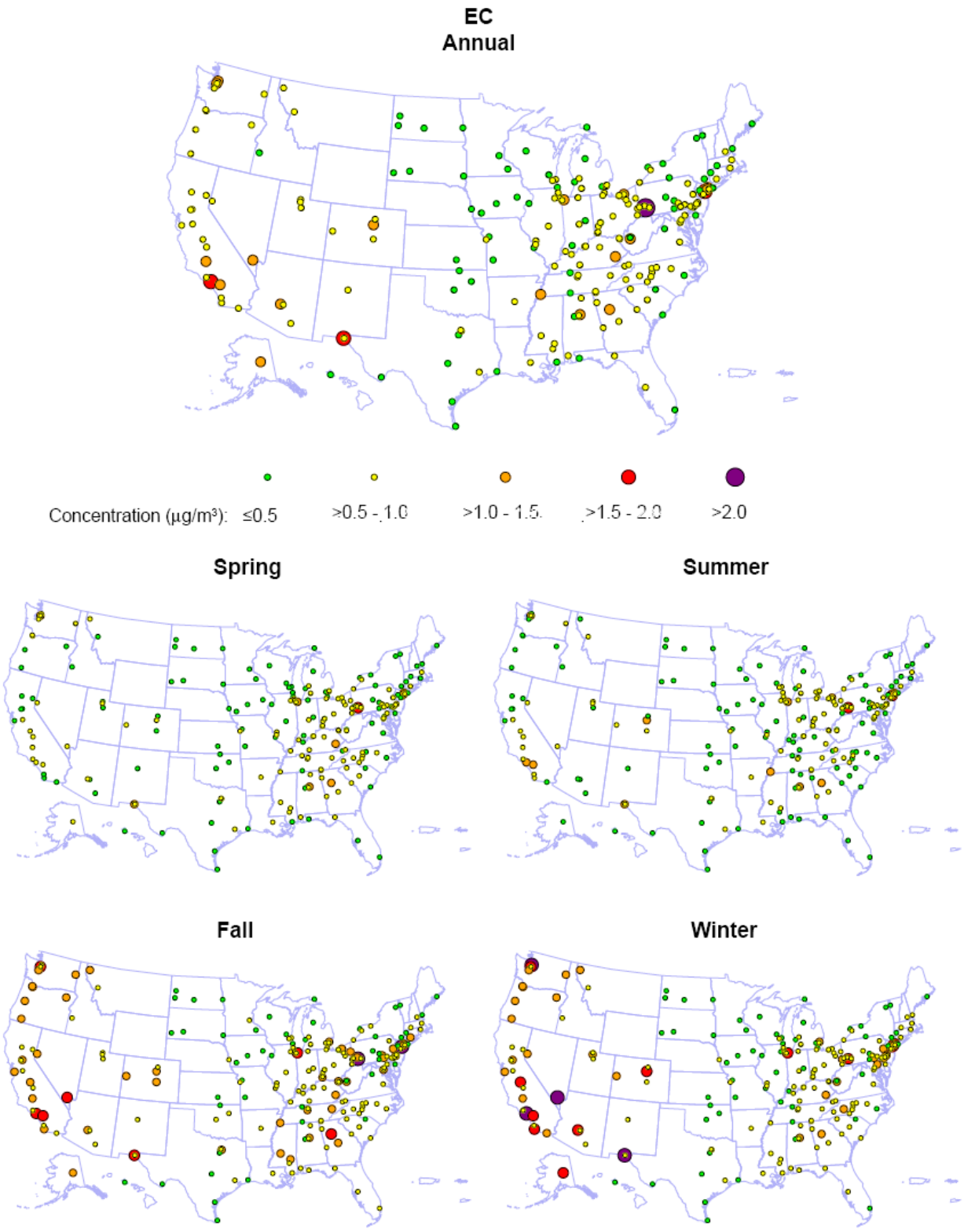


Figure 3-13. Three-yr avg 24-h $PM_{2.5}$ EC concentrations measured at CSN sites across the U.S., 2005-2007.

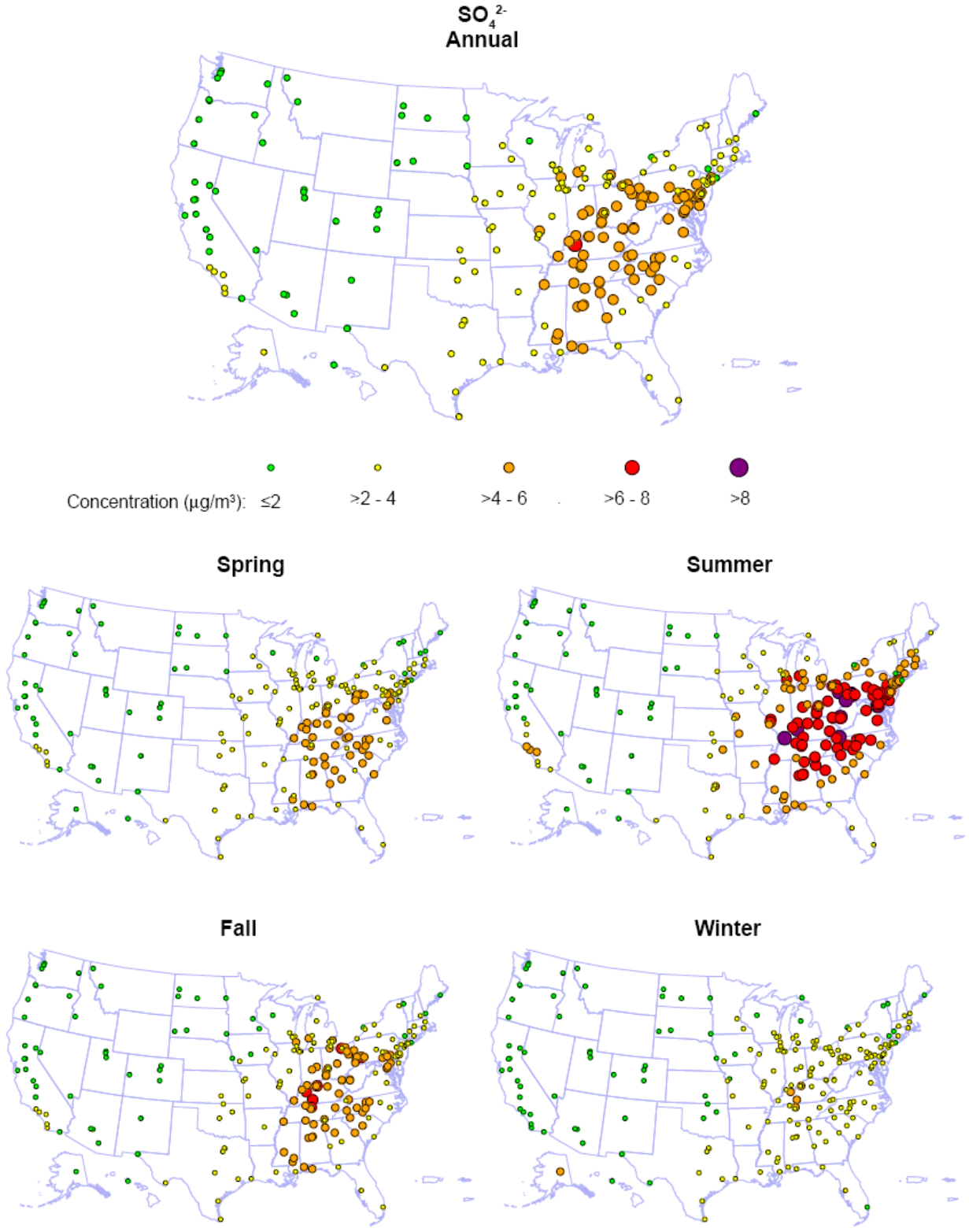


Figure 3-14. Three-yr avg 24-h $PM_{2.5}$ SO_4^{2-} concentrations measured at CSN sites across the U.S., 2005-2007.

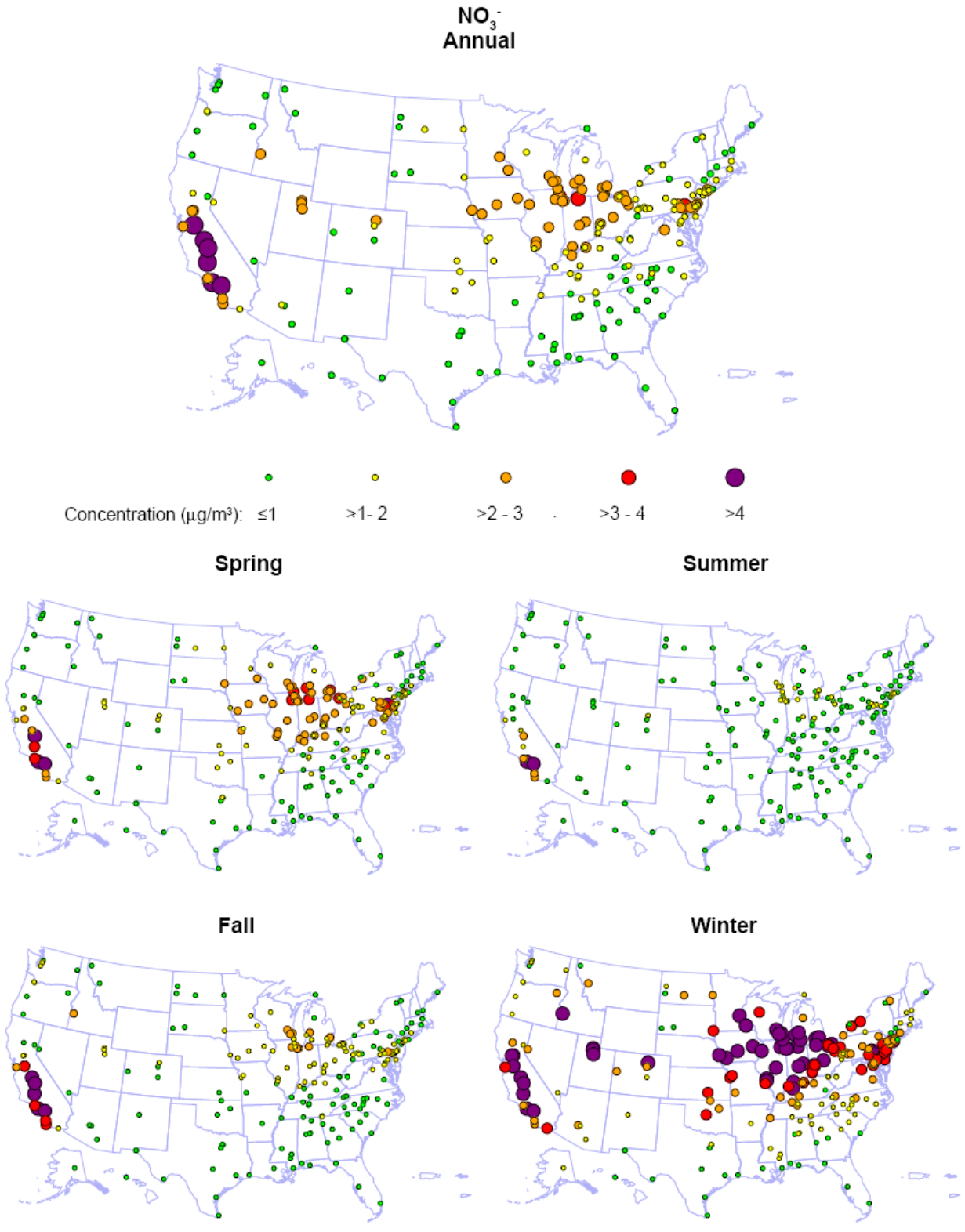


Figure 3-15. Three-yr avg 24-h $PM_{2.5}$ NO_3^- concentrations measured at CSN sites across the U.S., 2005-2007.

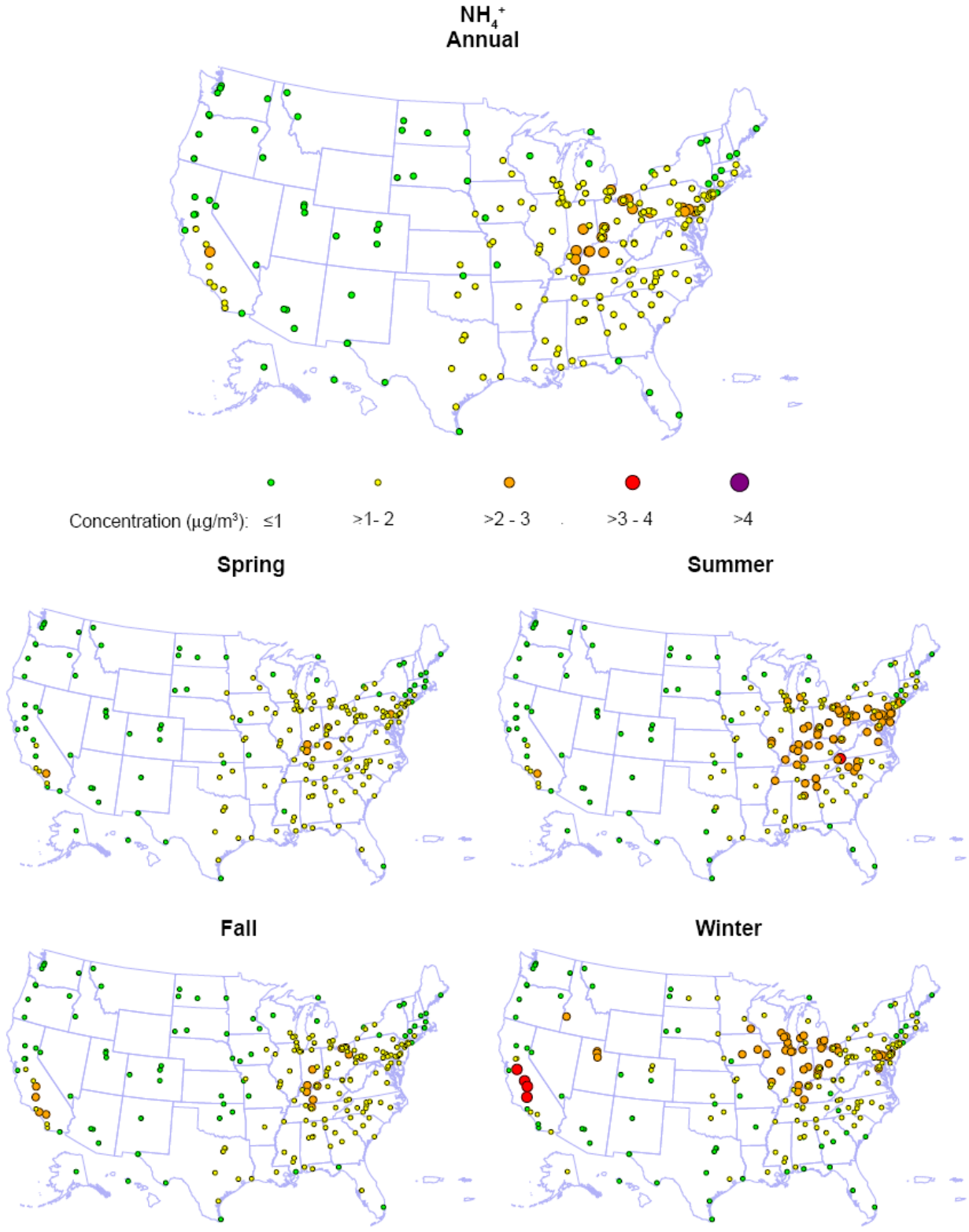


Figure 3-16. Three-yr avg 24-h $PM_{2.5}$ NH_4^+ concentrations measured at CSN sites across the U.S., 2005-2007.

Figure 3-17 shows the $PM_{2.5}$ compositional breakdown for the 15 CSAs/CBSAs. All available monitoring sites with co-located FRM $PM_{2.5}$ and CSN speciation data reporting in all four seasons for at least one calendar year from 2005-2007 were included. Furthermore, each season was required to contain five reported values for mass and the major $PM_{2.5}$ constituents. This resulted in a varying number of sites (ranging from one to seven, as indicated in the caption to Figure 3-17) used to create the averages shown in the figure. Variability in $PM_{2.5}$ composition within each CSA/CBSA where multiple monitors were available and trends in composition over time are discussed in subsequent sections.

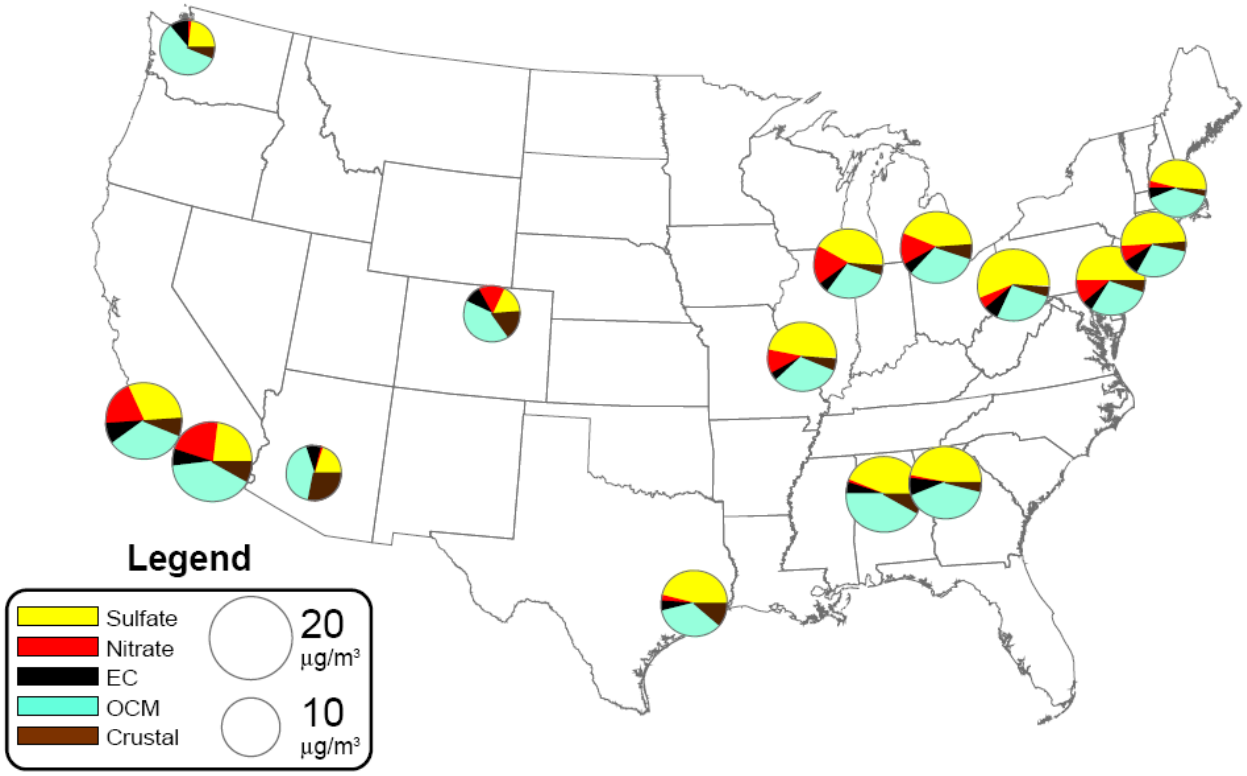


Figure 3-17. Three-yr avg $PM_{2.5}$ speciation estimates for 2005-2007 derived using the SANDWICH method. For the following 15 CSAs/CBSAs (with the number of sites per CSA/CBSA listed in parenthesis): Atlanta, GA (1); Birmingham, AL (3); Boston, MA (4); Chicago, IL (7); Denver, CO (2); Detroit, MI (4); Houston, TX (1); Los Angeles, CA (1); New York City, NY (7); Philadelphia, PA (6); Phoenix, AZ (2); Pittsburgh, PA (4); Riverside, CA (1); Seattle, WA (4); and St. Louis, MO (3). SO_4^{2-} and NO_3^- estimates include NH_4^+ and particle bound water and the circle area is scaled in proportion to FRM $PM_{2.5}$ mass as indicated in the legend.

On an annual average basis, SO_4^{2-} is a dominant PM component in the eastern U.S. cities. For the presented cities, this includes everything east of Houston where the SO_4^{2-} fraction of $PM_{2.5}$ ranges from 42% in Chicago to 56% in Pittsburgh on an annual average basis. OCM is the next largest component in the east ranging from 27% in Pittsburgh to 42% in Birmingham. In the west, OCM is the largest constituent on an annual basis, ranging from 34% in Los Angeles to 58% in Seattle. SO_4^{2-}, NO_3^- and crustal material are also important in many of the included western cities. In the west, fractional SO_4^{2-} ranges from 18% in Denver to 32% in Los Angeles while fractional NO_3^- is relatively large in Riverside (22%), Los Angeles (19%) and Denver (15%) and less important on an annual basis in Phoenix (1%) and Seattle (2%). Crustal material is particularly prevalent in Phoenix (28%). EC makes up a smaller fraction of the $PM_{2.5}$ (4-11%), but it is consistently present in all included cities regardless of region.

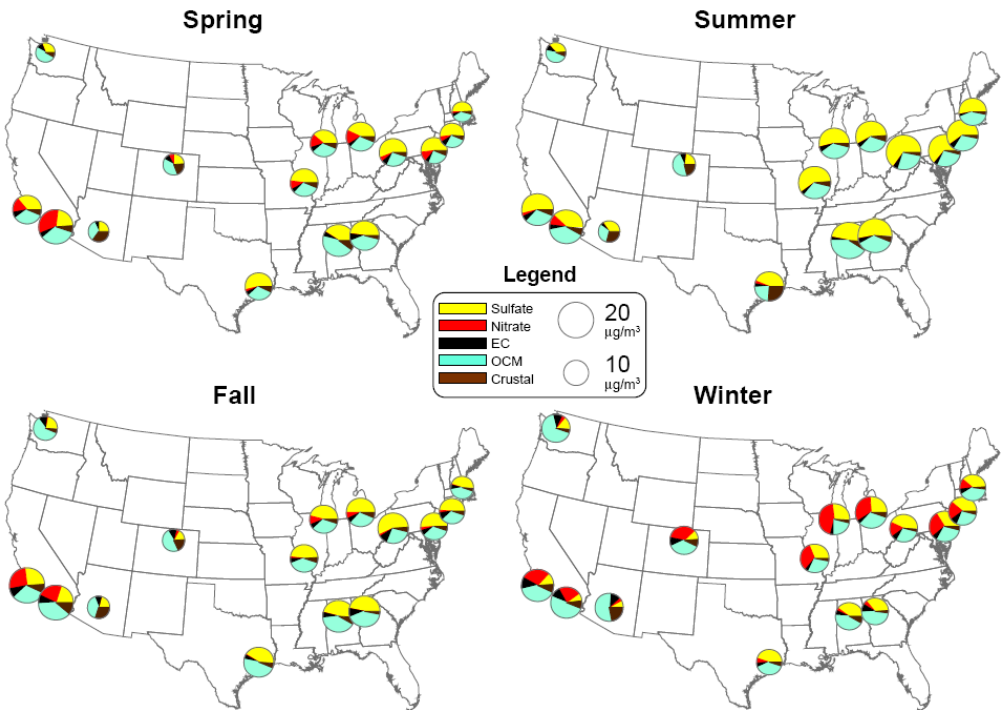


Figure 3-18. Seasonally-stratified 3-yr avg $PM_{2.5}$ speciation estimates for 2005-2007 derived using the SANDWICH method. For the following 15 CSAs/CBSAs: Atlanta, GA; Birmingham, AL; Boston, MA; Chicago, IL; Denver, CO; Detroit, MI; Houston, TX; Los Angeles, CA; New York City, NY; Philadelphia, PA; Phoenix, AZ; Pittsburgh, PA; Riverside, CA; Seattle, WA; and St. Louis, MO. SO_4^{2-} and NO_3^- estimates include NH_4^+ and particle bound water and the circle area is scaled in proportion to FRM $PM_{2.5}$ mass as indicated in the legend.

The seasonal variation in $PM_{2.5}$ composition across the 15 CSAs/CBSAs is shown in Figure 3-18 where the seasons are defined as before. SO_4^{2-} dominates in most metropolitan areas in the summertime, while NO_3^- becomes important in the colder wintertime months. Notable exceptions include Denver, Phoenix, Riverside, and Seattle where summertime SO_4^{2-} makes up a smaller fraction of the $PM_{2.5}$ mass compared with other regions. Likewise, NO_3^- is less pronounced in the wintertime in Atlanta, Birmingham, Houston, Phoenix, and Seattle compared with other regions. Los Angeles and Riverside exhibit elevated NO_3^- from fall through spring. Crustal material is a substantial summertime component in Houston (26%), and is generally low elsewhere in the East in all seasons. In the West, crustal material represents a substantial component year-round in Phoenix and Denver.

The only PM size fraction routinely collected at CSN network sites is $PM_{2.5}$, resulting in less available information on speciated $PM_{10-2.5}$. Edgerton et al. (2005, 088686; 2009, 180385) published speciated measurements for $PM_{2.5}$ and $PM_{10-2.5}$ obtained using dichotomous samplers from four locations included in the Southeastern Aerosol Research and Characterization (SEARCH) study: Yorkville, GA, Centreville, AL, Birmingham, AL and Atlanta, GA. Samples were collected between 1999 and 2003 on a 1-in-3 day or 1-in-6 day schedule, depending on site. Speciated measurements for both $PM_{2.5}$ and $PM_{10-2.5}$ included SO_4^{2-}, NO_3^-, NH_4^+, and major metal oxides (MMO). In addition, OC and either black carbon (BC) or EC were reported for $PM_{2.5}$ over the entire study period and for $PM_{10-2.5}$ for a subset of samples extending from April 2003 to April 2004.

For the Atlanta and Birmingham SEARCH sites, the annual average NO_3^- mass fraction was approximately equal for $PM_{2.5}$ (5.6% and 5.0%, respectively, for Atlanta and Birmingham) and $PM_{10-2.5}$ (4.9% and 3.3%). Likewise, the OC mass fraction was approximately equal for $PM_{2.5}$ (26% and 26%) and $PM_{10-2.5}$ (24% and 27%). MMO contributed an order of magnitude smaller mass fraction to $PM_{2.5}$ (2.6% and 4.7%) than $PM_{10-2.5}$ (38% and 35%). In contrast, SO_4^{2-} contributed an order of

magnitude greater mass fraction to $PM_{2.5}$ (25.1% and 24.1%) than $PM_{10-2.5}$ (2.8 and 2.1%). BC also contributed a larger mass fraction of $PM_{2.5}$ (8.6% and 10.5%) than EC did for $PM_{10-2.5}$ (2.9% and 2.4%). Based on these findings, MMO are present primarily in the thoracic coarse mode, while SO_4^{2-} and EC/BC are present primarily in the fine mode. NO_3^- and OC are present in both modes in approximately equal mass fractions. These results are specific to Atlanta and Birmingham and may not represent other geographic regions.

Information about the composition of ambient UFPs directly emitted by sources is still sparse compared to that for the larger size modes. However, their composition is expected to reflect that of their sources. As noted in Section 3.3 (and references therein), particle number emissions from motor vehicles are dominantly in the UF size range. The composition of gasoline vehicle emissions consists mainly of a mix of OC, EC and small quantities of trace metals and sulfates, with OC constituting anywhere from 26-88% of PM. Diesel PM is generally comprised of an EC and trace metal ash core onto which organic material and nucleation-mode SO_4^{2-}condense. With the introduction of new diesel emissions standards in 2007, total emissions have decreased dramatically, particularly for carbon. In areas where atmospheric nucleation is the dominant source of UFPs, sulfate along with ammonium, and secondary organic compounds are the likely major components of UFPs.

In a study conducted at several urban sites in Southern California, Cass et al. (2000, 020680) found that the composition of UFPs ranged from 32-67% OC, 3.5-17.5% EC, 1-18% SO_4^{2-}, 0-19% NO_3^-, 0-9% NH_4^+, 1-26% metal oxides, 0-2% Na, and 0-2% Cl. Thus carbon, in various forms, was found to be the major contributor to the mass of UFPs. However, ammonium was found to contribute 33% of the mass of UFPs at one site in Riverside. Fe was the most abundant metal found in the UFPs. Chung et al. (2001, 017105) found that carbon was the major component of the mass of UFPs in a study conducted during January of 1999 in Bakersfield, CA. However, in the study of Chung et al. (2001, 017105), the contribution of carbonaceous species (OC and EC; typically 20-30%) was much lower than that found in the cities in Southern California. They found that Ca was the dominant cation, accounting for about 20% of the mass of UFPs in their samples. Sizable contributions from Si (0-4%) and Al (6-14%) were also found. MOUDIs are used to collect size-segregated filter samples in the UFP compositional analyses described above. Coarse particle bounce is a concern when using MOUDIs and further studies, including scanning electron microscopy, may be needed to quantify the effect of this sampling artifact on UFP compositional analyses.

Herner et al. (2005, 135983) reported a gradual increase in OC mass fraction as particle size decreases from 1 µm (20% OC) to 100 nm (80% OC) in the San Joaquin Valley of California. Sardar et al. (2005, 180086) found OC to be the major component of UFPs at four locations in California, with higher OC mass fraction in the wintertime relative to summertime. EC and SO_4^{2-} were also present in the UFP samples, but at much smaller mass fractions. EC was present year-round, whereas SO_4^{2-} had a summertime increase. More detailed chemical characterization of the OC fraction of ambient UFPs is extremely limited, but recent studies have identified specific organic molecular markers affiliated with motor vehicle emissions including hopanes and PAHs (Fine et al., 2004, 141283; Ning et al., 2007, 156809; Phuleria et al., 2007, 117816).

As noted in the 2004 PM AQCD (U.S. EPA, 2004, 056905), primary biological aerosol particles (PBAP), which include microorganisms, fragments of living things, and organic compounds of miscellaneous origin in surface deposits on filters, are not distinguishable in analyses of total OC. A clear distinction should be made between PBAP and primary OC that is produced by organisms (e.g., waxes coating the surfaces of organisms) and precursors to secondary OC such as isoprene and terpenes. Indeed, the fields of view of many photomicrographs of PM samples obtained by scanning electron microscopy are often dominated by large numbers of pollen spores, plant and insect fragments, and microorganisms. Bioaerosols such as pollen, fungal spores, and most bacteria are expected to be found mainly in the coarse size fraction (see Figure 3-2 for an illustrative example of a pollen particle). However, allergens from pollens can also be found in respirable particles (Edgerton et al., 2009, 180385; Taylor, 2002, 025693). Matthias-Maser et al. (2000, 155972) summarized information about the size distribution of PBAP in and around Mainz, Germany in what is perhaps the most complete study of this sort. Matthias-Maser found that PBAP constituted up to 30% of total particle number and volume in the approximate size range from 0.35-50 µm on an annual basis. Additionally, whereas the contribution of PBAP to the total aerosol volume did not change appreciably with season, the contribution of PBAP to total particle number ranged from about 10% in December and March to about 25% in June and October. Bauer et al. (2008, 189986) measured contributions of fungal spores to OC at an urban and a suburban site in Vienna, Austria in spring and summer. Fungal spores at the suburban site contributed on average 10% to OC in PM_{10}

and 5% at the urban site. At the suburban site, in summer, fungal spores accounted on average for 60% of the OC (0.56 µg/m^3) in $PM_{10-2.1}$ (2.6 µg/m^3). The contribution to $PM_{2.1}$ was estimated to be about 10% that in $PM_{10-2.1}$. Womiloju et al. (2003, 179954) estimated that fungal spores contribute 14-22% of OC in $PM_{2.5}$ in and around Toronto.

Edgerton et al. (2009, 180385) found that PBAP contributed 60-70% of OC (average ~1.7 µg/m^3) in $PM_{10-2.5}$ at an urban and a rural site in Alabama in fall of 2000 and spring of 2001. The percentage contributions were similar at both sites and higher concentrations were found in spring than in fall. Although results for the U.S. are more limited, they are broadly consistent with the results of the other studies in illustrating the importance of PBAP, at least for fungal spores in OC.

3.5.1.2. Urban-Scale Variability

$PM_{2.5}$

Data from the 15 CSAs/CBSAs were used to investigate urban-scale variability in PM reported to AQS. $PM_{2.5}$ has a longer residence time in the atmosphere compared to $PM_{10-2.5}$ resulting from a slower V_d. As a result, $PM_{2.5}$ exhibits increased spatial homogeneity with relatively less localized influence from point sources. Maps of $PM_{2.5}$ monitor locations and box plots of seasonal $PM_{2.5}$ mass concentration data are provided for Boston (Figure 3-19 and Figure 3-20), Pittsburgh (Figure 3-21 and Figure 3-22), and Los Angeles (Figure 3-23 and Figure 3-24). Figures A-37 through A-80 in Annex A contain similar information for all 15 CSAs/CBSAs under investigation. With very few exceptions, the $PM_{2.5}$ concentration is quite uniformly distributed across the monitors. Los Angeles has one monitor (Site I) that reported noticeably less $PM_{2.5}$ in all four seasons than the rest of the monitors in the region. This monitor is located at Lancaster CA, separated from the rest of the Los Angeles region by the San Gabriel Mountains. In general, however, $PM_{2.5}$ varies approximately the same magnitude between monitors as it does between seasons for the 15 selected cities.

Table 3-11 through Table 3-13 contain pair-wise monitor site comparison statistics for $PM_{2.5}$ in Boston, Pittsburgh, and Los Angeles, respectively. Tables A-20 through A-34 in Annex A contain the same statistics for $PM_{2.5}$ measured within all 15 of the CSAs/CBSAs investigated. Comparison statistics shown include the Pearson correlation coefficient (R), the 90th percentile of the absolute difference in concentrations (P90), the coefficient of divergence (COD) and the number of paired observations (n). The COD provides an indication of the variability across the monitoring sites in each CSA/CBSA and is defined as follows:

$$COD_{jk} = \sqrt{\frac{1}{p}\sum_{i=1}^{p}\left(\frac{X_{ij} - X_{ik}}{X_{ij} + X_{ik}}\right)^2}$$

Equation 3-2

where X_{ij} and X_{ik} represent observed concentrations averaged over some measurement averaging period i (hourly, daily, etc.) at sites *j* and *k*, and *p* is the number of paired observations. A COD of 0 indicates there are no differences between concentrations at paired sites (spatial homogeneity), while a COD approaching 1 indicates extreme spatial heterogeneity.

Temporal correlations between 24-h $PM_{2.5}$ concentrations in Boston range from 0.61 to 0.97 in Table 3-11. The lowest correlation in this CSA was between Site A located in Fall River, MA, 1 km from the Narragansett Bay and Site L located in Nashua, NH, on the bank of the Merrimack River, 120 km north. The highest correlation was between Sites P and R, located less than a kilometer apart in Providence, RI.

In Pittsburgh, 24-h $PM_{2.5}$ correlations range from 0.65 to 0.97. The lowest correlation in this CSA was between Sites B and D, located diametrically opposite downtown Pittsburgh and 33 km apart. The highest correlation was for Sites K and D, located 21 km apart and both west of downtown. The prevailing wind in Pittsburgh is from the west, which explains the higher correlation between the two upwind sites.

In Los Angeles, 24-h $PM_{2.5}$ correlations range from 0.21 to 0.96. The lowest correlation was between Sites I and J located 123 km apart and separated by the San Gabriel Mountains as discussed

earlier. The highest correlation was for sites G and H, located 3.7 km apart and both in Long Beach, CA. Therefore, while distance between monitors plays an important role in how well any two monitors correlate, other factors such as meteorology and topography can be important as well.

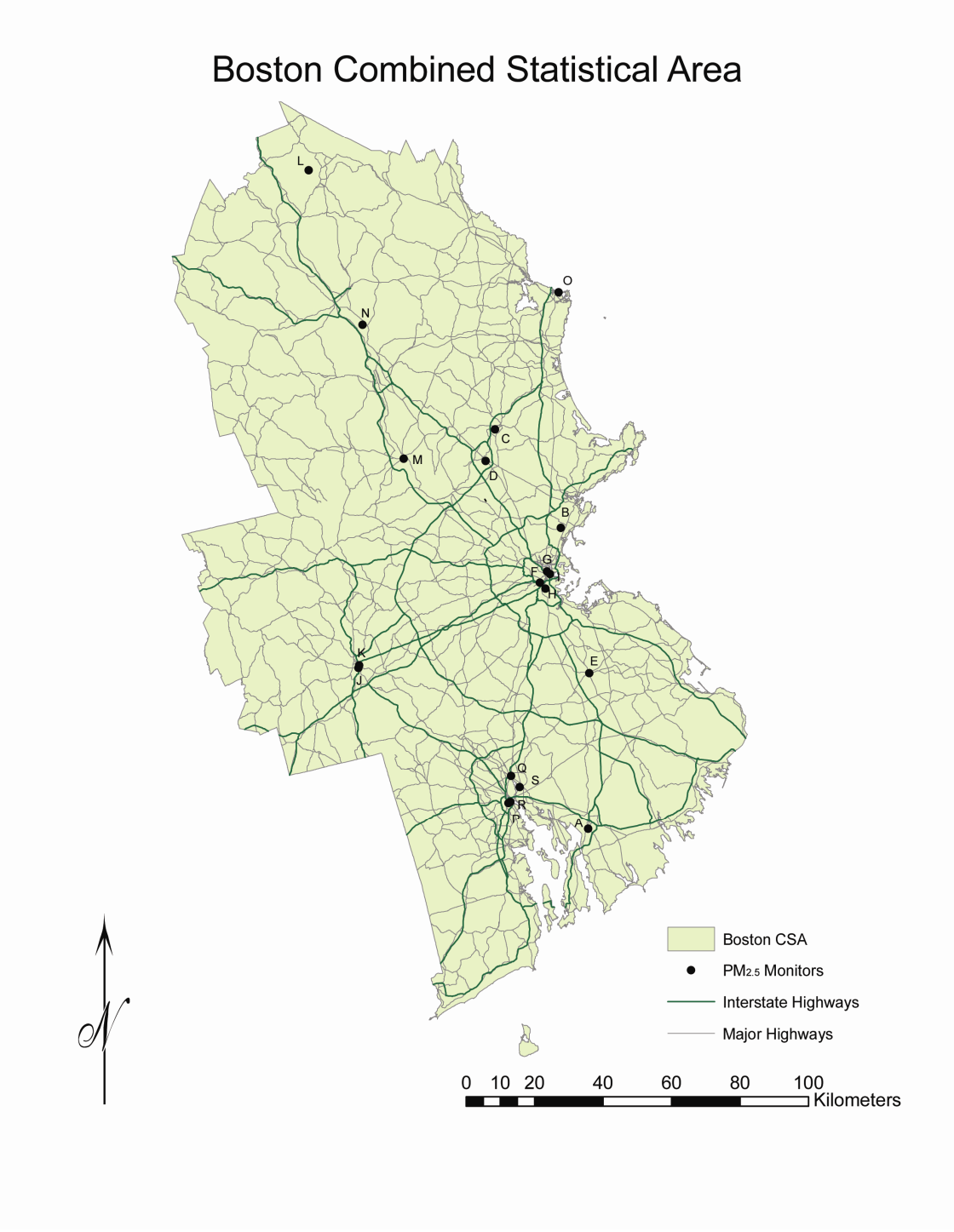


Figure 3-19. Locations of $PM_{2.5}$ monitors and major highways, Boston, MA.

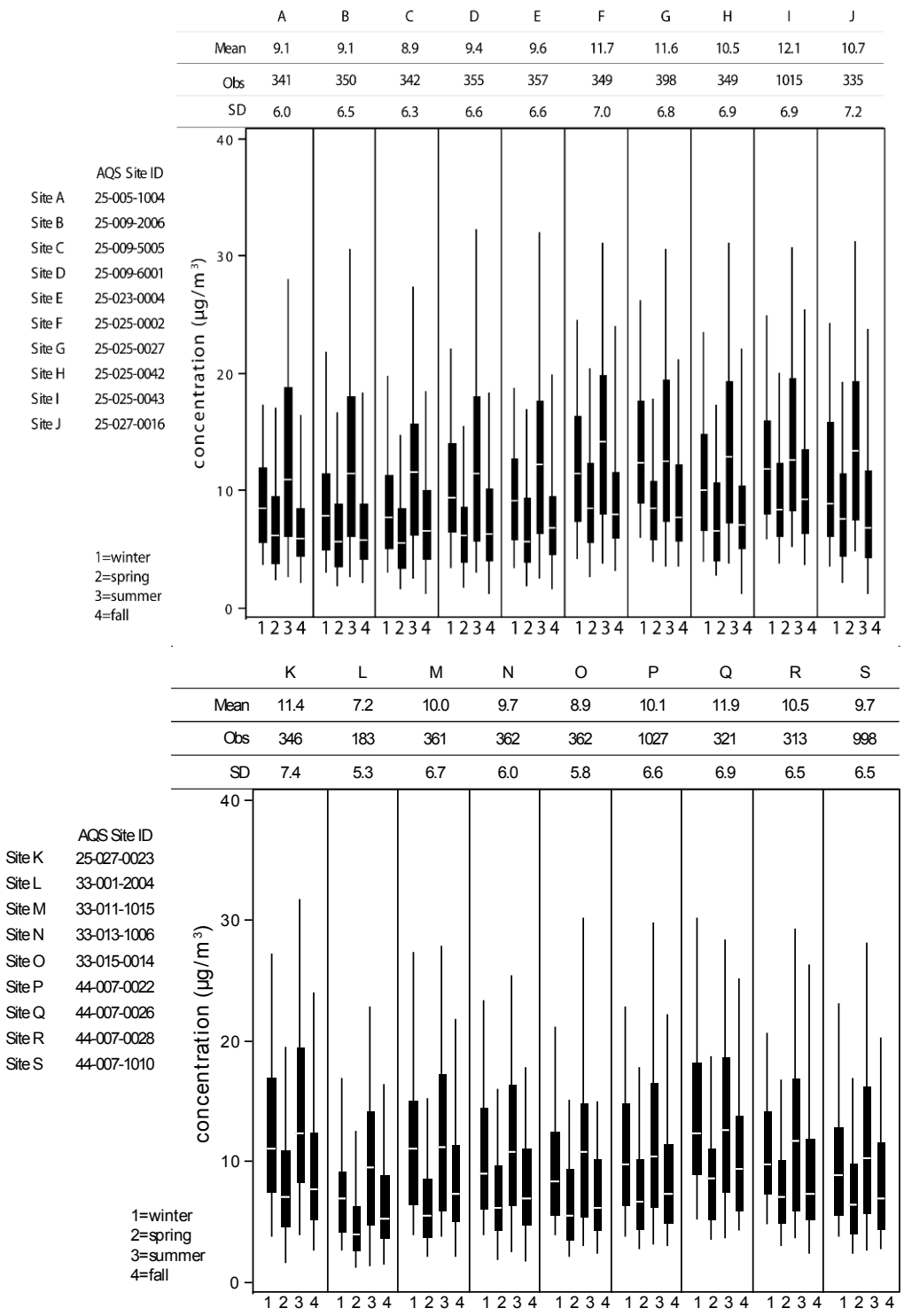


Figure 3-20. Seasonal distribution of 24-h avg $PM_{2.5}$ concentrations by site for Boston, MA, 2005-2007. Box plots show the median and interquartile range with whiskers extending to the 5th and 95th percentiles at each site during (1) winter (December-February), (2) spring (March-May), (3) summer (June-August) and (4) fall (September-November).

Table 3-11. Inter-sampler comparison statistics for each pair of 24-h $PM_{2.5}$ monitors reporting to AQS for Boston, MA.

Site	A	B	C	D	E	F	G	H	I	J
A	1.00	0.80	0.77	0.71	0.84	0.79	0.78	0.79	0.79	0.77
	(0.0, 0.00)	(6.6, 0.21)	(6.2, 0.22)	(6.9, 0.23)	(4.8, 0.19)	(8.1, 0.23)	(7.7, 0.24)	(6.8, 0.22)	(7.9, 0.25)	(7.5, 0.24)
	341	326	318	323	329	318	319	325	338	310
B		1.00	0.92	0.87	0.87	0.90	0.90	0.90	0.90	0.85
		(0.0, 0.00)	(4.1, 0.17)	(4.1, 0.18)	(4.7, 0.19)	(6.3, 0.21)	(6.2, 0.23)	(4.9, 0.19)	(7.1, 0.26)	(5.5, 0.21)
		350	328	331	339	326	323	333	343	317
C			1.00	0.90	0.85	0.90	0.89	0.90	0.88	0.86
			(0.0, 0.00)	(3.5, 0.17)	(5.3, 0.21)	(6.3, 0.23)	(6.3, 0.24)	(5.0, 0.20)	(6.8, 0.26)	(6.2, 0.21)
			342	321	331	316	318	326	336	311
D				1.00	0.80	0.88	0.88	0.86	0.86	0.87
	LEGEND			(0.0, 0.00)	(5.6, 0.20)	(5.8, 0.21)	(5.8, 0.22)	(4.6, 0.19)	(7.0, 0.26)	(5.8, 0.19)
	Pearson R			355	336	324	329	332	345	313
E	**(P90, COD)**				1.00	0.90	0.90	0.89	0.87	0.87
	n				(0.0, 0.00)	(5.9, 0.19)	(5.8, 0.21)	(5.0, 0.19)	(6.9, 0.24)	(5.4, 0.20)
					357	330	333	340	350	322
F						1.00	0.94	0.94	0.92	0.92
						(0.0, 0.00)	(3.8, 0.14)	(3.5, 0.15)	(4.5, 0.17)	(5.4, 0.18)
						349	324	324	339	310
G							1.00	0.94	0.94	0.89
							(0.0, 0.00)	(4.0, 0.16)	(4.3, 0.15)	(5.7, 0.20)
							398	325	338	308
H								1.00	0.93	0.89
								(0.0, 0.00)	(4.7, 0.19)	(5.0, 0.17)
								349	342	318
I									1.00	0.86
									(0.0, 0.00)	(6.9, 0.23)
									1015	330
J										1.00
										(0.0, 0.00)
										335

Site	K	L	M	N	O	P	Q	R	S
A	0.77	0.61	0.71	0.68	0.73	0.87	0.81	0.85	0.86
	(8.1, 0.23)	(8.3, 0.29)	(8.0, 0.23)	(7.9, 0.23)	(7.0, 0.22)	(5.3, 0.18)	(7.2, 0.23)	(5.6, 0.20)	(5.2, 0.18)
	320	173	324	334	331	326	292	285	306
B	0.86	0.80	0.87	0.83	0.88	0.86	0.80	0.85	0.85
	(6.6, 0.21)	(6.2, 0.23)	(5.3, 0.19)	(6.0, 0.21)	(4.7, 0.18)	(5.6, 0.19)	(7.9, 0.26)	(5.7, 0.21)	(6.0, 0.19)
	329	175	331	341	336	335	300	288	314
C	0.86	0.89	0.93	0.90	0.93	0.83	0.79	0.81	0.82
	(6.9, 0.21)	(4.8, 0.23)	(4.4, 0.17)	(4.6, 0.19)	(3.8, 0.18)	(5.9, 0.21)	(7.8, 0.26)	(6.2, 0.23)	(6.0, 0.21)
	321	173	323	335	328	329	290	281	309
D	0.88	0.79	0.91	0.85	0.86	0.80	0.75	0.79	0.80
	(6.4, 0.19)	(5.7, 0.25)	(3.5, 0.16)	(4.7, 0.19)	(4.2, 0.18)	(6.2, 0.20)	(7.8, 0.25)	(6.2, 0.21)	(5.8, 0.20)
	325	174	329	339	334	342	300	287	321
E	0.87	0.72	0.83	0.79	0.84	0.91	0.86	0.88	0.91
	(6.3, 0.20)	(8.3, 0.27)	(5.8, 0.17)	(6.3, 0.20)	(4.8, 0.18)	(4.5, 0.17)	(6.3, 0.22)	(4.9, 0.18)	(3.9, 0.17)
	333	179	338	347	343	343	306	295	324
F	0.91	0.78	0.90	0.85	0.85	0.89	0.86	0.88	0.89
	(4.7, 0.17)	(9.6, 0.33)	(5.3, 0.18)	(6.4, 0.20)	(7.5, 0.22)	(5.2, 0.16)	(6.0, 0.16)	(4.9, 0.16)	(5.5, 0.17)
	323	168	323	334	330	336	295	281	316
G	0.90	0.77	0.90	0.85	0.87	0.88	0.86	0.87	0.88
	(5.0, 0.19)	(9.0, 0.33)	(5.3, 0.19)	(6.3, 0.20)	(7.0, 0.22)	(5.5, 0.17)	(5.3, 0.17)	(5.2, 0.17)	(5.7, 0.19)
	320	172	326	335	329	383	296	282	356
H	0.90	0.75	0.88	0.83	0.84	0.89	0.86	0.87	0.88
	(4.4, 0.17)	(9.4, 0.30)	(4.9, 0.18)	(5.6, 0.21)	(6.8, 0.21)	(4.5, 0.16)	(6.0, 0.19)	(4.5, 0.16)	(5.1, 0.17)
	327	175	332	341	336	335	299	289	314
I	0.87	0.75	0.86	0.82	0.83	0.88	0.84	0.85	0.87
	(6.1, 0.20)	(10.0, 0.36)	(6.7, 0.22)	(7.2, 0.23)	(8.2, 0.25)	(6.1, 0.20)	(6.0, 0.16)	(6.0, 0.18)	(6.3, 0.21)
	341	181	352	356	357	957	314	306	936
J	0.95	0.73	0.87	0.84	0.80	0.90	0.86	0.87	0.88
	(3.0, 0.14)	(9.2, 0.28)	(5.2, 0.18)	(5.9, 0.20)	(7.5, 0.22)	(5.0, 0.17)	(5.9, 0.20)	(5.3, 0.17)	(5.2, 0.18)
	316	167	314	326	323	321	283	272	302
K	1.00	0.71	0.88	0.85	0.81	0.89	0.86	0.87	0.88
	(0.0, 0.00)	(10.3, 0.31)	(6.0, 0.16)	(6.5, 0.19)	(8.2, 0.22)	(5.2, 0.16)	(5.8, 0.18)	(5.5, 0.16)	(5.5, 0.18)
	346	170	326	337	332	331	296	286	313
L		1.00	0.89	0.91	0.90	0.68	0.63	0.72	0.69
		(0.0, 0.00)	(6.7, 0.24)	(5.9, 0.23)	(4.8, 0.21)	(10.0, 0.29)	(12.1, 0.35)	(9.1, 0.30)	(9.8, 0.29)
		183	176	181	177	181	153	149	164
M			1.00	0.94	0.90	0.83	0.81	0.82	0.84
			(0.0, 0.00)	(3.8, 0.13)	(4.6, 0.16)	(5.5, 0.16)	(7.4, 0.20)	(5.8, 0.17)	(5.1, 0.16)
			361	341	336	345	300	288	326
N				1.00	0.90	0.77	0.75	0.78	0.78
				(0.0, 0.00)	(4.4, 0.17)	(6.7, 0.19)	(8.1, 0.22)	(6.4, 0.20)	(6.2, 0.19)
				362	346	347	309	297	327
O					1.00	0.80	0.75	0.79	0.80
		LEGEND			(0.0, 0.00)	(5.8, 0.19)	(8.8, 0.25)	(6.8, 0.21)	(6.0, 0.19)
		Pearson R			362	348	304	292	330
P		**(P90, COD)**				1.00	0.95	0.97	0.97
		n				(0.0, 0.00)	(3.6, 0.14)	(2.0, 0.09)	(2.1, 0.08)
						1027	307	299	943
Q							1.00	0.92	0.94
							(0.0, 0.00)	(3.1, 0.13)	(4.0, 0.16)
							321	268	290
R								1.00	0.94
								(0.0, 0.00)	(2.7, 0.12)
								313	280
S									1.00
									(0.0, 0.00)
									998

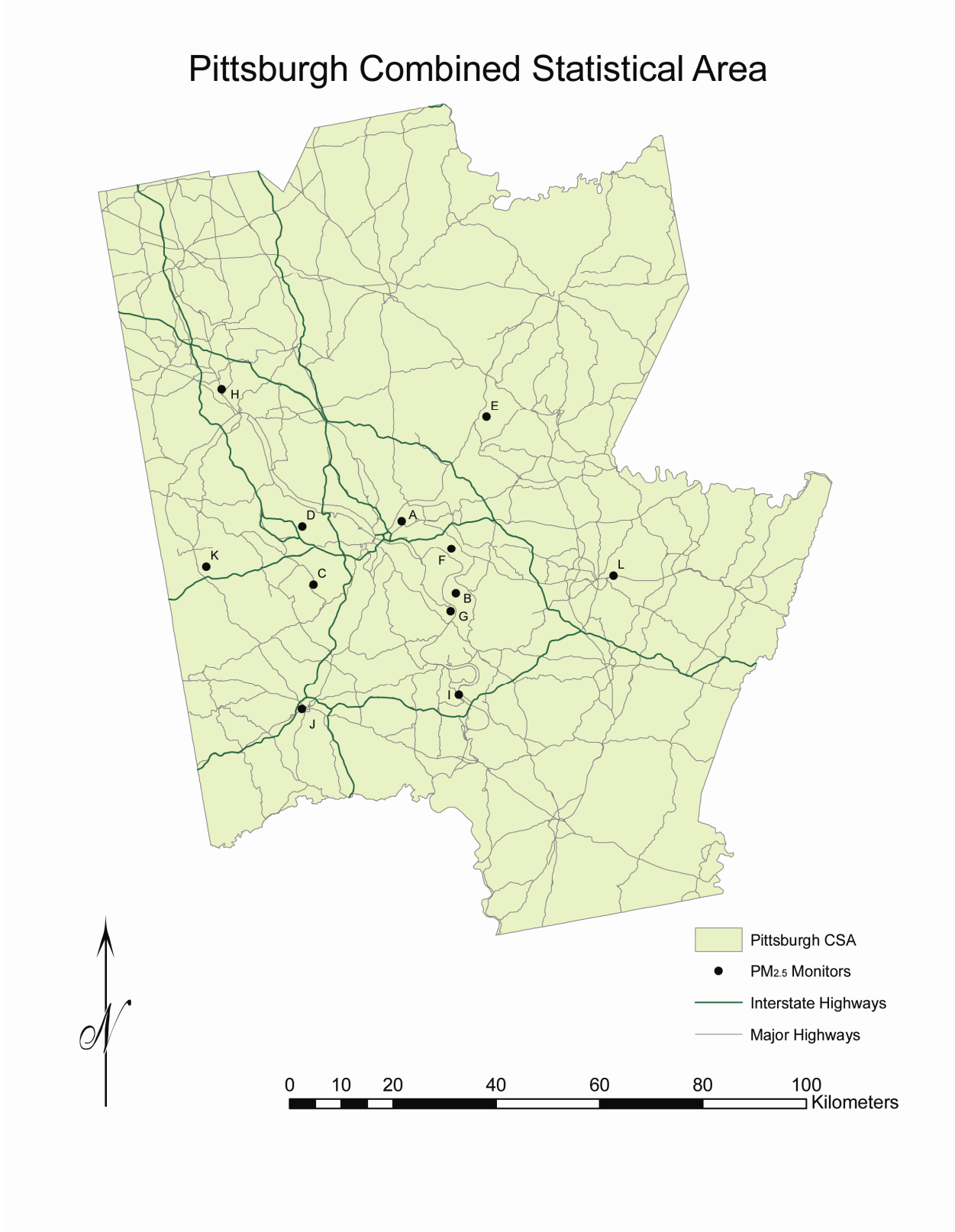


Figure 3-21. Locations of $PM_{2.5}$ monitors and major highways, Pittsburgh, PA.

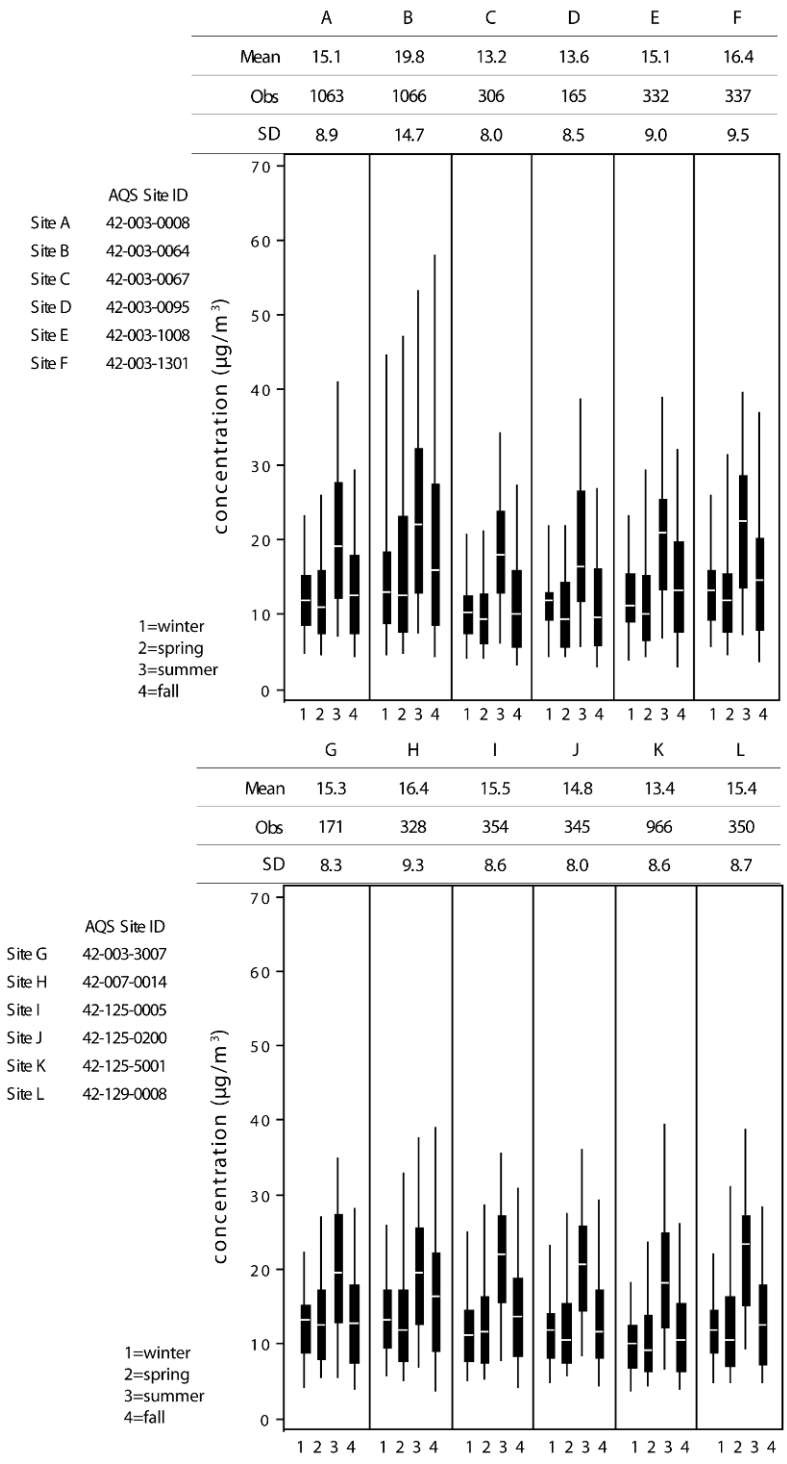


Figure 3-22. Seasonal distribution of 24-h avg $PM_{2.5}$ concentrations by site for Pittsburgh, PA, 2005-2007. Box plots show the median and interquartile range with whiskers extending to the 5th and 95th percentiles at each site during (1) winter (December-February), (2) spring (March-May), (3) summer (June-August) and (4) fall (September-November).

Table 3-12. Inter-sampler comparison statistics for each pair of 24-h $PM_{2.5}$ monitors reporting to AQS for Pittsburgh, PA.

	A	B	C	D	E	F	G	H	I	J	K	L
A	1.00	0.79	0.95	0.92	0.93	0.95	0.95	0.85	0.90	0.93	0.91	0.88
	(0.0, 0.00)	(15.9, 0.19)	(5.6, 0.13)	(4.7, 0.11)	(4.7, 0.11)	(4.9, 0.10)	(3.8, 0.10)	(6.4, 0.13)	(6.4, 0.13)	(5.0, 0.12)	(6.0, 0.13)	(5.6, 0.12)
	1063	1035	298	164	323	329	170	319	344	337	934	340
B		1.00	0.71	0.65	0.80	0.85	0.76	0.69	0.71	0.68	0.68	0.67
		(0.0, 0.00)	(16.9, 0.24)	(17.4, 0.25)	(14.4, 0.19)	(12.5, 0.14)	(15.7, 0.20)	(17.0, 0.19)	(15.7, 0.21)	(17.8, 0.23)	(19.3, 0.25)	(15.9, 0.21)
		1066	303	165	329	335	171	324	350	341	938	346
C			1.00	0.93	0.90	0.91	0.94	0.80	0.93	0.96	0.95	0.91
			(0.0, 0.00)	(2.8, 0.09)	(6.6, 0.16)	(8.7, 0.17)	(6.0, 0.14)	(9.4, 0.19)	(6.7, 0.15)	(4.6, 0.12)	(4.5, 0.10)	(6.5, 0.15)
			306	144	282	282	148	268	290	286	270	286
D				1.00	0.84	0.87	0.91	0.79	0.89	0.91	0.97	0.85
				(0.0, 0.00)	(6.4, 0.15)	(8.5, 0.16)	(5.8, 0.13)	(9.2, 0.17)	(5.9, 0.13)	(4.6, 0.11)	(3.1, 0.08)	(6.5, 0.15)
				165	153	161	158	156	158	155	146	157
E					1.00	0.90	0.90	0.84	0.85	0.86	0.88	0.83
					(0.0, 0.00)	(6.4, 0.13)	(6.5, 0.13)	(6.8, 0.14)	(8.3, 0.16)	(7.7, 0.16)	(7.6, 0.15)	(7.3, 0.15)
					332	313	157	295	320	315	290	318
F		**LEGEND**				1.00	0.91	0.82	0.88	0.88	0.89	0.86
		Pearson R				(0.0, 0.00)	(6.7, 0.13)	(7.4, 0.14)	(7.1, 0.15)	(7.9, 0.15)	(8.8, 0.17)	(7.0, 0.14)
		(P90, COD)				337	167	302	327	319	296	322
G		**n**					1.00	0.78	0.94	0.93	0.90	0.91
							(0.0, 0.00)	(7.3, 0.16)	(4.0, 0.10)	(5.0, 0.11)	(6.6, 0.15)	(5.0, 0.13)
							171	159	163	159	149	161
H								1.00	0.80	0.78	0.82	0.70
								(0.0, 0.00)	(8.4, 0.15)	(8.2, 0.17)	(9.0, 0.18)	(9.2, 0.18)
								328	317	309	288	314
I									1.00	0.93	0.89	0.88
									(0.0, 0.00)	(5.0, 0.11)	(7.2, 0.16)	(6.0, 0.13)
									354	334	310	339
J										1.00	0.93	0.88
										(0.0, 0.00)	(5.5, 0.12)	(5.9, 0.13)
										345	302	331
K											1.00	0.86
											(0.0, 0.00)	(6.9, 0.15)
											966	306
L												1.00
												(0.0, 0.00)
												350

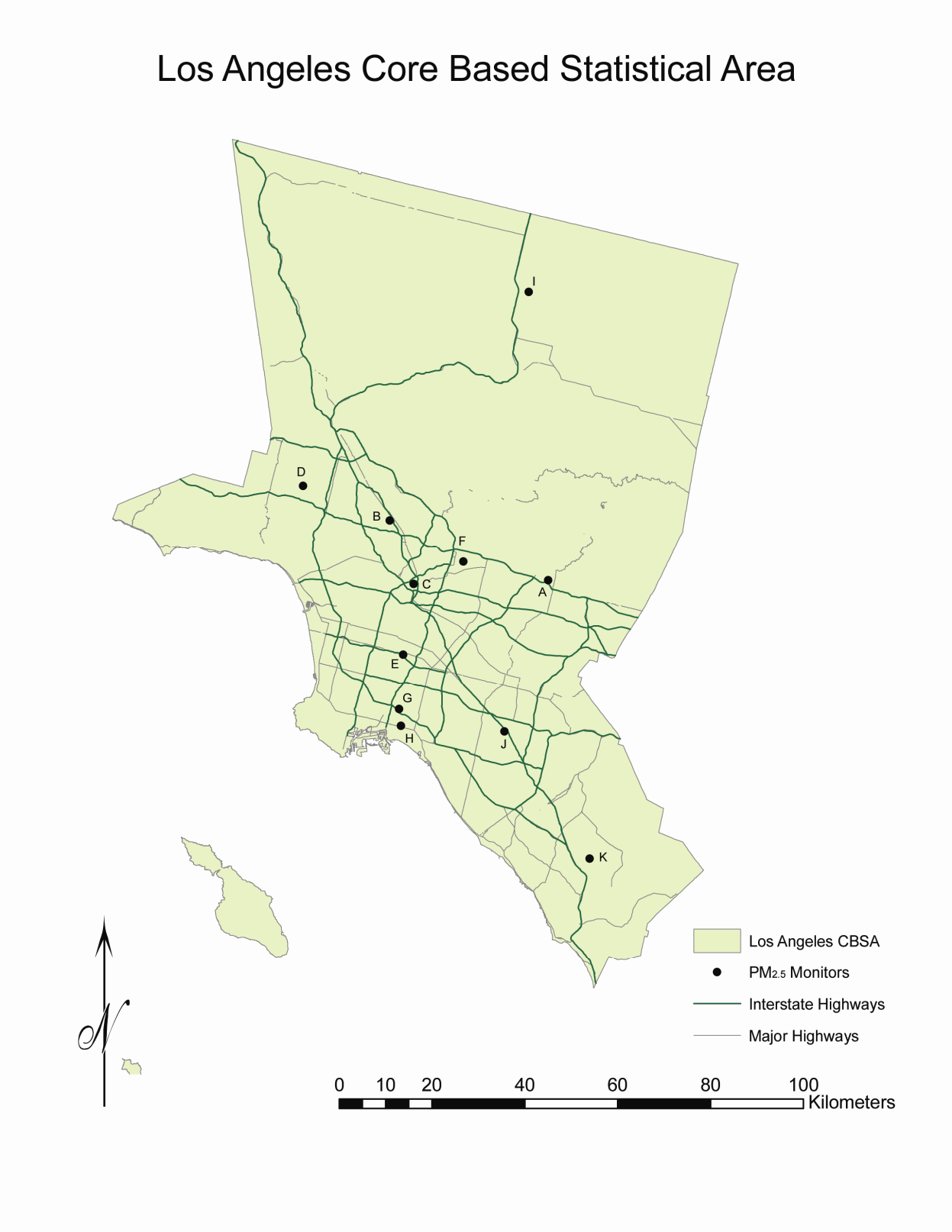


Figure 3-23. Locations of $PM_{2.5}$ monitors and major highways, Los Angeles, CA.

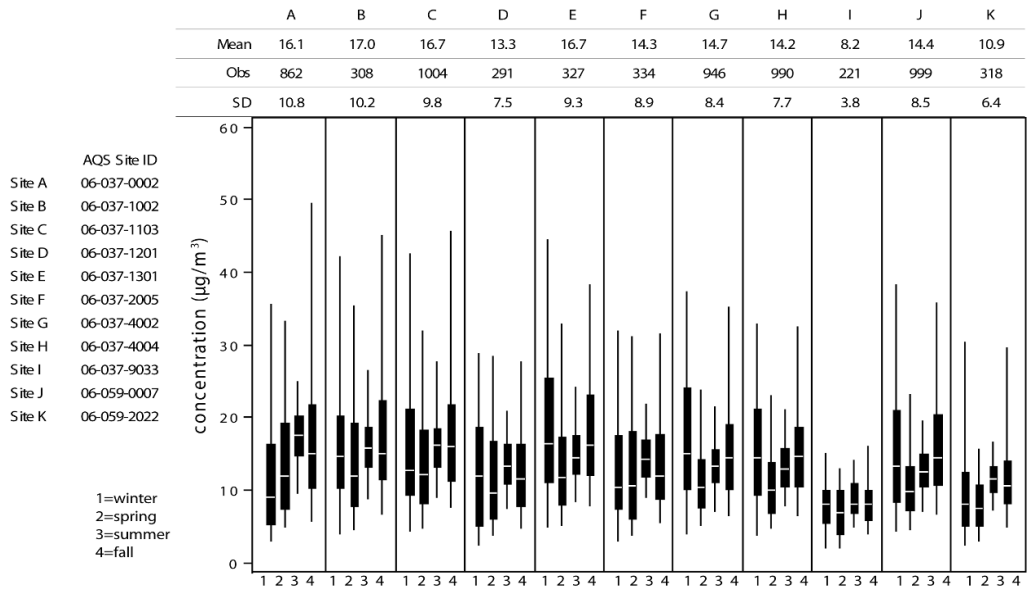


Figure 3-24. Seasonal distribution of 24-h avg $PM_{2.5}$ concentrations by site for Los Angeles, CA, 2005-2007. Box plots show the median and interquartile range with whiskers extending to the 5th and 95th percentiles at each site during (1) winter (December-February), (2) spring (March-May), (3) summer (June-August) and (4) fall (September-November).

Table 3-13. Inter-sampler comparison statistics for each pair of 24-h $PM_{2.5}$ monitors reporting to AQS for Los Angeles, CA.

	A	B	C	D	E	F	G	H	I	J	K
A	1.00	0.86	0.87	0.81	0.80	0.88	0.68	0.64	0.30	0.70	0.82
	(0.0, 0.00)	(9.0, 0.18)	(7.7, 0.16)	(9.0, 0.19)	(9.7, 0.21)	(5.8, 0.14)	(11.5, 0.22)	(12.4, 0.23)	(18.0, 0.36)	(10.5, 0.21)	(11.4, 0.23)
	862	252	803	238	262	269	761	793	179	804	259
B		1.00	0.92	0.87	0.83	0.88	0.77	0.73	0.31	0.74	0.71
		(0.0, 0.00)	(5.5, 0.11)	(9.1, 0.19)	(9.0, 0.15)	(7.6, 0.15)	(9.8, 0.17)	(11.6, 0.18)	(24.1, 0.38)	(11.9, 0.19)	(15.0, 0.27)
		308	293	250	278	279	268	282	177	292	277
C			1.00	0.80	0.89	0.92	0.84	0.79	0.29	0.82	0.78
			(0.0, 0.00)	(9.6, 0.20)	(5.8, 0.11)	(6.4, 0.13)	(9.0, 0.15)	(10.0, 0.17)	(18.6, 0.38)	(9.4, 0.16)	(13.2, 0.25)
			1004	274	315	319	880	913	213	920	305
D				1.00	0.69	0.77	0.63	0.60	0.41	0.64	0.60
				(0.0, 0.00)	(10.9, 0.23)	(7.4, 0.18)	(11.3, 0.22)	(11.1, 0.22)	(14.8, 0.31)	(9.6, 0.21)	(11.6, 0.23)
				291	263	263	256	268	164	274	261
E					1.00	0.79	0.95	0.92	0.34	0.88	0.76
					(0.0, 0.00)	(9.1, 0.19)	(5.9, 0.11)	(7.6, 0.13)	(19.7, 0.39)	(8.2, 0.15)	(13.7, 0.27)
					327	301	289	301	192	307	291
F						1.00	0.70	0.70	0.33	0.69	0.72
		LEGEND				(0.0, 0.00)	(10.5, 0.18)	(9.2, 0.19)	(14.8, 0.34)	(9.8, 0.19)	(9.9, 0.21)
		Pearson R				334	290	302	184	311	293
G		**(P90, COD)**					1.00	0.96	0.23	0.92	0.78
		n					(0.0, 0.00)	(4.0, 0.09)	(17.0, 0.35)	(5.4, 0.12)	(11.0, 0.21)
							946	859	194	882	277
H								1.00	0.26	0.91	0.78
								(0.0, 0.00)	(15.3, 0.34)	(5.9, 0.12)	(9.5, 0.21)
								990	208	914	294
I									1.00	0.21	0.31
									(0.0, 0.00)	(18.3, 0.35)	(9.7, 0.28)
									221	205	180
J										1.00	0.84
										(0.0, 0.00)	(9.8, 0.19)
										999	298
K											1.00
											(0.0, 0.00)
											318

To further investigate the relationship between correlation and distance, Figure 3-25 through Figure 3-27 plot inter-sampler correlation as a function of distance between monitors for $PM_{2.5}$ in

Boston, Pittsburgh, and Los Angeles. These three cities were selected to illustrate how this relationship varies across urban areas with different topography and climatology as well as different $PM_{2.5}$ sources, compositions and monitor densities. Plots are provided in Annex A for all 15 CSAs/CBSAs under investigation beginning with Figure A-39. The Boston data exhibit the strongest relationship between inter-sampler correlation and distance, with average inter-sampler correlation remaining higher than 80% when samplers are 95 km apart ($R^2 = 0.55$). This small amount of variability is expected given the consistency between distributions shown in the corresponding box plots (Figure 3-20). The Pittsburgh data show some reductions in inter-sampler correlations at short distances, with the samplers at Sites B and G having only 76% correlation with a distance of less than 4 km. Site B is located in Liberty, PA, a mountainous suburb of Pittsburgh where emissions from steel manufacturing and frequent stable conditions in the planetary boundary layer cause localized events of elevated concentration. In contrast, Site G is in the neighboring town of Clairton, PA, located at a lower elevation on the bank of the opposite side of the Monongahela River from Liberty. On average, inter-sampler correlation remained higher than 80% when samplers were separated by 61 km, but in this case with much greater scatter ($R^2 = 0.22$) than observed in the Boston data. This scatter is driven by the measurements at Site B; Figure 3-22 shows an elevated mean and variability for this site compared with other monitors situated around the Pittsburgh CSA. When data from Site B are removed, the inter-sampler correlation vs. distance plot for Pittsburgh $PM_{2.5}$ resembles the one from Boston (with R^2 increasing to 0.68). The Los Angeles data exhibit a much steeper slope, with average inter-sampler correlation remaining higher than 80% when samplers are 29 km apart ($R^2 = 0.74$). This suggests that other factors, such as mountainous topography separating monitors, the distribution of traffic, re suspension of crustal components, and occurrence of stable boundary layers, may cause more spatial variation in the $PM_{2.5}$ concentration profile within the Los Angeles region when compared with other parts of the country. The Site I monitor, separated from the rest of the Los Angeles region by the San Gabriel Mountains as mentioned above, provides the low correlations grouped in the lower right portion of Figure 3-27. It should also be noted in examining Figure 3-19, Figure 3-21, and Figure 3-23 that some monitors are often located close to major interstate highways while others in the same urban area are not. These differences in proximity of monitors to nearby major roads may also result in lower inter-monitor correlations.

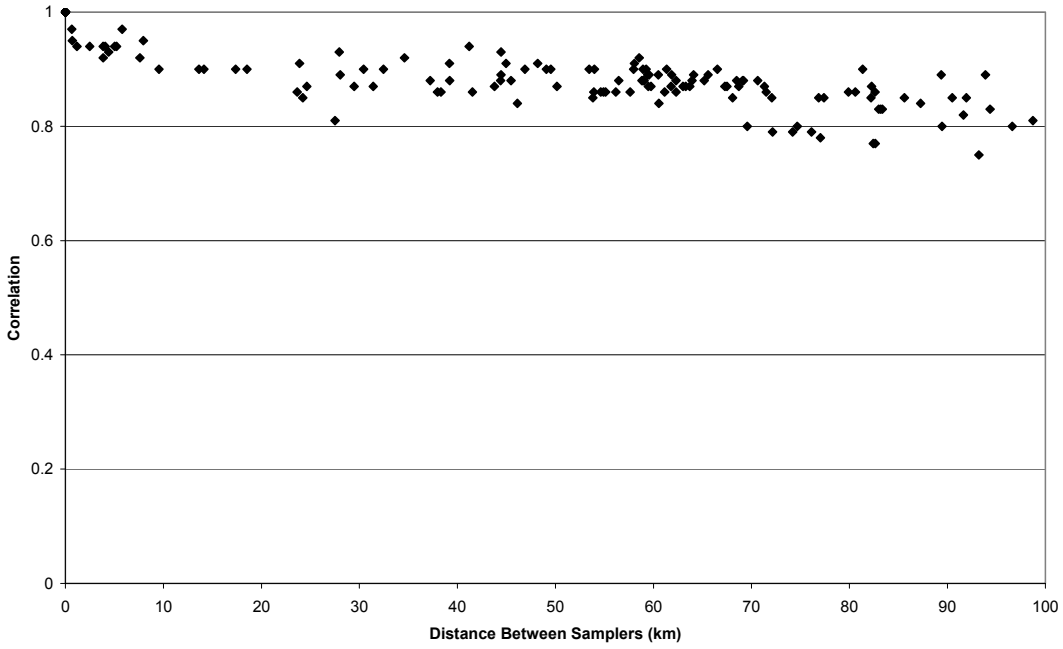


Figure 3-25. Inter-sampler correlations for 24-h $PM_{2.5}$ as a function of distance between monitors in Boston, MA.

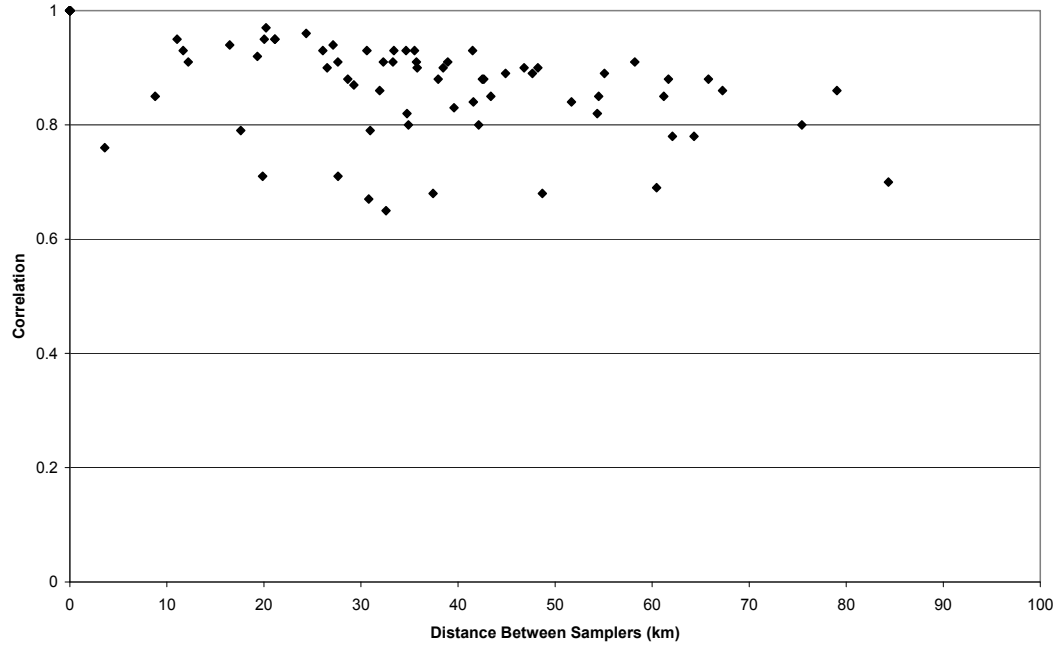


Figure 3-26. Inter-sampler correlations for 24-h $PM_{2.5}$ as a function of distance between monitors in Pittsburgh, PA.

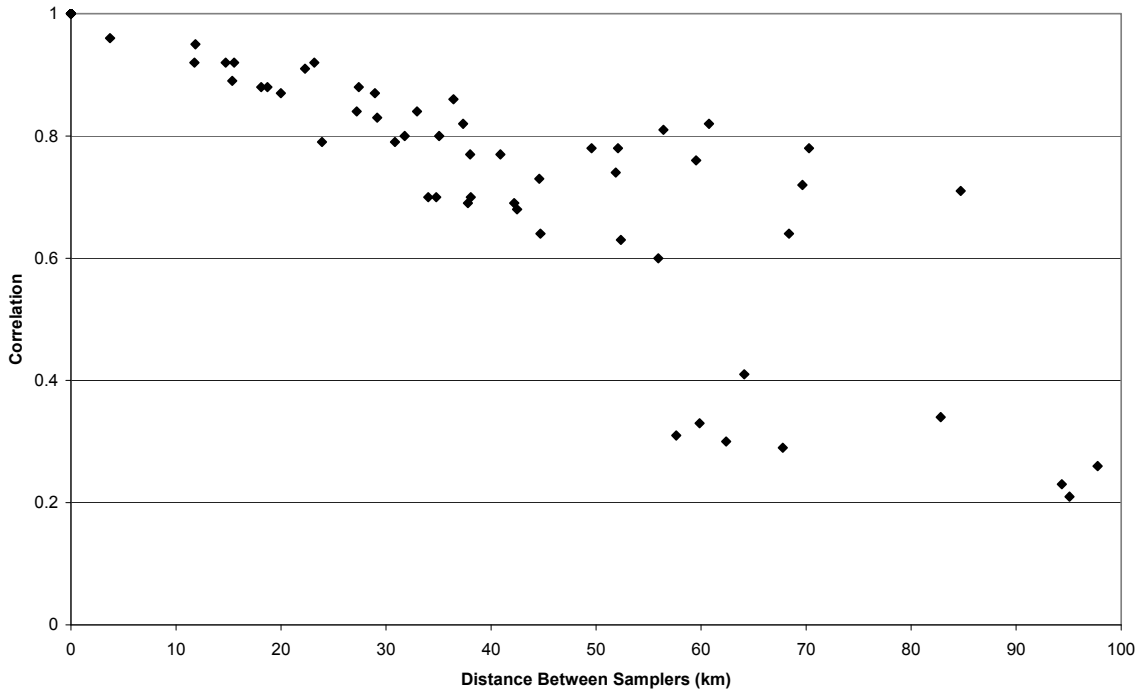


Figure 3-27. Inter-sampler correlations for 24-h $PM_{2.5}$ as a function of distance between monitors in Los Angeles, CA.

$PM_{10-2.5}$

Given the limited number of co-located low-volume FRM PM_{10} and FRM $PM_{2.5}$ monitors, only a very limited investigation into the intra-urban spatial variability of $PM_{10-2.5}$ was possible using AQS data. Of the 15 cities under investigation, only six (Atlanta, Boston, Chicago, Denver, New York and Phoenix) contained data sufficient for calculating $PM_{10-2.5}$ according to the data completeness and monitor specification requirements discussed earlier. Figure 3-28 contains box plots of $PM_{10-2.5}$ for one or two available sites per CSA/CBSA providing adequate $PM_{10-2.5}$ concentration data. For Boston, the correlation between the two sites for $PM_{10-2.5}$ was 0.45 compared with 0.73 for $PM_{2.5}$ alone and 0.84 for PM_{10} alone (using the same two monitoring sites). For New York, the correlation was slightly higher for the two sites: 0.74 for $PM_{10-2.5}$ compared with 0.93 for $PM_{2.5}$ alone and 0.82 for PM_{10} alone. The COD for $PM_{10-2.5}$ also increases in both cities compared with $PM_{2.5}$ and PM_{10} alone, suggesting less spatial homogeneity for thoracic coarse particles compared with fine particles. Wilson and Suh (1997, 077408) reported $PM_{10-2.5}$ correlations between eight sites in Philadelphia ranging from 0.14 to 0.63 with an average of 0.38. This was considerably less than the corresponding average correlation for $PM_{2.5}$ ($r = 0.90$) and PM_{10} ($r = 0.87$) from the same study. Thornburg et al. (2009, 190999) also reported a high degree of spatial variability in $PM_{10-2.5}$ in Detroit with between-monitor correlations ranging from 0.03 to 0.76. These results suggest that local sources can have a substantial impact on $PM_{10-2.5}$ concentrations, resulting in a higher degree of spatial variability in $PM_{10-2.5}$ relative to $PM_{2.5}$ or PM_{10}.

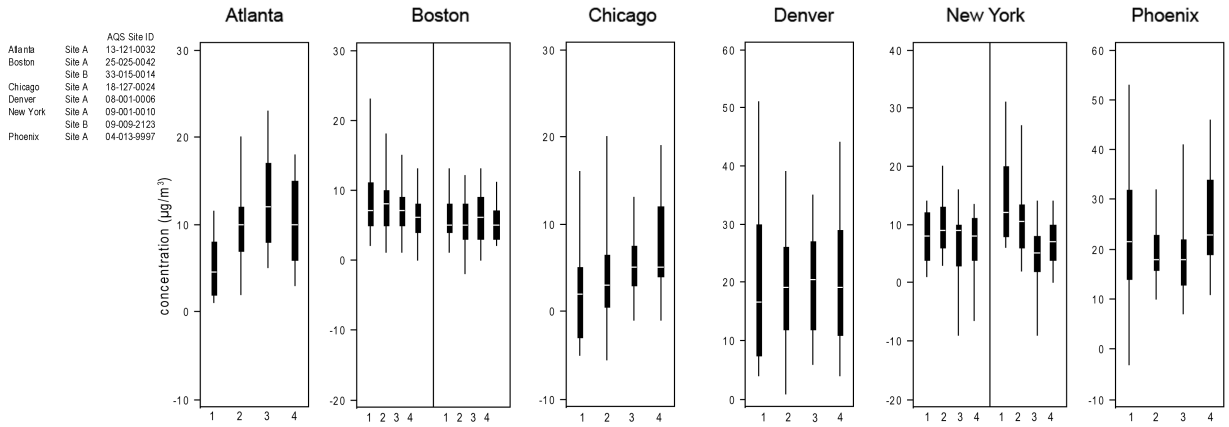


Figure 3-28. Seasonal distribution of 24-h avg $PM_{10-2.5}$ concentrations by site for Atlanta, GA; Boston, MA; Chicago, IL; Denver, CO; New York City, NY; and Phoenix, AZ; 2005-2007. Box plots show the median and interquartile range with whiskers extending to the 5th and 95th percentiles at each site during (1) winter (December-February), (2) spring (March-May), (3) summer (June-August) and (4) fall (September-November). Note the different concentration scales on the y-axes.

PM_{10}

PM_{10} mass concentration has been shown to vary as much as a factor of five over urban-scale distances of 100 km or less, and by a factor of 2 or more on scales as small as 30 km in an analysis of California air quality (Alexis et al., 2001, 079886). This can be attributed to the rapid V_d and resulting short atmospheric lifetime of the coarse-mode particles making up much of PM_{10} mass. As a result, local emission sources often dominate PM_{10} annual average mass at certain monitors. Data from the 15 CSAs/CBSAs were used to investigate urban variability in PM_{10} reported to the AQS database.

Maps of PM_{10} monitor locations and box plots of seasonal PM_{10} mass concentration data are provided for Boston (Figure 3-29 and Figure 3-30), Pittsburgh (Figure 3-31 and Figure 3-32), and Los Angeles (Figure 3-33 and Figure 3-34) similar to the $PM_{2.5}$ maps and box plots shown earlier in Figure 3-19 through Figure 3-24. Annex A, Figures A-82 through A-125 incorporate similar information for all 15 CSAs/CBSAs. Table 3-14 through Table 3-16 contain pair wise, within-city comparison statistics (R, P90, COD and n, as defined above) for PM_{10} measured at the available monitors in Boston (Table 3-14), Pittsburgh (Table 3-15) and Los Angeles (Table 3-16); all 15 CSAs/CBSAs are included in Annex A, Tables A-35 through A-49.

Boston is an example of a city with a wide range in concentrations measured at different sites. Inter-monitor variation in PM_{10} is frequently larger than the seasonal variation measured at any given site. Pairwise correlations between monitors in Boston range from 0.45 to 0.95 in Table 3-14. Pittsburgh is an example of a city with a large number of PM_{10} monitors providing consistent values with a select few reporting higher concentrations (sites D, H, I and K in Figure 3-32). This illustrates the potential influence of localized point or area sources or topography. Correlations between monitors in Pittsburgh range from 0.47 to 0.97 in Table 3-15. Los Angeles shows a high degree of between-season and within-season variability, which is on the order of the between-monitor variation. Correlations between monitors in Los Angeles range from 0.29 to 0.93 in Table 3-16. Once again, the lowest correlations are with the monitor separated from the other monitors by the San Gabriel Mountains (Site E in Figure 3-33).

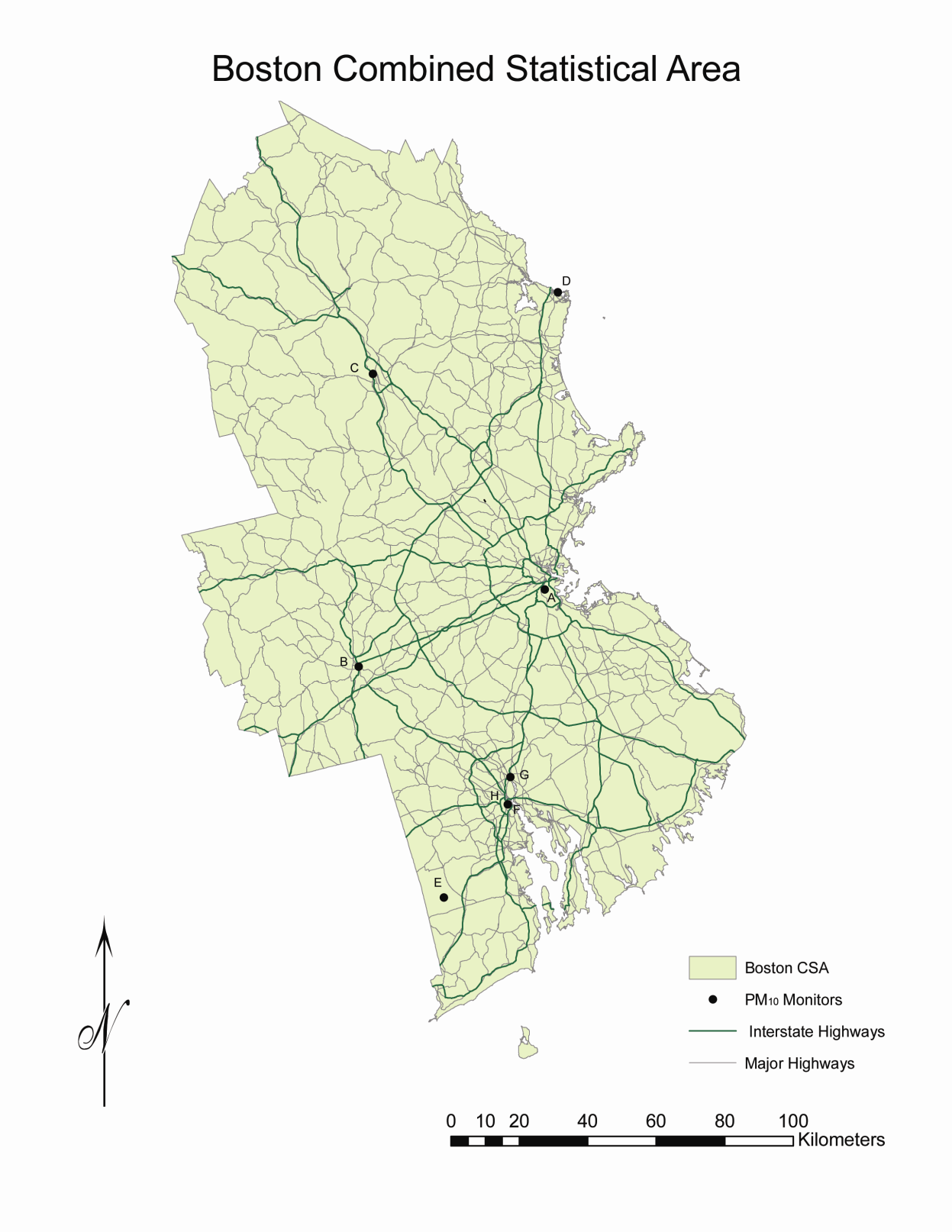


Figure 3-29. Locations of PM_{10} monitors and major highways, Boston, MA.

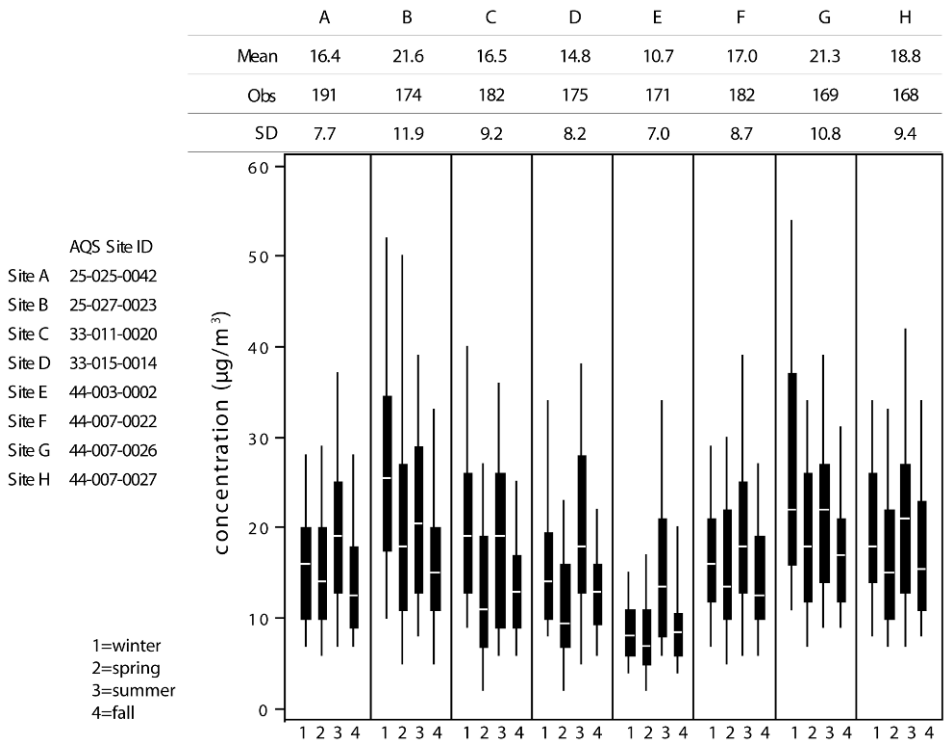


Figure 3-30. Seasonal distribution of 24-h avg PM_{10} concentrations by site for Boston, MA, 2005-2007. Box plots show the median and interquartile range with whiskers extending to the 5th and 95th percentiles at each site during (1) winter (December-February), (2) spring (March-May), (3) summer (June-August) and (4) fall (September-November).

Table 3-14. Inter-sampler comparison statistics for each pair of 24-h PM_{10} monitors reporting to AQS for Boston, MA.

Site	A	B	C	D	E	F	G	H
A	1.00	0.69	0.69	0.73	0.71	0.84	0.70	0.79
	(0.0, 0.00)	(15.0, 0.22)	(12.0, 0.20)	(10.0, 0.22)	(13.0, 0.30)	(8.0, 0.14)	(15.0, 0.20)	(10.0, 0.17)
	191	169	179	173	171	182	169	167
B		1.00	0.66	0.56	0.45	0.69	0.77	0.65
		(0.0, 0.00)	(17.0, 0.24)	(19.0, 0.28)	(24.0, 0.39)	(15.0, 0.21)	(12.0, 0.17)	(16.0, 0.20)
		174	167	161	158	169	156	154
C			1.00	0.72	0.47	0.62	0.64	0.59
			(0.0, 0.00)	(10.0, 0.22)	(17.0, 0.33)	(12.0, 0.21)	(16.0, 0.26)	(16.0, 0.24)
			182	170	168	179	166	164
D				1.00	0.63	0.68	0.59	0.69
				(0.0, 0.00)	(11.0, 0.29)	(10.0, 0.23)	(19.0, 0.30)	(13.0, 0.26)
				175	163	173	161	158
E		LEGEND			1.00	0.84	0.58	0.80
		Pearson R			(0.0, 0.00)	(13.0, 0.29)	(22.0, 0.38)	(15.0, 0.33)
		(P90, COD)			171	171	161	157
F		n				1.00	0.81	0.95
						(0.0, 0.00)	(11.0, 0.16)	(5.0, 0.11)
						182	169	167
G							1.00	0.79
							(0.0, 0.00)	(10.0, 0.13)
							169	154
H								1.00
								(0.0, 0.00)
								168

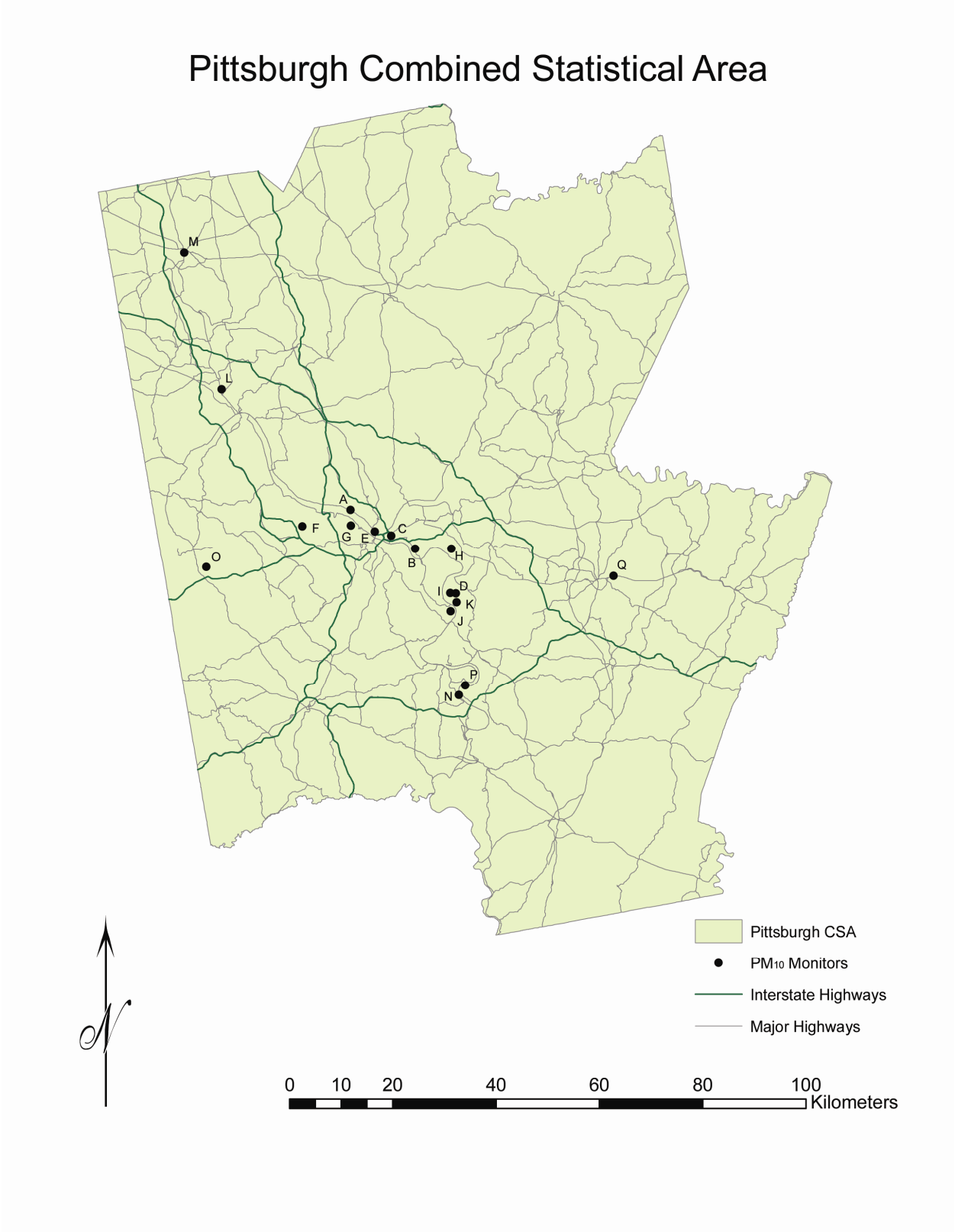


Figure 3-31. Locations of PM_{10} monitors and major highways, Pittsburgh, PA.

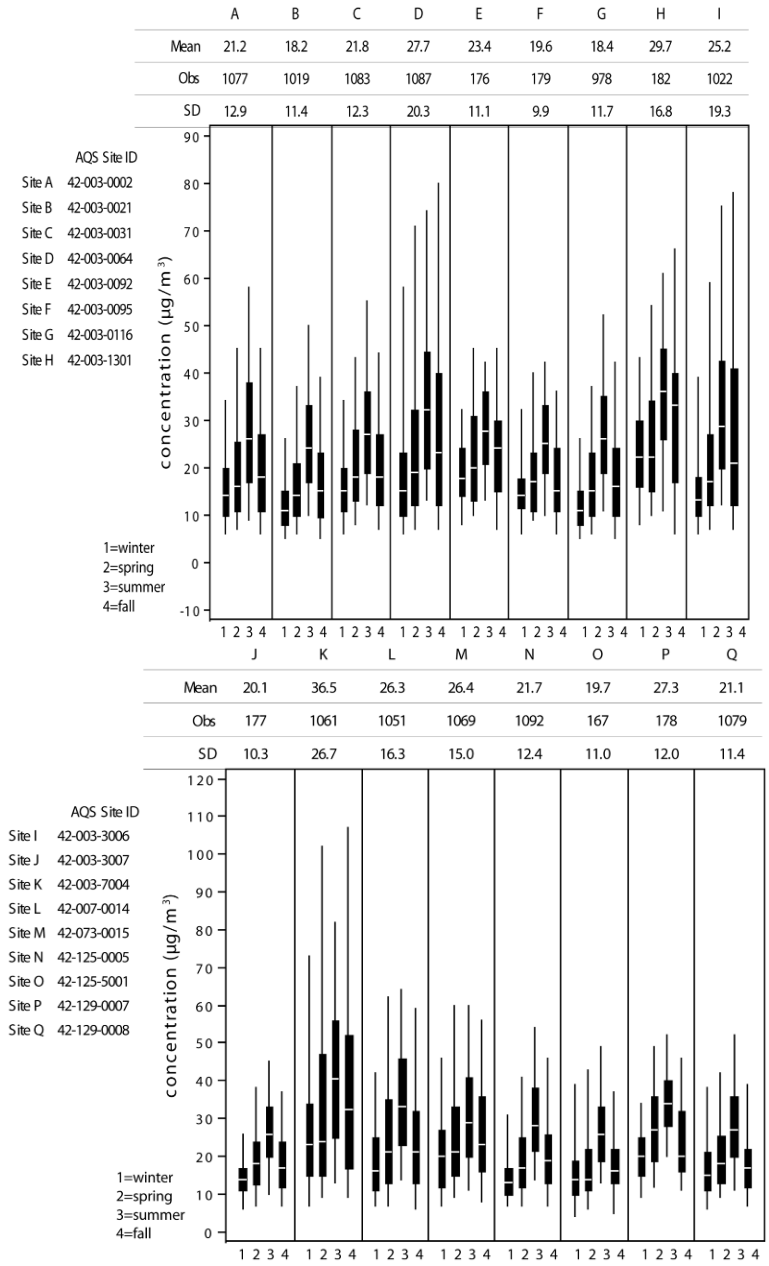


Figure 3-32. Seasonal distribution of 24-h avg PM_{10} concentrations by site for Pittsburgh, PA, 2005-2007. Box plots show the median and interquartile range with whiskers extending to the 5th and 95th percentiles at each site during (1) winter (December-February), (2) spring (March-May), (3) summer (June-August) and (4) fall (September-November).

Table 3-15. Inter-sampler comparison statistics for each pair of 24-h PM_{10} monitors reporting to AQS for Pittsburgh, PA.

Site	A	B	C	D	E	F	G	H	I
A	1.00	0.93	0.93	0.80	0.92	0.89	0.93	0.79	0.86
	(0.0, 0.00)	(9.0, 0.15)	(8.0, 0.14)	(23.0, 0.21)	(8.0, 0.12)	(14.0, 0.18)	(8.0, 0.14)	(16.0, 0.17)	(18.0, 0.18)
	1077	1002	1065	1070	175	178	960	181	1005
B		1.00	0.96	0.80	0.91	0.92	0.97	0.81	0.89
		(0.0, 0.00)	(8.0, 0.15)	(29.0, 0.24)	(11.0, 0.20)	(6.0, 0.16)	(5.0, 0.10)	(25.0, 0.29)	(22.0, 0.20)
		1019	1007	1012	163	166	911	169	954
C			1.00	0.81	0.94	0.93	0.94	0.77	0.87
			(0.0, 0.00)	(23.0, 0.20)	(6.0, 0.11)	(7.0, 0.12)	(8.0, 0.13)	(21.0, 0.22)	(19.0, 0.17)
			1083	1075	173	176	966	179	1010
D				1.00	0.72	0.66	0.76	0.83	0.88
				(0.0, 0.00)	(21.0, 0.20)	(26.0, 0.24)	(27.0, 0.24)	(14.0, 0.18)	(16.0, 0.14)
				1087	176	179	970	182	1014
E					1.00	0.90	0.90	0.78	0.77
					(0.0, 0.00)	(10.0, 0.14)	(10.0, 0.17)	(20.0, 0.20)	(20.0, 0.19)
	LEGEND				176	173	154	175	166
F	Pearson R					1.00	0.94	0.70	0.74
	(P90, COD)					(0.0, 0.00)	(7.0, 0.12)	(25.0, 0.27)	(25.0, 0.22)
	n					179	157	178	168
G							1.00	0.70	0.87
							(0.0, 0.00)	(22.0, 0.28)	(20.0, 0.19)
							978	160	910
H								1.00	0.76
								(0.0, 0.00)	(17.0, 0.20)
								182	171
I									1.00
									(0.0, 0.00)
									1022

	J	K	L	M	N	O	P	Q
A	0.84	0.76	0.88	0.85	0.86	0.77	0.78	0.86
	(14.0, 0.20)	(40.0, 0.30)	(15.0, 0.18)	(16.0, 0.19)	(11.0, 0.16)	(16.0, 0.22)	(15.0, 0.19)	(11.0, 0.15)
	176	1044	1033	1052	1074	166	177	1061
B	0.93	0.76	0.88	0.81	0.91	0.76	0.83	0.88
	(7.0, 0.16)	(43.0, 0.36)	(19.0, 0.23)	(20.0, 0.26)	(10.0, 0.16)	(12.0, 0.19)	(18.0, 0.28)	(10.0, 0.18)
	164	986	982	994	1016	157	165	1003
C	0.90	0.75	0.88	0.83	0.89	0.78	0.88	0.90
	(8.0, 0.13)	(39.0, 0.30)	(14.0, 0.17)	(15.0, 0.19)	(9.0, 0.12)	(12.0, 0.18)	(13.0, 0.19)	(9.0, 0.12)
	174	1049	1039	1057	1080	164	175	1067
D	0.73	0.84	0.80	0.78	0.76	0.57	0.64	0.74
	(24.0, 0.22)	(24.0, 0.22)	(20.0, 0.18)	(20.0, 0.20)	(25.0, 0.20)	(28.0, 0.26)	(20.0, 0.25)	(26.0, 0.21)
	177	1055	1043	1061	1084	167	178	1071
E	0.86	0.65	0.83	0.80	0.84	0.77	0.84	0.85
	(10.0, 0.16)	(36.0, 0.29)	(16.0, 0.16)	(14.0, 0.17)	(12.0, 0.14)	(14.0, 0.19)	(13.0, 0.16)	(11.0, 0.15)
	171	169	169	172	176	161	172	174
F	0.90	0.57	0.82	0.75	0.86	0.83	0.84	0.86
	(7.0, 0.12)	(41.0, 0.34)	(20.0, 0.20)	(19.0, 0.22)	(11.0, 0.14)	(9.0, 0.15)	(16.0, 0.22)	(9.0, 0.14)
	174	172	172	175	179	164	175	177
G	0.92	0.73	0.87	0.78	0.89	0.81	0.84	0.86
	(7.0, 0.13)	(45.0, 0.35)	(18.0, 0.21)	(19.0, 0.24)	(9.0, 0.15)	(11.0, 0.17)	(17.0, 0.26)	(10.0, 0.16)
	156	955	938	952	975	146	157	967
H	0.74	0.68	0.77	0.78	0.74	0.60	0.65	0.76
	(23.0, 0.26)	(26.0, 0.22)	(15.0, 0.18)	(17.0, 0.18)	(21.0, 0.22)	(27.0, 0.29)	(19.0, 0.22)	(21.5, 0.24)
	176	175	175	178	182	167	177	180
I	0.79	0.83	0.82	0.78	0.81	0.66	0.69	0.78
	(22.0, 0.20)	(30.0, 0.25)	(16.0, 0.17)	(18.0, 0.20)	(20.0, 0.17)	(26.0, 0.24)	(21.0, 0.25)	(22.0, 0.19)
	166	992	978	998	1019	158	167	1009
J	1.00	0.66	0.79	0.72	0.88	0.78	0.86	0.86
	(0.0, 0.00)	(44.5, 0.33)	(18.0, 0.20)	(18.0, 0.22)	(8.0, 0.13)	(11.0, 0.17)	(16.0, 0.21)	(8.0, 0.15)
	177	170	170	173	177	163	173	175
K		1.00	0.74	0.75	0.70	0.47	0.58	0.68
		(0.0, 0.00)	(31.0, 0.26)	(33.0, 0.24)	(40.0, 0.30)	(44.0, 0.36)	(34.0, 0.30)	(43.0, 0.30)
		1061	1017	1035	1058	160	171	1048
L			1.00	0.87	0.85	0.70	0.74	0.80
			(0.0, 0.00)	(13.0, 0.16)	(16.0, 0.17)	(22.0, 0.24)	(17.0, 0.21)	(18.0, 0.19)
			1051	1025	1048	160	171	1035
M				1.00	0.74	0.64	0.67	0.77
				(0.0, 0.00)	(18.0, 0.21)	(19.0, 0.26)	(17.0, 0.22)	(18.0, 0.19)
				1069	1067	163	174	1053
N					1.00	0.72	0.86	0.86
					(0.0, 0.00)	(13.0, 0.18)	(14.0, 0.20)	(10.0, 0.14)
					1092	167	178	1076
O						1.00	0.75	0.69
						(0.0, 0.00)	(18.0, 0.25)	(14.0, 0.19)
						167	163	165
P							1.00	0.84
							(0.0, 0.00)	(15.0, 0.21)
							178	176
Q								1.00
								(0.0, 0.00)
								1079

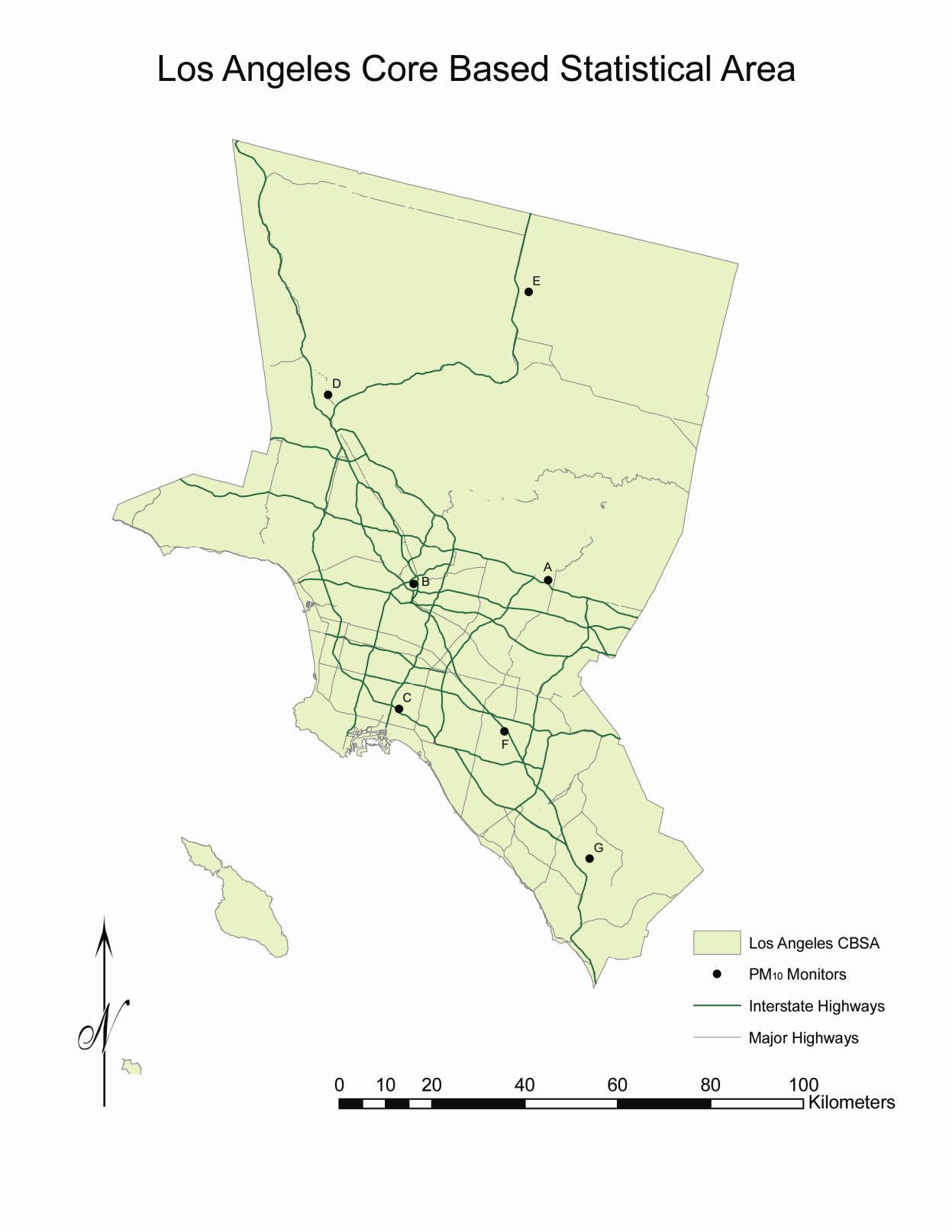


Figure 3-33. Locations of PM_{10} monitors and major highways, Los Angeles, CA.

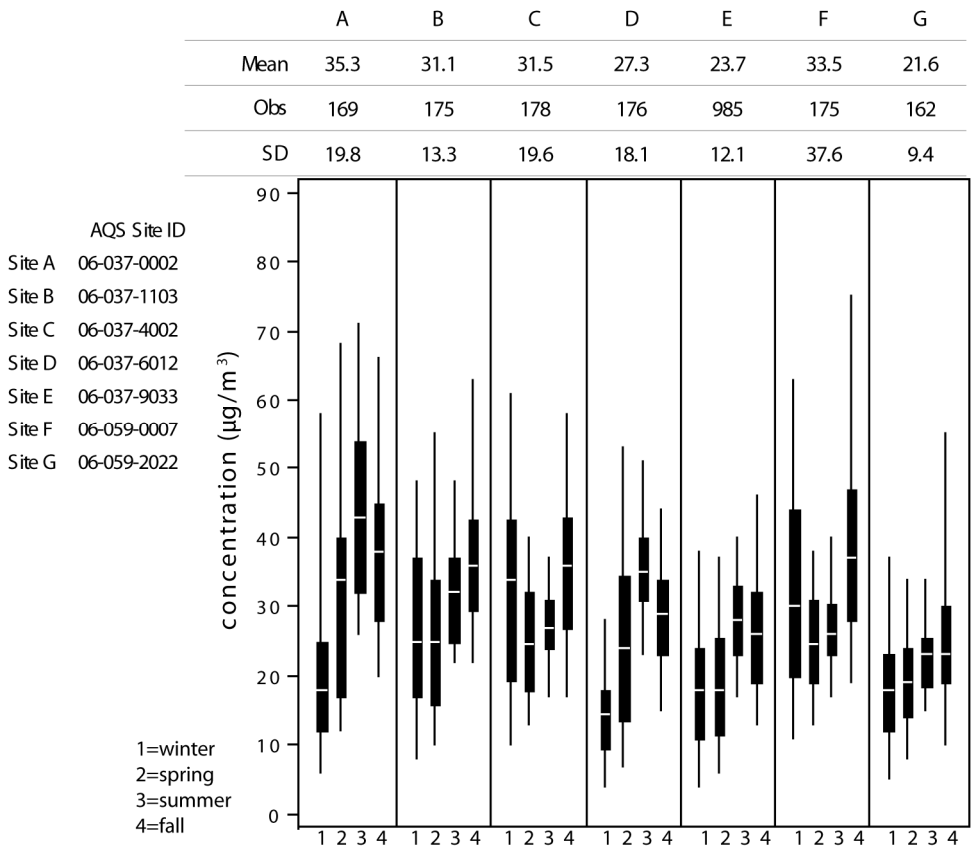


Figure 3-34. Seasonal distribution of 24-h avg PM_{10} concentrations by site for Los Angeles, CA, 2005-2007. Box plots show the median and interquartile range with whiskers extending to the 5th and 95th percentiles at each site during (1) winter (December-February), (2) spring (March-May), (3) summer (June-August) and (4) fall (September-November).

Table 3-16. Inter-sampler comparison statistics for each pair of 24-h PM_{10} monitors reporting to AQS for Los Angeles, CA.

Site	A	B	C	D	E	F	G
A	1.00	0.73	0.44	0.73	0.47	0.41	0.65
	(0.0, 0.00)	(17.0, 0.17)	(27.0, 0.24)	(24.0, 0.22)	(28.0, 0.26)	(29.0, 0.24)	(30.0, 0.28)
	169	153	154	157	169	155	143
B		1.00	0.61	0.57	0.52	0.42	0.73
		(0.0, 0.00)	(14.0, 0.14)	(21.0, 0.24)	(23.0, 0.23)	(15.0, 0.16)	(20.0, 0.23)
		175	159	159	173	162	149
C			1.00	0.65	0.43	0.93	0.73
	LEGEND		(0.0, 0.00)	(27.0, 0.28)	(22.0, 0.24)	(11.0, 0.11)	(21.0, 0.22)
	Pearson R		178	158	176	159	148
D	(P90, COD)			1.00	0.70	0.65	0.57
	n			(0.0, 0.00)	(16.0, 0.20)	(26.0, 0.28)	(19.5, 0.24)
				176	175	161	150
E					1.00	0.29	0.38
					(0.0, 0.00)	(26.0, 0.25)	(20.0, 0.24)
					985	173	159
F						1.00	0.65
						(0.0, 0.00)	(21.5, 0.22)
						175	150
G							1.00
							(0.0, 0.00)
							162

Figure 3-35 through Figure 3-37 illustrate the relationship between inter-sampler correlation and distance between sites for PM_{10} measurements obtained in Boston, Pittsburgh and Los Angeles. Annex A contains similar plots for all 15 CSAs/CBSAs under investigation beginning with Figure A-84. In each plot, substantially more scatter is observed when compared to those for $PM_{2.5}$ (Figure 3-25 through Figure 3-27). This is consistent with the variability observed in the seasonal box plots of concentration shown in Figure 3-30, Figure 3-32, and Figure 3-34. The Boston data exhibit the strongest relationship between inter-sampler correlation and distance, with average inter-sampler correlation remaining higher than 80% when samplers are 44 km apart ($R^2 = 0.61$). The lowest correlations on this plot originate from comparisons between Site B (rural Worcester, MA) and samplers located at Sites E (West Greenwich, RI) and G (Providence, RI). Boston is subject to long range transport of SO_4^{2-}, which is a regional pollutant and is a major component of $PM_{2.5}$ and PM_{10} in the eastern U.S. The Pittsburgh data shows some lower inter-sampler correlations, with one sampler pair having only 66% correlation within a distance of 2 km. On average, inter-sampler correlation remained higher than 80% when samplers were also separated by 44 km, but in this case with much greater scatter ($R^2 = 0.28$) than observed in the Boston data. As seen for the Pittsburgh PM_{10} box plots in Figure 3-32, sites D, H, I, and K have elevated means and high variability that is driving the observed scatter. These four sites are all located in mountainous suburbs of Pittsburgh (North Braddock, PA, Liberty, PA, Lincoln Boro, PA, and Beaver Falls, PA, respectively), where emissions from steel manufacturing and frequent stable conditions in the planetary boundary layer cause localized events of elevated concentration. When those four sites are removed, scatter decreases greatly ($R^2 = 0.56$). The Los Angeles data exhibit a much steeper slope, with average inter-sampler correlation remaining higher than 80% when samplers are only 30 km apart ($R^2 = 0.56$). The lower inter-sampler correlations in part reflect the fact that some of these monitoring sites are separated from each other by hills or, in the case of one sited at Lancaster, CA (Site I), by the San Gabriel Mountains. The Los Angeles data exhibit greater scatter than the Pittsburgh data. However, the smallest inter-sampler separation distance is 23 km, and there are relatively fewer PM_{10} samplers. Given the present data, it is not possible to judge how data would correlate on smaller spatial scales.

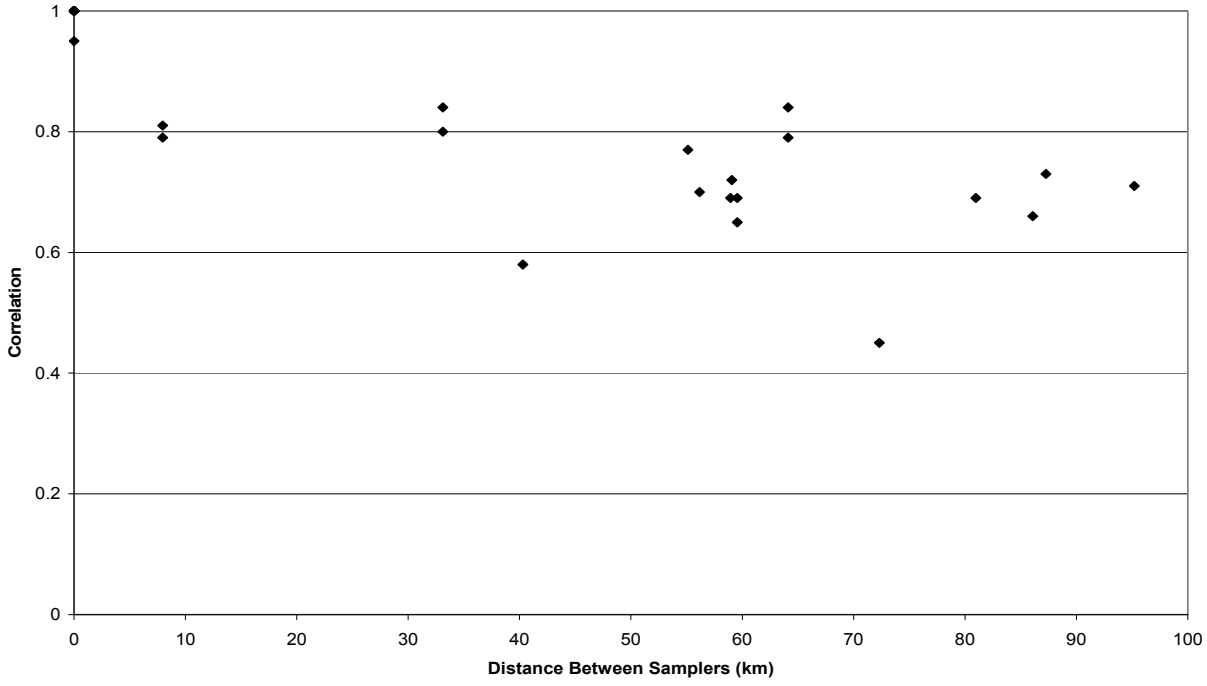


Figure 3-35. Inter-sampler correlations for 24-h PM_{10} as a function of distance between monitors in Boston, MA.

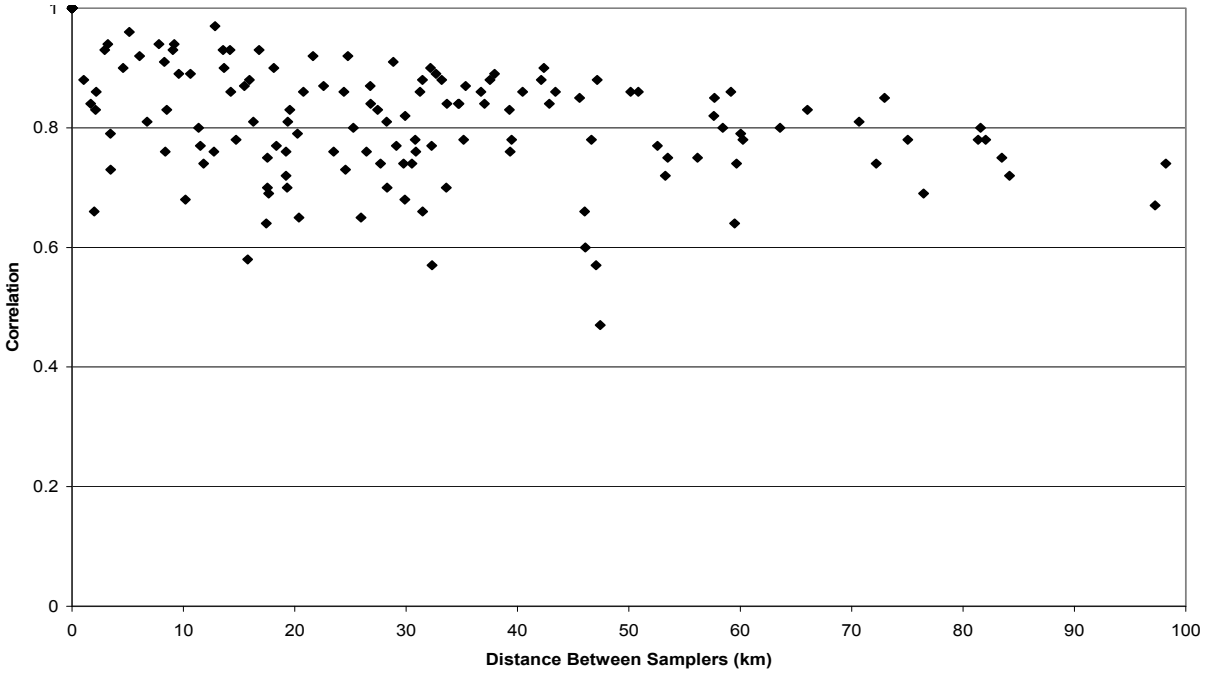


Figure 3-36. Inter-sampler correlations for 24-h PM_{10} as a function of distance between monitors in Pittsburgh, PA.

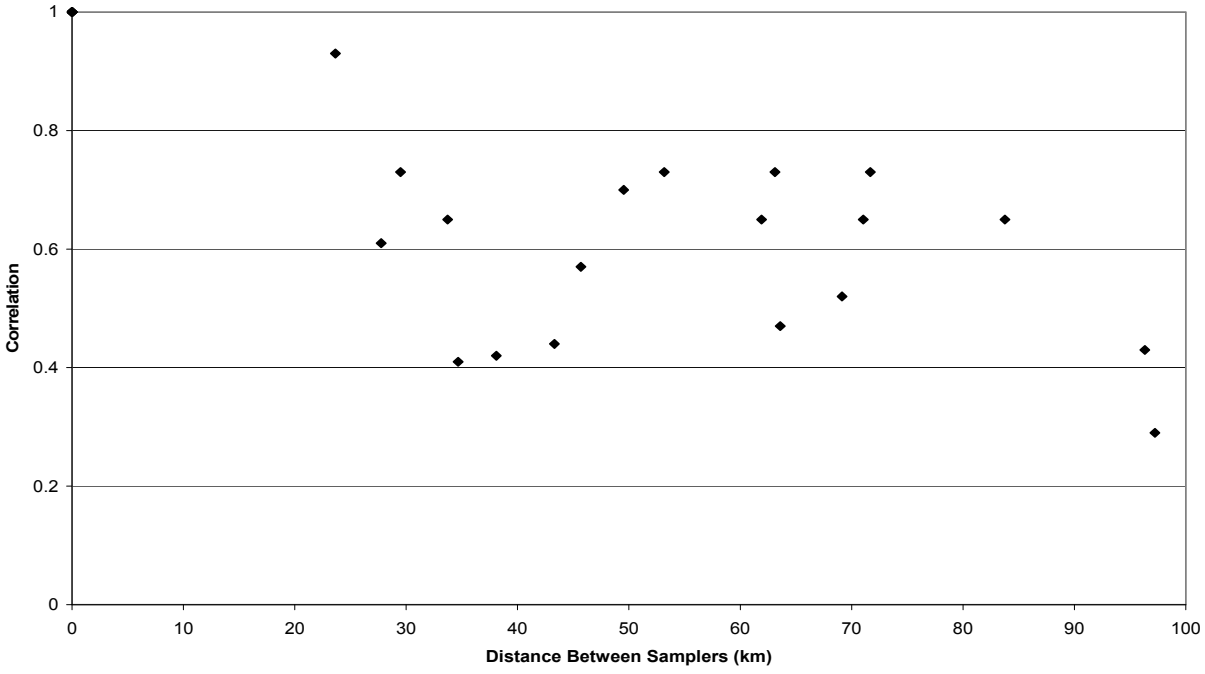
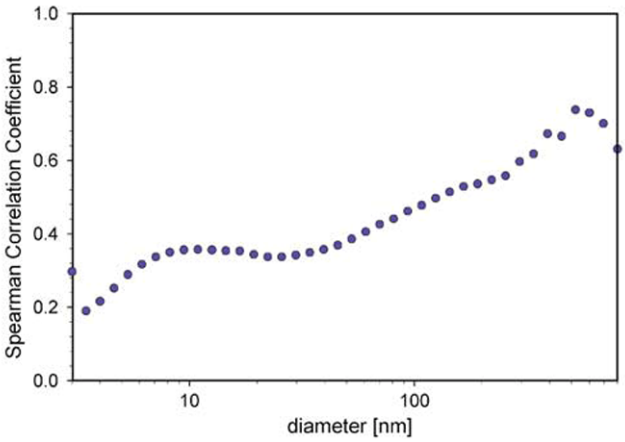


Figure 3-37. Inter-sampler correlations for 24-h PM_{10} as a function of distance between monitors in Los Angeles, CA.

UFPs

Relatively few studies compare UFP measurements at multiple locations within an urban center. An early study by Buzorius et al. (1999, 081205) suggested spatial homogeneity in total particle number concentrations between multiple locations in Helsinki, Finland. They found correlations in 10-min average at three sites within the city as high as 0.84. The sites, however, were relatively close together (2 km) and all near the same roadway. There was a high degree of correlation between traffic intensity and total aerosol number concentrations, suggesting that traffic was the primary source of the measured particles and the driving force behind the high correlations. Weekend correlations (0.28-0.47) and correlations with a fourth monitor located 22 km outside the city (0.05-0.64) were much lower.

Tuch et al. (2006, 157060) found more spatial heterogeneity in UFP concentrations measured for an entire year at two locations 1.5 km apart in Leipzig, Germany. Figure 3-38 shows the correlation as a function of particle size (mobility diameter) dropping off as the particle size decreases from 0.5 at 100 nm down to 0.2 at 3 nm. Table A-50 in Annex A contains correlation coefficients of hourly and daily average particle number, surface area and volume concentrations as a function of particle diameter adapted from the Tuch et al. (2006, 157060) study. For all days (N = 5481 hourly observations), the correlation between UFPs (10-100 nm) measured at the two sites was 0.31.



Source: Reprinted with Permission of Nature Publishing Group from Tuch et al. (2006, 157060)

Figure 3-38. Bin-wise Spearman correlation coefficients in aerosol particle number concentrations between the lft (urban background) and the Eisenbahn-strasse (city/urban center) sites in Leipzig, Germany.

The two sites represented in Figure 3-38 and Table A-44 were relatively close to each other, but one was located in a mixed semi-industrial region while the other was in a street canyon in a residential neighborhood near busy roadways. This suggests a high degree of spatial heterogeneity in UFPs driven primarily by differences in nearby source characteristics. Sioutas et al. (2005, 088428) reviewed studies of the distribution of UFPs and came to the similar conclusion that mobile sources make a large contribution to UFPs and therefore UFP concentrations can exhibit substantial variability in space and time. This is to be expected since UFP concentrations drop off much quicker with distance from roadways than larger particle sizes (Levy et al., 2003, 052661; Reponen et al., 2003, 088425; Zhu et al., 2005, 157191). Hagler et al. (2009, 191185) showed similar exponential decreases in UFP number concentrations with distance from the road for multiple locations in the U.S. Neighborhood-scale variability and near-roadway concentration gradients for UFPs are discussed further in Section 3.5.1.3.

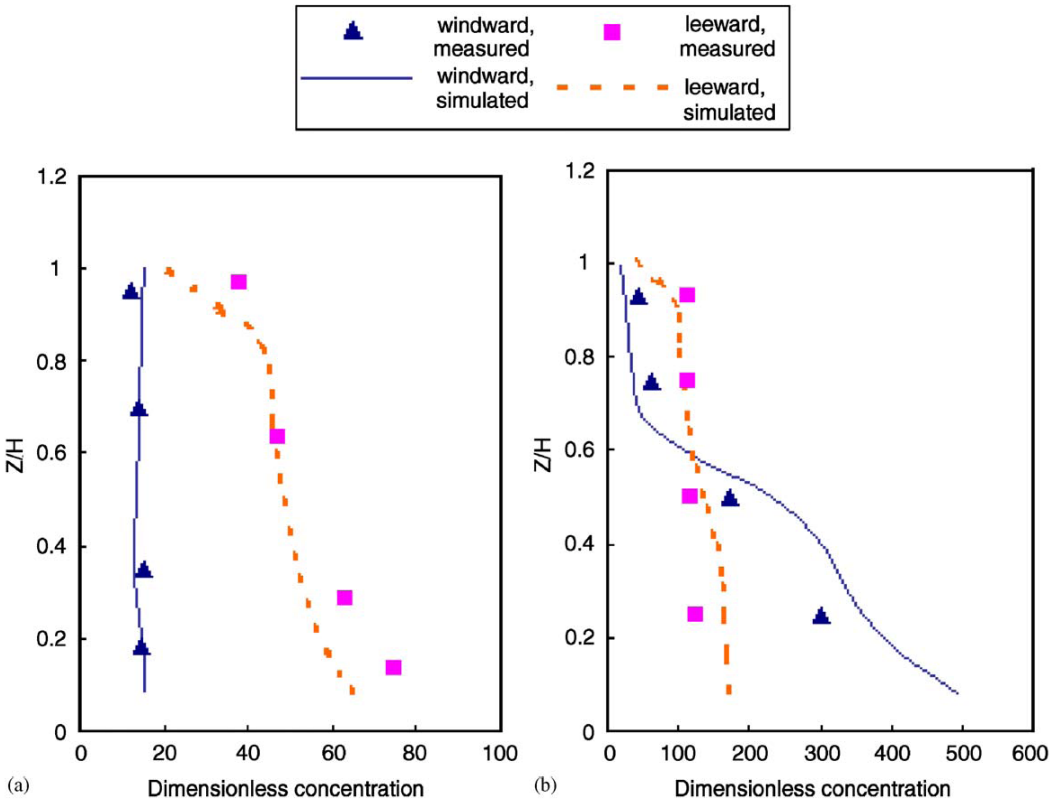
PM Constituents

The pie charts showing $PM_{2.5}$ composition that were generated using the SANDWICH method for the 15 CSAs/CBSAs presented earlier in Figure 3-17 and Figure 3-18 represent the average of all available monitors within each region. Individual pie charts for each monitor are included in Figures A-127 through A-141 in Annex A and provide an indication of the urban-scale spatial variability in $PM_{2.5}$ composition. In the instances where multiple monitors were available, there was a fair degree of spatial homogeneity in $PM_{2.5}$ bulk chemistry within each metropolitan area. Some notable exceptions exist, however. Birmingham and Detroit show variation in the amount of crustal material, both spatially and seasonally. Denver exhibits some spatial variation in NO_3^- during the winter, the season with the highest measured $PM_{2.5}$ mass. Several sites in New York and one in Pittsburgh have elevated fractions of EC relative to the other sites within the respective cities, and several sites in New York have been shown to have elevated Ni concentrations in $PM_{2.5}$ samples when compared with surrounding areas (Peltier and Lippmann, 2009, 197455; Peltier et al., 2008, 197452). In Phoenix, high winter $PM_{2.5}$ mass is site specific and appears to be associated with high OC; the crustal component also varies and is inversely proportional to total measured mass.

3.5.1.3. Neighborhood-Scale Variability

Neighborhood scale spatial variability in the particle concentration profile is affected by land and building topography, meteorology, particle size distribution, particle composition, and particle volatility. Population density at the neighborhood scale is also an important determinant of the spatial distribution of PM concentration because population density impacts source prevalence, source magnitude, topographical-driven ventilation, and heat island effects (Crist et al., 2008, 156372; Makar et al., 2006, 155959; Mfula et al., 2005, 123359; Rigby and Toumi, 2008, 156050).

A number of computational and wind tunnel modeling street canyon studies have demonstrated the potential variability in pollutant concentrations within a street canyon (Borrego et al., 2006, 155697; Chang and Meroney, 2003, 090298; Kastner-Klein and Plate, 1999, 001961; So et al., 2005, 110746; Xiaomin et al., 2006, 156165). Influential parameters include street canyon height to width ratio (H/W), source positioning, wind speed and direction, building shape and upstream configuration of buildings. Figure 3-39 shows pollutant concentrations obtained from wind tunnel and computational fluid dynamics simulations of transport and dispersion in an infinitely long street canyon with a line source centered at the bottom of the canyon (Xiaomin et al., 2006, 156165). When the canyon height was equal to the street width (typical of moderate density suburban or urban fringe residential neighborhoods) and lower background wind speed existed, concentrations on the leeward canyon wall were four times those of the windward wall near ground level. When the canyon height was twice the street width (typical of higher-density urban planning) and background winds were somewhat higher, near ground level concentrations on the windward canyon wall were roughly three times higher than those measured at the leeward wall. Baldauf et al. (2008, 191017; 2009, 191766) noted that the presence of noise barriers, vegetation, or changes in topography adjacent to the road can also alter particle dispersion characteristics. Specifically, depressed road segments, where the road bed is below the surrounding terrain, leads to increased air turbulence and pollutant dispersion. These results suggest that micro- and neighborhood-scale variation related to urban topography may have a significant impact on pollutant concentrations at this scale.



Source : Reprinted with Permission of Elsevier Ltd. From Xiaomin et al. (2006, 156165).

Figure 3-39. Dimensionless concentration as a function of height at windward and leeward locations and street canyon aspect ratios (H/W). (a) Dimensionless concentration on the windward and leeward sides of the canyon when H/W = 1 and wind speed = 3 m/s. (b) Dimensionless concentration on the windward and leeward sides of the canyon when H/W = 2 and wind speed = 5 m/s. Computational fluid dynamics modeling was performed, and measurements were obtained in wind tunnel simulations.

$PM_{2.5}$ and PM_{10}

Knowledge of neighborhood-scale variability is important for interpreting data from $PM_{2.5}$ and PM_{10} community monitors. Figure 3-40 shows data derived from the 15 CSAs/CBSAs for $PM_{2.5}$ and PM_{10} discussed in Section 3.5.1.2. This figure is limited to the inter-sampler correlations obtained for sampler pairs located within a distance of 4 km (i.e., neighborhood scale). $PM_{2.5}$ data exhibit a flatter slope, with average correlation maintained at 93% within 4 km ($R^2 = 0.22$). There is more scatter and variability among the PM_{10} data, with an average correlation of 70% within 4 km ($R^2 = 0.03$). The degree of variability in PM_{10} compared with $PM_{2.5}$ relates to transport and dispersion of the $PM_{10-2.5}$ component of PM_{10} compared with $PM_{2.5}$. However, differences in composition, source location, topography, and monitor height—all of which could affect concentrations—could drive the relatively high degree of scatter for both size classes, considering the low computed R^2 values for each of these curves.

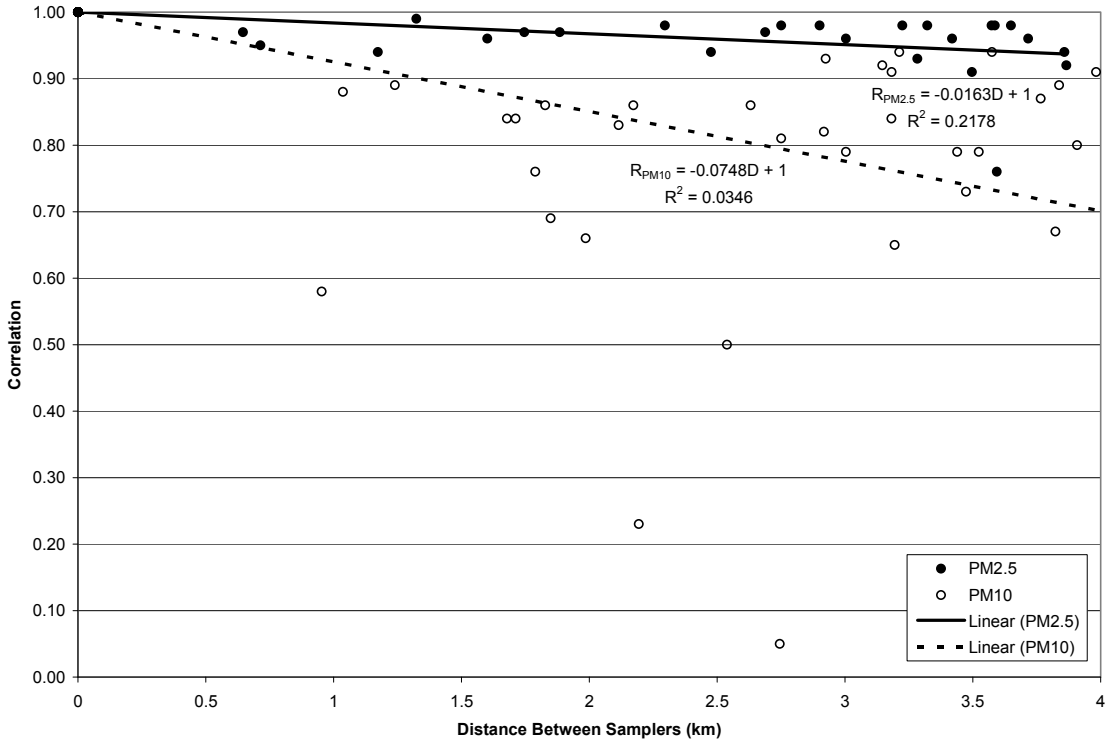


Figure 3-40. Inter-sampler correlations for 24-h $PM_{2.5}$ and PM_{10} as a function of distance between monitors for samplers located within 4 km (neighborhood scale).

Isakov et al. (2007, 156588) compared $PM_{2.5}$ concentrations from a central monitoring site in Wilmington, DE with $PM_{0.3}$ measurements taken on a mobile platform driven through mostly quite residential streets within a 4 km×4 km grid containing the central monitor. Correlations were generally high (average r = 0.87) over all time periods and locations monitored, consistent with the range of correlations for $PM_{2.5}$ shown in Figure 3-40.

$PM_{10-2.5}$

Neighborhood-scale variability in $PM_{10-2.5}$ was investigated by Chen et al. (2007, 147318) in the Raleigh/Durham area of NC. The average correlation between 26 residential monitors located throughout the region and a centrally located monitor representing a maximum inter-sampler range of 60 km was found to be 0.75 for $PM_{10-2.5}$ compared with 0.92 and 0.94 for $PM_{2.5}$ and PM_{10}, respectively. Based on this study, neighborhood-scale variability is greater for $PM_{10-2.5}$ than for $PM_{2.5}$ or PM_{10}, matching the conclusion drawn above on the broader urban-scale.

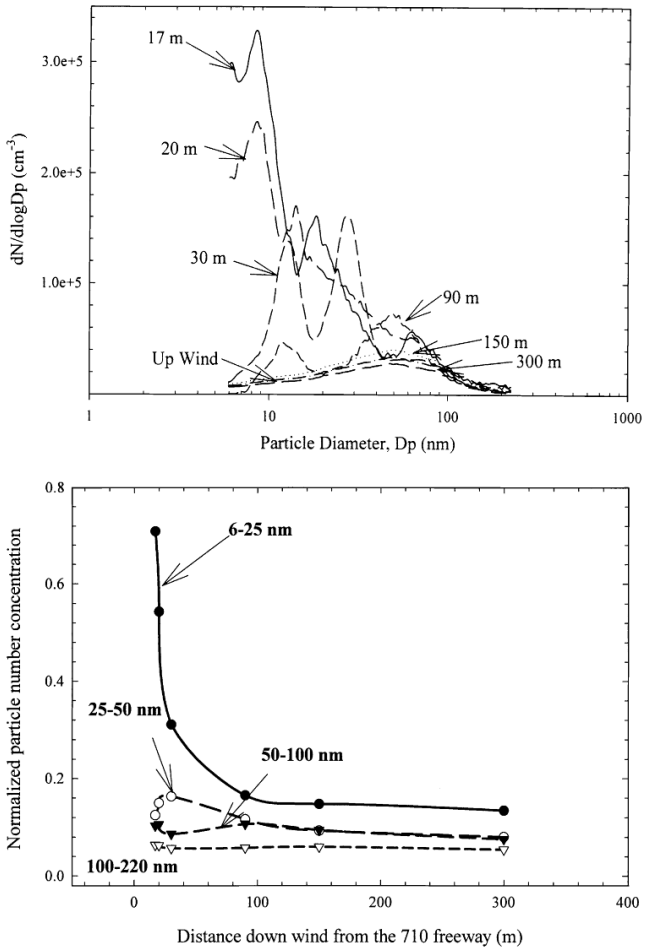
UFPs

Moore et al. (2009, 191004) monitored UFP concentrations throughout the Ports of Los Angeles and Long Beach, through which an interstate highway runs and found that concentrations varied by a factor of 5-7 across sites with substantial differences in the daily concentration time series at each site. Such variability reflects diversity of the sources (some near the Interstate, some near the Port), and the influence of changing meteorology over an urban area. In a mobile platform sampling study, Westerdahl et al. (2005, 086502) and Fruin et al. (2008, 097183) also reported substantial peaks in UFP concentration when sampling at highways in comparison with a background site (the University of Southern California) using the same data set.

Near roadway environments can exhibit high concentration gradients, particularly for UFPs. Ntziachristos et al. (2007, 089164) observed that the near-road particle size distribution was

substantially higher in the UF mobility diameter range and that these results were very sensitive to meteorology (rain) and time of day. Baldauf et al. (2008, 190239) reported elevated UFP number concentrations downwind of a highway in Raleigh, NC, when compared to measurements approximately 100 m upwind of the road. Hagler et al. (2009, 191185) noted a 5-12% decrease in number concentrations per 10 m distance from the road for a number of studies in the U.S. with unobstructed air flow.

After initial emission from a motor vehicle, the evolution of the PM distribution within the plume is a function of (1) the turbulence that dilutes the plume and (2) evaporation or condensation of the volatile portion of the aerosol that results from rapid cooling of the exhaust. Figure 3-41 shows the size distribution measured by Zhu et al. (2002, 041553) at distances of 17-300 m away from the roadway (in this case, Highway 710 in Los Angeles) and at an upwind site. It can be seen that a mode originally measured around 9 nm increases in diameter and decreases in number concentration as distance from the highway increases. Smaller secondary modes appear around 30 m from the roadway with multiple modes at some particle sizes. By 150 m away from the highway, the size distribution flattens with a small mode around 50 nm. It is clear from the bottom figure that the number concentration of larger particles (i.e., 100-220 nm) does not vary as much as UFPs (<100 nm) with increasing distance downwind from the roadway.



Source: Reprinted with Permission of Elsevier Ltd. From Zhu et al. (2002, 041553).

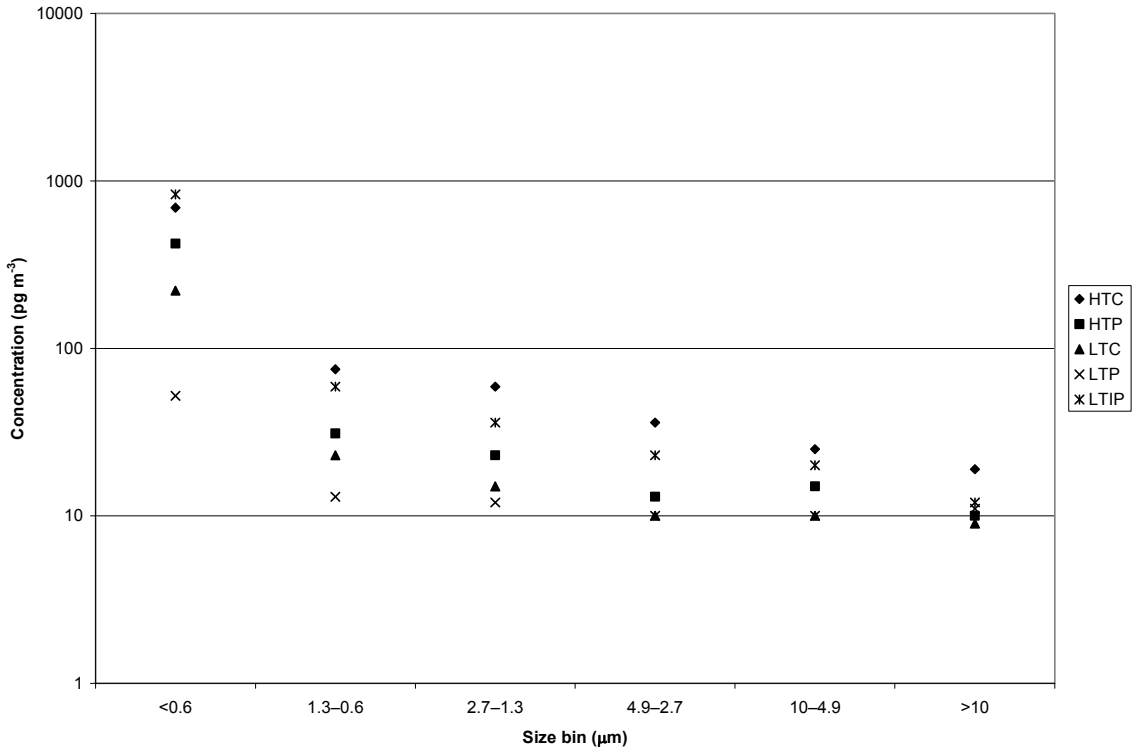
Figure 3-41. Particle size distributions measured at various distances from the 710 freeway in Los Angeles, CA (top), and particle number concentration as a function of distance from the 710 freeway (bottom).

Zhou and Levy (2007, 098633) performed a meta-analysis of traffic-related air pollution literature and found that background pollution and meteorology can have important impacts on the size of the elevated concentration region around the highway. Zhu et al. (2002, 041553) and Zhang et al. (2005, 157185) noted in field measurements of UFPs that small particles can be lost due to evaporation or to coagulation during Brownian diffusion to form bigger particles, resulting in an upward shift in mode diameter with distance from the roadway. Studies of particle sizes on roads (Kittelson et al., 2006, 156649; Kittelson et al., 2006, 156648), in tunnels (Venkataraman et al., 1994, 002475), and upwind and downwind of roads (Zhu et al., 2002, 041553) suggest that for well-maintained spark-ignition vehicles, a large fraction of the mass of particles emitted from the vehicles are in the nuclei mode (i.e., smaller than accumulation mode). High-speed highway driving may be associated with a larger fraction of particle mass being emitted in the UF size range, while lower speed operation results in a higher mass fraction in the accumulation mode (Cadle et al., 2001, 017192). In situations in which the dilution rates are lower than in a short tunnel or downwind of a road way, condensation of vapors can give rise to particles in the accumulation mode (Kittelson, 1998, 051098). Diesel engines, in particular, emit black carbon in the lower end of the accumulation mode, with number emissions dominated by semi-volatile material in the nuclei mode (Kittelson, 1998, 051098; Kittelson et al., 2006, 156649; Kittelson et al., 2006, 156648). Sharp gradients in black carbon mass have been observed along roadways with high diesel traffic (Zhu et al., 2002, 041553). As the traffic pollution moves downwind, the UFPs may grow into the accumulation mode by coagulation or condensation. In addition to Gaussian dispersion and wind eddies caused by the presence of natural and anthropogenic barriers, Sahlodin et al. (2007, 114058) demonstrated that turbulence produced by vehicles can result in modification of the plume emanating from the highway. Hence, on-road turbulence could potentially alter the aerosol size distribution. This added turbulence could cause some evaporation of tiny nucleation particles that have not absorbed or adsorbed onto soot nuclei, which may affect the rate of coagulation (Jacobson et al., 2005, 191187). The roadway configuration may also affect particle transport and dispersion. Depressed road sections, where the road bed is below the surrounding terrain, leads to increased air turbulence and mixing as air flows up and out of the road depression. This configuration can result in lower particulate concentrations and flatten concentration decay curves away from the road. On the other hand, configurations with the road bed at-grade with surrounding terrain, or elevated above the surrounding terrain with solid fill material resulted in the highest pollutant concentrations and sharpest concentration gradients downwind from the road.

PM Constituents

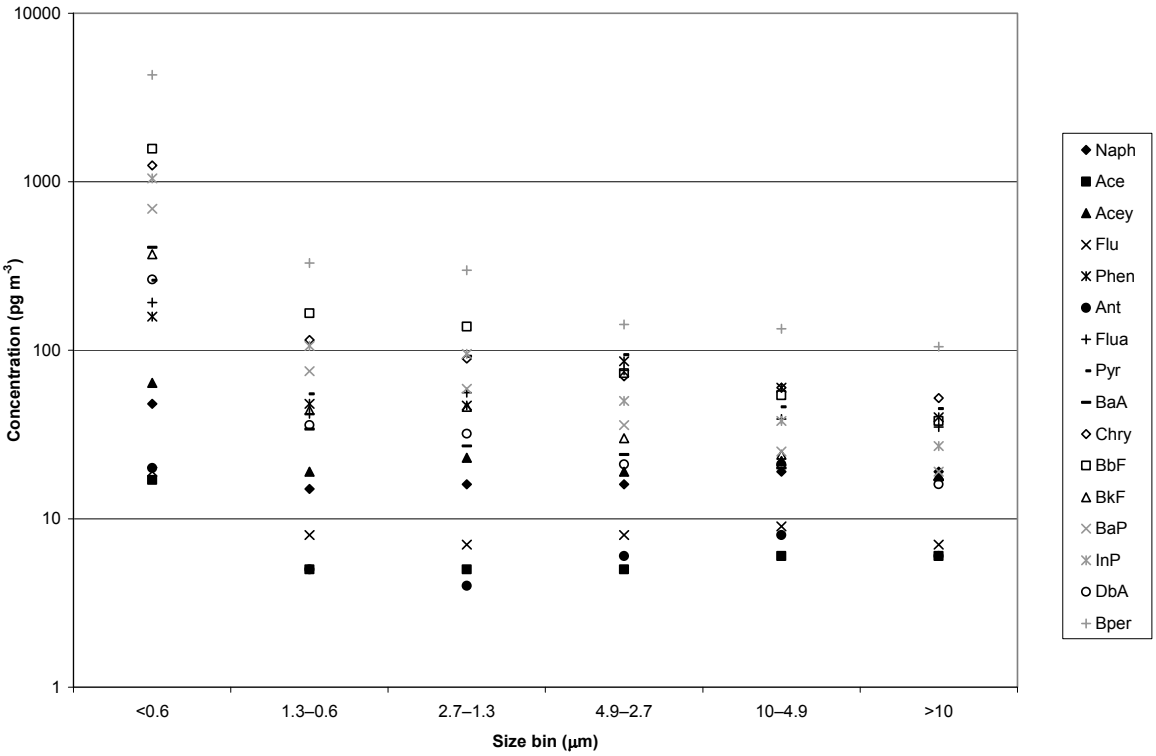
The composition of PM will also vary on the neighborhood-scale in response to local sources and differential dispersion, resulting in variable spatial distribution of individual components. Krudysz et al. (2008, 190064) investigated spatial variation in size-fractionated (<0.25 µm, 0.25-2.5 µm, >2.5 µm) PM composition data at four sites located within 3-6 km of each other in the Long Beach, CA area. Inter-site R^2 values in the 0.25-2.5 µm size range were higher for mass (ranging from 0.56-0.91) than for EC (0.02-0.71) for pair wise site comparisons. Spatial heterogeneity in all size ranges investigated was also found for several elements associated with motor vehicle emissions and resuspended road dust including Cu, Mg, Ba, Ca and Al. Viana et al. (2008, 156135) observed higher concentrations of crustal elements in $PM_{2.5}$ and PM_{10} samples in rural neighborhoods and higher concentrations of combustion-derived $PM_{2.5}$ and PM_{10}, such as EC and NO_3^-, in higher density urban areas. Gutiérrez-Dabán et al. (2005, 155818) examined the mass distribution of various PAHs under different traffic and urban density conditions. Figure 3-42 displays the distributions for benz[a]pyrene (BaP) at high and low traffic sites at the urban center, periphery, and industrial areas in Seville, Spain (Gutiérrez-Dabán et al., 2005, 155818). Concentrations were nearly an order of magnitude lower for the low traffic urban periphery location when compared with the high traffic or industrial locations. Particles smaller than ~ 600 nm had roughly an order of magnitude higher concentration than those at larger sizes and tended to have a larger spread in concentrations among sampling sites. Figure 3-43 shows the distributions for sixteen PAHs at a high traffic location at the city center in Seville, Spain (Gutiérrez-Dabán et al., 2005, 155818). PAH species varied in concentration by up to two orders of magnitude for each particle size bin, and the highest concentrations of individual PAHs were generally found for particles smaller than approximately 600 nm. Olson and McDow (2009, 191188) reported decreases by a factor of 1.04-2.37 in select PAH and organic source marker concentrations when comparing measurements 10 m and 275 m from a highway in Raleigh, North Carolina. Phuleria et al. (2006, 156867) sampled

UFPs and $PM_{2.5}$ concentrations and PAH species at the mouth of the Caldecott Tunnel in Orinda, CA and found that the two size classes were highly correlated ($R^2 = 0.97$). Given the size differentials of each size bin presented in the Gutiérrez-Dabán et al. (2005, 155818) study, it is possible that the $PM_{2.5}$ sampled at the tunnel mouth in the latter study represented secondary $PM_{2.5}$ that grew from UFP emissions trapped within the tunnel.



Source: Adapted with Permission of Springer-Verlag from Gutiérrez-Dabán et al. (2005, 155818).

Figure 3-42. Mass distributions for BaP at a high traffic urban center (HTC), high traffic urban periphery (HTP), low traffic urban center (LTC), low traffic urban periphery (LTP), and low traffic industrial urban periphery (LTIP) in Seville, Spain.



Source: Adapted with Permission of Springer-Verlag from Gutiérrez-Dabán et al. (2005, 155818).

Figure 3-43. Mass distributions for 16 PAHs at a high traffic city center in Seville, Spain.

3.5.2. Temporal Variability

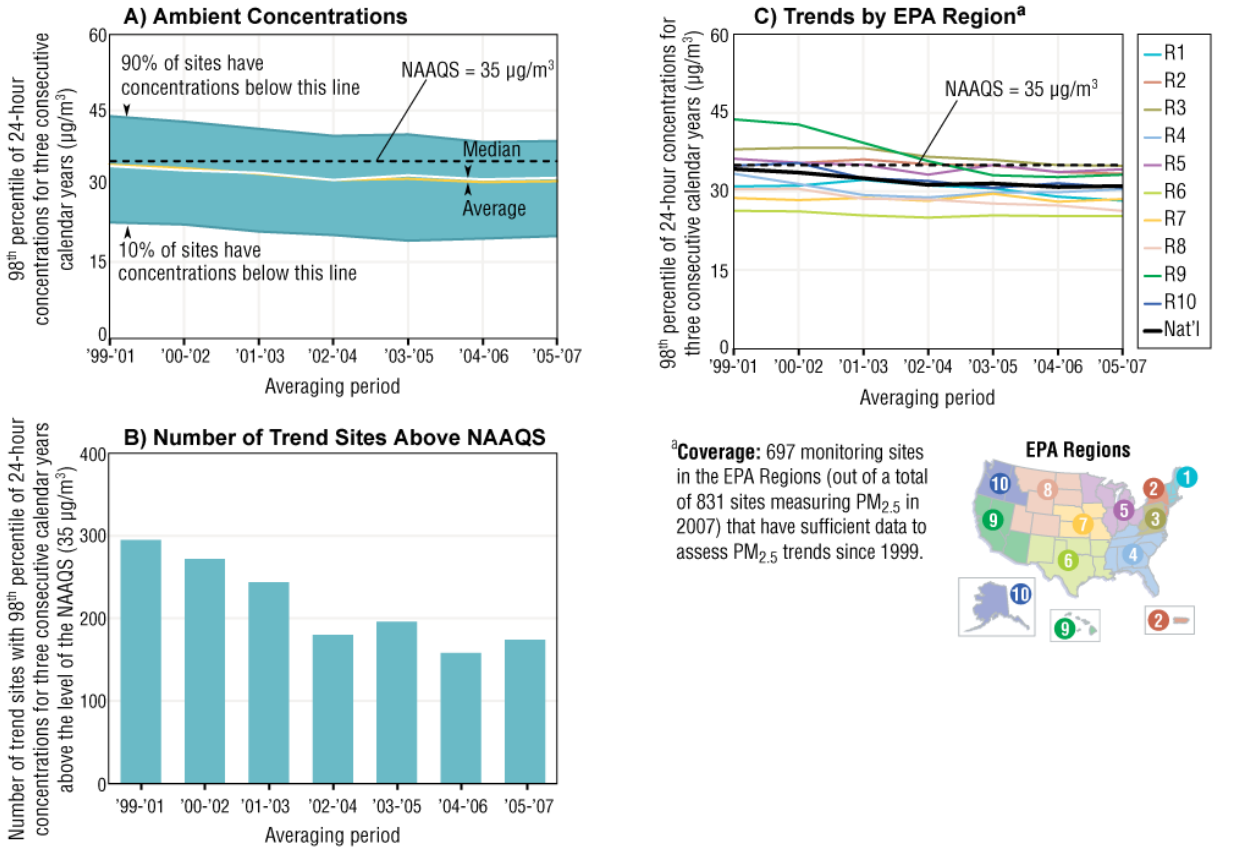
Temporal variability is another important factor in characterizing PM. This section addresses trends as well as seasonal and hourly variability. Trends in $PM_{2.5}$ and PM_{10} are addressed in Section 3.5.2.1 based on AQS data. Seasonality is coupled with spatial variability and has been discussed in the regional context above. Section 3.5.2.2 below briefly investigates the seasonality on a finer time scale, thereby addressing issues relating to the seasonal definitions used earlier. Section 0 addresses hourly patterns, an issue particularly important to understanding the behavior of PM concentrations in reference to sources, human activity patterns and exposure. Hourly patterns are investigated using AQS data on a national basis for $PM_{2.5}$ and PM_{10}. Data for UFPs and PM constituents are presented where available.

3.5.2.1. Regional Trends

This section summarizes available information on trends in PM mass and composition. Mass concentration trends are based on AQS data and incorporate 9 years (1999-2007) of $PM_{2.5}$ data and 20 years (1988-2007) of PM_{10} data. Composition trends are based on six years of available CSN data (2002-2007). Several monitoring sites were excluded from the following trend analyses to provide a consistent basis for comparison over the desired years of monitoring. This included exclusion of sites when there was no corresponding site in later or earlier years. Region-average trends were calculated to facilitate presentation and extrapolation of the results. These region-averages, however, may not necessarily represent the trends that are being observed at any individual monitor or geographical location within the specified region.

$PM_{2.5}$

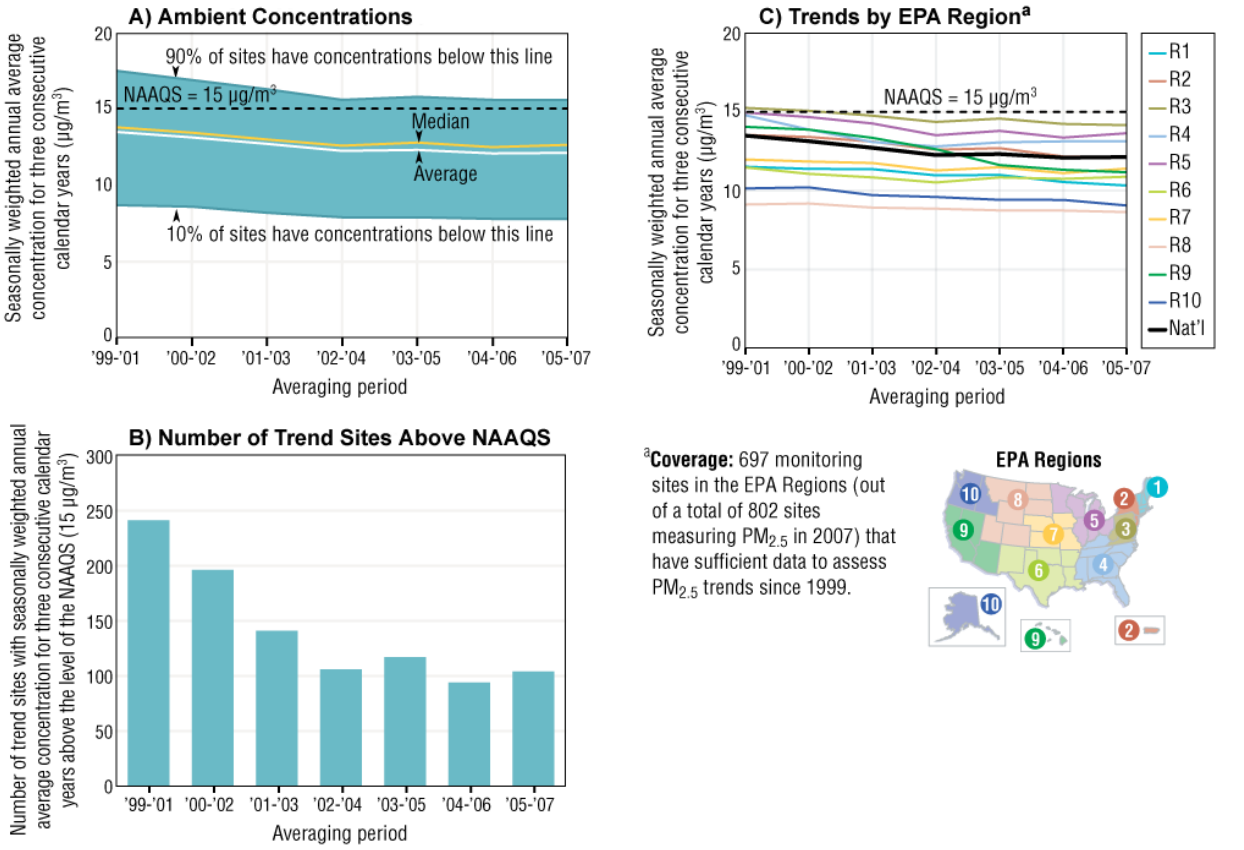
Figure 3-44 shows trends in U.S. ambient 24-h $PM_{2.5}$ concentrations from 1999-2007. In the period 2005-2007, the 3-yr avg of the 98th percentile of 24-h $PM_{2.5}$ concentrations fell 10% relative to the 1999-2001 period (see Figure 3-44A). The number of sites reporting values greater than the 24-h NAAQS was shown to decline 40% in Figure 3-44B. Figure 3-44C illustrates the downward trend in the 98th percentile of 24-h $PM_{2.5}$ concentrations for three consecutive calendar years in all U.S. EPA regions. This trend is most pronounced in Region 9 incorporating Arizona, California and Nevada where this value dropped 25% from the 1999-2001 period to the 2005-2007 period.



Source: U.S. EPA (2008, 157076)

Figure 3-44. Ambient 24-h $PM_{2.5}$ concentrations in the U.S., 1999-2007, showing A) ambient concentrations, B) number of trends sites above the 24-h NAAQS and C) trends by U.S. EPA Region.

Figure 3-45 contains similar trend information for the annual $PM_{2.5}$ NAAQS. The seasonally weighted 3-yr avg $PM_{2.5}$ concentrations for the years 2005-2007 were at the lowest since national monitoring began in 1999 (Figure 3-45A). The seasonally weighted 3-yr avg fell 10% between the 1999-2001 averaging period and the 2005-2007 averaging period. The number of sites reporting concentrations above the annual average $PM_{2.5}$ NAAQS fell 56% over these same periods in Figure 3-45B. Figure 3-45C illustrates the annual trends in $PM_{2.5}$ by U.S. EPA region. Declines were the greatest in Region 9 again where annual $PM_{2.5}$ concentrations fell 20% from the 1999-2001 averaging period to the 2005-2007 averaging period.

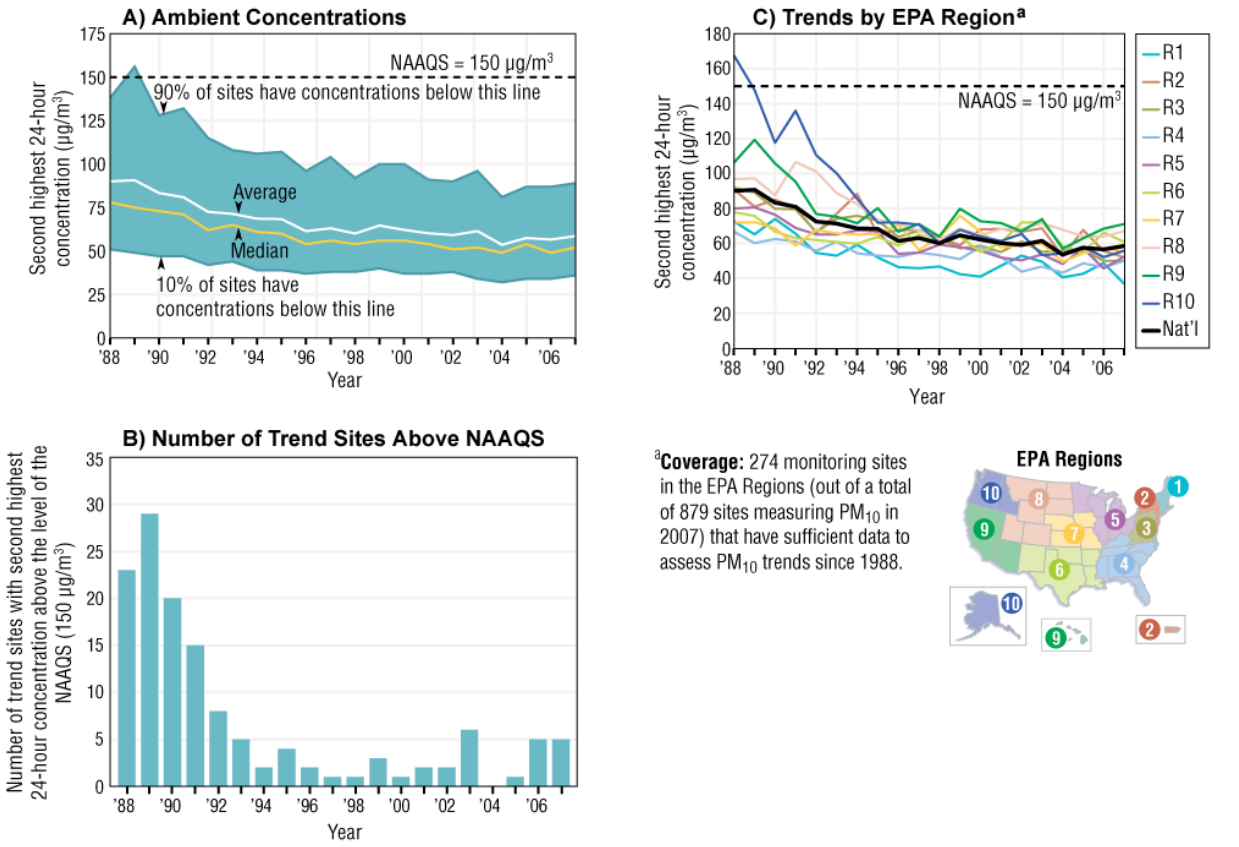


Source: U.S. EPA (2008, 157076).

Figure 3-45. Ambient annual $PM_{2.5}$ concentrations in the U.S., 1999-2007, showing A) ambient concentrations, B) number of trends sites above the annual NAAQS and C) trends by U.S. EPA Region.

PM_{10}

Figure 3-46 shows trends in U.S. ambient 24-h PM_{10} concentrations from 1988-2007. In 2007, the U.S. national average second highest PM_{10} concentration was 37% lower than in 1988 (Figure 3-46A). Of 281 sites used in this trend analysis, the number reporting concentrations above the 24-h PM_{10} NAAQS (150 µg/m^3) fell from 23 in 1988 to 5 in 2007 with a max of 29 in 1989 (Figure 3-46B). Figure 3-46C shows trends in the second highest 24-h PM_{10} concentrations broken down by U.S. EPA region. All regions exhibit an overall decrease from 1988-2007. Largest decreases occurred in EPA Region 10, which incorporates Washington, Oregon, Idaho and Alaska. Most of the decrease occurred between 1988-1995.

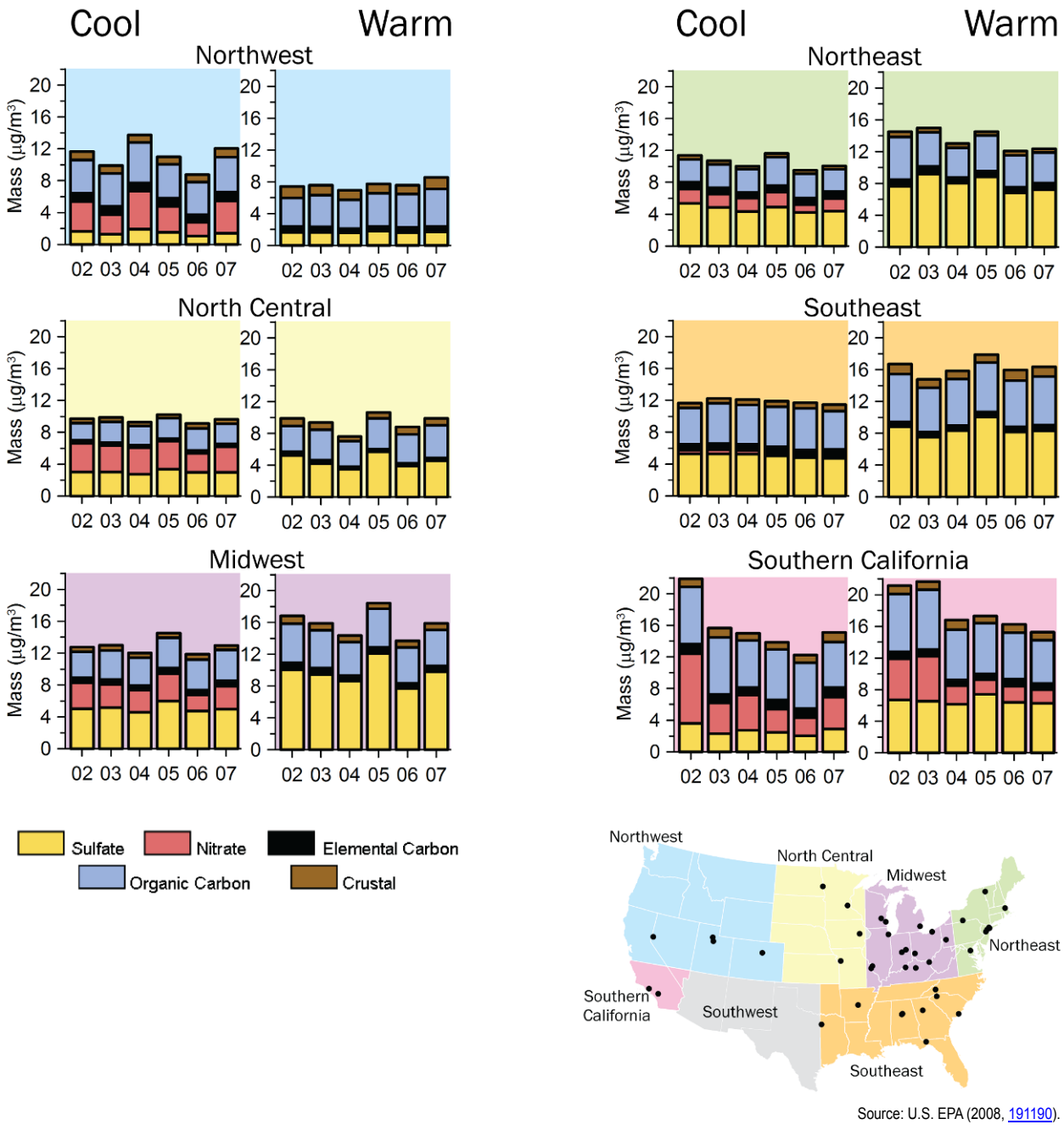


Source: U.S. EPA (2008, 157076).

Figure 3-46. Ambient 24-h PM_{10} concentrations in the U.S., 1988-2007, showing A) ambient concentrations, B) number of trends sites above the 24-h NAAQS and C) trends by U.S. EPA Region.

PM Constituents

The SANDWICH method discussed in Section 3.5.1.1 for estimating $PM_{2.5}$ composition from FRM mass measurements and CSN bulk composition measurements was used to evaluate trends in $PM_{2.5}$ constituents. Figure 3-47 includes stacked bar charts of $PM_{2.5}$ composition from 2002 to 2007 stratified by region and season. The regions used in Figure 3-47 were selected based on common aerosol characteristics including trends, seasonality, size distributions and/or composition as described in chapter 6 of the 1996 PM AQCD (U.S. EPA, 1996, 079380) and differ from the EPA regions used in the preceding figures. Figure 3-47 is based on 42 monitoring locations reporting complete CSN data with 2002 being the first year with sufficient speciation data. The Southwest region incorporating Arizona, New Mexico and parts of Texas and Oklahoma did not contain any complete data and therefore is not represented in this analysis. Two seasons representing different temperature ranges–cool (October-April) and warm (May-September)–were considered in the figure since many $PM_{2.5}$ components exhibit strong seasonal dependence.



Source: U.S. EPA (2008, 191190).

Figure 3-47. Regional and seasonal trends in annual $PM_{2.5}$ compostion from 2002 to 2007 derived using the SANDWICH method. Data from the 42 monitoring locations shown on the map were stratified by region and season including cool months (October-April) and warm months (May-September). SO_4^{2-} and NO_3^- estimates include NH_4^+ and particle bound water.

Most of the components showed little discernable trend over the 6-yr period. SO_4^{2-} showed a peak during the warm months of 2005 in the Southeast, Northeast and Midwest, partly due to atypical weather conditions (U.S. EPA, 2008, 191190). However, no trend over the 6-yr time period is present for SO_4^{2-} in any of the regions or seasons. The same is true for EC and crustal material. A slight decline in OC was observed for the Northeast during warm months and in Southern California year-round. The largest decline was for NO_3^- in Southern California during both cool and warm

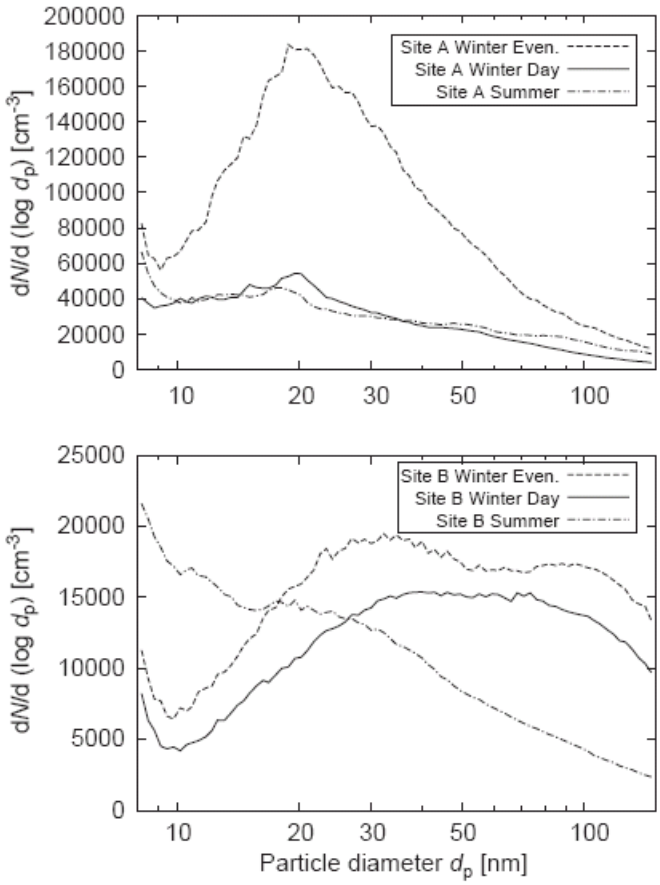
months. A smaller decline in NO_3^- is also observed in the other regions with the exception of the Northwest where no discernible trend is present. This analysis is limited in time and space by the availability of CSN data so a high degree of uncertainty remains regarding $PM_{2.5}$ compositional trends. However, with the exception of NO_3^- concentrations in Southern California, no major changes in $PM_{2.5}$ composition are evident based on available CSN data from 2002-2007. This is consistent with Figure 3-44 and Figure 3-45 where the downward trend in $PM_{2.5}$ mass begins to level off after 2002.

3.5.2.2. Seasonal Variations

Many of the figures and tables presented in the preceding sections have included a seasonal break-down based on the following climatological seasons: winter (December-February), spring (March-May), summer (June-August) and fall (September-November). Figures A-142 through A-156 in Annex A show bar charts of $PM_{2.5}$ composition by individual month, illustrating intra-annual variability on a finer time scale. The same 15 CSAs/CBSAs are investigated and included in these plots; they are generated from the same data used in the seasonal and annual pie charts based on the SANDWICH method discussed in Section 3.5.1.1 and illustrated in Figure 3-17 and Figure 3-18.

Monthly plots for most of the areas reveal heterogeneity in PM composition within the 3-month long seasonal bins defined earlier. This is especially true in the spring and fall when daily average weather conditions (e.g., temperature) are changing most rapidly, driving fluctuation in $PM_{2.5}$ composition on relatively short timescales in many cities. For example, the NO_3^- mass in Los Angeles (Figure A-129) and Riverside (Figure A-134) can vary from a small fraction to the most prevalent fraction of $PM_{2.5}$ mass in a month's time based on the 3-yr aggregate data. Therefore, selecting a different delineation point for the seasons can have an influence on the seasonal composition analysis, specifically for constituents that fluctuate rapidly (e.g., NO_3^-).

Relatively little is known about the seasonal variability in UFPs. Kuhn et al. (2005, 129448) and Zhu et al. (2004, 156184) found that the concentrations in the UF mode in Los Angeles, CA can be much higher during winter, particularly during evenings, because atmospheric dilution is reduced in response to lower mixing heights (Figure 3-48). Jeong et al. (2004, 180350) made similar observations in Rochester, NY, suggesting an inverse relationship between temperature and UFP formation in the 11-470 nm size range. Singh et al. (2006, 190136) reported higher particle number concentrations during winter months, relative to summer and spring, at urban sites in Southern California, and that afternoon particle number concentrations in warm months either occurred during a peak in ozone concentrations or followed shortly thereafter, suggesting a role for photochemistry in addition to meteorological changes in the formation of aerosols. The study also reported increased concentrations of 60-200 nm particles during a labor strike at the Port of Long Beach, suggesting contributions from idling ships. Moore et al. (2009, 191004) also report higher particle number concentrations during cooler months at 14 sites in Long Beach, San Pedro, and Wilmington, CA, a location with diverse industrial and transportation sources. However, they noted substantial heterogeneity in seasonal trends between sites with seasonal numerical size distributions not generalizable across the study area with a maximum monitor separation of under 10 km.



Source:Reprinted with Permission of Elsevier Ltd. from Kuhn et al. (2005, 129448).

Figure 3-48. UFP size distribution at highway (site A) and background (site B) sites in Los Angeles, CA, during summer and winter seasons, with winter broken into day and evening distributions.

Studies reporting higher cold-season particle number concentrations are consistent with vehicle emission studies that found particle emission rates elevated during lower ambient temperatures (Baldauf et al., 2005, 191184; Mathis et al., 2005, 155970; U.S. EPA, 2008, 191767). Mathis et al. (2005, 155970) found that cold-start conditions produce roughly an order of magnitude greater PM number emissions in gasoline engines and more than two orders of magnitude higher PM number emissions in diesel engines when compared with warm start conditions.

3.5.2.3. Hourly Variability

Hourly $PM_{2.5}$ and PM_{10} measurements are conducted at many sites using beta gauge or TEOM monitors. Many of the hourly measurements for PM_{10} have FRM or FEM status. All available hourly data from FRM, FEM and FRM-like monitors in the 15 CSAs/CBSAs discussed earlier were used to investigate diel variation in PM. Of the 15 CSAs/CBSAs, Atlanta, Chicago, Pittsburgh, Seattle and St. Louis had qualifying hourly $PM_{2.5}$ and PM_{10} data available. Houston and New York had only qualifying $PM_{2.5}$ data. Denver, Detroit, Los Angeles, Philadelphia, Phoenix, and Riverside had only qualifying hourly PM_{10} data. Birmingham and Boston had no qualifying hourly $PM_{2.5}$ or PM_{10} data.

Diel plots for $PM_{2.5}$ stratified by weekdays and weekends for seven of the 15 CSAs/CBSAs with available data between 2005 and 2007 are included in Annex A, Figures A-157 through A-163. In most cities investigated, a morning $PM_{2.5}$ peak is present starting at approximately 6:00 a.m., corresponding with the start of the morning rush hour just before the break-up of overnight stagnation. In Pittsburgh, dispersion behavior during the night results in elevated $PM_{2.5}$

concentrations throughout the night that blend in with any morning peak. With the exception of Pittsburgh, all seven metropolitan areas show two distinct daily peaks on both the weekdays and weekends. The evening $PM_{2.5}$ concentration peak is broader than the morning peak and extends to overnight hours, reflecting the concentration increase caused by a drop in boundary layer height at night. Figure 3-49 compares the two-peak diel distribution in $PM_{2.5}$ for Seattle with the one-peak distribution in $PM_{2.5}$ for Pittsburgh Since these figures represent the distribution of hourly observations over a 3-yr period, any fluctuations or changes in the timing of the daily peaks would result in a broadening of the curves shown in the diel plot.

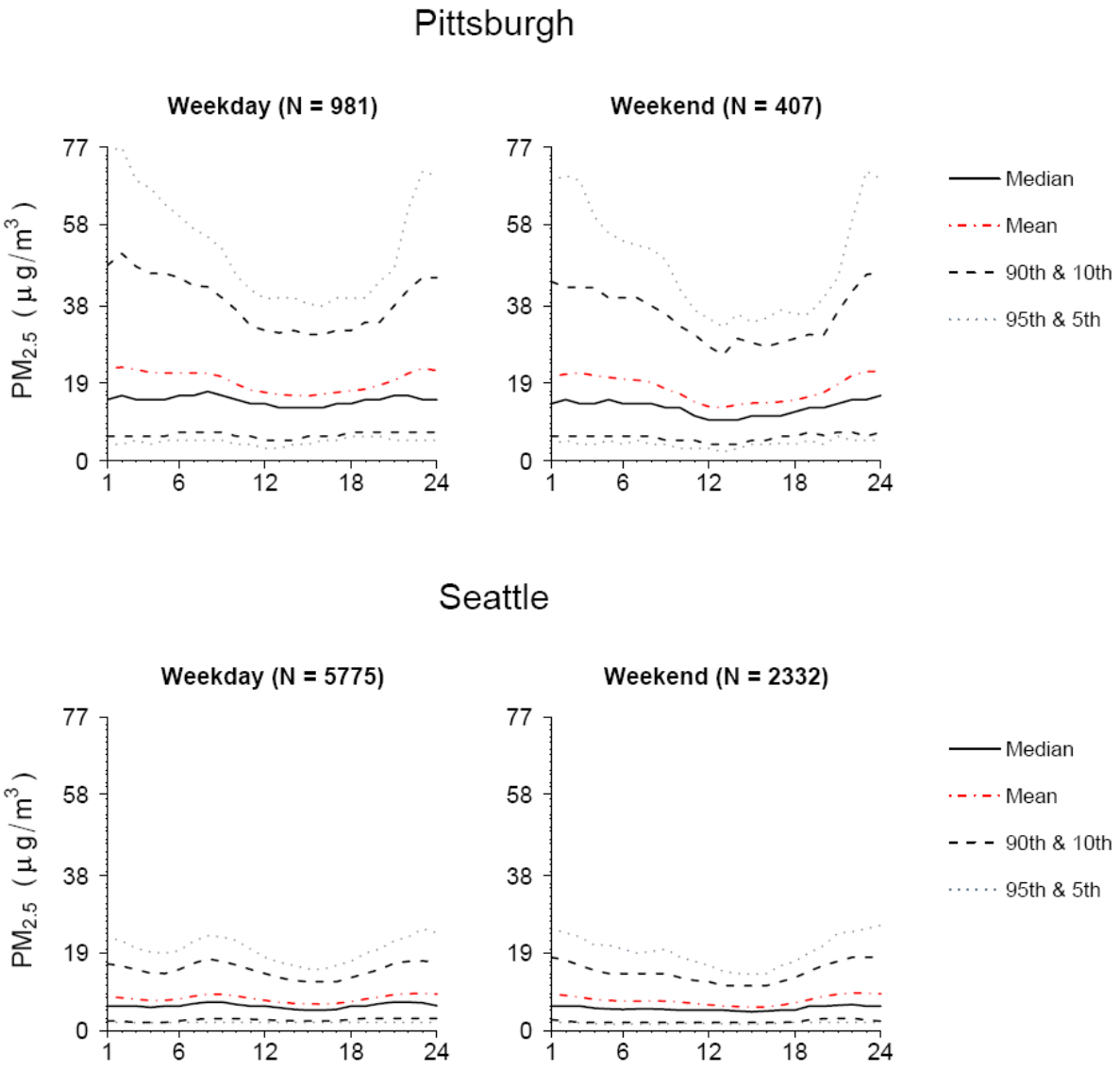


Figure 3-49. Diel plot generated from hourly FRM-like $PM_{2.5}$ data ($\mu g/m^3$) stratified by weekday (left) and weekend (right) for Pittsburgh, PA, and Seattle, WA, 2005-2007. Included are the number of monitor days (N) and the median, mean, 5th, 10th, 90th and 95th percentiles for each hour of the day shown on the horizontal axis.

Annex A, Figures A-164 through A-174 show diel patterns for PM_{10} stratified by weekdays and weekends for eleven of the 15 CSAs/CBSAs with available data between 2005 and 2007. All cities show a gradual morning increase in mean PM_{10} starting at approximately 6:00 a.m. on weekdays, corresponding with the start of the morning rush hour before the break-up of overnight stagnation. The magnitude and duration of this peak, however, varies considerably by area. Phoenix shows the most pronounced morning PM_{10} peak concentration, which drops off during the day and reappears in the evening. In contrast, Chicago shows a less pronounced peak with the PM_{10} concentration remaining elevated throughout the day. Figure 3-50 shows the diel plots of PM_{10} for Chicago and Phoenix. In both instances, the weekend diel pattern is similar in shape to the weekday pattern with less pronounced peaks. Once again, any fluctuations in the timing of the daily peaks could result in a broadening of the peaks in the 3-yr composite diel figures.

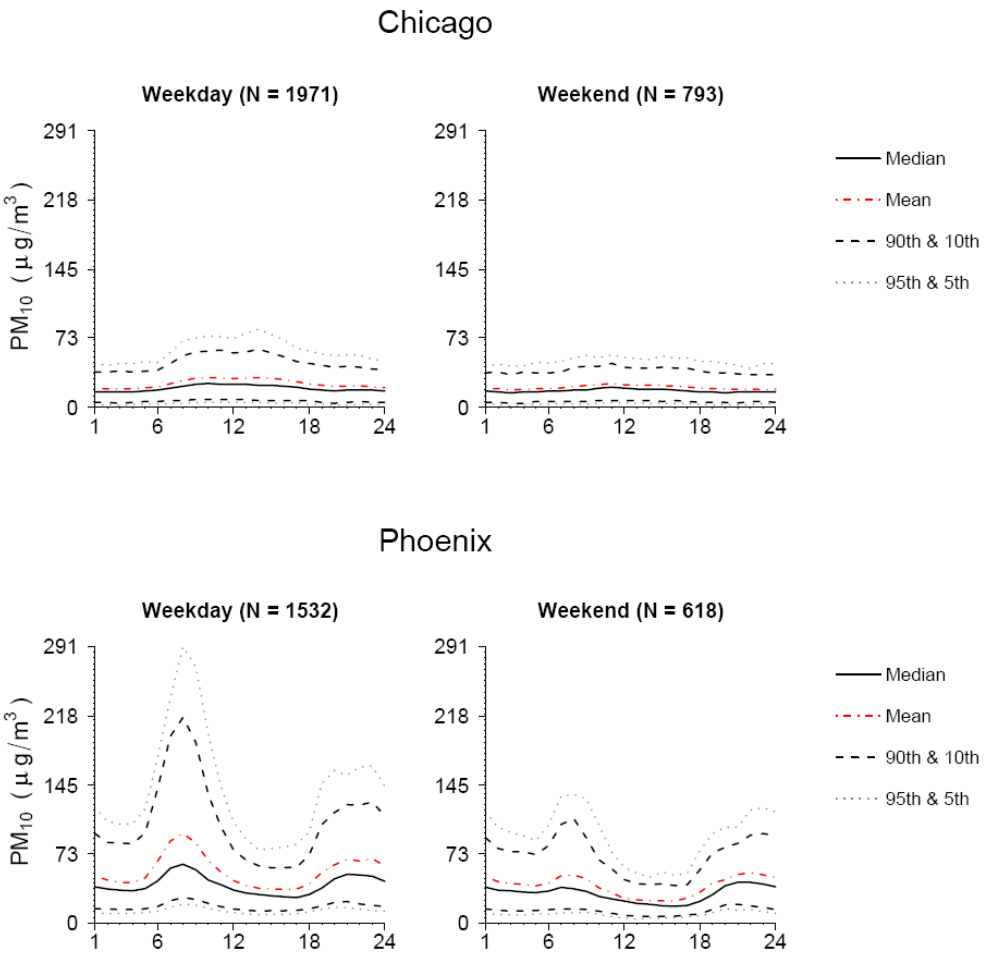
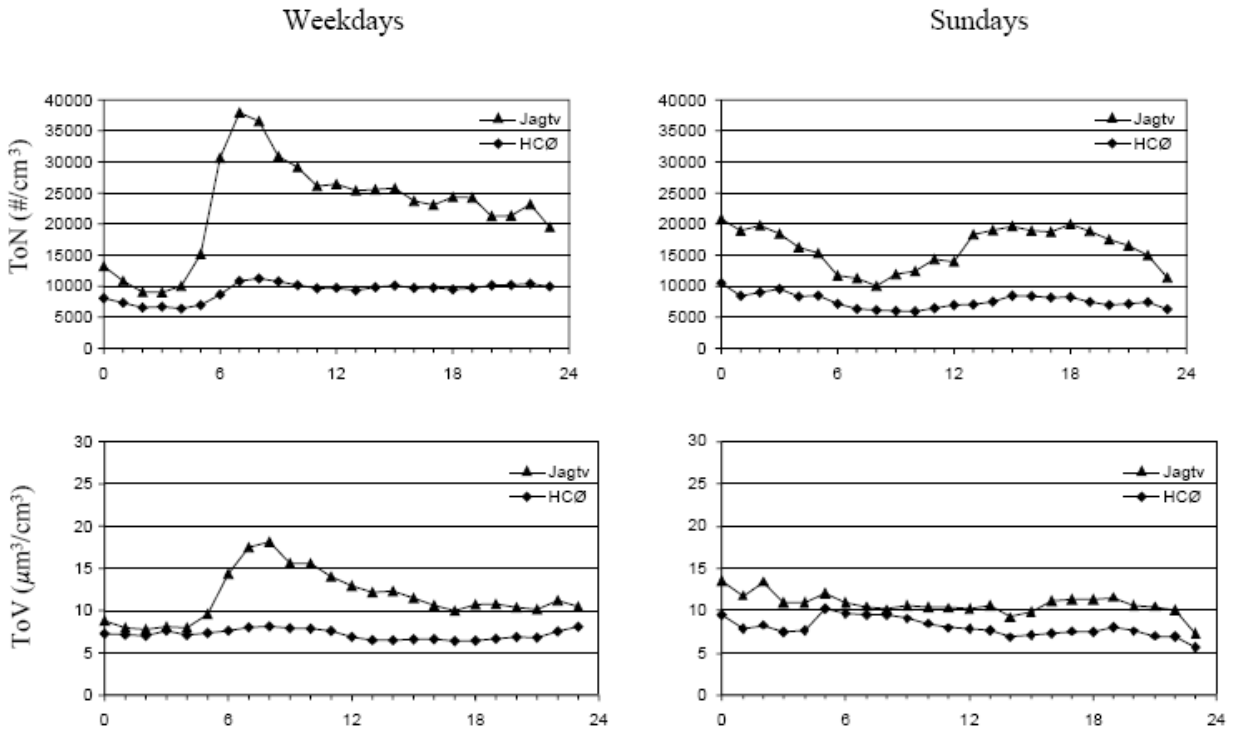


Figure 3-50. Diel plots generated from hourly FEM PM_{10} data (µg/m^3) stratified by weekday (left) and weekend (right) for Chicago, IL, and Phoenix, AZ, 2005-2007. Included are the number of monitor days (N) and the median, mean, 5th, 10th, 90th and 95th percentiles for each hour of the day shown on the horizontal axis.

UFPs in urban environments have been shown to exhibit a similar two-peaked diel pattern in Los Angeles (Moore et al., 2007, 122445; Sardar et al., 2005, 180086) and the San Joaquin Valley (Herner et al., 2005, 135983) in CA, Rochester, NY (Jeong et al., 2004, 180350), Raleigh, NC (Baldauf et al., 2008, 190239) as well as in Kawasaki City, Japan (Hasegawa et al., 2005, 157355) and Copenhagen, Denmark (Ketzel et al., 2003, 131251). Figure 3-51 from the Denmark study

shows a large peak in total particle number (dominated by UFPs) corresponding with the morning rush hour. The morning peak is absent on Sundays, however. Many studies also show a broad afternoon UFP concentration peak, which likely originates from a combination of evening rush-hour traffic, decreased atmospheric dilution and formation of UFPs through nucleation involving products of active photochemistry. Nucleation likely plays an important role since the afternoon peak is present on weekends whereas the morning traffic related peak is absent. This is consistent with observations of particle counts in Atlanta peaking during the mid-afternoon for particles <10 nm (Woo et al., 2001, 011702) resulting from nucleation.



Source: Adapted with Permission of Elsevier Science Ltd. From Ketzel et al. (2003, 131251)

Figure 3-51. Average diel variation in total particle number (ToN) and total particle volume (ToV) on weekdays (left column) and Sundays (right column) from two sites in Denmark: one in a busy street canyon (Jagtv) and one measuring urban background (HCØ).

Hourly variability in particle-phase OC and EC were investigated by Bae et al. (2004, 156243) in the urban St. Louis atmosphere. OC diel patterns were similar during weekdays and weekends with a broad morning and evening concentration peak most likely reflecting daily fluctuations in atmospheric mixing height. Weekend EC diel patterns were similar to those for OC, but the weekday patterns showed more abrupt EC concentration peaks in the morning and afternoon, coinciding with rush-hour traffic. The divergent weekday patterns between OC and EC suggests motor vehicles or other EC sources with temporal profiles tracking traffic patterns are primarily responsible for the daily fluctuations in EC concentrations in St. Louis.

3.5.3. Statistical Associations with Copollutants

Associations between different PM size fractions and between PM and other copollutants including SO_2, NO_2, CO and O_3 are investigated in this section. AQS data were obtained from all available co-located monitors across the U.S. after application of a completeness criterion of 11 or

more observations per quarter. Pearson correlation coefficients (r) were calculated using 2005-2007 data. The results are displayed graphically in Figure 3-52 for correlations with $PM_{2.5}$ mass concentration and Figure 3-53 for correlations with PM_{10} mass concentration. The different PM size fractions are compared and contrasted in this section using temporal correlations which should not be confused with average PM mass fraction (e.g., $PM_{2.5}/PM_{10}$) comparisons discussed in Section 3.5.1.1.

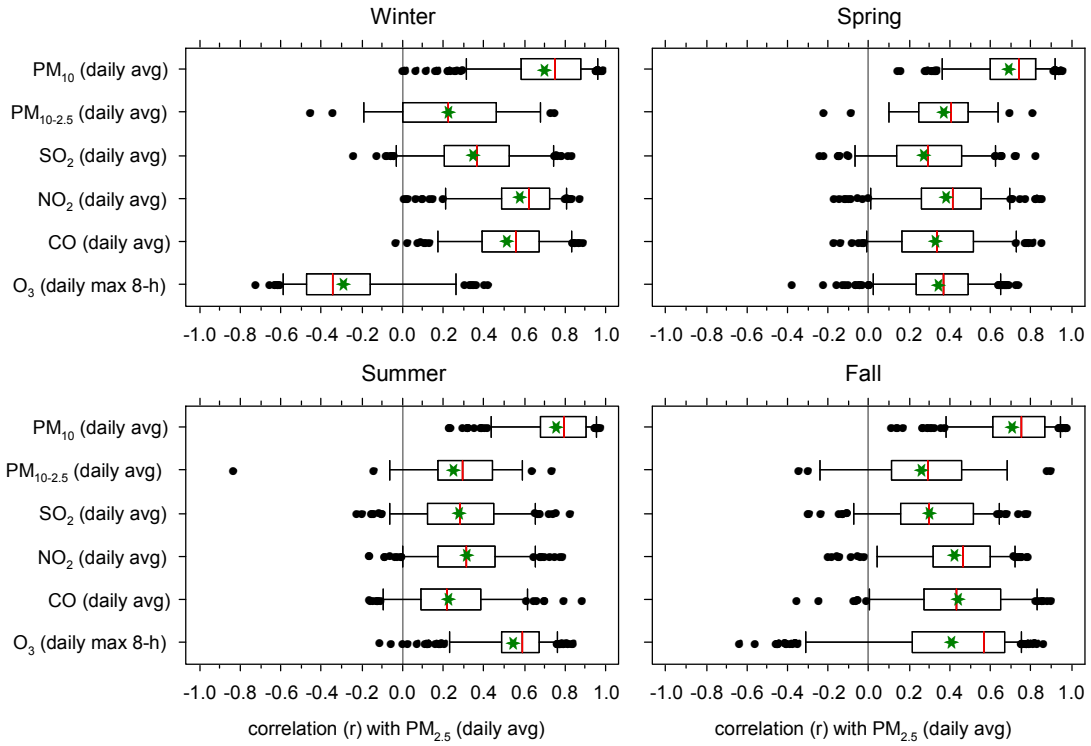


Figure 3-52. Distribution of correlations between 24-h avg $PM_{2.5}$ and co-located 24-h avg PM_{10}, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily max 8-h avg O_3 for the U.S. stratified by season (2005-2007). Statistics shown include the mean (green star), median (red line), inner quartile range (box), 5th/95th percentiles (whiskers) and outliers (black circles).

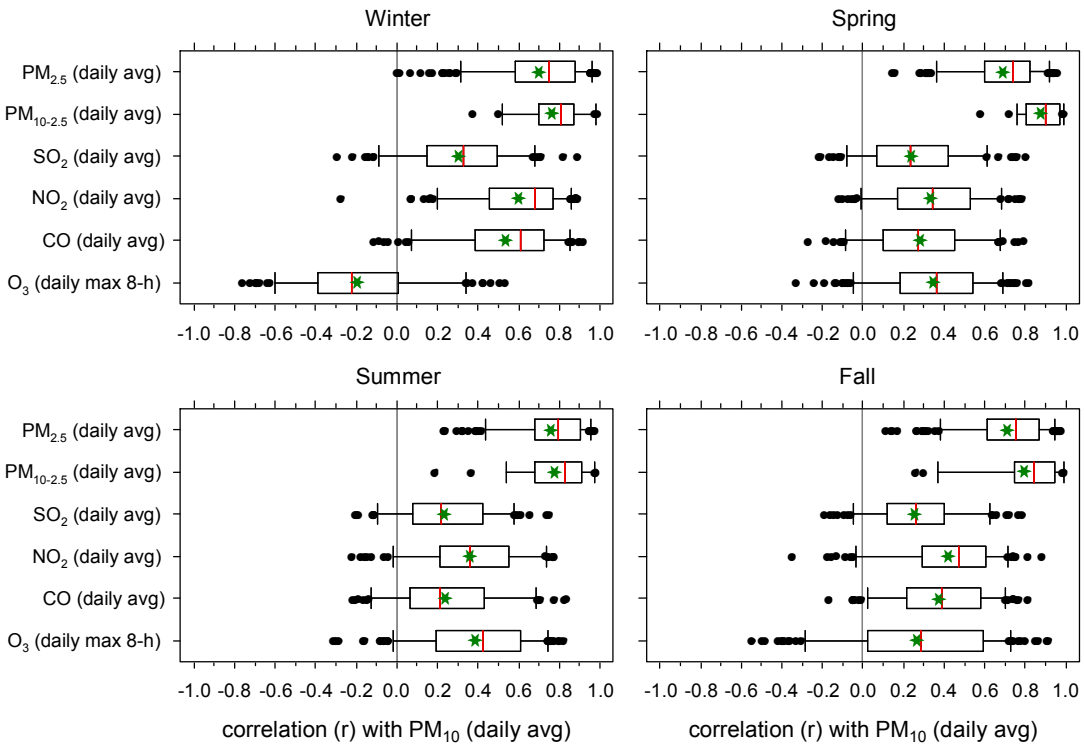


Figure 3-53. Distribution of correlations between 24-h avg PM_{10} and co-located 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily max 8-h avg O_3 for the U.S. stratified by season (2005-2007). Statistics shown include the mean (green star), median (red line), inner quartile range (box), 5th/95th percentiles (whiskers) and outliers (black circles).

For both $PM_{2.5}$ and PM_{10} national composite copollutant correlations, there is considerable spread in the observed correlations in all four seasons. On average, $PM_{2.5}$ and PM_{10} correlate with each other better than with the gaseous copollutants. The correlations between $PM_{2.5}$ and PM_{10} are all positive but span the range from just above zero to near one. This illustrates the wide variability in correlation between these two PM metrics. Fewer points are available for correlation with $PM_{10-2.5}$ because only data from low-volume FRM/FRM-like samplers were used to calculate $PM_{10-2.5}$. The available data suggest a stronger correlation between PM_{10} and $PM_{10-2.5}$ than between $PM_{2.5}$ and $PM_{10-2.5}$ on a national basis.

Correlations among copollutants for individual CSAs/CBSAs are included in Annex A, Figure A-175 through Figure A-188 for $PM_{2.5}$ and Figure A-189 through Figure A-202 for PM_{10}. Each data point in these figures represents a co-located monitor pair. Seattle did not have sufficient co-located data to be included with the other CSAs/CBSAs. As can be seen from the individual CSAs/CBSAs, there can be considerable variation in the correlations even within an individual urban area. For example, correlations between 24-h average $PM_{2.5}$ and PM_{10} concentrations measured at the five co-located monitor pairs in Boston between 2005 and 2007 ranged from 0.42 to 0.88 during winter and reach as high as 0.98 during the summer (Figure A-177).

Few locations within the 15 CSAs/CBSAs contained adequate data for calculating correlations with $PM_{10-2.5}$ using low-volume PM data: Boston and New York had two locations each, Atlanta, Chicago, Denver and Phoenix had only one location and the remaining CSAs/CBSAs had no locations. Correlations between $PM_{2.5}$ and $PM_{10-2.5}$ varied substantially by CSA/CBSA and season and no general patterns were observed in the limited data set analyzed here. In contrast, correlations between PM_{10} and $PM_{10-2.5}$ did show some trends by location and season and were greater in all locations than correlations between $PM_{2.5}$ and $PM_{10-2.5}$. The highest correlations between PM_{10} and

$PM_{10-2.5}$ were observed in Denver and Phoenix with correlations above 0.88 during all seasons. Atlanta, Boston, Chicago and New York all had lower correlations between PM_{10} and $PM_{10-2.5}$ ($0.30 \leq r \leq 0.88$), particularly during the fall ($0.30 \leq r \leq 0.56$). The lowest correlations between PM_{10} and $PM_{10-2.5}$ were observed in New York in the fall and Boston in the summer where they dropped to 0.30 and 0.38, respectively, at one of the two monitor locations in each city. In the four eastern CSAs/CBSAs investigated, correlations between PM_{10} and $PM_{10-2.5}$ were highest in the spring, in agreement with the national averages shown in Figure 3-53. In Denver and Phoenix, there was less seasonal dependence in the correlation.

A similar analysis of correlations between PM size fractions by region was reported in Table 3-1 of the 2004 PM AQCD (U.S. EPA, 2004, 056905) and Figure 2-20 of the 2005 OAQPS Staff Paper (U.S. EPA, 2005, 090209). In all regions, correlations between PM_{10} and $PM_{10-2.5}$ were greater than those for $PM_{2.5}$ and $PM_{10-2.5}$. Correlations between PM_{10} and $PM_{10-2.5}$ were found to be largest in the southwest and the upper Midwest and smallest in the southeast and the northeast. While these regional analyses used different data inclusion criteria for estimating $PM_{10-2.5}$ than the criteria used in this analysis for the individual CSAs/CBSAs, the results are generally consistent: higher correlations between PM_{10} and $PM_{10-2.5}$ mass concentrations compared with $PM_{2.5}$ and $PM_{10-2.5}$ mass concentrations in all regions and higher correlations between PM_{10} and $PM_{10-2.5}$ mass concentrations in the west compared to the east.

The correlation between PM and the gaseous pollutants included in Figure 3-52 and Figure 3-53 also showed a large range in values based on the national composite data. There was little seasonal variability in the mean correlation between PM and SO_2. NO_2 and CO, however, showed higher correlations with PM on average in winter than in the other seasons. This is possibly driven by meteorology with increased frequency of stagnation events in colder months as well as potential concurrent increases in emissions of these compounds from motor vehicles with colder temperatures. The correlation between daily max 8-h avg O_3 and 24-h avg PM showed the highest degree of seasonal variability with positive correlations on average in summer (0.56 for $PM_{2.5}$ and 0.39 for PM_{10}) and negative correlations on average in winter (-0.30 for $PM_{2.5}$ and -0.18 for PM_{10}). During the transition seasons, spring and fall, correlations were mixed but on average were still positive. $PM_{2.5}$ is both primary and secondary in origin, whereas O_3 is only secondary. Photochemical production of O_3 and secondary PM in the planetary boundary layer (PBL) is much slower during the winter than during other seasons. Primary pollutant concentrations (e.g., primary $PM_{2.5}$ components, NO and NO_2) in many urban areas are elevated in winter as the result of heating emissions, cold starts and low mixing heights. O_3 in the PBL during winter is mainly associated with air subsiding from above the boundary layer following the passage of cold fronts, and this subsiding air has much lower PM concentrations than are present in the PBL. Therefore, a negative association between O_3 and PM is frequently observed in the winter. During summer, both O_3 and secondary $PM_{2.5}$ are produced in the PBL and in the lower free troposphere at faster rates compared to winter, and so they tend to be positively correlated. Bell et al. (2007, 093256) also observed wintertime minima in same-day correlations between 24-h avg PM (both $PM_{2.5}$ and PM_{10}) and 24-h avg O_3 using data from 98 U.S. urban communities. The average correlations were positive in winter, unlike those shown in Figure 3-53. Furthermore, the highest national average correlations were in spring and fall in the Bell et al. (2007, 093256) analysis rather than summer as observed in Figure 3-52 and Figure 3-53. This discrepancy could be a result of the different averaging times used for O_3 or the selection of different monitoring networks and/or time periods.

For the $PM_{2.5}$ city-specific correlations shown in Annex A , Figure A-175 through Figure A-188, all selected cities with sufficient data showed negative correlations in the wintertime with daily max 8-h avg O_3 (including Birmingham, Boston, Chicago, Denver, Houston, Los Angeles, Philadelphia, Phoenix, Pittsburgh, Riverside and St. Louis). The remaining four CSAs/CBSAs had insufficient data. In Baltimore, Sarnat et al. (2001, 019401) found a significant (at the $p < 0.05$ level) positive (0.67) and negative (-0.72) correlation between daily $PM_{2.5}$ and O_3 in the summer (June 19-August 23, 1998) and winter (February 2-March 13, 1999), respectively. For PM_{10}, the city-specific correlations with max 8-h avg O_3 shown in Annex A, Figure A-189 through Figure A-202 were more variable. Birmingham, Boston, and St. Louis all showed positive wintertime correlations between PM_{10} and daily maximum 8-h avg O_3 while Denver, Detroit, Houston, Los Angeles and Phoenix showed negative wintertime correlations. The remaining seven CSAs/CBSAs had insufficient data. These copollutant correlations illustrate the importance of considering seasonality when assessing temporal relationships between air pollutants, particularly PM and O_3.

3.6. Mathematical Modeling of PM

There are two main classes of models used to study atmospheric PM, receptor models and CTMs. Receptor models are statistical models whereas CTMs are numerical models, i.e., they approximate derivatives by finite difference approximations. Finite element models are also numerical models but have not been used as extensively for applications described here, and so are not discussed further. Receptor models are diagnostic in their approach, in that they try to derive source contributions at monitoring locations using either ambient data alone or in combination with data for the chemical composition of sources or in combination with meteorological data. Three-dimensional CTMs are formulated in a prognostic, or predictive manner, that is, they attempt to predict species concentrations by solving a set of coupled, non-linear partial differential equations (continuity equations) for chemical species that include terms based on emissions inventories, atmospheric transport, chemical transformations, and deposition. Monitoring data is used to evaluate the performance of CTMs. Each of these approaches has its own advantages and disadvantages.

3.6.1. Estimating Source Contributions to PM Using Receptor Models

Methods for analyzing the composition of ambient PM samples in terms of contributions from different sources are reviewed in this section. Associations between exposures to ambient PM, as represented by ambient monitors, and health outcomes have been extensively studied. Some health studies, described in Section 6.6, have used source apportionment modeling to evaluate relationships between health outcomes and PM (mainly $PM_{2.5}$) from different sources. This section is intended to provide background concerning the uses of source apportionment techniques in such studies. Understanding the contribution of different emissions sources to ambient PM has also been used extensively in evaluating air quality data for use in developing control strategies.

3.6.1.1. Receptor Models

Receptor models have been used mainly as part of the development of air quality management plans. However, there have been several publications relating apportioned source types based on receptor models to human health effects. Discussions in this section will focus mainly on those methods that have been used to relate health outcomes to sources. More complete descriptions of a large number of types of receptor models currently in use are given in Watson et al. (2008, 157128), who summarize the properties of these methods, including the strengths and weaknesses. This compilation of receptor models, broken down into different approaches (i.e., chemical mass balance, factor analysis, tracer-based, meteorology based) is included in Tables A-51 through A-54 in Annex A.

Receptor models such as the chemical mass balance (CMB) model (Watson et al., 1990, 004848) relate source category contributions to ambient PM concentrations based on analyses of the compositional profiles of ambient and source emissions samples. It uses as its basis a mass balance equation that represents all chemical species in an aerosol sample as linear combinations of contributions from a fixed number of independent sources plus an error term representing the portion of the measurement that cannot be fit by the model.

The compositional profiles used in receptor models can be extensive (see for example the SPECIATE data base, http://www.epa.gov/ttnchie1/software/speciate/index.html) for a comprehensive collection of results from a large number of studies. As an example, several studies have identified EC and over 100 organic carbon compounds in gasoline PM emissions, including alkanes, PAHs, oxy-PAHs, steranes, hopanes, and organic acids (Maricq, 2007, 155973; Schauer et al., 1999, 010582; Schauer et al., 2002, 035332). This breakdown in identifiable groups of organic compounds is illustrated in Figure 3-54 and Table 3-17 shows emissions factors for trace elements. Data for the compositional profiles for several other important sources of PM that could be used for CMB modeling are shown in Table A-55 in Annex A.

Source categories are amenable to refinement and to analysis as information on tracers becomes available. For example, PBAP have long been known to be significant constituents of the atmospheric aerosol, but not many studies have evaluated their contributions, largely because of the lack of suitable tracers and the additional equipment needs for sampling and analysis of bioaerosols.

Bauer et al. (2008, 189986) reviewed studies estimating the contribution of fungal spores to $PM_{2.5}$ and $PM_{10-2.5}$ as fungal spores were expected to be major contributors to PBAP. They proposed the use of arabitol and mannitol as unique tracers with an estimated accuracy of ± 50% to apportion the contribution of fungal spores to OC in both $PM_{2.5}$ and $PM_{10-2.5}$. They estimated 24-h avg contributions of ~ 40% to OC in $PM_{10-2.5}$ during spring and summer in Vienna, with a smaller contribution to $PM_{2.5}$.

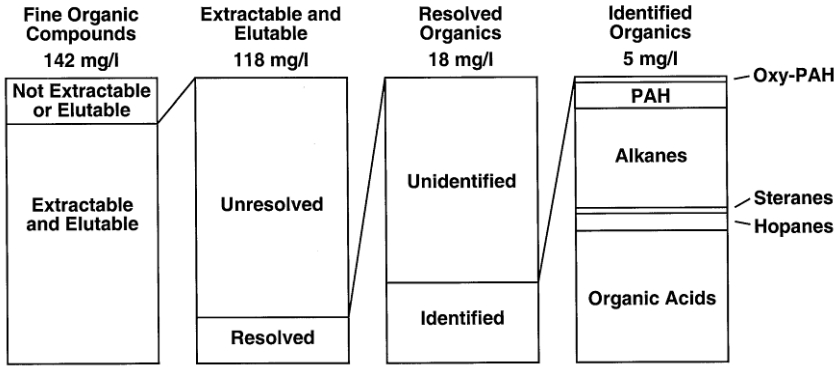


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Figure 3-54. Schematic of organic composition of particulate emissions from gasoline-fueled vehicles.

One recently-identified concern in the application of CMB-based receptor models with detailed organic marker compounds is the photochemical stability of those species. Robinson et al. (2006, 156918) reported evidence of significant summertime photooxidation of hopanes and long-chain alkenoic acids, low-volatility compounds often used as mobile source and cooking emissions, respectively. Seasonal differences in hopanes/EC ratios differed in a manner consistent with oxidation. Photochemical loss of particle-phase marker species mass complicates the interpretation of model results, as long-range transport and photochemistry may result in the loss of markers for distant sources. Furthermore, photochemical breakdown of organic marker species may cause losses in CMB model performance criteria and possible bias in source contribution estimates. The photooxidation of condensed-phase organic compounds also may affect the polarity and volatility of these compounds.

In other methods, various forms of factor analysis are used that rely on the varying mix of species present in ambient observations of compositional data to derive the source contributions. Standard factor analytic approaches such as Principal Component Analysis (PCA) have been used, but PCA alone can apportion only the variance, not the mass, in an aerosol composition data set. Additional steps in particular the identification of source tracers is required in Absolute Principal Components Scores (APCS) to apportion mass from PCA (Miller et al., 2002, 030661; Thurston and Spengler, 1985, 056074). However, it can be difficult to find suitable tracers for some sources because many elements are emitted by more than one source. In Positive Matrix Factorization (PMF) (Paatero and Tapper, 1994, 086998), the ambient compositional data matrix is decomposed into the product of a matrix representing the source contributions and one representing the source profiles. Solutions are obtained by minimizing an object function with respect to these two matrices, and solutions are subject to non-negativity constraints. PMF also allows for the treatment of missing data and data near or below detection limits by weighting elements inversely according to their uncertainties. The PMF approach requires a large number of samples (n typically >50) and are most often applied to time series data, whereas CMB can be applied to a single sample. Both the CMB and the PMF approaches find solutions based on least squares fitting and minimization of an object function. Both methods provide error estimates for the solutions based on estimates of the errors in the input parameters. It should be noted, though, that the error estimates for both methods often contain subjective judgments about the magnitude of the analytical and monitoring errors.

Table 3-17. Example of emissions factors (ng/km) for trace elements under variable speed and steady speed driving conditions for PM emitted by diesel and gasoline engines. Note that emissions are highly variable.

Element	Diesel		Gasoline	
	Transient	**Steady State**	**Transient**	**Steady State**
Al	9108 (5224)	2706	2273 (545)	252
Ca	69,443 (23,640)	16,128	18,247 (3044)	2324
Fe	22,910 (21,448)	2036	10,266 (9928)	138
K	4672 (752)	1191	1935 (558)	117
Mg	3087 (461	997	5183 (1706)	183
Na	7736 (1751)	1945	2237 (1125)	321
Ba	583 (349)	73	331 (55)	4.8
Be	26 (12)	23	6.7 (1.1)	1.5
Cr	634 (354)	93	138 (6.7)	8.6
Cu	1944 (679)	627	1745 (1803)	16
Li	13 (0.2)	7.9	3.0 (1.4)	0.9
Mn	368 (183)	76	152 (85)	3.4
Ni	2310 (656)	644	107 (0.7)	21
Pb	793 (593)	79	237 (2.3)	11
S	23,750 (5295)	6713	8705 (3375)	349
Ti	2036 (320)	345	118 (9.3)	24
V	28 (9.4)	11	15 (11)	1.8
Zn	21,118 (4422)	5620	4650 (1225)	198

Standard deviations are presented in parenthesis when multiple tests have been averaged.

Source: Adapted with Permission of Elsevier Ltd. from Geller et al. (2006, 139644)

The nature of the solutions in terms of source categories is different in the CMB and PMF approaches. In the CMB approach, the composition of the source emissions is assumed to be known based on measurements. These assumptions may or may not reflect the composition of emissions affecting a particular site at any given time or place. However, there may be variations in the composition of individual source categories (e.g., soils, motor vehicle emissions) across a given airshed and even in the composition of the same source with time. Source profiles can also be altered between emission and receptor locations resulting from atmospheric reactions, depending on the source type and species under analysis. The CMB technique was developed for apportioning source categories of primary PM and was not formulated to include sources of secondary PM. CMB might not explain all the mass or produce a valid result unless there is information for the composition of all major sources affecting a given site, and there is confidence that the existing source profiles are specific to those sources. For example, Volckens et al. (2008, 105465) describe PAH emission profiles from hand-held gasoline lawn and garden equipment as found in some CMB source profiles for motor vehicles.

In PMF, the source solutions are more general in that they contain information about the entrainment of emissions from additional sources during transport, the time dependence of the composition of emissions from particular sources, the formation of secondary species and local differences in source compositions. PMF differs from CMB because it derives the mix of factors from measured data. However, the procedure used to find a solution results in some rotational ambiguity (Paatero and Tapper, 1994, 086998). The assignment of sources to PMF factors depends largely on past experience and judgments. Judgments are based to large extent on comparison with data for source profiles and also on the factors that could modify the assignments. These issues are

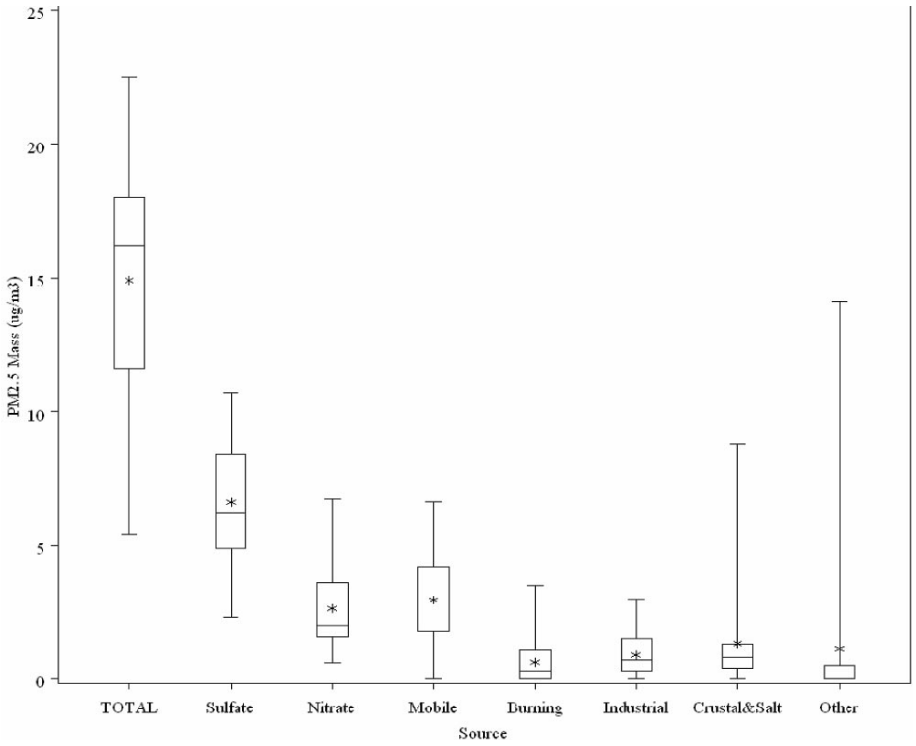
alleviated to some degree by incorporating information about local wind fields and other physical parameters.

The UNMIX model takes a geometric approach that exploits the covariance of the ambient data to determine the number of independent sources, the composition and contributions of the sources, and corresponding uncertainties (Henry, 1997, 020941). UNMIX uses PCA to find edges in m-dimensional space, where m is the number of ambient species. Success of the UNMIX model hinges on the ability to find these "edges" in the ambient data from which the number of source types and the source compositions are extracted. In simplest terms, the approach can be seen to be similar to that for deriving ternary mixing diagrams, except there is extension to higher dimensionality. Measurement errors in the ambient data "fuzz" the edges, making them difficult to find. UNMIX employs an "edge-finding" algorithm to find the best edges in the presence of error. UNMIX does not make explicit use of errors or uncertainties in the ambient concentrations, unlike the methods outlined above. Rather they are implicitly incorporated into the analyses. PMF and UNMIX have also used data for particle size distributions to obtain further information about sources.

Partial least squares (PLS) is another mathematical model related to PCA which has been used in a limited number of PM toxicology studies to establish a relationship between PM constituents and health outcomes (McDonald et al., 2004, 087458; Seagrave et al., 2006, 091291; Veranth et al., 2006, 087479). Although not really a receptor model and not designed as such, PLS shares some similarities with certain receptor models; and more importantly attempts to link PM components with health outcomes. Unlike PCA and other receptor models discussed in this section, PLS incorporates both predictor variables (e.g., PM component concentrations) and outcome variables (e.g., toxicological responses) into one coupled regression model. Like PCA, PLS groups the observable variables into a reduced number of latent variables, thereby reducing the dimensionality of the model. Typically, PM toxicology studies have been limited to two-component models (two latent variables on the predictor side compared with two on the outcome side), thereby producing a 2×2 loading plot revealing relationships between predictors and outcomes. PLS is particularly useful when there are more predictor variables than observations, which is a situation that other multivariate factor analysis approaches do not handle well. However, since PLS is a variance based approach, it shares the same shortcomings discussed earlier for PCA. PLS has also traditionally been limited to two-component applications even though this is not a strict mathematical limitation.

Results from Receptor Models

Results from receptor modeling calculations indicate that $PM_{2.5}$ is most often produced mainly by fossil fuel combustion. Fugitive dust, found mainly in the $PM_{10-2.5}$ size range, represents the largest source of measured ambient PM_{10} in many locations in the western U.S. Quoted uncertainties in the source apportionment of constituents in ambient aerosol samples typically range from 10 to 50%. It is apparent that a relatively small number of broadly defined source categories, compared to the total number of chemical species that typically are measured in ambient monitoring-source receptor model studies, are needed to account for the majority of the observed mass of PM in these studies. Trying to be more specific about contributions from source categories could result in ambiguity. For example, some stationary sources (e.g., agriculture use engines) and quite different mobile sources (e.g., trucks and locomotives) rely on diesel power and ancillary data is required to resolve contributions from these sources. Compilations of source attribution studies using CMB for PM_{10} have appeared in the 2004 PM AQCD (U.S. EPA, 2004, 056905) and using PMF for $PM_{2.5}$ in Engel-Cox and Weber (2007, 156419). Results of the compilation by Engel-Cox and Weber (2007, 156419) for the eastern U.S. are shown in Figure 3-53. There are only three main source categories in the figure constituting most of the $PM_{2.5}$ mass (i.e., sulfate, nitrate, mobile). Two of these are predominantly secondary and not identified by sources of precursors. Tables A-56 and A-57 in Annex A list results of other receptor modeling studies for $PM_{2.5}$ and PM_{10}, many of which are in the western U.S.

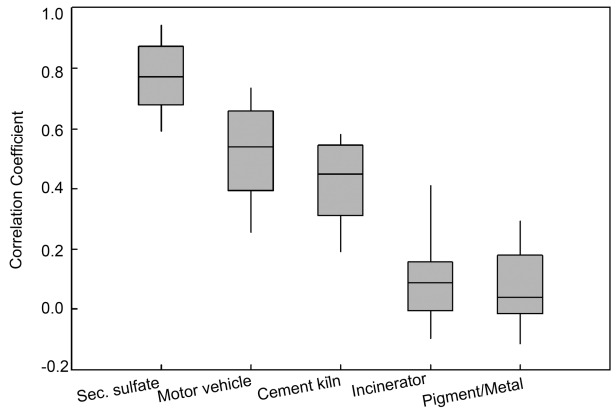


Source: Reprinted with Permission of Air & Waste Management Association from Engel-Cox and Weber (2007, 156419).

Figure 3-55. Source category contributions to $PM_{2.5}$ at a number of sites in the East derived using PMF.

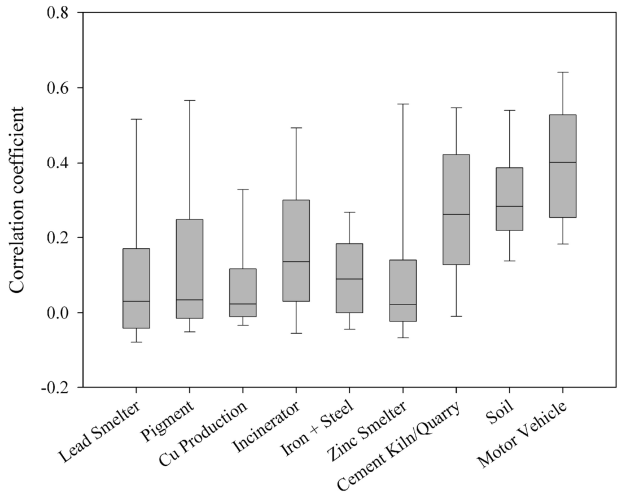
Spatial Variability in Source Contributions to PM Based on Receptor Models

Spatial variability in source contributions across urban areas is an important consideration in assessing the likelihood of exposure measurement error in epidemiologic studies relating health endpoints to sources. Arguments similar to those for using ambient concentrations as surrogates for personal exposures apply here. Studies for $PM_{2.5}$ (Kim et al., 2005, 083181; Wongphatarakul et al., 1998, 049281) indicate that intra-urban variability increases in the following order: regional sources (e.g., secondary SO_4^{2-} originating from EGUs) < area sources (e.g., on-road mobile sources) < point sources (e.g., stacks). This point is illustrated in Figure 3-56. The only study available for $PM_{10-2.5}$ (Hwang et al., 2008, 134420) indicates a similar ordering, but without a regional component (resulting from the short lifetime of coarse PM compared to transport times on the regional scale) as shown in Figure 3-57.



Source: Reprinted with Permission of ACS from Kim et al. (2005, 083181)

Figure 3-56. Pearson correlation coefficients for source category contributions to $PM_{2.5}$ between the 10 Regional Air Pollution Study/Regional Air Monitoring System (RAPS/RAMS) monitoring sites in St. Louis.



Source: Reprinted with Permission of ACS from Hwang et al. (2008, 194533)

Figure 3-57. Pearson correlation coefficients for source contributions to $PM_{10-2.5}$ between the 10 Regional Air Pollution Study/Regional Air Monitoring System (RAPS/RAMS) monitoring sites in St. Louis.

3.6.2. Chemistry Transport Models

CTMs are the prime tools used to compute the interactions among atmospheric pollutants and their transformation products, the production of secondary aerosols, the evolution of particle size distribution, and transport and deposition of pollutants. CTMs are driven by emissions inventories for primary species such as NO_X, SO_X, NH_3, VOCs, and primary PM, and by meteorological fields produced by other numerical prediction models. Values for meteorological state variables such as winds and temperatures are taken from operational analyses, reanalyses, or weather circulation models. In most cases, these are off-line meteorological analyses, meaning that they are not modified

by radiatively active species generated by the air quality model (AQM). Work to integrate meteorology and chemistry was done in the mid-1990s by Lu et al. (1997, 048202 and references therein; 1997, 191768) although limits to computing power prevented their wide-spread application. More recently, new, integrated models of meteorology and chemistry are now available as well; see, for example, Binkowski et al. (2007, 090563) and the Weather Research and Forecast model with chemistry (WRF-Chem) (http://ruc.fsl.noaa.gov/wrf/WG11).

CTMs have been developed for application over a wide range of spatial scales ranging up from neighborhood to global. CTMs are used to: (1) obtain better understanding of the processes controlling the formation, transport, and destruction of gas- and particle-phase criteria and hazardous air pollutants; (2) understand the relations between concentrations of secondary pollutant products and concentrations of their precursors; (3) understand relations among the concentration patterns of various pollutants that may exert adverse effects; and (4) evaluate how changes in emissions propagate through the atmospheric system to secondary products and deposition.

Emissions of precursor compounds can be divided into anthropogenic and natural source categories. Natural sources can be further divided into biogenic from vegetation, microbes, and animals, and abiotic from biomass burning, lightning, and geogenic sources. However, the distinction between natural sources and anthropogenic sources is often difficult to make in practice, as human activities affect directly or indirectly emissions from what would have been considered natural sources during the preindustrial era. Thus, emissions from plants and animals used in agriculture have been referred to as anthropogenic or biogenic in different applications. Wildfire emissions may be considered natural, except that forest management practices can lead to buildup of fuels on the forest floor, thereby altering the frequency and severity of forest fires.

The initial conditions, or starting concentration fields of all species computed by a model, and the boundary conditions, or concentrations of species along the horizontal and upper boundaries of the model domain throughout the simulation, must be specified at the beginning of the simulation. Both initial and boundary conditions can be estimated from models or data or, more generally, model + data hybrids. Because data for vertical profiles of most species of interest are very sparse, results of model simulations over larger, usually global, domains are often used. As might be expected, the influence of boundary conditions depends on the lifetime of the species under consideration and the time scales for transport from the boundaries to the interior of the model.

Each of the model components described above has associated uncertainties and the relative importance of these uncertainties varies with the modeling application. The largest errors in photochemical modeling are still thought to arise from the meteorological and emissions inputs to the model (Russell and Dennis, 2000, 035563). While the effects of poorly specified boundary conditions propagate through the model's domain, the effects of these errors remain undetermined. Because many meteorological processes occur on spatial scales smaller than the model's vertical or horizontal grid spacing and thus are not calculated explicitly, parameterizations of these processes must be used. These parameterizations introduce additional uncertainty. Because the chemical production and loss terms in the continuity equations for individual species are numerically coupled, the chemical calculations must be performed iteratively until calculated concentrations converge to within some preset criterion. The number of iterations and the convergence criteria chosen also can introduce error.

CTMs in current use mostly have one of two forms. The first, grid-based or Eulerian air quality models subdivide the region to be modeled, the modeling domain, into a three-dimensional array of grid cells. Spatial derivatives in the species continuity equations are cast in finite-difference form over this grid and a system of equations for the concentrations of all the chemical species in the model are solved numerically at each grid point. Time-dependent continuity or mass conservation equations are solved for each species including terms for transport, chemical production and destruction, and emissions and deposition (if relevant), in each grid cell. Chemical processes are simulated with ordinary differential equations, and transport processes are simulated with partial differential equations. Because of a number of factors such as the different time scales inherent in different processes, the coupled, nonlinear nature of the chemical process terms, and computer storage limitations, not all of the terms in the equations are solved simultaneously in three dimensions. Instead, operator splitting, in which terms in the continuity equation involving individual processes are solved sequentially, is used.

In the second common CTM formulation, trajectory or Lagrangian models, a number of hypothetical air parcels are specified as though following wind trajectories. In these models, the

original system of partial differential equations is transformed into a system of ordinary differential equations.

A less common approach is to use a hybrid Lagrangian-Eulerian model, in which certain aspects of atmospheric chemistry and transport are treated with a Lagrangian approach and others are treaded in an Eulerian manner (e.g., Stein et al., 2000, 048341).

Each approach has advantages and disadvantages. The Eulerian approach is more general in that it includes processes that mix air parcels and allows integrations to be carried out for long periods during which individual air parcels lose their identity. There are, however, techniques for including the effects of mixing in Lagrangian models such as FLEXPART (Zanis et al., 2003, 053423), ATTILA (Reithmeier and Sausen, 2002, 053447), and CLaMS (McKenna et al., 2002, 053445). Because both the accuracy and the computational intensity of Eulerian models depend strongly on the size of the horizontal and vertical grid spacing, speed and fidelity to actual atmospheric conditions must sometimes be traded-off; that is to say, while finer grid spacing will often capture effects missed at larger grid intervals, models set up in this way require longer to solve. In a similar manner, the accuracy of Lagrangian models depends on the number of air parcels deployed; thus they, too, become computationally intensive when higher-order accuracy is desired. More detailed discussion of CTM applications appears in the 2008 ISA for NO_X and SO_X – Ecological Criteria (U.S. EPA, 2008, 157074).

3.6.2.1. Global Scale

Global-scale CTMs are used to address issues associated with climate change and stratospheric O_3 depletion to characterize long-range air pollution transport, and to provide boundary conditions for the regional-scale models. The CTMs include parameterizations of atmospheric transport; the transfer of solar radiation through the atmosphere; chemical reactions; and removal to the surface by turbulent motions and precipitation for emitted pollutants. The upper boundaries of the CTMs extend anywhere from the tropopause (~8 km at the poles to ~16 km in the tropics) to the mesopause at ~80 km in order to obtain more realistic boundary conditions for problems involving stratospheric dynamics and chemistry.

Global simulations are typically conducted with a horizontal grid spacing of 200 km or more, although some models such as GEOS-Chem have been run at grid spacings of about 100 km (e.g., Wu et al., 2008, 190039) and efforts are being made to achieve even higher spatial resolution. Simulations of the effects of long-range transport at particular locations link multiple horizontal resolutions from the global to the local scale. Finer resolution can only improve scientific understanding to the extent that the governing processes are more accurately described at that scale. Consequently, there is a crucial need for observations at the appropriate scales to evaluate the scientific understanding represented by the models.

3.6.2.2. Regional Scale

Most major regional-scale air-related modeling efforts at EPA use the Community Multi-scale Air Quality modeling system (CMAQ) (Byun and Ching, 1999, 156314; Byun and Schere, 2006, 090560). A number of other modeling platforms using Lagrangian and Eulerian frameworks were reviewed in the 2006 O_3 AQCD (U.S. EPA, 2006, 088089) and in Russell and Dennis (2000, 035563). The capabilities of a number of CTMs designed to study local- and regional-scale air pollution problems were summarized by Russell and Dennis (2000, 035563). Evaluations of the performance of CMAQ are given in Arnold et al. (2003, 087579), Eder and Yu (2005, 089229), Appel et al. (2005, 089227), and Fuentes and Raftery (2005, 087580). CMAQ's horizontal domain can extend from a few hundred kilometers on a side to the entire hemisphere. CMAQ is most often driven by the MM5 mesoscale meteorological model (Seaman, 2000, 035562), though it may be driven by other meteorological models including WRF and the Regional Atmospheric Modeling System (RAMS); see http://atmet.com. Simulations of pollution episodes over regional domains have been performed with a horizontal resolution as low as 1 km; see the application and general survey results reported in Ching et al. (2006, 090300). However, simulations at such high resolutions require better parameterizations of meteorological processes such as boundary layer fluxes, deep convection and clouds (Seaman, 2000, 035562). Finer spatial resolution is necessary to resolve features such as urban heat island circulation; sea, bay, and land breezes; mountain and valley breezes; and the nocturnal low-level jet, all of which can affect pollutant concentrations.

The most common approach to setting up the horizontal domain is to nest a finer grid within a larger domain of coarser resolution. However, there are other strategies such as the stretched grid and the adaptive grid. In a stretched grid, the grid's resolution continuously varies throughout the domain, thereby eliminating any potential problems with the sudden change from one resolution to another at the boundary. Caution should be exercised in using such a formulation because certain parameterizations like those for convection might be valid on a relatively coarse grid scale but may not be valid on finer scales. Adaptive grids are not fixed at the start of the simulation, but instead adapt to the needs of the simulation as it evolves. They have the advantage that they can resolve processes at relevant spatial scales. However, they can be very slow if the situation to be modeled is complex. Additionally, if adaptive grids are used for separate meteorological, emissions, and photochemical models, there is no reason a priori why the resolution of each grid should match, and the gains realized from increased resolution in one model will be wasted in the transition to another model. The use of finer horizontal resolution in CTMs will necessitate finer-scale inventories of land use and better knowledge of the exact paths of roads, locations of factories, and, in general, better methods for locating sources and estimating their emissions.

The vertical resolution of these CTMs is variable and usually configured to have more layers in the PBL and fewer higher up. Because the height of the boundary layer is of critical importance in simulations of air quality, improved resolution of the boundary layer height would likely improve air quality simulations. Additionally, current CTMs do not adequately resolve fine-scale features such as the nocturnal low-level jet in part because little is known about the nighttime boundary layer.

CTMs require time-dependent, three-dimensional wind fields for the period of simulation. The winds may be generated either by a model using initial fields alone or with four-dimensional data assimilation to improve the model's performance; i.e., model equations can be updated periodically to bring results into agreement with observations. Modeling series durations can range from simulations of several days duration, the typical time scale for individual O_3 episodes, to several months or multiple seasons of the year. The current trend in modeling applications is towards annual simulations. This trend is driven in part by the need to improve understanding of observations of periods of high wintertime PM (Blanchard et al., 2002, 047598) and the need to simulate O_3 episodes occurring in spring, fall, and winter.

Chemical kinetics mechanisms representing the important reactions occurring in the atmosphere are used in CTMs to estimate the rates of chemical formation and destruction of each pollutant simulated as a function of time. Mechanisms that treat the reactions of all individual reactive species explicitly are computationally too demanding to be incorporated into CTMs for regulatory use. Similarly, very extensive "master mechanisms" (Derwent et al., 2001, 047912) that include approximately 10,500 reactions involving 3,603 chemical species (Derwent et al., 2001, 047912) can be combined into mechanisms that group together compounds with similar chemistry. Because of different approaches to the lumping of organic compounds into surrogate groups for computational efficiency, chemical mechanisms can produce different results under similar conditions. The Carbon Bond chemical mechanisms starting with CB-IV (Gery et al., 1989, 043039), the RADM II mechanism (Stockwell et al., 1990, 043095), the SAPRC (e.g., Carter, 1990, 042893; Wang et al., 2000, 048357; Wang et al., 2000, 048365), and the RACM mechanisms can be used in CMAQ. Jimenez et al. (2003, 156611) provided brief descriptions of the features of the main mechanisms in use and compared concentrations of several key species predicted by seven chemical mechanisms in a box-model simulation over 24 h.

CMAQ and other state-of-the-science CTMs incorporate processes and interactions of aerosol-phase chemistry (Binkowski and Roselle, 2003, 191769; Gaydos et al., 2007, 139738; Zhang and Wexler, 2008, 191770). There have also been several attempts to study the feedbacks of chemistry on atmospheric dynamics using meteorological models like MM5 and WRF (Grell et al., 2000, 048047; Liu et al., 2001, 048201; Lu et al., 1997, 048202; Park et al., 2001, 044169). This coupling is necessary to accurately simulate feedbacks which may be caused by the heavy aerosol loading found in forest fire plumes (Lu et al., 1997, 048202; Park et al., 2001, 044169) or in heavily polluted areas. Photolysis rates in CMAQ can now be calculated interactively with model produced O_3, NO_2, and aerosol fields (Binkowski et al., 2007, 090563).

Spatial and temporal characterizations of anthropogenic and biogenic precursor emissions must be specified as inputs to a CTM. Emissions inventories have been compiled on grids of varying resolution for many hydrocarbons, aldehydes, ketones, CO, NH_3, and NO_X. Emissions inventories for many species require the application of algorithms for calculating the dependence of emissions on physical variables, such as temperature, and to convert the inventories into formatted emission

files which can be used by a CTM. For example, preprocessing of emissions data for CMAQ often is done by the Spare-Matrix Operator Kernel Emissions (SMOKE) system (http://smoke-model.org). For many species, information concerning the temporal variability of emissions is lacking, so long-term annual averages are used in short-term, episodic simulations. Annual emissions estimates are often modified by the emissions model to produce emissions more characteristic of the time of day and season. Significant errors in emissions can occur if inappropriate time dependence is used. Additional complexity arises in model calculations because different chemical mechanisms can include different species, and inventories constructed for use with one mechanism must be adjusted to reflect these differences in another.

3.6.2.3. Local or Neighborhood Scale

The grid spacing in regional CTMs, usually between 1 and 12 km^2, is usually too coarse to resolve spatial variations on the neighborhood scale. The interface between regional scale models and models of smaller exposure scales is provided by smaller scale dispersion models. Several models could be used to simulate concentration fields near roads, each with its own set of strengths and weaknesses. The California Department of Transportation's most recent line dispersion model is CALINE4; see http://www.dot.ca.gov/hq/env/air/pages/calinesw.htm. The CALINE family of models is not supported by the California Department of Transportation for modeling of highway-source PM, however, but only for roadway CO, although PM work with CALINE has been performed for more than ten years; see Wu et al. (2009, 191773) and references therein.

In addition, AERMOD (http://www.epa.gov/scram001/dispersion_prefrec.htm) is a steady-state plume model formulated as a replacement to the ISC3 dispersion model. In the stable boundary layer (SBL), it assumes the concentration distribution to be Gaussian in both the vertical and horizontal dimensions. In the convective boundary layer, the horizontal distribution is also assumed to be Gaussian, but the vertical distribution is described with a bi-Gaussian probability density function (pdf). AERMOD has provisions that can be applied to flat and complex terrain and multiple source types (including, point, area and volume sources) in both urban and rural areas. It incorporates air dispersion based on the structure of turbulence in the PBL and scaling concepts and is meant to treat surface and elevated sources, in both simple and complex terrain in rural and urban areas. The dispersion of emissions from line sources like highways in AEROMOD is handled as a source with dimensions set using an area or volume source algorithm in the model; however, actual emissions are usually not in steady state and there are different functional relationships between buoyant plume rise in point and line sources. Moreover, most simple dispersion models including AERMOD are designed without chemical mechanisms and so cannot produce secondary pollutants from their primary emissions .

There are also non-steady state models that incorporate plume rise explicitly from different types of sources. For example, CALPUFF (http://www.src.com/calpuff/calpuff1.htm), which is EPA's recommended dispersion model for transport in ranges >50 km, is a non-steady-state puff dispersion model that simulates the effects of time- and space-varying meteorological conditions on pollution transport, transformation, and removal and has provisions for calculating dispersion from surface sources. However, CALPUFF was not designed to treat the dispersion of emissions from roads, and like AERMOD does not include production of secondary pollutants. The distinction between a steady-state and time varying model could be unimportant for long time scales; however, at short time scales, the temporal variability in traffic emissions could result in underestimation of peak concentration and exposures.

3.6.3. Air Quality Model Evaluation for Air Concentrations

Urban and regional air quality is determined by a complex system of coupled chemical and physical processes including emissions of pollutants and pollutant precursors, complex chemical reactions, physical transport and diffusion, and wet and dry deposition. NO_X in these systems has long been known to (1) act nonlinearly in the production of O_3 and other secondary pollutants (Dodge, 1977, 038646); and (2) involve complicated cross-media environmental issues, such as acidic or nutrient deposition to sensitive biota and degradation of visibility.

NO_Y species emitted and transformed from emissions control the production and fate of both O_3 and aerosols by sustaining or suppressing OH cycling. Correctly characterizing the interrelated

NO_Y and OH dynamics for O_3 formation and fate in the polluted troposphere depends on new techniques using combinations of several NO_Y species for diagnostically probing the complex atmospheric dynamics in typical urban and regional airsheds.

Evaluation results from a recent EPA exercise of CMAQ in the Tampa Bay, FL, airshed are presented here as an example of the present level of skill of state-of-the-science AQMs for predicting atmospheric concentrations of some of the relevant species for this PM NAAQS assessment. This modeling series exercised CMAQ version 4.4 and with the University of California at Davis (UCD) sectional aerosol module in place of the standard CMAQ modal aerosol module and was driven by meteorology from MM5 v3.6 and with NEI emissions as augmented by continuous emissions monitoring data where available. The UCD size-segregated module was preferred for this application because of the importance of sea salt particles in the bay airshed. Testing of this new engineering extension to CMAQ (termed CMAQ-UCD below) revealed that its performance was very similar to that of CMAQ's standard modal module; hence, model behavior and performance reported here can stand as a general indication of CMAQ's skill.

The CTM was run with 21 vertical layers for the month of May 2002. For this evaluation, CMAQ-UCD was run in a one-way nested series of three domains with 32 km, 8 km, and 2 km horizontal grid spacings from the CONUS (32 km) to central Florida and the eastern Gulf of Mexico (2 km). Depictions of the 8 km and 2 km domains used here zoomed over the central Tampa area are shown in Figure 3-58 and Figure 3-59.

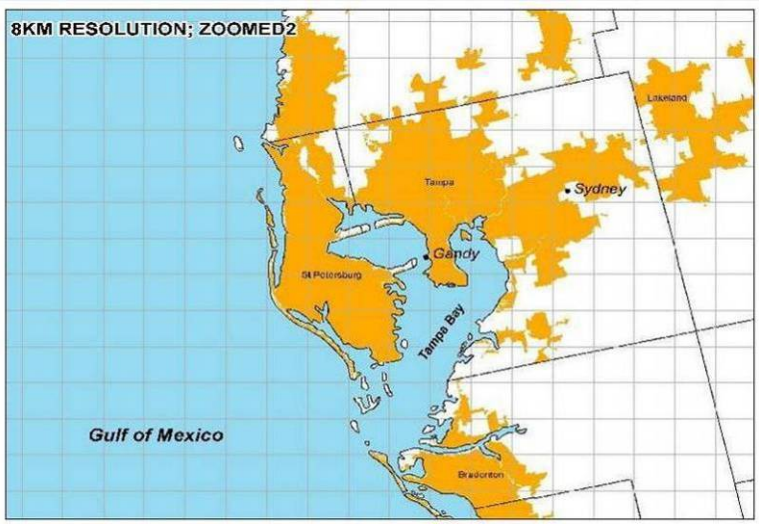


Figure 3-58. Eight km southeast U.S. CMAQ-UCD domain zoomed over Tampa Bay, FL.

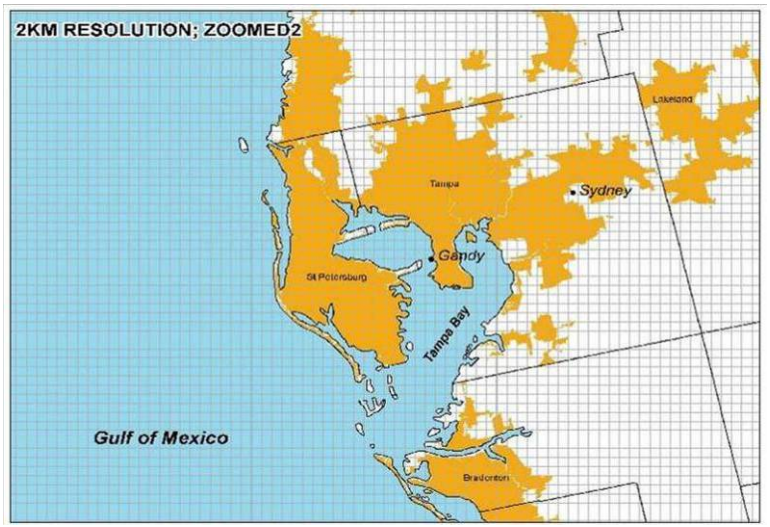


Figure 3-59. Two km southeast U.S. CMAQ-UCD domain zoomed over Tampa Bay, FL.

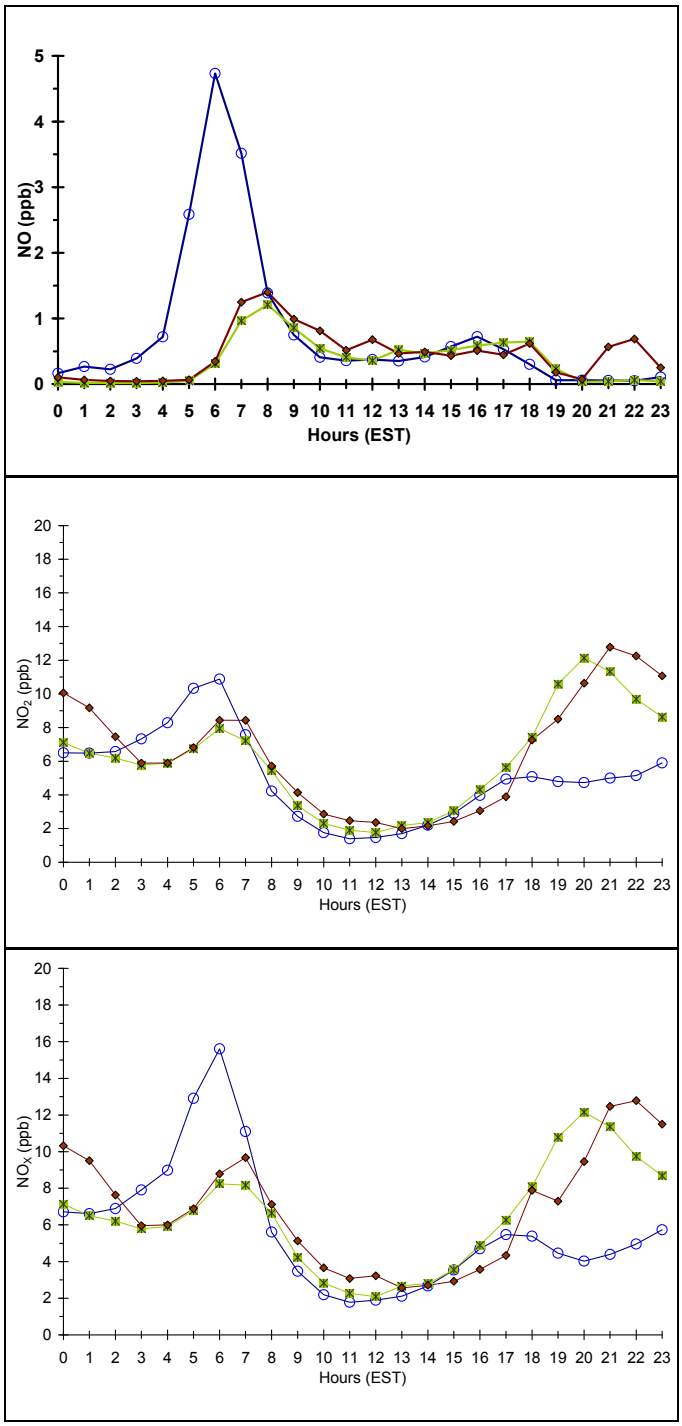


Figure 3-60. Hourly average CMAQ-UCD predictions and measured observations of NO (top), NO_2 (middle), and total NO_X (bottom) concentrations for May 1-31, 2002. Green squares = 8 km solution, red diamonds = 2 km solution, blue circles = observations.

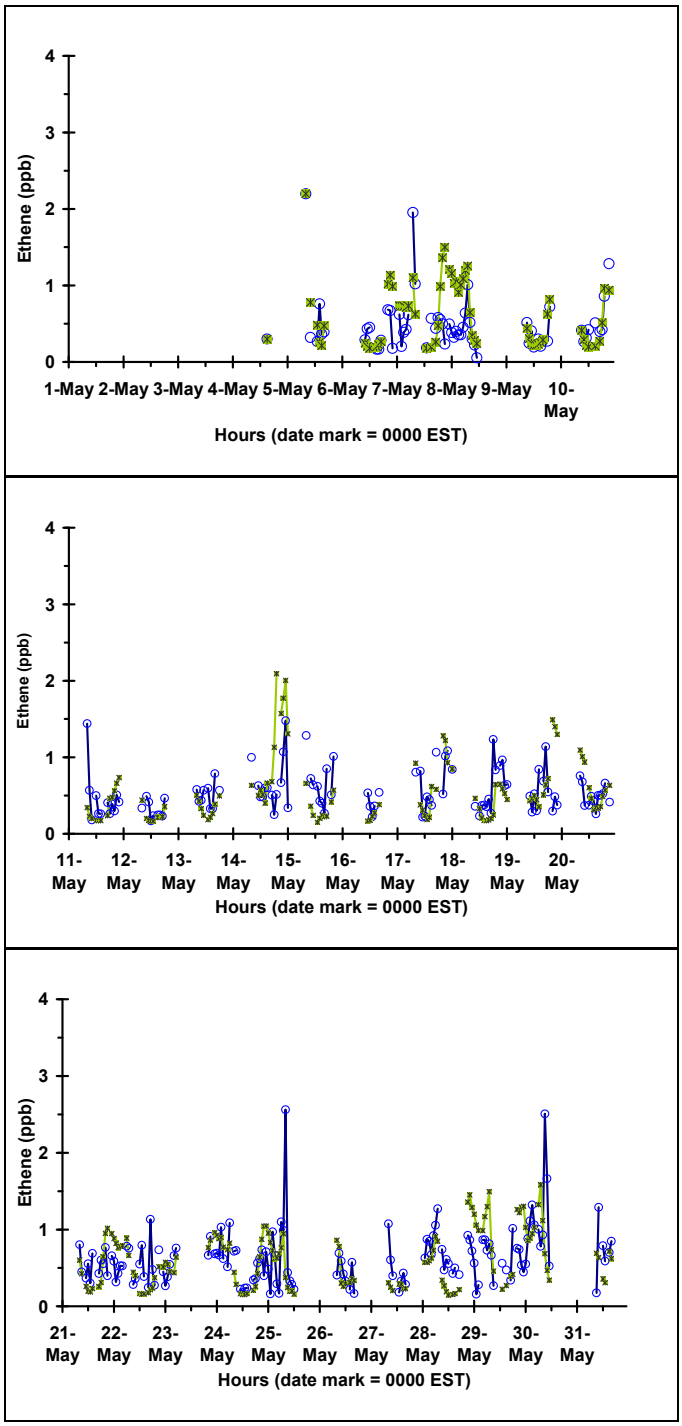


Figure 3-61. CMAQ-UCD predictions and measured observations of ethene concentrations at Sydney, FL for May 1-31, 2002. Green squares = 8 km solution, blue circles = observations.

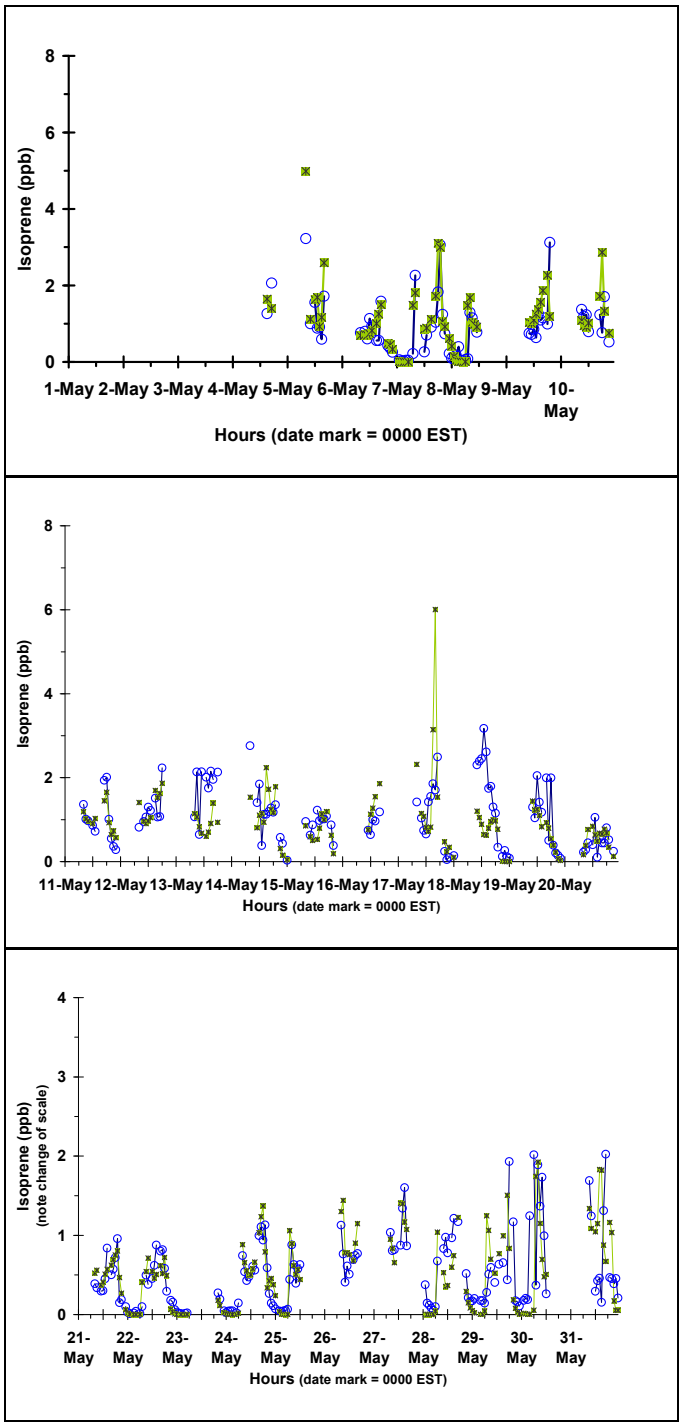


Figure 3-62. CMAQ-UCD predictions and measured observations of isoprene concentrations at Sydney, FL for May 1-31, 2002. Green squares = 8 km solution, blue circles = observations.

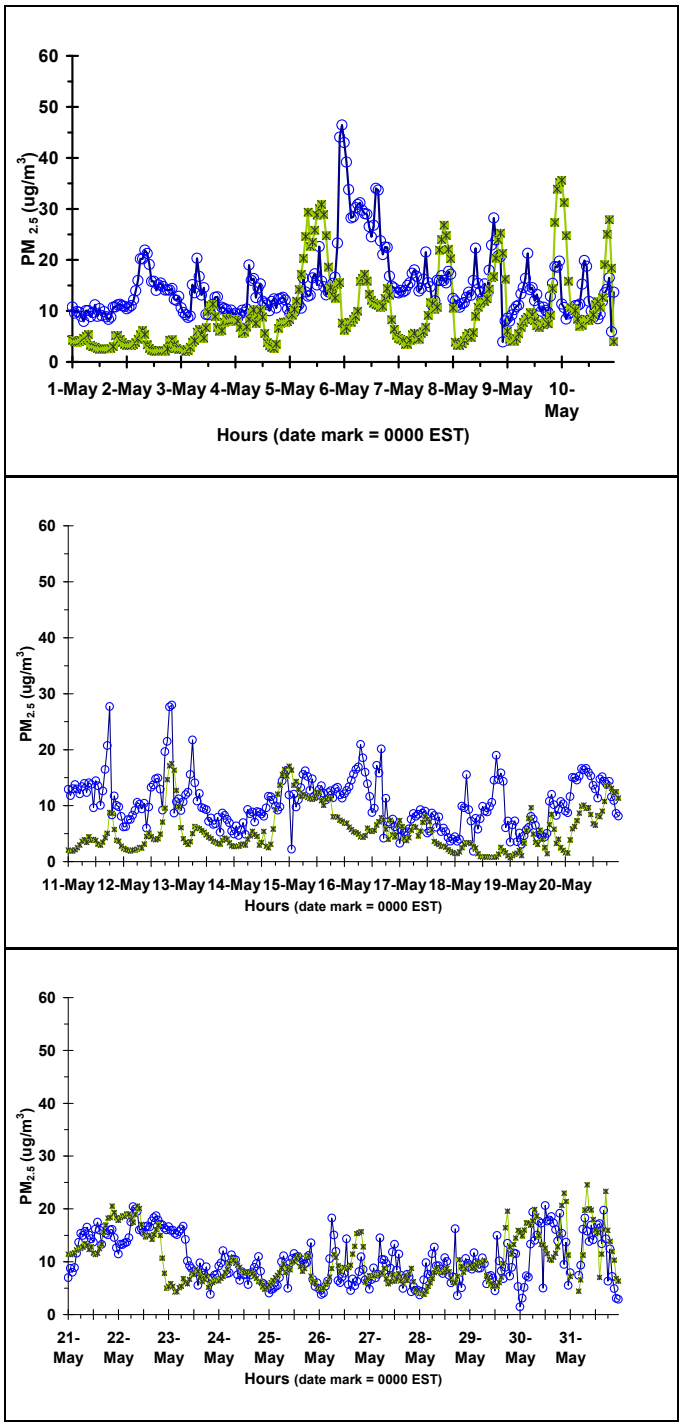


Figure 3-63. CMAQ-UCD predictions and measured observations of $PM_{2.5}$ concentrations at Sidney, FL for May 1-31, 2002. Green squares = 8 km solution, blue circles = observations.

3.6.3.1. Ground-based Comparisons of Photochemical Dynamics

Errors in the NO_X concentrations in the model, most likely from on-road emissions, affected NO_X predictions shown in Figure 3-60, but CMAQ-UCD's general responses were reasonable. The model also replicated anthropogenic and biogenic VOC emissions well; see Figure 3-61 and Figure 3-62, respectively. After initial errors leading to underprediction in the first 21 days, CMAQ-UCD's predictions of hourly $PM_{2.5}$ concentrations and trends over the whole month also replicated the observed concentrations well (Figure 3-63).

3.6.3.2. Predicted Chemistry for Nitrates and Related Compounds

Particulate NO_3^- (pNO_3^-) plays a crucial and complex role in the health of aquatic and estuarine ecosystems and human drinking water systems. Gas-phase NO_3^- replacement of Cl^- on sea salt particles is often favored thermodynamically and the V_d of the coarse pNO_3^- formed through this replacement is more than an order of magnitude greater than for fine pNO_3^-. Over open bodies of salt water such as the Gulf of Mexico and Tampa Bay, FL, pNO_3^- from this reaction dominates dry deposition and is estimated to be of the same order as pNO_3^- wet deposition.

However, total NO_3^- concentrations are driven, buffered, and altered by a wide range of photochemical gas-phase reactions, heterogeneous reactions, and aerosol dynamics, making them especially difficult to model. Because pNO_3^- is derived mostly from gas-phase HNO_3 and will interact with Na^+, NH_4^+, Cl^-, and SO_4^{2-}, all these species and the physical parameters governing their creation, transport, transformation, and fate must be accurately replicated to predict pNO_3^- with high fidelity. This has historically been a difficult problem for numerical process models, owing in large part to the pervasive dearth of reliable ambient measurements of NO_3^- in its various forms. Normalized mean error (NME) for the large-scale Eulerian CTM-predicted pNO_3^- has typically been on the order of a factor of 3 greater than the NME for particulate SO_4^{2-} (pSO_4^{2-}) (Odman et al., 2002, 092474; Pun et al., 2003, 047775).

SO_4^{2-}, NH_4^+, Na^+, and Cl^- were all predicted to within a factor of 2 and with no significant bias during the photochemical day in the 8 km CMAQ-UCD solution, although a significant bias in Na^+ and Cl^- was evident in the 2 km solution for two near-water sites. This grid-size dependent bias is still being explored. Size segregation maxima were correct to within two size bins every day for which there were observations for both SO_4^{2-} and NH_4^+ (0.2 to 1.0 μm), and Na^+ and Cl^- (2.0-10.0 μm). Cl^- concentrations were greatly overpredicted during dark hours, but were nearer to observed values during the photochemical day. CMAQ-UCD performance for HNO_3 and NH_3 are shown in Figure 3-64 and Figure 3-65, respectively.

Figure 3-66 shows that CMAQ-UCD systematically underpredicted the hourly time series of measured pNO_3^- concentrations at the Sydney supersite, the only location with discrete pNO_3^- data. These time series data establish that CMAQ-UCD's largest errors were on 4 days in the first 2 wk of the month, but that the total peak pNO_3^- concentrations were nearly all underpredicted.

Since pNO_3^- is derived in large part from gas-phase HNO_3, its underprediction may be due to an underprediction of HNO_3 concentrations or an underrepresentation of the gas- to aerosol-phase change. At Sydney, FL, in fact, both these conditions held. Figure 3-64 depicts the model's bias for HNO_3 underprediction in both the 8 km and 2 km solutions, except for four days of very large peak overpredictions. This pattern of underpredictions was especially evident overnight. On 8 other days the model overpredicted the one hour peak concentration as well, though not so substantially, but the chief effect was still one of an artificial and inappropriate N limitation in the model.

A time series molar equivalent ratio of HNO_3 to total NO_3 depicts which phase stores the NO_3^- and how that storage ratio changes over time. Figure 3-67 shows that at Sydney, FL, CMAQ-UCD stored too much NO_3^- in the gas phase as HNO_3 (and recall that the daytime HNO_3 concentrations were sometimes overpredicted by the model) and too little in the gas phase overnight, when the model was regularly low against the measurements; compare Figure 3-64 and Figure 3-65. Note again here the similarity of the 8 km and 2 km solutions in this comparison.

Interestingly, the 23-h integrated data did not reveal this important difference in NO_3^- form between the model and measurements as Figure 3-68 shows in the stacked bar percentage plots of fine and coarse pNO_3^- together with gas-phase HNO_3. Both the 8 km (Figure 3-68, middle panel) and the 2 km (Figure 3-68, bottom panel) solutions predicted distributions between the two general ranges of aerosol size, and between gas and aerosol phases, with good fidelity to the daily observations (Figure 3-68, top panel) at Sydney, FL. This result illustrates that while discrete time

series data are crucial for diagnosing model behavior, on the integrated total daily and longer basis used for computing total annual N loads, CMAQ-UCD predicted approximately the correct distributions for pNO_3^-, even though the total NO_3^- concentration prediction was biased low.

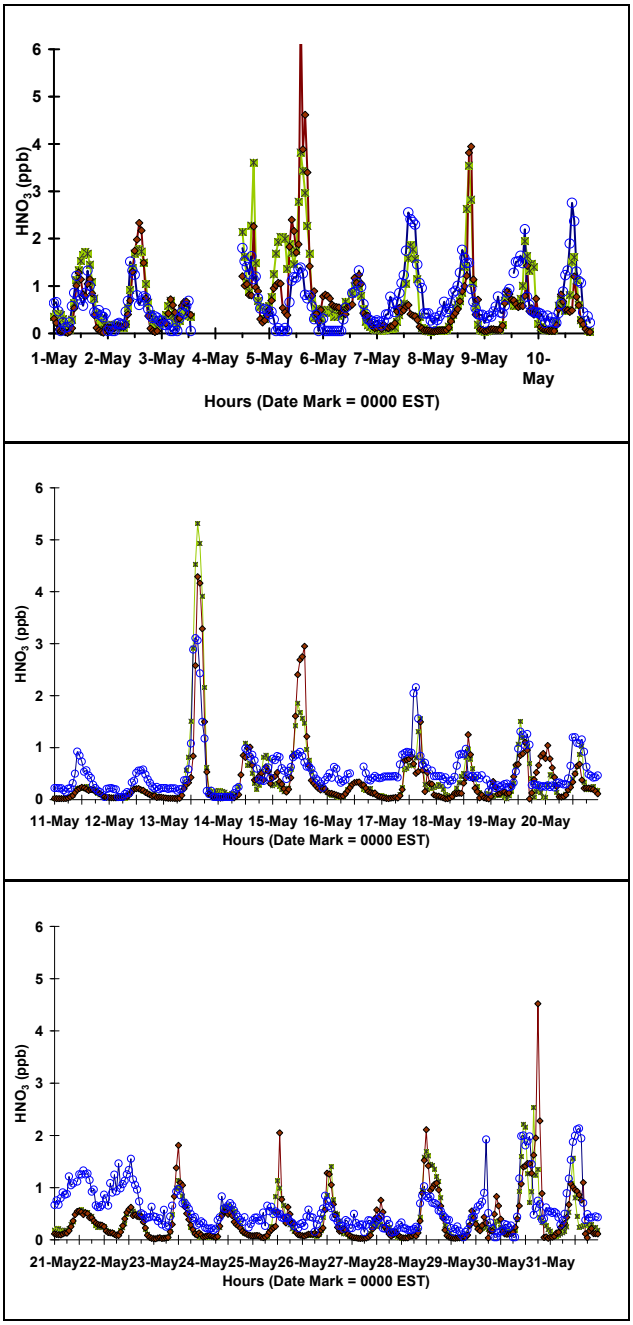


Figure 3-64. CMAQ-UCD predictions of HNO_3^- concentrations and corresponding measured observations at Sydney, FL, for May 1-31, 2002. Green x = 8 km solution, red diamonds = 2 km solution, blue circles = observations.

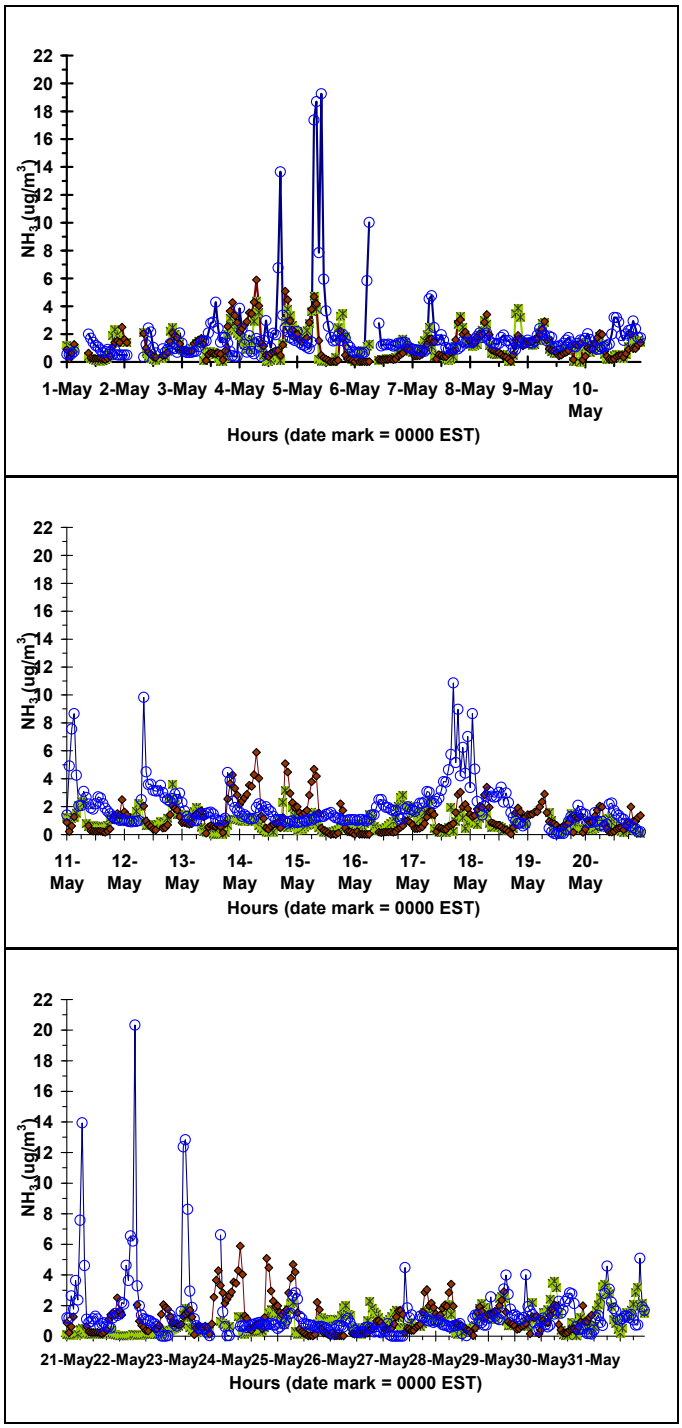


Figure 3-65. CMAQ-UCD predictions of NH_3 concentrations and corresponding measured observations at Sydney, FL, for May 1-31, 2002. Green x = 8 km solution, red diamonds = 2 km solution, blue circles = observations.

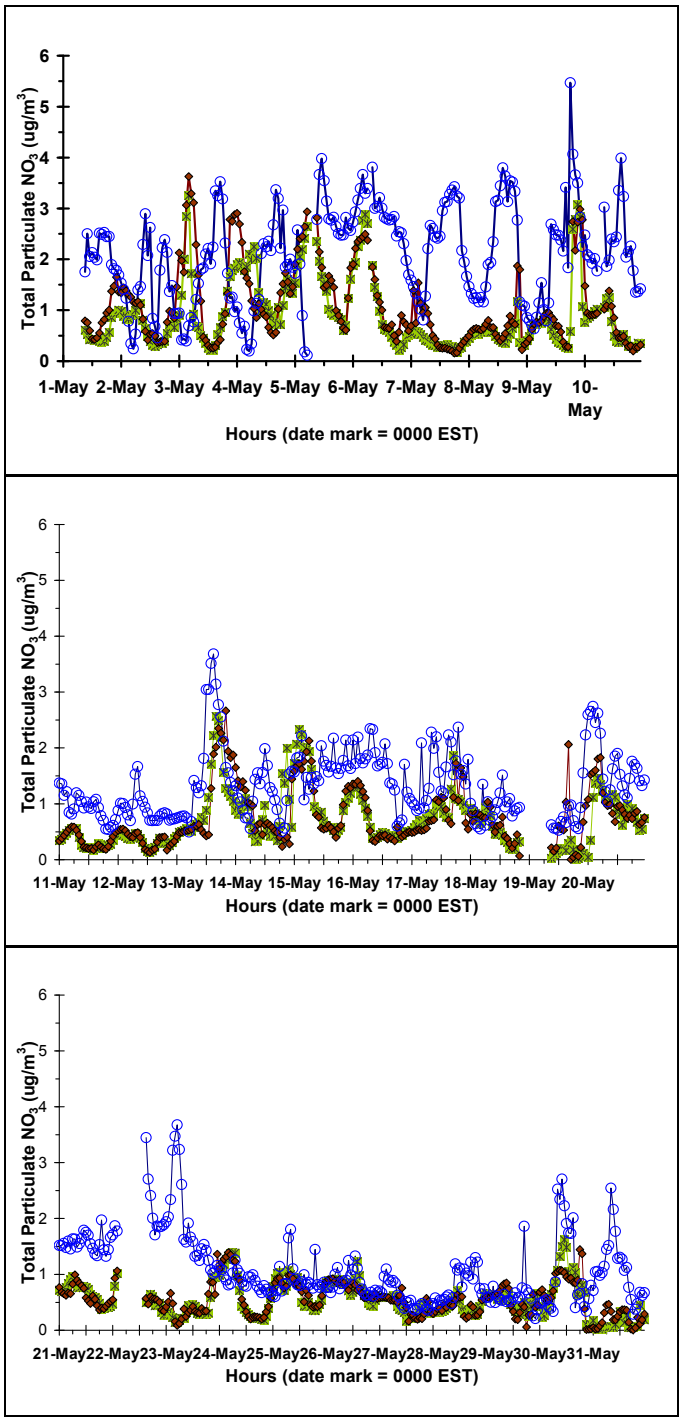


Figure 3-66. CMAQ-UCD predictions of pNO_3^- concentrations and corresponding measured observations at Sydney, FL, for 1-31 May, 2002. Green x = 8 km solution, red diamonds = 2 km solution, blue circles = observations.

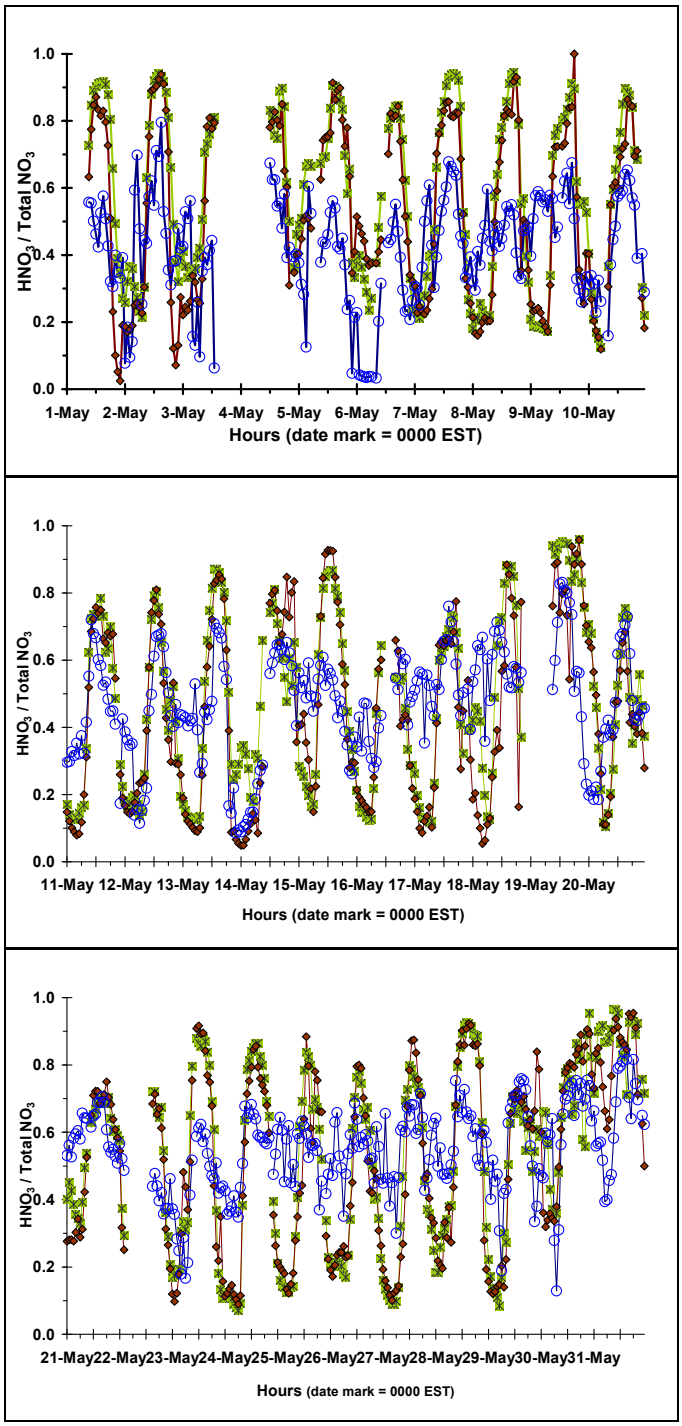


Figure 3-67. CMAQ-UCD predictions of the ratio of HNO_3 to total NO_3 and corresponding measured observations at Sydney, FL, for May 1-31, 2002. Green x = 8 km solution, red diamonds = 2 km solution, blue circles = observations.

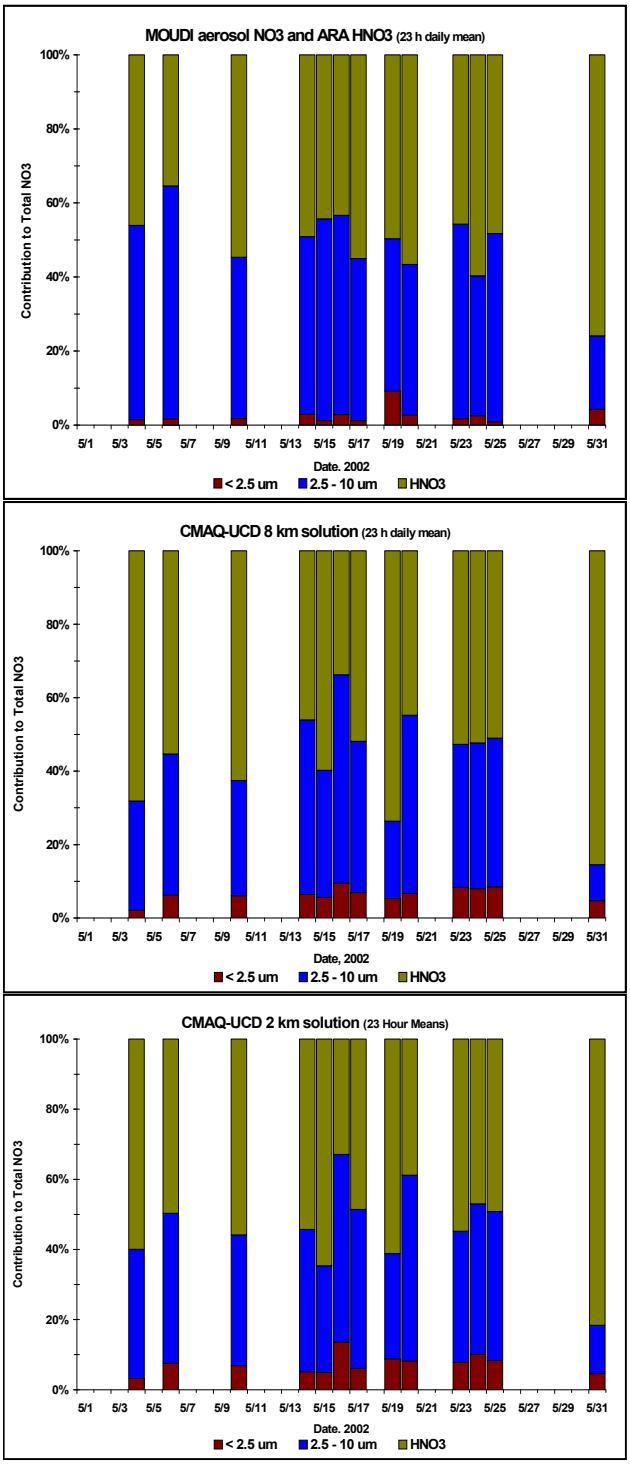


Figure 3-68. CMAQ-UCD predicted size and chemical-form fractions of total NO_3^- for days in May 2002 with measured observations. Measured concentrations (top panel); 8 km solution (middle panel); 2 km solution (bottom panel). Red bars = pNO_3^- <2.5 µm; blue bars = pNO_3^- 2.5-10 µm; green bars = HNO_3.

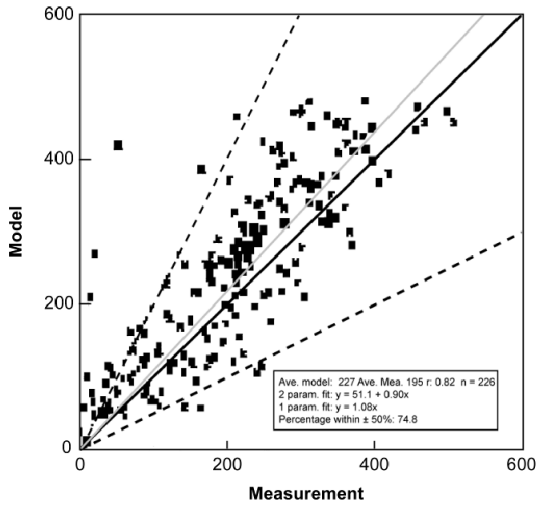
While inorganic aerosol anion totals were dominated by NO_3^- in the coarse fraction and by SO_4^{2-} in the fine fraction, there was sufficient NH_X ($NH_X = NH_3 + NH_4^+$) at Sydney, FL, to form fine aerosol NH_4NO_3 in some circumstances. Figure 3-65 depicts the hourly mass concentration of NH_3 at Sydney, FL, showing again the strong similarity of the 8 km and 2 km solutions. Each solution, however, underpredicted the measured NH_3 concentrations consistently, and especially for the nine very large excursions of 10-20 $\mu g/m^3$ during the month.

Overall, CMAQ-UCD was found to be operationally sound in this evaluation of its 8 km and 2 km solutions for the Tampa Bay airshed using the ground-based and aloft data (not shown here) from the May 2002 field intensive. Moreover, results from diagnostic tests of the model's photochemical dynamics were generally in excellent agreement with results from the ambient atmosphere. However, CMAQ-UCD was biased low in this application for total NO_3 and for NO_3 present as gas-phase HNO_3. In addition, the model was biased low for the HO_X radical reservoir species CH_2O and H_2O_2 (not shown here), though this bias appeared to have been limited to these species. Performance of the new UCD aerosol module was judged to be entirely adequate, allocating aerosols by chemical makeup to the appropriate size fractions. Model performance for fine-mode aerosols was also judged to be fully adequate.

3.6.4. Evaluating Concentrations and Deposition of PM Components with CTMs

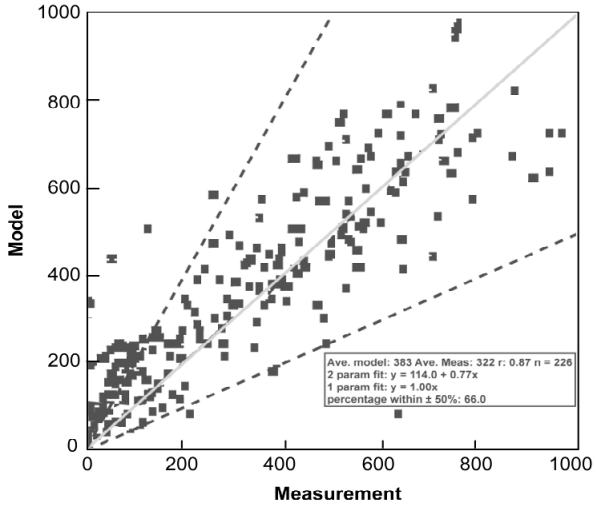
3.6.4.1. Global CTM Performance

The wet and dry deposition processes described in Section 3.3 are of necessity highly parameterized in all CTMs. While all current models implement resistance schemes for dry deposition, the V_d generated from different models can vary highly across terrain types (Stevenson et al., 2006, 089222).The accuracy of wet deposition in global CTMs is tied to spatial and temporal distribution of model precipitation and the treatment of chemical scavenging. Dentener et al. (2006, 088434) compared wet deposition across 23 models with available measurements around the globe. Figure 3-69 and Figure 3-70 extract results of a comparison of the 23-model mean versus observations over the eastern U.S. for pNO_3^- and pSO_4^{2-} deposition, respectively. The mean model results were strongly correlated with the observations ($r > 0.8$), and usually captured the magnitude of wet deposition to within a factor of two over the eastern U.S. Dentener et al. (2006, 088434) concluded that 60-70% of the participating models captured the measurements to within 50% in regions with quality controlled observations.



Source: Adapted with Permission of American Geophysical Union from Dentener et al. (2006, 088434).

Figure 3-69. Scatter plot of total nitrate (HNO_3 plus pNO_3^-) wet deposition (mg N/m^2/yr) of the model mean versus measurements for the North American Deposition Program (NADP) network. Dashed lines indicate a factor of two. The gray line is a linear regression through zero.



Source: Adapted with Permission of American Geophysical Union from Dentener et al. (2006, 088434).

Figure 3-70. Scatter plot of total SO_4^{2-} wet deposition (mg S/m^2/yr) of the model mean versus measurements for the National Atmospheric Deposition Program (NADP) network. Dashed lines indicate a factor of two. The gray line is a linear regression through zero.

3.6.4.2. Regional CTM Performance

Regional CTM performance for concentration and deposition of some of the most relevant PM species is illustrated here with examples from CMAQ version 4.6.1 as configured and run for

exposure and risk assessments reported in the *Risk and Exposure Assessment for the Review of the Secondary National Ambient Air Quality Standards for Oxides of Nitrogen and Oxides of Sulfur* (U.S. EPA, 2009, 191774); additional details on the model configuration and application are found there. A map of the 36 km parent domain and two 12 km (east and west) progeny domains appears in Figure 3-71.

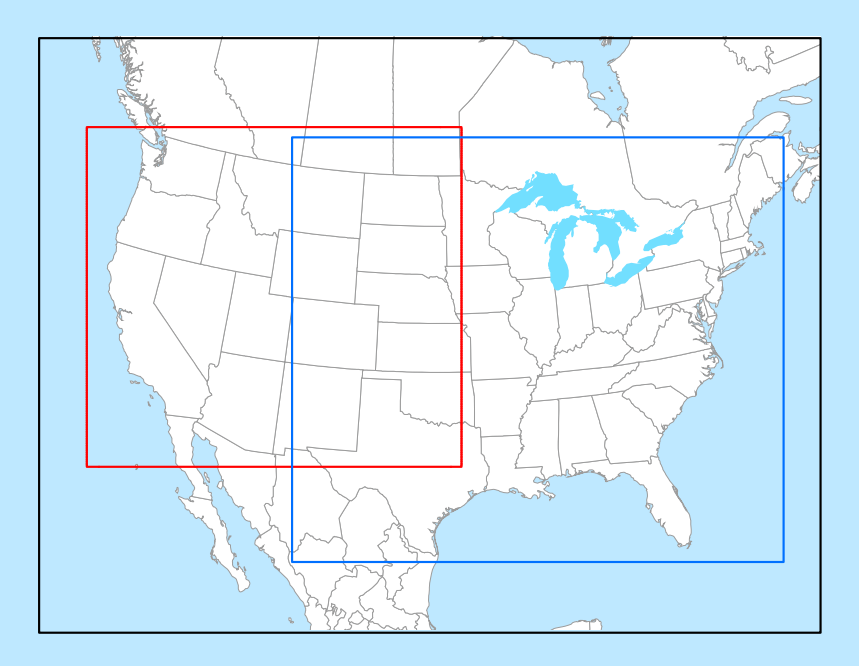


Figure 3-71. CMAQ modeling domains for the OAQPS risk and exposure assessments: 36 km outer parent domain in black; 12 km western U.S. (WUS) domain in red; 12 km eastern U.S. (EUS) domain in blue.

Comparisons from the 2002 annual run of CMAQ for the exposure assessment are shown here against measured concentrations and deposition totals from nodes in three networks: IMPROVE, CSN (labeled STN in the plots) and CASTNet. Comparisons were made as model-observation pairs at all sites having sufficient data for the seasonal or the 2002 annual time period in the two 12 km east and west domains and were evaluated with the following descriptive statistics: correlation, root mean square error, normalized mean bias, and normalized mean error.

Summertime pSO_4^{2-} concentrations are well predicted by CMAQ, to within a factor of 2 at nearly every point, and with R^2 >0.8 across all three networks (Figure 3-72). This result tracks the generally well-predicted SO_4^{2-} concentrations found in earlier CMAQ evaluations: see Eder and Yu (2005, 089229), Mebust et al. (2003, 156749) and Tesche et al. (2006, 157050). Since pSO_4^{2-} concentrations are strongly a function of precipitation, care must be taken to ensure that the meteorological solution driving individual CMAQ chemical applications produces precipitation fields with low bias as discussed by Appel et al. (2008, 155660).

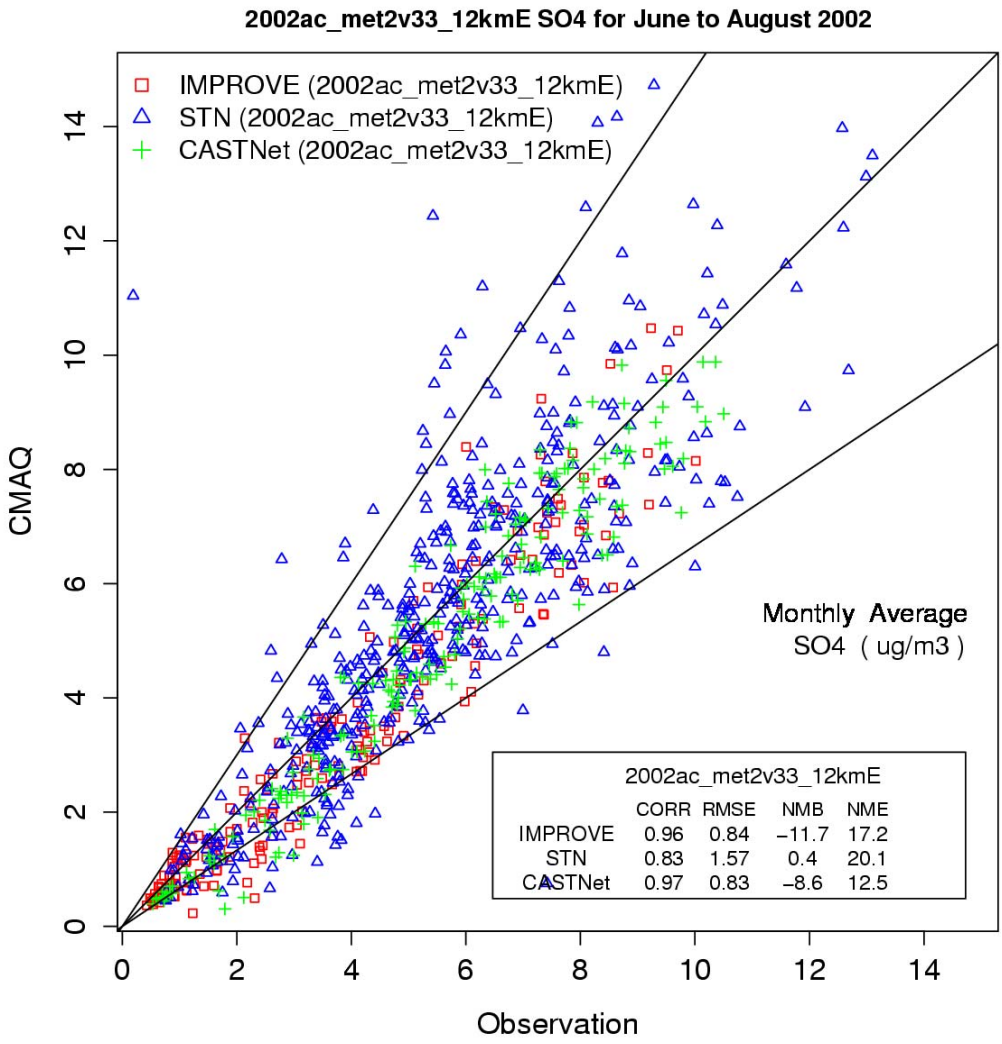


Figure 3-72. 12-km EUS Summer sulfate PM. Each data point represents a paired monthly averaged (June/July/August) observation and CMAQ prediction at a particular IMPROVE, STN, and CASTNet site. Solid lines indicate a factor of two around the 1:1 line shown between them.

Wintertime pNO_3^- (Figure 3-73) and total NO_3 (HNO_3+pNO_3^-) (Figure 3-74) concentrations are predicted less well by CMAQ, but NO_3 is a pervasively difficult species to measure and model. Still, at the CASTNet nodes where the total NO_3 concentrations are higher than they are at all but a few of the remote IMPROVE sites, CMAQ predicts concentrations for nearly every node to within a factor of 2 and with an R^2 >0.8. These CMAQ-predicted concentrations, coupled with modeled cloud and precipitation fields produce wet deposition fields for SO_4^{2-} and NO_3^- in the east domain as shown in Figure 3-75 and Figure 3-76, respectively.

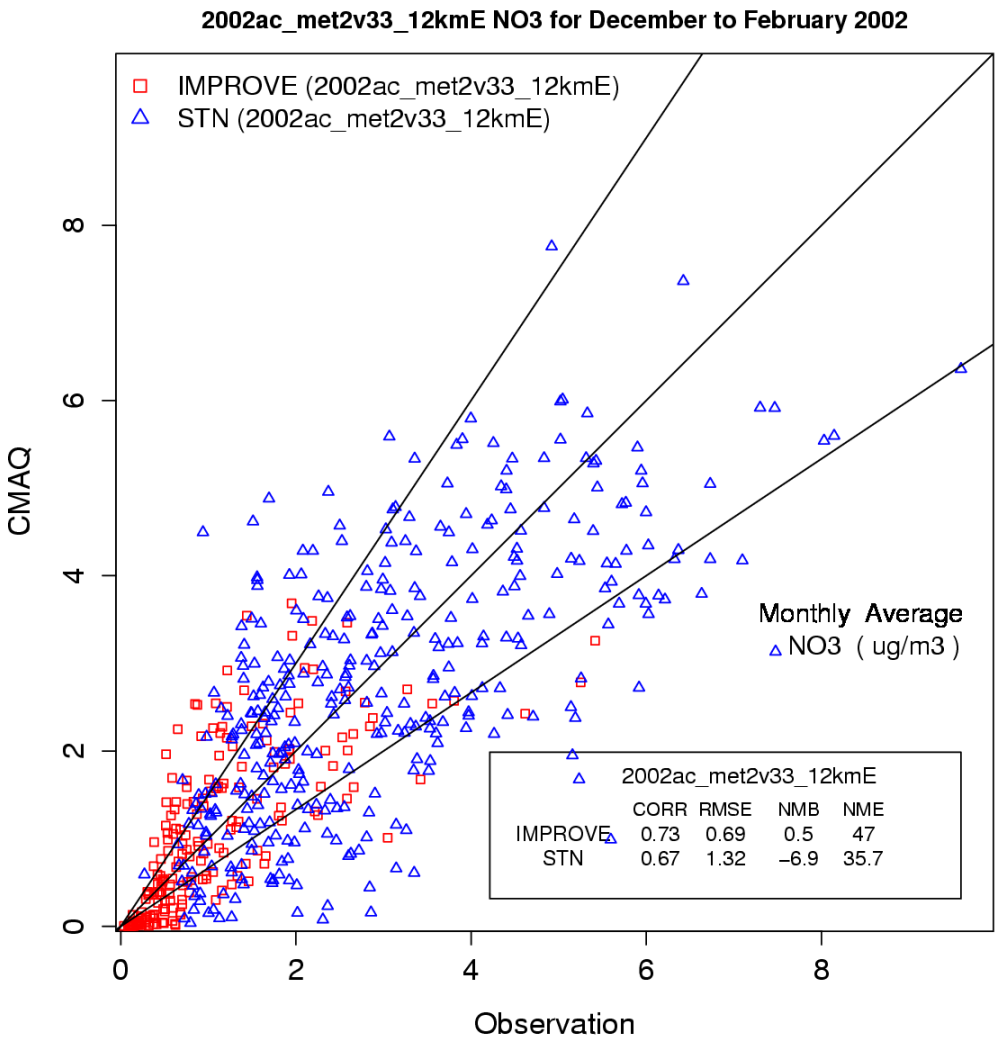


Figure 3-73. 12-km EUS Winter nitrate PM. Each data point represents a paired monthly averaged (December/January/February) observation and CMAQ prediction at a particular IMPROVE and STN site. Solid lines indicate a factor of two around the 1:1 line shown between them.

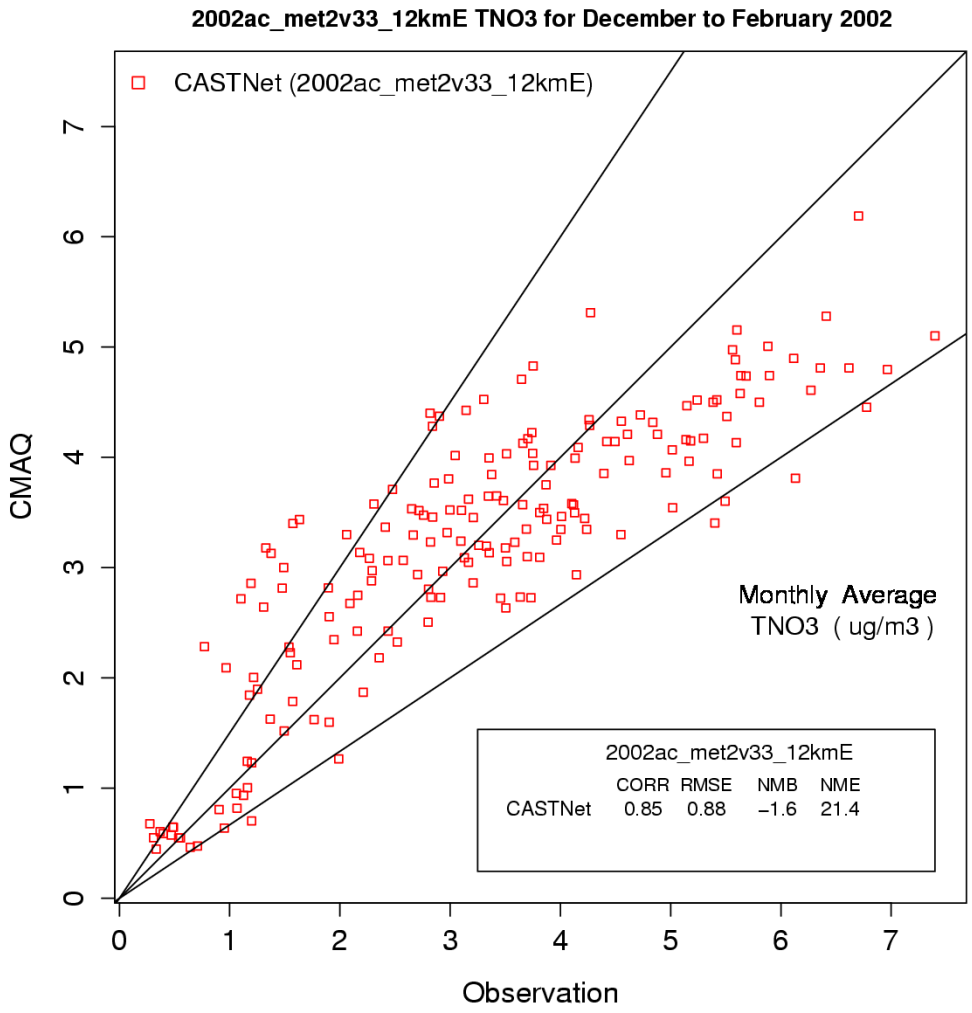


Figure 3-74. **12-km EUS Winter total nitrate (HNO_3 + total pNO_3^-). Each data point represents a paired monthly averaged (December/January/February) observation and CMAQ prediction at a particular CASTNet site. Solid lines indicate a factor of two around the 1:1 line shown between them.**

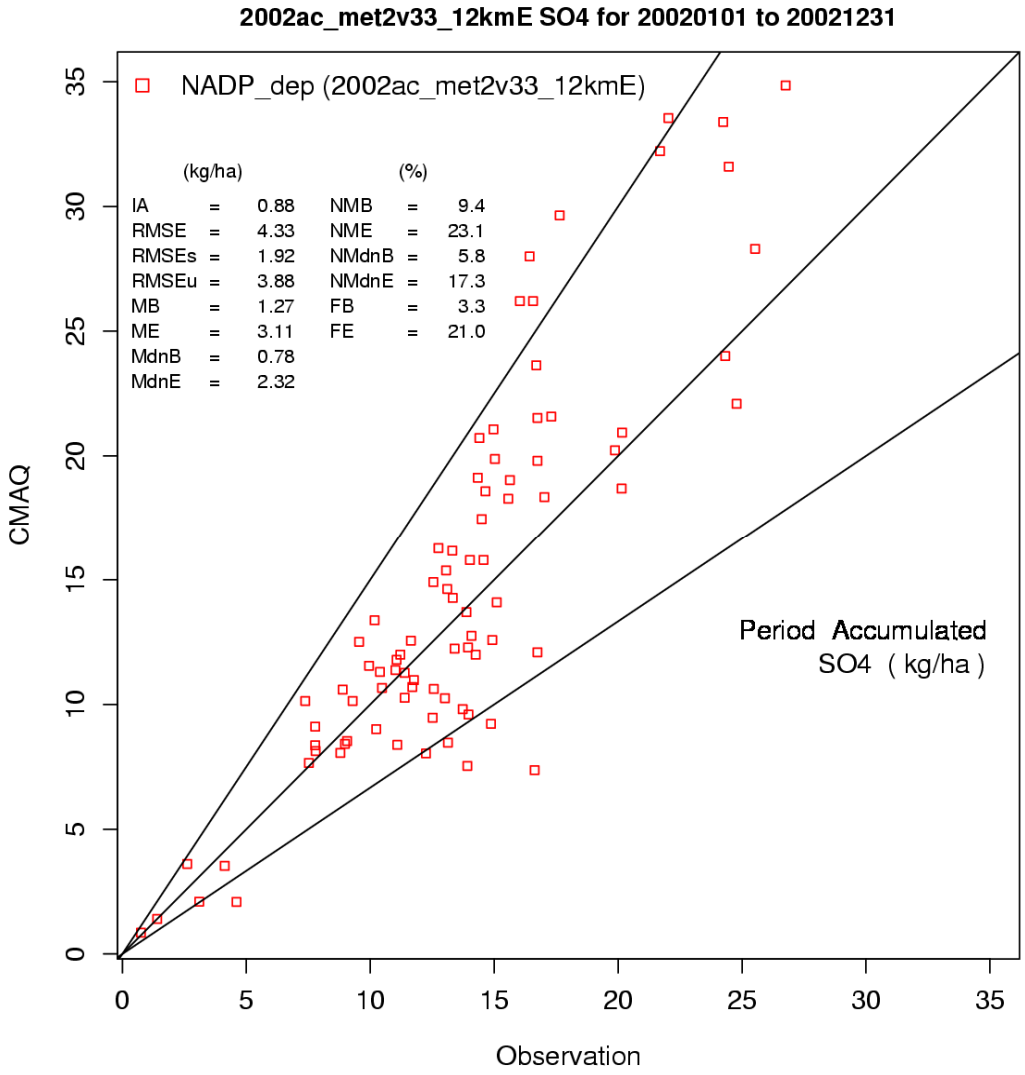


Figure 3-75. 12-km EUS annual sulfate wet deposition. Each data point represents an annual average paired observation and CMAQ prediction at a particular NADP site. Solid lines indicate the factor of 2 around the 1:1 line shown between them.

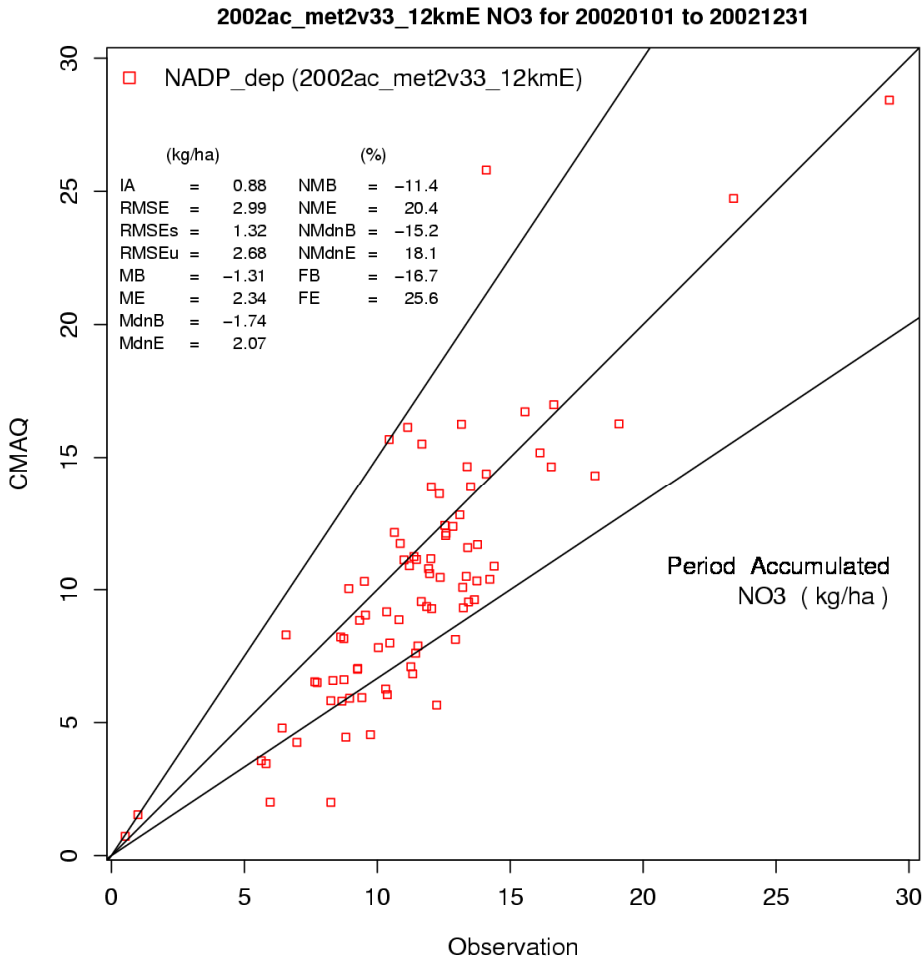


Figure 3-76. 12-km EUS annual nitrate wet deposition. Each data point represents an annual average paired observation and CMAQ prediction at a particular NADP site. Solid lines indicate a factor of two around the 1:1 line shown between them.

Importantly, CMAQ captured the chief spatial patterns and magnitudes of air concentrations and wet deposition relevant to computing concentration and deposition budgets, as shown in Figure 3-77 for concentrations and Figure 3-78 for deposition. More specifically, CMAQ's predictions of NH_3 and SO_4^{2-} for both high and low concentration sites are well within the range of observed measurements (Figure 3-79).

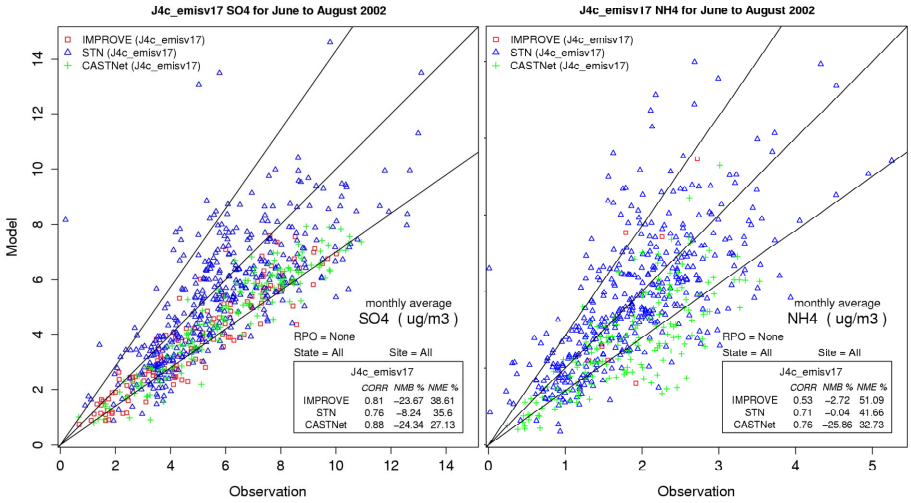


Figure 3-77. CMAQ vs. measured air concentrations from east-coast sites in the IMPROVE, CSN (labeled STN), and CASTNet sites in the summer of 2002 for sulfate (left) and ammonium (right). Solid lines indicate a factor of 2 around the 1:1 line shown between them.

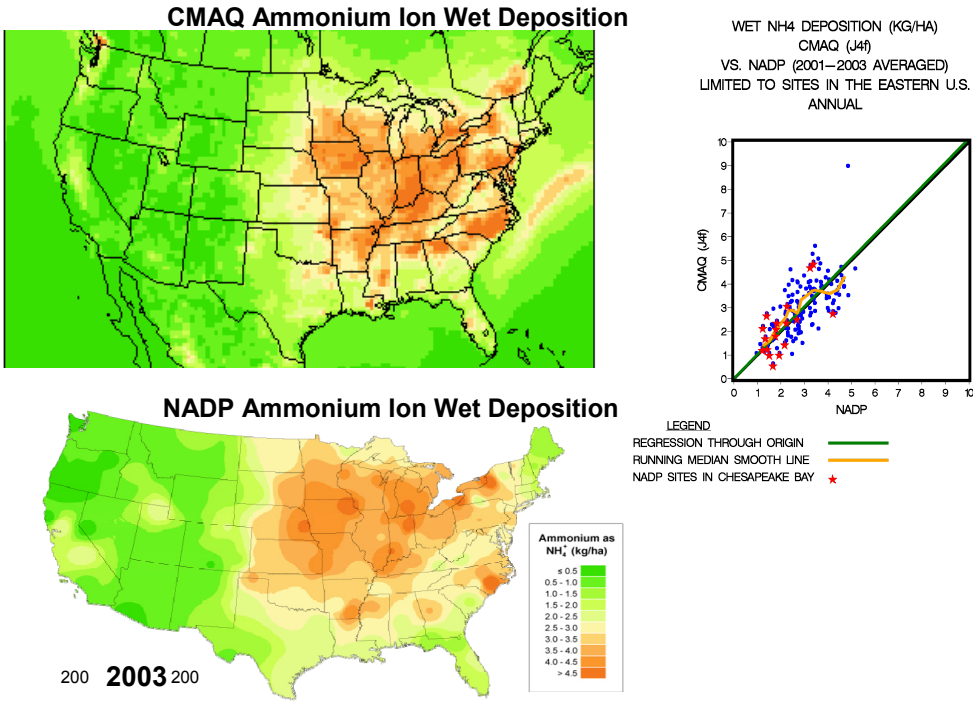


Figure 3-78. Comparison of CMAQ-predicted and NADP-measured NH_4^+ wet deposition : (top left) CMAQ prediction; (bottom left) NADP-measurements; (right) regression and smoothed median line through CMAQ predictions and NADP measurements with sites in the Chesapeake Bay watershed highlighted.

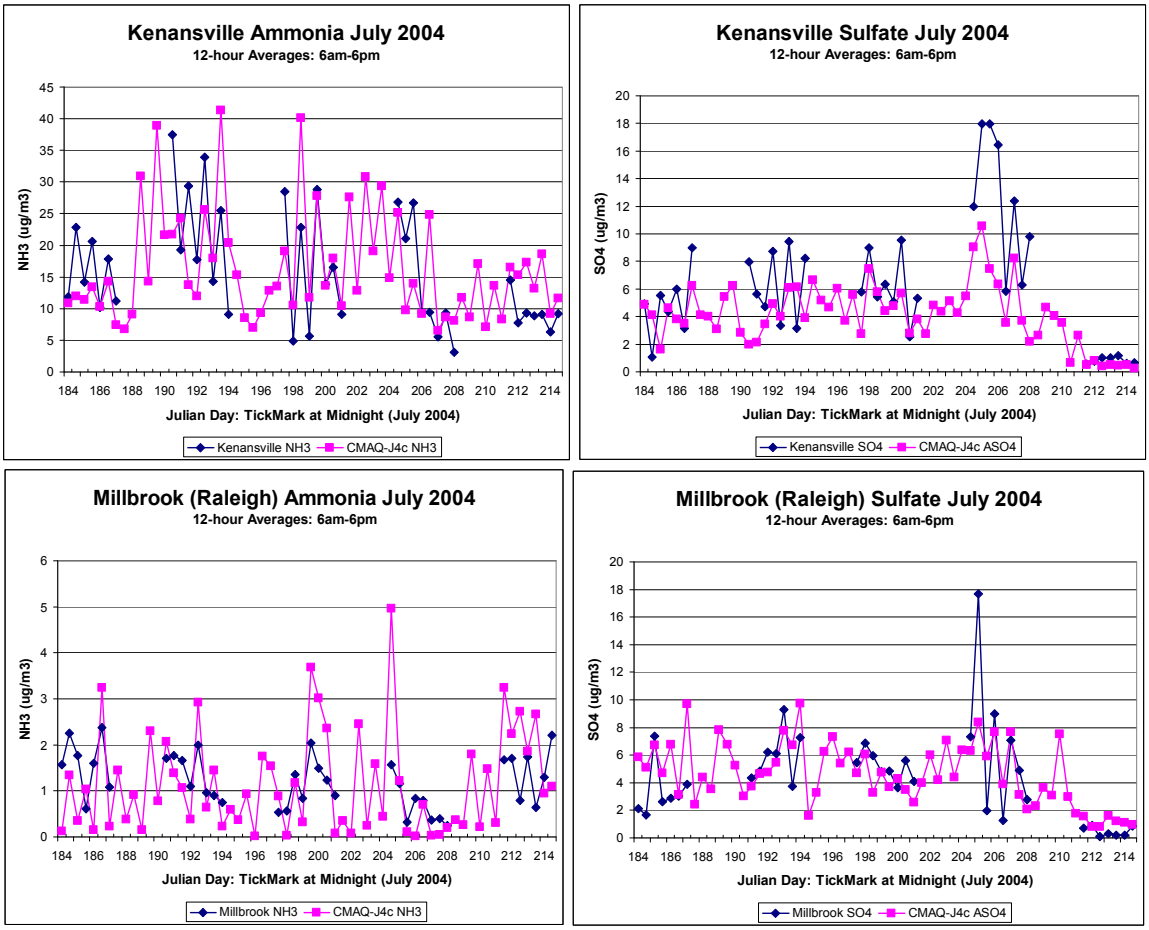


Figure 3-79. CMAQ-predicted (red symbols and lines) and 12-h measured (blue symbols and lines) NH_3 and SO_4^{2-} surface concentrations at high and low concentration grid cells in North Carolina in July 2004. (top left) High concentration NH_3 in Kenansville; (top right) high concentration SO_4^{2-} in Kenansville; (bottom left) low concentration NH_3 in Raleigh; (bottom right) low concentration SO_4^{2-} in Raleigh.

Deposition velocities are difficult to estimate for reasons described in Section 3.3.3. Recent work in EPA's Atmospheric Modeling and Analysis Division with CMAQ showed that the original V_d for NH_3 was very likely too high and should be nearer to the values for SO_2 deposition, or even lower over some land use surface types. A sensitivity study with the model was performed to test the effects of changing V_d for NH_3 on the fraction of NH_3 available for transport away from grid cells with high emissions concentrations. Comparisons were made for the surface grid cells and total column NH_3 concentrations.

In the highest emissions grid cells during June 2002, the surface NH_X budget was dominated by turbulent transport or vertical mixing moving a majority of the surface NH_3 emissions up and away from the surface into the mixed layer. Figure 3-80 depicts the NH_X budget under the base case (Base V_d) and the sensitivity case (SO_2 V_d) for which the NH_3 V_d was set equal to the SO_2 V_d. Lower NH_3 V_d decreased NH_X deposition to the surface from 15 to 8%, leaving more NH_X for transport horizontally, 22% up from 20% in the base case, and vertically, 69% up from 64% in the base case. Typically, ~67% of surface emissions were moved aloft where most was advected away from the high emissions grid cell, with a small fraction converted to pNH_4^+ and an even smaller fraction wet-deposited to the surface. The total column analyses for NH_3 and NH_X are shown in Figure 3-81.

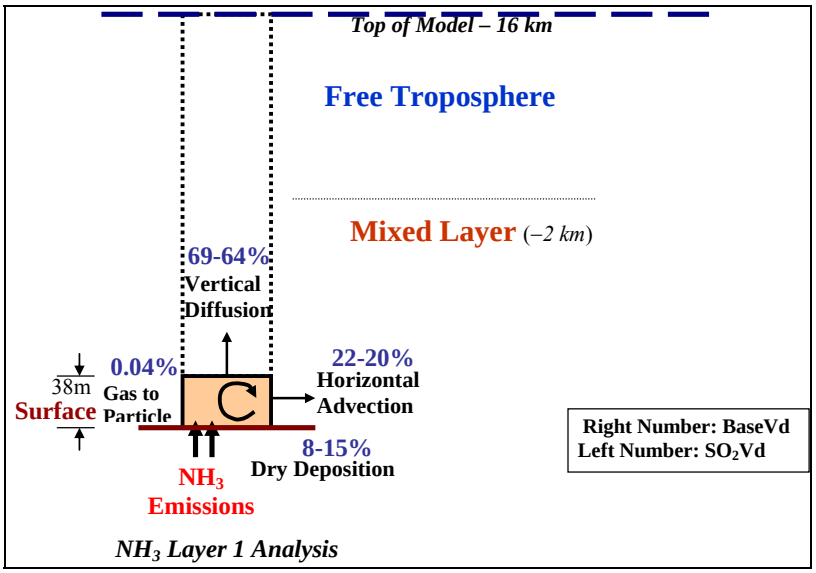


Figure 3-80. Surface grid cell (layer 1) analysis of the sensitivity of NH_X deposition and transport to the change in NH_3 V_d in CMAQ.

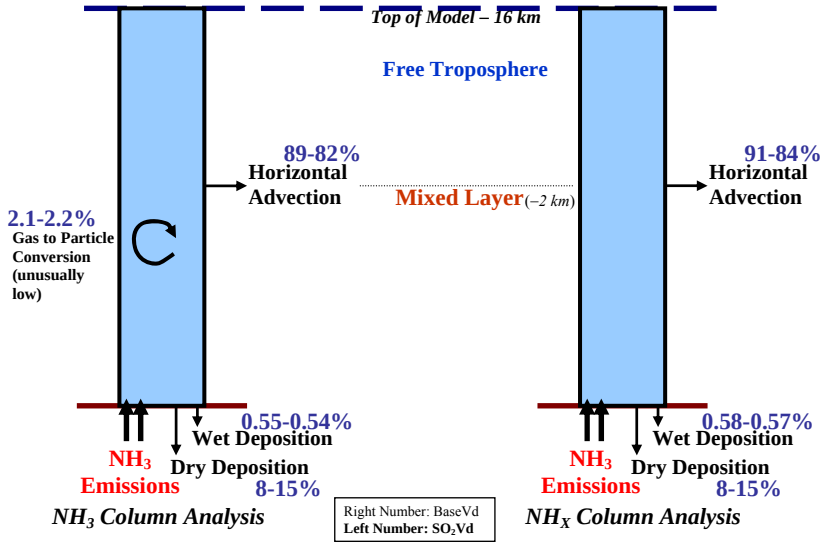


Figure 3-81. Total column analysis for NH_3 (left) and NH_X (right) showing modeled NH_3 emissions, transformation, and transport throughout the mixed layer and up to the free troposphere.

Local total deposition (wet + dry) is a significant but not dominant loss pathway for surface NH_3 emissions. In these simulations, CMAQ deposited ~25% of the NH_3 emissions from the single high concentration grid cell in Sampson County, NC, back into that grid cell. By far, the largest contribution to the local deposition total was dry deposition. Dry-to-wet deposition ratios for the Sampson County high emissions grid cell and surrounding surface grid cells ranged from 2 to 10.

Deposition to grid cells farther away from the high concentration, immediately surrounding grid cells, was significantly affected by the change in NH_3 V_d tested in this case. Figure 3-82 depicts

the range of influence of the high concentration grid cell, where that range is defined to be the distance by which 50% of the emissions attributable to that grid cell have deposited. The range of influence of the high concentration Sampson County grid cell was extended in the V_d sensitivity tested here from ~180 km in the base case to ~400 km in the case using the lower, more realistic V_d for NH_3. The areal extent of this difference in range of influence is mapped in Figure 3-83.

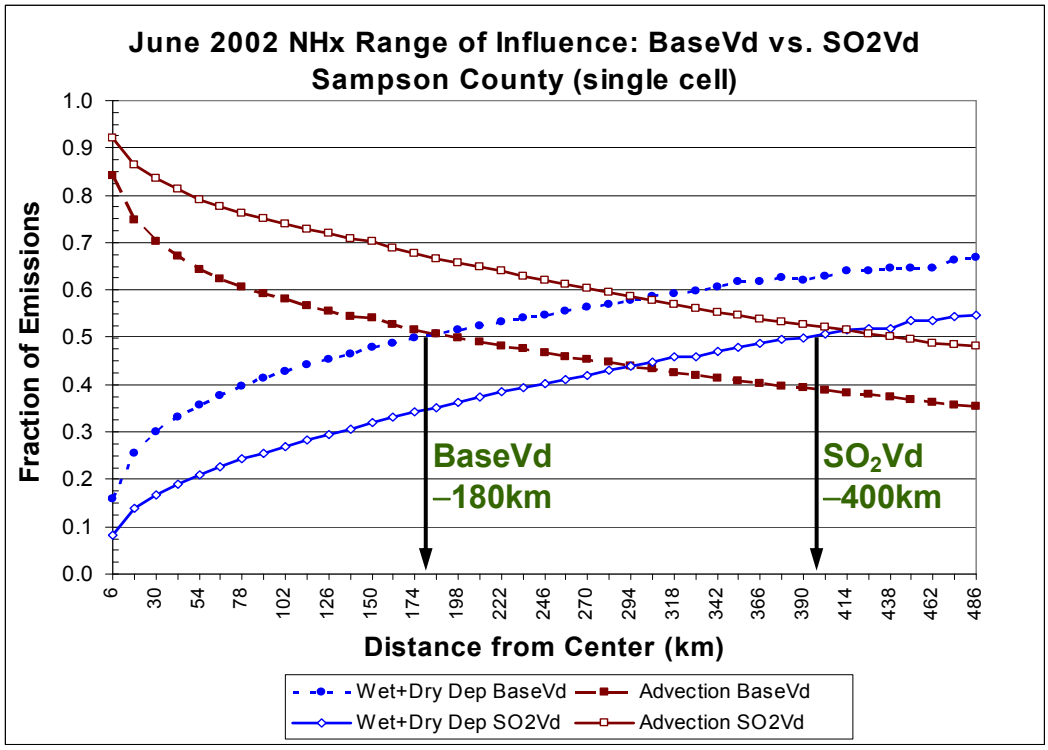


Figure 3-82. Range of influence (where 50% of emitted NH_3 deposits) from the high concentration Sampson County grid cell in the June 2002 CMAQ simulation of V_d sensitivities. Base case and sensitivity case total deposition (blue symbols and lines); base case and sensitivity case advection totals (red symbols and lines).

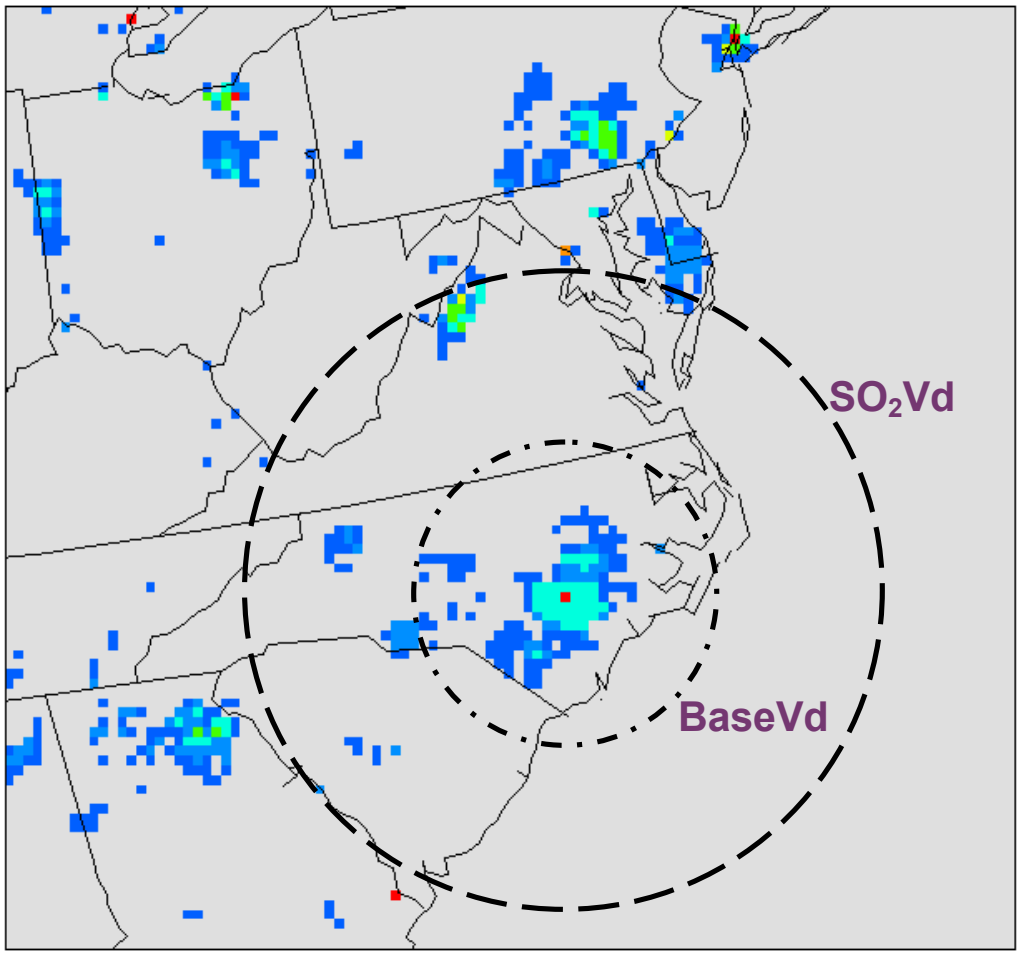


Figure 3-83. Areal extent of the change in NH_X range of influence as predicted by CMAQ for the Sampson County high concentration grid cell (center of range circles) in June 2002 using the base case and sensitivity case V_d.

3.7. Background PM

The background concentrations of PM that are useful for risk and policy assessments informing decisions about the NAAQS are referred to as policy-relevant background (PRB) concentrations. PRB concentrations have historically been defined by EPA as those concentrations that would occur in the U.S. in the absence of anthropogenic emissions in continental North America defined here as the U.S., Canada, and Mexico. For this document, PRB concentrations include contributions from natural sources everywhere in the world and from anthropogenic sources outside continental North America. Background concentrations so defined facilitated separation of pollution that can be controlled by U.S. regulations or through international agreements with neighboring countries from those that were judged to be generally uncontrollable by the U.S. Over time, consideration of potential broader ranging international agreements may lead to alternative determinations of which PM source contributions should be considered by EPA as part of PRB.

3.7.1. Contributors to PRB Concentrations of PM

Contributions to PRB concentrations of PM include both primary and secondary natural and anthropogenic components. Natural sources include wind erosion of natural surfaces (Gillette and Hanson, 1989, 030212); volcanic production of SO_4^{2-}; PBAP; wildfires producing EC, OC, and inorganic and organic PM precursors; and SOA produced by oxidation of biogenic hydrocarbons such as isoprene and terpenes. However, human intervention can be involved in the formation of SOA, as production of natural SOA depends to a large extent on the presence of anthropogenic NO_X. As described earlier in Section 3.3, prescribed fires are considered part of PRB. In addition to emissions from forest fires in the U.S., emissions from forest fires in other countries can be transported to the U.S. For example, Boreal forest fires in Canada (Mathur, 2008, 156742) and Siberia (Generoso et al., 2007, 155786) and tropical forest fires in the Yucatan Peninsula and Central America (Wang et al., 2006, 157109) have affected PM concentrations in the U.S. PRB PM varies across the contiguous Unites States (CONUS) by region and season as a function of the complex mechanisms of transport, dispersion, deposition, and reentrainment.

Dust from the Sahara desert and the Sahel in North Africa (Chiapello et al., 2005, 156339) affects mainly the eastern U.S.; dust from the Gobi and Taklimikan deserts in Asia (VanCuren and Cahill, 2002, 157087; Yu et al., 2008, 157168) have the largest effects in the western U.S. but also affect air quality in the eastern U.S. Husar et al. (2001, 024947) report that the average PM_{10} concentration at 25 reporting stations throughout the northwestern U.S. reached 65 $\mu g/m^3$ during an episode in the last week in April 1998, compared to an average of 10-25 $\mu g/m^3$ during the rest of April and May. This was accompanied by visual reports of milky-white discoloration of the normally blue sky in non-urban areas along the west coast.

PRB contributions to $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10} can also be viewed as coming from two conceptually separate components: a reasonably consistent "baseline" component and an episodic component. The baseline component consists of contributions that are generally well characterized by a reasonably consistent distribution of daily values each year, although there is variability by region and season. The episodic component consists of infrequent, sporadic contributions from natural high-concentration events occurring over shorter periods of time (e.g., hours to several days) both within North America (e.g., volcanic eruptions, large forest fires, dust storms) and outside North America (e.g., transport related to dust storms from deserts in North Africa and China and storms at sea). These episodic natural events, as well as events like the uncontrolled biomass burning in Central America, are essentially uncontrollable and do not necessarily occur in all years.

In-situ measurements provide evidence for the transport of anthropogenic PM from Asia on Mt. Batchelor, OR (Jaffe et al., 2003, 052229). These data show sporadic but well correlated increases in CO, O_3, total Hg, and aerosol backscatter associated with air coming from Asia. The ITCT-2K2 campaign also found evidence for the oxidation of SO_2 to H_2SO_4 during trans-Pacific transport of Asian emissions. If particulate SO_4^{2-} were to be formed in the polluted boundary layer where it originated, it would likely be deposited prior to transport across the Pacific Ocean (Brock et al., 2004, 156295). Thus, primary species emitted directly and secondary species formed during transport contribute to PRB concentrations. Satellite data have provided images to track clouds of dust and pollution across the oceans and have been used for some quantitative estimation of the flux of material leaving continents. Yu et al. (2008, 157168) used optical thickness data to estimate

column loadings from the MODIS along with satellite assimilated wind fields to estimate the transport of PM from Asia. Three-dimensional, global-scale CTMs have also been used to estimate intercontinental transport of PM pollution (UNCEC, 2007, 157078) and trans-Pacific transport of mineral dust from Asian deserts (Fairlie et al., 2007, 141923) and the Sahara Desert (McKendry et al., 2007, 156748).

Estimates for the contribution of PBAP are highly problematic. Heald and Spracklen (2009, 190014) estimated the contribution of fungal spores to $PM_{2.5}$ based on GEOS-Chem simulations of mannitol, considered to be a unique tracer for fungal spores (Bauer et al., 2008, 189986). They estimated an annual mean contribution of fungal spores to OC ranging from <0.1 $\mu g/m^3$ in the desert Southwest to ~ 0.5 $\mu g/m^3$ in the more humid Southeast. It should be noted that these are model derived estimates that still require evaluation against measurements in the U.S. They do, however, provide the only quantitative estimates of PBAP concentrations across the continental U.S.

3.7.1.1. Estimates of PRB Concentrations in Previous Assessments

Estimates of PRB concentrations reported in the 1996 PM AQCD (U.S. EPA, 1996, 079380) and earlier PM AQCDs were based in large measure on estimates by Trijonis et al. (1990, 157058) for the National Acid Precipitation Assessment Program (NAPAP) as shown in Table 3-18. The importance of different sources is likely to be quite different for natural background compared to current conditions in the US, resulting in large changes in relations among different size fractions. For example, $PM_{10-2.5}$ might be expected to dominate under certain conditions in the absence of primary and secondary $PM_{2.5}$ from anthropogenic sources. Different approaches for estimating PRB concentrations in the western and eastern U.S. were taken in the 2004 PM AQCD (U.S. EPA, 2004, 056905). Data obtained at IMPROVE monitoring sites in the western U.S. shown in Figure 3-84 were chosen as estimates of the distribution of daily average PRB concentrations in the West because they were thought to be among the least likely influenced by regional pollution sources especially at the upper end of the concentration distribution. This conclusion was drawn from back trajectory analyses and examination of the trace elemental composition at IMPROVE sites. Because of likely unresolved contamination from pollution sources at other IMPROVE sites, it was recommended to use averaged data from these sites throughout the West. Concentrations distributions from 1988 through 2001 can be found in Appendix 3E of the 2004 PM AQCD (U.S. EPA, 2004, 056905). Median concentrations were ~3 $\mu g/m^3$. Little interannual variability was observed below the 90th percentile values. However, at the upper end of the concentration distribution substantial interannual variability was observed due mainly to forest fires and dust transport from Asian deserts. It was also recognized that this method would likely overestimate PRB concentrations.

Table 3-18. Estimates of annual average natural background concentrations of $PM_{2.5}$ and PM_{10} ($\mu g/m^3$) from Trijonis et al. (1990, 157058). Estimates of $PM_{10-2.5}$ were obtained by subtraction.

	$PM_{2.5}$	PM_{10}	$PM_{10-2.5}$
East	2-5	5-11	≤ 1-9
West	1-4	4-8	≤ 1-7

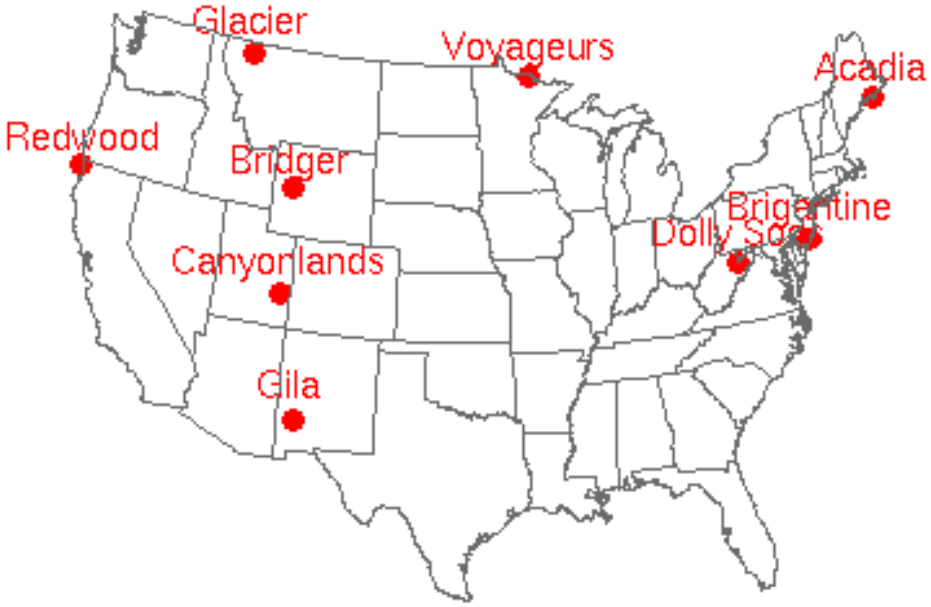


Figure 3-84. IMPROVE monitoring site locations.

Table 3-19 shows annual and quarterly average $PM_{2.5}$ concentrations measured at the IMPROVE sites shown in Figure 3-84 for 2004. Annual average concentrations tend to be slightly higher in the East, particularly in Brigantine and Dolly Sods. When the data are broken down by season, a more complex picture emerges. The highest concentrations in the East and Midwest are found during the 3rd calendar quarter, whereas in the West highest quarterly averages can occur during other quarters. As can also be seen from a comparison with values shown in Table 3-18, $PM_{2.5}$ values measured in the East are much higher than the PRB concentration estimates by Trijonis et al. (1990, 157058) for the NAPAP.

Table 3-19. Annual and quarterly mean $PM_{2.5}$ concentrations ($\mu g/m^3$) measured at IMPROVE sites in 2004.

	Mean	January-March	April-June	July-September	October-December
EAST					
Acadia	4.5	3.9	4.6	6.0	3.5
Brigantine	9.5	8.1	11.3	11.6	7.3
Dolly Sods	9.5	6.7	9.8	15.5	5.7
MIDWEST					
Voyageurs	3.8	4.1	3.1	4.2	3.6
WEST					
Bridger	2.1	1.2	3.1	2.8	1.3
Canyonlands	2.6	2.2	3.2	2.9	2.1
Gila	2.9	2.0	4.0	3.8	1.8
Glacier	4.8	4.6	4.2	5.3	5.0
Redwood	3.5	2.7	3.6	3.7	3.9

Thus, estimating daily average PRB concentrations in the eastern U.S. using observations is highly problematic because of the widespread mixing of precursors and anthropogenic PM generated in the East. Therefore, results from receptor modeling studies using PMF by Song et al. (2001, 036064) were used in the 2004 PM AQCD (U.S. EPA, 2004, 056905) for the East to separate contributions from likely regional pollution sources from natural and imported pollution. The "background" sources contribute about 7% to annual average $PM_{2.5}$ concentrations at Underhill, VT and about 12% at Brigantine, NJ, i.e., values between 1 and 2 $\mu g/m^3$. These sites were chosen because they were outside of urban areas making it easier to separate pollution from background components. However, some contribution of regional anthropogenic pollution was still present.

The PM Staff Paper (U.S. EPA, 2006, 157071) adopted a different approach for estimating PRB concentrations. This approach separated out components mainly thought to be emitted by regional pollution sources such as SO_4^{2-}, which are obtained directly from observations at many more IMPROVE sites than are shown in Figure 3-84, and to use the remaining PM components in both the East and the West to estimate PRB. Removing regional pollution from data obtained at IMPROVE sites is problematic as it involves assumptions about the relative contributions of regional pollution and background sources. Although sulfate in the East is mainly produced by regional pollution sources, it is not the only component with a regional pollution source. By comparison, sulfate is a very minor component of $PM_{2.5}$ in the West, leading to substantial overestimates in populated states like California. Annual mean estimates in the continental U.S. ranged from 2.5 $\mu g/m^3$ in the Central West (ID, MT, WY, ND, SD, CO, UT, NZ, AZ) to 5.2 $\mu g/m^3$ for the Southwest Coast (most of California), the latter value likely reflecting contributions from local, non-sulfate pollution.

In general, the methods outlined in both these documents are of limited utility for two reasons: (1) they lack detailed spatial coverage across the whole U.S., since both methods rely on monitoring data that are limited both spatially and temporally; and (2) PM measurements from even the limited, remote sites used in the previous estimates of PRB can not be completely devoid of contributions from anthropogenic PM. Because of these limitations, numerical modeling can provide superior PM background estimates, as described just below.

3.7.1.2. Chemistry Transport Models for Predicting PRB Concentrations

CTMs can be used to estimate the PRB concentrations of atmospheric components including PM using a "zero-out" approach in which anthropogenic emissions inside continental North America are set to zero while global biogenic emissions and anthropogenic emissions outside continental

North America remain. Numerical modeling can provide more precision in the estimate of PRB PM than measurements since even the most remote measurement sites like some of those in the IMPROVE network (see the discussion in Section 3.7.1.1) will necessarily be affected by non-local non-biogenic pollution, thereby confusing the contributions from these sources. Numerical models are also capable of supplying estimates of PRB concentrations at much higher spatial and temporal resolution than can be obtained by relying on measurements obtained at even the most remote monitoring sites. In this approach, the monitoring data are used to evaluate the CTM's performance.

For this assessment, the global-scale circulation model GEOS-Chem was coupled with the regional scale air quality model CMAQ (Section 3.6.2.2) to simulate one year of air quality data over the CONUS in two series of runs, the first annual series with all anthropogenic and biogenic emissions included and the second annual series with the zero-out approach employed.

The global-scale scale circulation model was set up as follows. GEOS-Chem, version 7, was used, with modifications to include aromatic and biogenic SOA formation; emissions were computed from a variety of sources including the Global Emissions Inventory Activity (GEIA) (Benkovitz et al., 1996, 156267), and Emissions Database for Global Atmospheric Research, version 2 (EDGAR) (Olivier et al., 1996, 156828; Olivier et al., 1999, 156829).

Particularized emissions in specific areas used the European Monitoring and Evaluation Program (EMEP) for Europe (Auvray and Bey, 2005, 156237), BRAVO (Kuhns and Knipping, 2005, 156663) for Mexico, and Streets et al. (2006, 157019) for Asia. Emissions from these studies were supplemented with data from Martin et al. (2002, 089380) for additional NO_X emissions from biofuels, lightning, and ship traffic, Bond et al. (2004, 056389) for global primary organic aerosols, and Cooke et al. (1999, 156365) and Park et al. (2003, 156842) for U.S. primary organic aerosols. Biomass burning emissions are not climatological, but were computed with GFEDv2 (Giglio et al., 2006, 156469; van der Werf et al., 2006, 157084); monthly values computed using active fire observations from MODIS; global dust fields computed off-line using GOCART (see emissions from DEAD: http://dust.ess.uci.edu/dead/) to make annual adjustments to photolysis rates and heterogeneous-phase chemistry.

The regional CTM was set up as follows. CMAQ, version 4.7, (excluding the dynamic coarse mode updates) was used with the SAPRC_99 chemical mechanism and AERO5 aerosol module; emissions were processed through SMOKE (http://smoke-model.org), version 2.4, based on the 2004 projections from the NEI with specific CEM, biogenics, and fire updates; MM5, version 3.7.4, was used with the Asymmetric Convective Mixing, version 2.2, PBL scheme; and data nudging was used to analyze fields for winds and temperature.

Model Evaluation

Details from evaluations of the performance of a number of CMAQ applications are given in Arnold et al. (2003, 087579), Eder and Yu (2006, 142721), Appel et al. (2005, 089227), and Fuentes and Raftery (2005, 087580).

In an annual simulation series for 2002 using CMAQ, version 4.6.1, in two 12-km domains for the CONUS (Figure 3-85), predicted concentrations of summertime particulate SO_4, often a major determinant of surface-layer PM concentrations, were well-predicted by CMAQ at a 12-km grid spacing, to within a factor of 2 at nearly every point of comparison and with $R^2 > 0.8$ across all three national networks (CASTNet, IMPROVE and CSN); a more detailed description is included in the 2008 NO_XSO_X ISA (U.S. EPA, 2008, 157074). This result for CMAQ, version 4.6.1, for 2002 tracks the generally well-predicted SO_4^{2-} concentrations found in most earlier CMAQ evaluations: see Mebust et al. (2003, 156749), Eder and Yu (2006, 142721), and Tesche et al. (2006, 157050). Since particulate SO_4^{2-} concentrations are strongly a function of precipitation, care must be taken to ensure that the meteorological solution driving individual CMAQ chemical applications produces precipitation fields with low bias as discussed by Appel et al. (2008, 155660).

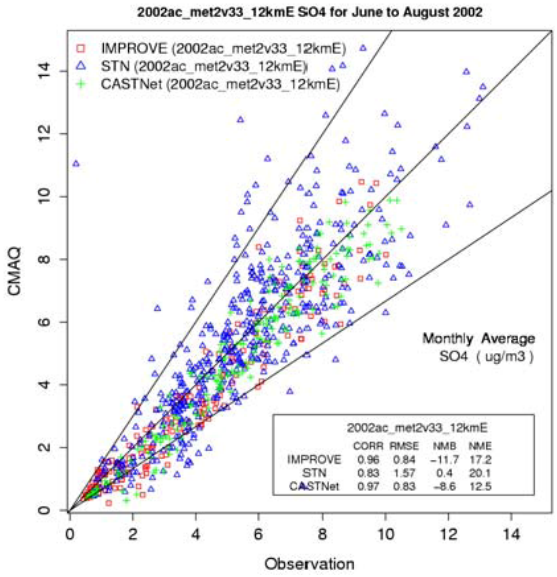


Figure 3-85. 12-km EUS Summer SO_4^{2-} PM. Each data point represents a paired monthly averaged (June/July/August) observation and CMAQ prediction at a particular IMPROVE, STN, and CASTNet site. Solid lines indicate the factor of 2 around the 1:1 line shown between them.

Wintertime particulate NO_3^- (Figure 3-86) and total NO_3 (HNO_3 + particulate NO_3^-) (Figure 3-87) concentrations are predicted as well by CMAQ; however, NO_3^- is a pervasively difficult species to measure and model. Still, at the CASTNet nodes where the total NO_3^- concentrations are higher than they are at all but a few of the remote IMPROVE sites, CMAQ predicts concentrations for nearly every node to within a factor of 2 and with an R^2 >0.8.

A "base case" in which conditions for 2004 including all the anthropogenic and natural sources both within and outside of continental North America was run for comparison with measurements. A PRB simulation was also run by shutting off the anthropogenic sources of primary PM and precursors to secondary PM inside continental North America.

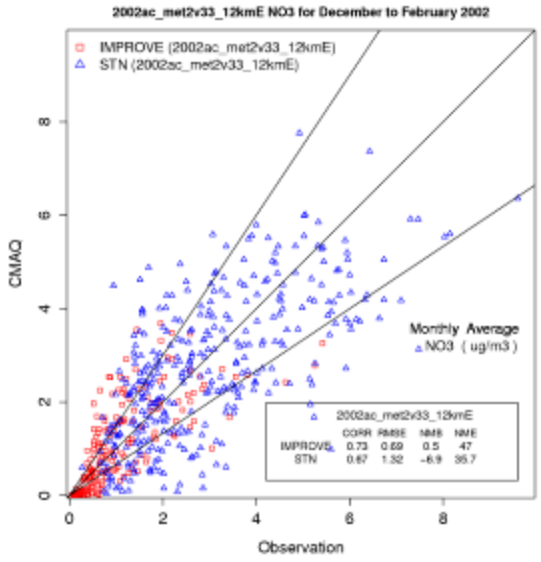


Figure 3-86 **12-km EUS Winter NO_3^- PM. Each data point represents a paired monthly averaged (December/January/February) observation and CMAQ prediction at a particular IMPROVE and STN site. Solid lines indicate the factor of 2 around the 1:1 line shown between them.**

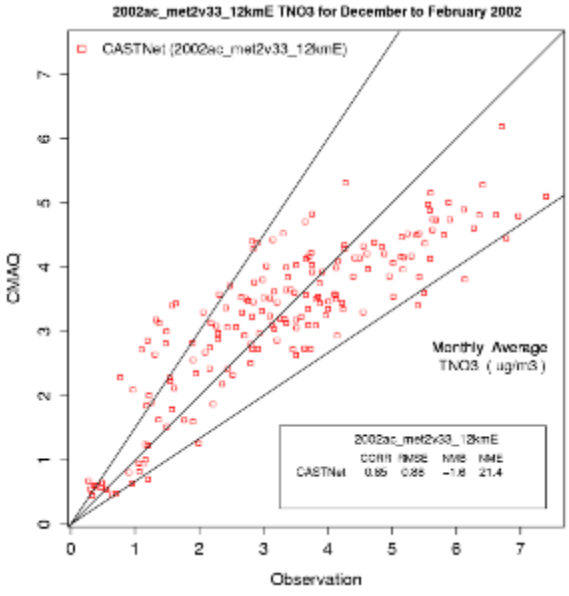


Figure 3-87. **12-km EUS Winter total nitrate (HNO_3 + total particulate NO_3^-). Each data point represents a paired monthly averaged (December/January/February) observation and CMAQ prediction at a particular CASTNet site. Solid lines indicate the factor of 2 around the 1:1 line shown between them.**

Figure 3-88 and Figure 3-89 show monthly average concentrations, and Figure 3-90 and Figure 3-91 show 24-h avg concentration distributions for 2004 predicted by CMAQ for the base case and for PRB. Measurements are also included for the five western and four eastern/midwestern IMPROVE sites shown in Figure 3-84. Wildfires could have affected the grid cell containing the midwestern Voyageurs site resulting in the high PRB values found for the July average compared to the PRB values for the rest of the year. The "base case" simulations tend to underestimate concentrations throughout most western sites as shown in Figure 3-89 and Figure 3-91. These underestimates are still within the range of a few $\mu g/m^3$. However, the base case simulation also greatly over-predicts $PM_{2.5}$ concentrations at the upper end of the distribution at the Redwoods site (Figure 3-91). This over-prediction results from emissions from wildfires in northern California that are included in the grid cell containing the Redwoods site, but may not have affected the site. However, wildfires indicated by MODIS would have affected other areas either close to these sites or could have affected other locations in between the IMPROVE sites. The simulated monthly average PRB concentrations in the east/midwest range from a minimum of 0.6 $\mu g/m^3$ at Acadia National Park (NP) in July to 3.7 $\mu g/m^3$ at Voyageurs NP in July. However, most values are <1 $\mu g/m^3$. The monthly average PRB concentrations calculated for the West tend to be lower than for the East and range from 0.2 $\mu g/m^3$ at Bridger and Glacier NPs in January and February, respectively, to 8.7 $\mu g/m^3$ at Redwoods NP in November. Excluding values at Redwoods NP which greatly exceed measurements, the highest monthly average concentration was 3.7 $\mu g/m^3$ at Voyageurs NP in the East/Midwest and 2.4 $\mu g/m^3$ at Gila NP in the West.

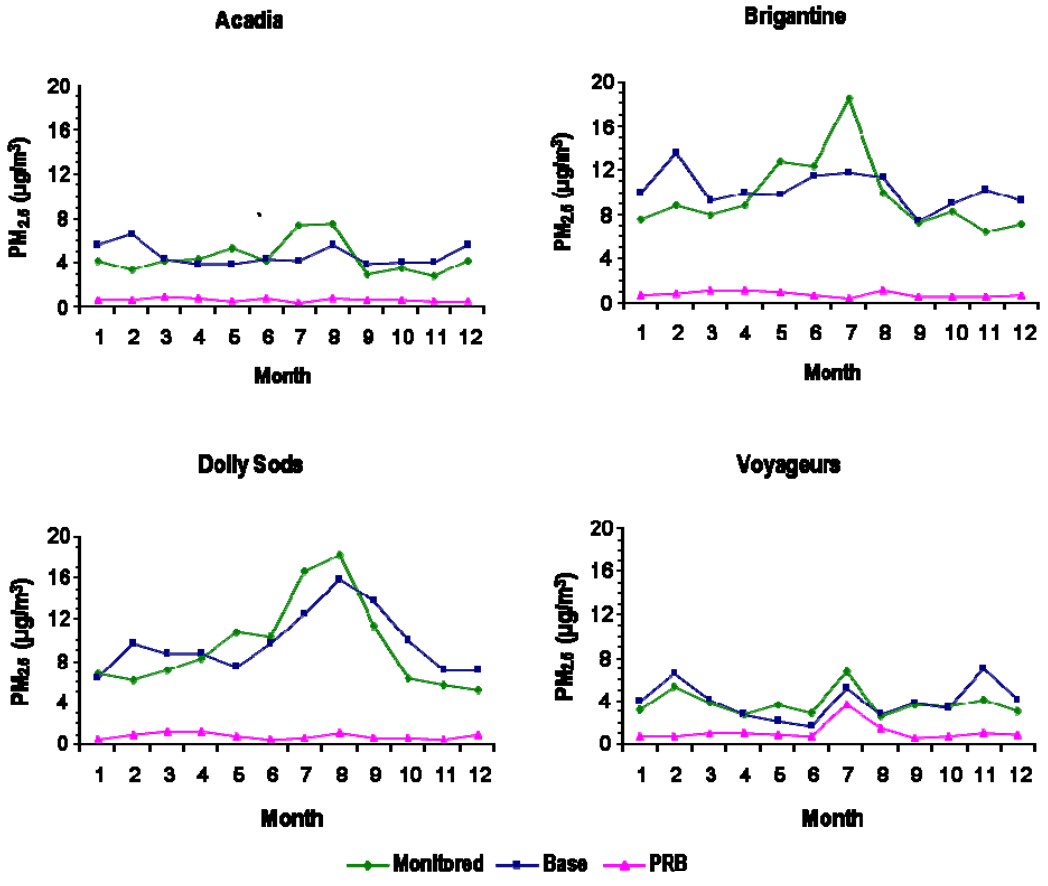


Figure 3-88. Monthly average of $PM_{2.5}$ concentrations measured at IMPROVE sites in the East and Midwest for 2004. Also shown are distributions of $PM_{2.5}$ concentrations calculated by CMAQ for the base case and for PRB.

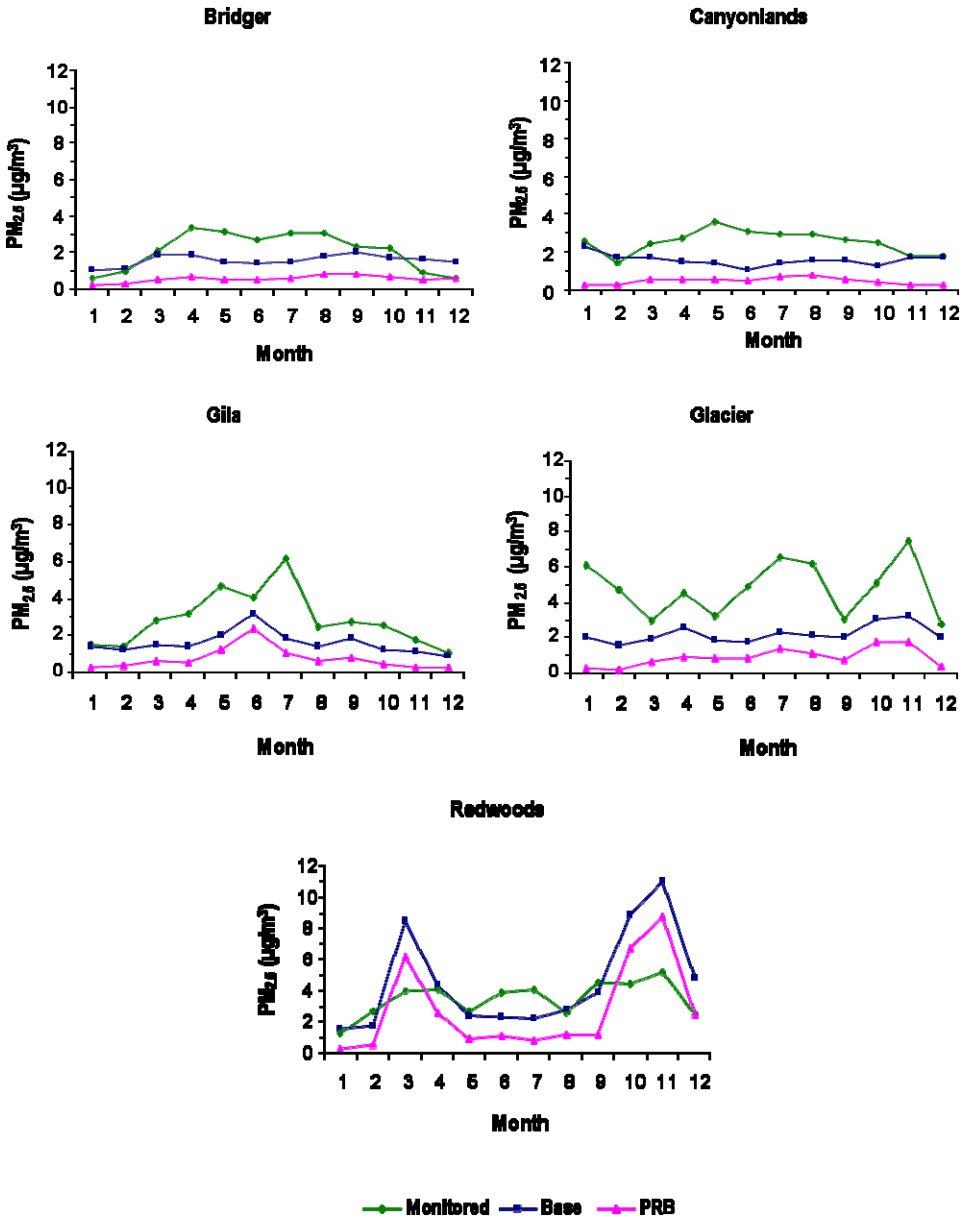


Figure 3-89. Monthly average of $PM_{2.5}$ concentrations measured at IMPROVE sites in the West for 2004. Also shown are distributions of $PM_{2.5}$ concentrations calculated by CMAQ for the base case and for PRB.

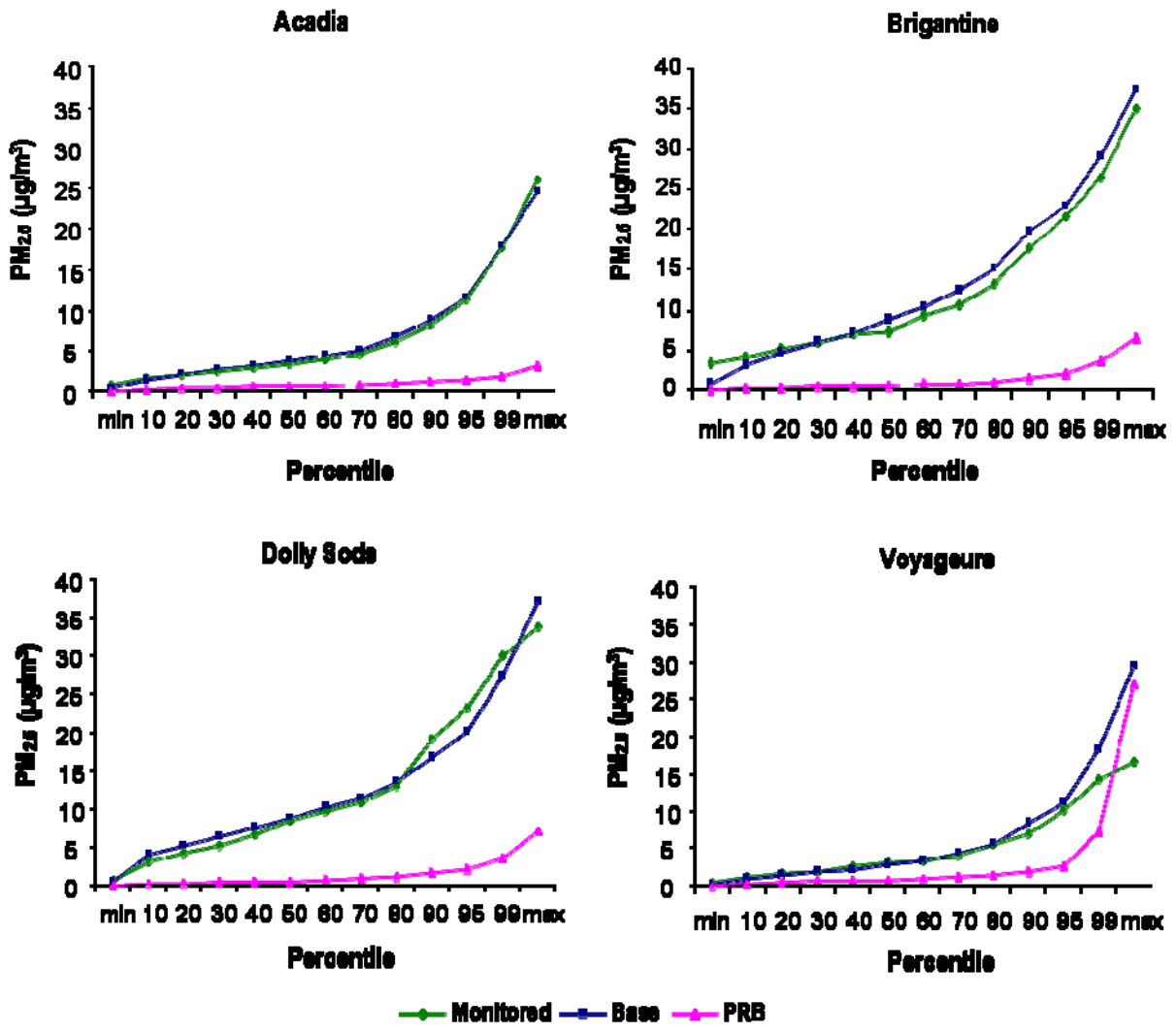


Figure 3-90. Distribution of $PM_{2.5}$ concentrations measured at IMPROVE sites in the East and Midwest for 2004. Also shown are distributions of $PM_{2.5}$ concentrations calculated by CMAQ for the base case and for PRB.

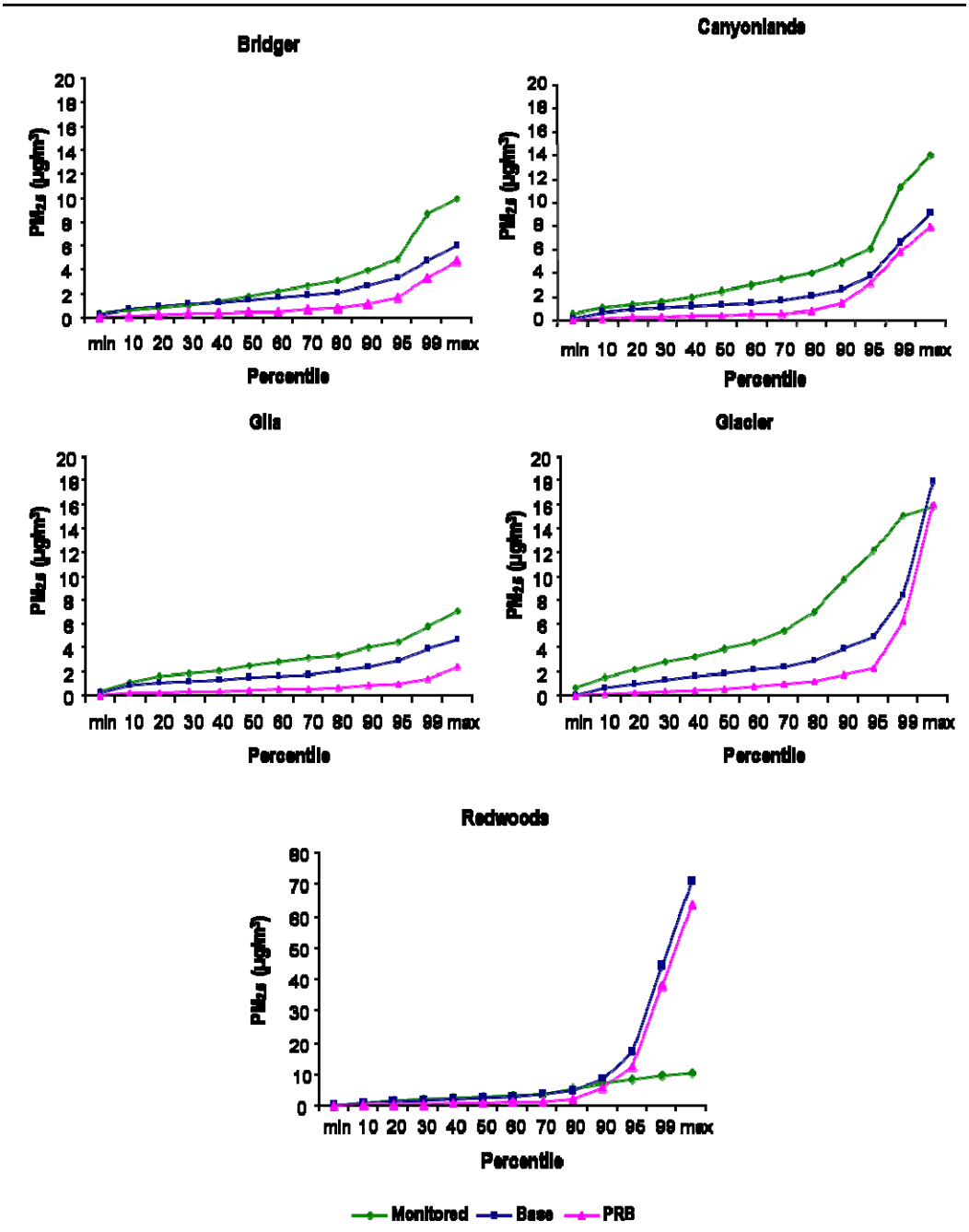


Figure 3-91. Distribution of $PM_{2.5}$ concentrations measured at IMPROVE sites in the West for 2004. Also shown are distributions of $PM_{2.5}$ concentrations calculated by CMAQ for the base case and for PRB. Note the scale change on the y-axis for Redwoods NP.

Table 3-20 gives the annual and quarterly average CMAQ predictions at IMPROVE sites for the "base case" and the ratio of CMAQ predictions to the measured concentrations at those sites in 2004. CMAQ performance for the annual average concentrations and most of the seasonal averages is very good in the East and Midwest, generally falling within 35%. In the West, CMAQ's prediction of $PM_{2.5}$ mass averages at these remote sites is generally too low in all seasons, often by 50%. Air quality model predictions in the mountainous West are often not as good as those over the flatter

terrain in the East and Midwest because the model's grid spacing (36 km in this case) smoothes over significant variation at the surface that results in differences at such remote sites. However, the model's trend relative to the geospatial difference is correct: the predicted $PM_{2.5}$ concentrations are lower at the western sites than they are at the eastern sites, just as the measurements are. Table 3-21 shows corresponding annual and quarterly mean PRB $PM_{2.5}$ concentrations at IMPROVE sites.

Table 3-20. Annual and quarterly mean $PM_{2.5}$ concentrations ($\mu g/m^3$) for the CMAQ "base case" at IMPROVE sites in 2004.

	Annual; mod/obs	Jan-March; mod/obs	Apr-Jun; mod/obs	Jul-Sep; mod/obs	Oct-Dec; mod/obs
EAST					
Acadia	4.7; 1.04	5.6; 1.44	4.0; 0.87	4.6; 0.77	4.6; 1.31
Brigantine	10.2; 1.07	10.9; 1.35	10.3; 0.91	10.2; 0.88	9.4; 1.29
Dolly Sods	9.8; 1.03	8.3; 1.24	8.6; 0.88	14.0; 0.90	8.0; 1.40
MIDWEST					
Voyageurs	4.0; 1.05	4.9; 1.19	2.2; 0.71	3.9; 0.93	4.9; 1.36
WEST					
Bridger	1.6; 0.76	1.3; 1.08	1.6; 0.52	1.8; 0.64	1.7; 1.30
Canyonlands	1.6; 0.62	1.9; 0.86	1.4; 0.44	1.5; 0.52	1.6; .76
Gila	1.6; 0.55	1.4; 0.70	2.2; 0.55	1.7; 0.45	1.1; 0.61
Glacier	2.2; 0.45	1.8; 0.39	2.1; 0.50	2.1; 0.40	2.8; 0.56
Redwood	4.6; 1.31	4.0; 1.48	3.0; 0.83	2.9; 0.78	8.4; 2.15

Table 3-22 illustrates CMAQ predictions of seasonal variation in the base case $PM_{2.5}$ concentrations across regions of the CONUS, while Table 3-23 shows CMAQ predictions of the seasonal variation in regional PRB $PM_{2.5}$ concentrations. Highest base case $PM_{2.5}$ concentrations were observed for the Northeast, Southeast, and industrial Midwest, with highest concentrations during the fall and winter (and comparably high concentrations in the summer for the Industrial Midwest). PRB $PM_{2.5}$ concentrations were highest on an annual basis in the Southeast, and peaking during the winter. In the summer, PRB $PM_{2.5}$ is roughly comparable for the Northwest and Southern California and elevated, but slightly lower for the Southwest. These results also likely indicate the influence of sources that are more strongly related to hot and dry conditions such as wildfires and dust suspension.

Table 3-21. Annual and quarterly mean $PM_{2.5}$ concentrations ($\mu g/m^3$) for the CMAQ PRB simulations at IMPROVE sites in 2004.

	Annual	January-March	April-June	July-September	October-December
EAST					
Acadia	0.70	0.76	0.76	0.65	0.65
Brigantine	0.77	0.86	0.91	0.70	0.63
Dolly Sods	0.79	0.88	0.83	0.75	0.66
MIDWEST					
Voyageurs	1.2	0.83	0.91	2.0	0.93
WEST					
Bridger	0.57	0.33	0.57	0.76	0.61
Canyonlands	0.49	0.38	0.54	0.68	0.35
Gila	0.74	0.42	1.4	0.80	0.32
Glacier	0.91	0.36	0.87	1.1	1.3
Redwood	2.8	2.4	1.5	1.1	6.1

Table 3-22. Annual and quarterly mean of the CMAQ-predicted base case $PM_{2.5}$ concentrations ($\mu g/m^3$) in the U.S. EPA CONUS regions in 2004.

	Annual	January-March	April-June	July-September	October-December
Northeast	9.76	10.74	8.38	9.55	10.38
Southeast	10.05	12.28	7.72	9.78	10.42
Industrial Midwest	11.38	12.22	9.37	11.89	12.00
Upper Midwest	6.70	8.83	4.95	5.34	7.67
Southwest	3.30	4.08	2.77	3.31	3.03
Northwest	2.72	2.49	2.21	2.71	3.44
Southern California	4.43	4.64	3.93	4.34	4.82

Table 3-23. Annual and quarterly mean of the CMAQ-predicted PRB $PM_{2.5}$ concentrations ($\mu g/m^3$) in the U.S. EPA CONUS regions in 2004.

	Annual	January-March	April-June	July-September	October-December
Northeast	0.74	0.85	0.78	0.67	0.68
Southeast	1.72	2.43	1.41	1.41	1.64
Industrial Midwest	0.86	0.89	0.89	0.94	0.73
Upper Midwest	0.84	0.79	0.93	0.99	0.66
Southwest	0.62	0.61	0.76	0.70	0.40
Northwest	1.01	0.48	0.81	1.42	1.32
Southern California	0.84	0.54	0.92	1.21	0.67

3.8. Issues in Exposure Assessment for PM and its Components

The purpose of this section is to present the latest exposure assessment studies to characterize the exposure of individuals and populations to PM of ambient origin. Such information will aid the interpretation of epidemiologic studies described in subsequent chapters of this ISA. This section includes descriptions of modeling and monitoring techniques used to capture personal PM exposure, observations reported in the literature at various relevant spatial scales, observations related to PM composition and PM in a mix of copollutants, and the effect of exposure estimates on epidemiologic results. Attention is given to use of community-based monitors at urban spatial scales and use of personal and microenvironmental exposure data to present how each metric can be used in exposure assessment and what errors and uncertainties exist for each approach. Understanding of exposure errors is important because exposure error can potentially bias an estimate of a health effect endpoint, or increase the size of confidence intervals around a health effect estimate. Typically, exposure error biases analyses of health effects towards the null (i.e., no relationship between exposure and health effect).

The information presented in this section builds upon the key findings of the 2004 PM AQCD (U.S. EPA, 2004, 056905). One key finding was that separation of total PM exposures into ambient and nonambient components reduces potential uncertainties in the analysis and interpretation of PM health effects data. At the time of the 2004 PM AQCD (U.S. EPA, 2004, 056905), one study reported that individual daily values of both the total and nonambient personal PM exposure were poorly correlated with the daily ambient PM concentrations, while individual daily values of ambient PM exposure and daily ambient PM concentrations were highly correlated. In pooled studies (different subjects measured on different days), individual, daily values of the total PM exposure were generally shown to be poorly correlated with the daily ambient PM concentrations. In longitudinal studies (each subject measured for multiple days), individual, daily values of the total PM personal exposure and the daily ambient PM concentrations were found to be highly correlated for some, but not all, subjects. Using the PTEAM study data, the 2004 PM AQCD (U.S. EPA, 2004, 056905) also analyzed exposure measurement errors in the context of time-series epidemiology to show that the error introduced by using ambient PM concentrations as a surrogate for ambient PM exposures negatively biases the estimation of health risk coefficients by the ratio of ambient PM exposure to ambient PM concentration. However, it was concluded that the health risk coefficient determined using ambient PM concentrations provides the correct information on the change in health risks that would be produced by a change in ambient concentrations.

Personal exposure to PM can vary considerably depending on PM size and composition, source strength and proximity, season, time of day, region of the country, population density of the environment, personal activity patterns, and ventilation of indoor environments. Table A-58 of Annex A, which summarizes findings from U.S. panel studies of personal exposure to PM with no

indoor sources published between 2002 and 2008 broken down by region of the country, illustrates this variability. For example, Table A-58 presents 24-h personal $PM_{2.5}$ exposures that range from roughly 1-55 μg/m^3 with highest exposures in the southwest and northeastern regions of the country and during the summer season. Section 3.8 is designed to present current theory and field results regarding exposure to PM. To illustrate the concept of personal exposure within various microenvironments, a general exposure model is presented in Section 3.8.1. New developments in techniques for measuring personal and indoor PM are presented in Section 3.8.2, followed by exposure modeling techniques in Section 3.8.3. In Section 3.8.4, exposure assessment field studies in the literature are presented. Attention is given to ambient exposure over multiple spatial scales including near-road, in-vehicle, and indoor environments. Section 3.8.5 presents issues related to PM composition and PM in multipollutant mixtures. Finally, implications of exposure assessment issues for epidemiologic studies are presented in Section 3.8.6.

3.8.1. General Exposure Concepts

A theoretical model of personal exposure is presented to highlight what is measurable and what uncertainties exist in this framework. An individual's time-integrated total exposure to airborne PM can be described based on a compartmentalization of the person's activities during a given time period:

$$E_T = \int C_j dt$$

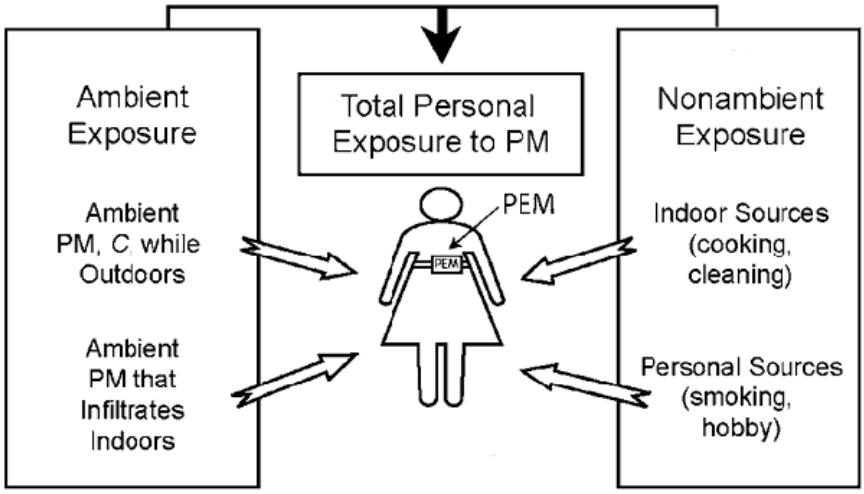
Equation 3-3

where E_T = total exposure over a time period of interest, C_j = airborne PM concentration at microenvironment j, and dt = portion of the time-period spent in microenvironment j. Equation 3-3 can be decomposed into a microenvironmental model that accounts for exposure to PM of ambient (E_a) and nonambient (E_{na}) origin of the form:

$$E_T = E_a + E_{na}$$

Equation 3-4

Figure 3-92 illustrates Equation 3-4. Examples of ambient PM sources include industrial and mobile source emissions, resuspended dust, biomass combustion, and secondary formation. Examples of nonambient sources include smoking, cooking, home heating, cleaning, and indoor air chemistry. PM concentrations generated by ambient and nonambient sources are subject to spatial and temporal variability that can affect estimates of exposure and resulting health effects. Exposure factors affecting interpretation of epidemiology are discussed in detail in Section 3.8.6.



Source: Adapted with permission of Nature Publishing Group from Wilson and Brauer (2006, 088933).

Figure 3-92. Model of total personal exposure to PM as a function of ambient and nonambient sources.

This assessment focuses on the ambient component of exposure because this is more relevant to the NAAQS review. E_a can be decomposed into the fraction of time spent in various outdoor and indoor microenvironments (Wallace et al., 2006, 089190; Wilson et al., 2000, 010288):

$$E_a = \sum f_o C_o + \sum f_i F_{\text{inf},i} C_{o,i}$$

Equation 3-5

where f = fraction of the relevant time period (equivalent to dt in Equation 3-2), subscript o = index of outdoor microenvironments, subscript i = index of indoor microenvironments, subscript o,i = index of outdoor microenvironments adjacent to a given indoor microenvironment i, and $F_{\text{inf},i}$ = infiltration factor for indoor microenvironment i. Equation 3-5 is subject to the constraint $\Sigma f_o + \Sigma f_i = 1$, and each term on the right hand side of the equation has a summation because it reflects various microenvironmental exposures. Here, "indoors" refers to being inside any aspect of the built environment, e.g., home, office buildings, enclosed vehicles (automobiles, trains, buses), and recreational facilities (movies, restaurants, bars). "Outdoor" exposure can occur in parks or yards, on sidewalks, and on bicycles or motorcycles.

F_{inf} represents the equilibrium fraction of the PM concentration outside the microenvironment that penetrates inside the microenvironment and remains suspended. It is a function of the microenvironmental air exchange characteristics and the particle properties. Assuming steady state conditions, the infiltration factor is a function of the penetration, P, of PM (a fractional quantity representing the portion of outdoor PM that passes through the building envelope), the air exchange rate, a, of the indoor microenvironment, and the rate of PM loss, k, within the indoor microenvironment: $F_{\text{inf}} = Pa/(a+k)$. Determination of E_a can be complicated by PM loss through chemical and physical processes in microenvironments, and the composition of PM can be modified during infiltration of outdoor air into microenvironments (Meng et al., 2007, 194618; Sarnat et al., 2006, 089166).

In the context of interpreting epidemiologic studies of the effects of ambient pollutants on human health, the association between E_a and concentrations from a central site monitor, C_a, is more relevant than the association between E_T and C_a because nonambient PM is uncorrelated with C_a, as discussed in Section 3.8.4. In ecologic studies of large panels or cohorts, C_a is often used in lieu of outdoor microenvironmental data to represent these exposures based on the availability of data. Thus it is often assumed that $C_o = C_a$ and that the fraction of time spent outdoors can be expressed cumulatively as f_o; the indoor terms still retain a summation because infiltration differs among

different microenvironments. Under these assumptions, an individual's exposure to ambient PM, first given in Equation 3-5, can be re-expressed as a function of C_a. The following approximation has been employed in the literature to describe ambient exposure based on these assumptions (Wallace et al., 2006, 089190; Wilson and Brauer, 2006, 088933; Wilson et al., 2000, 010288):

$$E_a = \left(f_o + \sum f_i F_{\text{inf},i}\right) C_a$$

Equation 3-6

Particle size, particle composition, meteorology, urban and natural topography, and other factors determine whether or not Equation 3-6 is a reasonable approximation for Equation 3-5. Errors and uncertainties inherent in the use of Equation 3-6 in lieu of Equation 3-5 are described in Section 3.8.6 with respect to implications for epidemiology. If concentration measured at a central site monitor is used to represent ambient concentration, then α, the ratio between personal exposure to ambient PM and the ambient concentration of PM, can be defined as:

$$\alpha = \frac{E_a}{C_a}$$

Equation 3-7

If the assumptions forming the basis for Equation 3-6 are valid, then α is the proportionality factor in Equation 3-6:

$$\alpha = f_o + \sum f_i F_{\text{inf},i}$$

Equation 3-8

α varies between 0 and 1. If a person's exposure occurs in a single microenvironment, the ambient component of a microenvironmental PM concentration can be represented as the product of the ambient concentration and F_{inf}. Wallace et al. (2006, 089190) note that time-activity data and corresponding estimates of F_{inf} for each microenvironmental exposure are needed to compute an individual's α with accuracy. If significant local sources and sinks are not captured by central site monitors, then the ambient component of outdoor air must be estimated using dispersion models, land use regression (LUR) models, receptor models, fine scale CTMs or some combination of these techniques. Modeling methods are described in Section 3.8.3.

3.8.2. Personal and Microenvironmental Exposure Monitoring

The purpose of this section is to present new discoveries related to measuring microenvironmental PM concentrations or personal exposure to PM. A review of over 100 personal and microenvironmental PM exposure studies published since 2002 (see Table A-58 of Annex A) reveals that the majority of the monitoring techniques in use were previously reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905) for PM. Detailed descriptions of these methodologies are provided in that document and therefore will not be repeated in this document. The following sections will include only findings from 2002 or later regarding monitoring and modeling methodologies in common use and significant advancements in understanding the capabilities and limitations of these methods for assessment of PM exposure.

3.8.2.1. New Developments in Personal Exposure Monitoring Instrumentation

Current personal exposure sampling methodology consists largely of integrated filter sampling using a cyclone or personal exposure monitor (PEM) to achieve a cut point at a desired particle size. This method of sampling facilitates speciation work because the filters can be archived for chemical and gravimetric analysis. Additionally, light scattering aerosol detection instruments, such as the personal DataRam (pDR) and SidePak personal aerosol monitor have seen some use in personal $PM_{2.5}$, PM_{10}, and PM_1 monitoring (e.g., Lewne et al., 2006, 090556; Wallace et al., 2006, 088211). Several researchers have noted that relative humidity causes overestimation of the particle mass in

light-scattering personal exposure monitors (e.g., Lowenthal et al., 1995, 045134; Ramachandran et al., 2003, 195017); a correction factor has been applied to concentrations to address this issue. In the DEARS, Williams et al. (2008, 191201) attempted to reduce humidity of the sample stream by placing a drying column upstream of the pDR's detector. Although this addressed the humidity issue, the drying column occasionally released particles and therefore caused artificial concentration peaks. For this reason, Williams et al. (2008, 191201) determined that the humidity correction approach is preferable.

One area of further development is in personal sampling of the thoracic and respirable particle size distribution. Variations of the cascade impactor have been developed for personal sampling and tested for use in field studies (Case et al., 2008, 155149; Lee et al., 2006, 098249; Singh et al., 2003, 156088). The model developed and tested by Lee et al. (2006, 098249) operates with a 1-µm cut point and therefore can characterize respirable particles well. The Case et al. (2008, 155149) two-stage cascade impactor separated $PM_{10-2.5}$ from $PM_{2.5}$ for personal monitoring and sampled within ± 20% of a reference method. Hsiao et al. (2009, 191001) developed a mini-cyclone with a 1 µm or 0.3 µm cut point for sampling accumulation mode and UFPs. The Personal Cascade Impactor Sampler (PCIS) has the capability to sample down to a cut point of 250 nm (Singh et al., 2003, 156088). For $PM_{2.5}$, the difference between the PCIS and the MOUDI cascade impactor was 11%, while the difference between the PCIS and the SMPS-APS was only 2%. Differences between the PCIS and the MOUDI for $PM_{2.5}$ species compared with the MOUDI was generally higher: 11% for SO_4^{2-}, 22% for NO_3^-, 19% for EC, and 94% for OC. Mass was overestimated by 3%, 16%, and 31% for $PM_{1-0.5}$, $PM_{0.5-0.25}$, and $PM_{0.25}$, respectively, when compared with the SMPS-APS. Similarly, Case et al. (2008, 155149) found a mass difference ranging from -11 to +10% for $PM_{10-2.5}$ with the Personal Respirable Particulate Sampler (PRPS), and Lee et al. (2006, 098249) found a mass difference of -6 to 0% for $PM_{2.5}$ and -6 to -1% for PM_{10} when comparing results from this device with those from the PEM. Leith et al. (2007, 098241) redesigned the Wagner-Leith passive sampler for measuring $PM_{10-2.5}$. In this work, the difference between a $PM_{10-2.5}$ FRM and the co-located passive sampler was within 1 standard deviation of concentrations measured by the FRM samplers.

A number of personal PM monitors are under development as part of the National Institutes of Health Genes, Environment, and Health Initiative (http://www.gei.nih.gov/exposurebiology/program/sensor.asp). Funded projects for miniature personal monitors include a platform that records real-time BC and PM concentrations and archives PM for further analysis, a badge containing a sensor array that detects several compounds found in diesel PM, a micro-nephelometer recording PM and endotoxin exposure, a complementary metal-oxide-semiconductor (CMOS) fitting in the nose to measure allergen PM, and a micro-thermofluidic nanoparticle sensor. The mini-cyclone cited above was designed to operate upwind of the micro-thermofluidic sensor (Hsiao et al., 2009, 191001). LeVine et al. (2009, 192091) and Schwartz et al. (2008, 192094) described use of the CMOS technology for real-time DNA detection. Mulchandani et al. (2001, 191003) reviewed amperometric biosensors used for organophosphate pesticide detection that are the basis of the diesel detection badge; several additional articles have been published by this group that describe applications of amperometric sensors.

3.8.2.2. New Developments in Microenvironmental Exposure Monitoring Instrumentation

The majority of developments since the 2004 PM AQCD (U.S. EPA, 2004, 056905) regarding microenvironmental PM characterization have involved real-time instrumentation in the UFP size range. Because these methods are also used for ambient sampling, they are described in Section 3.4 and in Annex Table A-59.

New developments in microenvironmental sampling for exposure assessment have also included construction, testing, and implementation of mobile environmental sampling laboratories for PM mass, particle count, and composition, as well as other criteria pollutants (CO, SO_2, NO_2, O_3). These mobile laboratories typically contain a suite of real-time equipment with short sampling intervals (e.g., 1-10 min), such as an SMPS with CPC, APS, laser photometers, and aethalometers for aerosols; monitors for the gaseous criteria pollutants; a weather station for meteorological variables; and a Global Positioning System (GPS) for position. Videotape or journal observations are sometimes logged simultaneously to track local on-road sources of pollution. One key application of mobile laboratory technology is assessment of the outdoor microscale environments and in-vehicle microenvironments on roadways for determining exposure during on-road transportation (Pirjola et

al., 2004, 117564; Sabin et al., 2005, 087728; Weijers et al., 2004, 104186; Westerdahl et al., 2005, 086502). For instance, Sabin et al. (2005, 087728) used videotape records to determine whether BC detected on a school bus was the result of local outdoor sources from other vehicles or "self-pollution" from the school bus's own engine exhaust. Westerdahl et al. (2005, 086502) used the GPS time series to determine that minima in the UFP time series corresponded to passage through residential areas of Long Beach and Pasadena, in contrast to the pollution spikes observed along highways. Studies have also shown that detection of PM from vehicle exhaust could be improved through use of combined measurement results to improve statistical analysis (Ntziachristos and Samaras, 2006, 116722).

3.8.3. Exposure Modeling

This section describes a variety of techniques used to model PM exposure. Many of these methods are used in combination to link ambient PM levels in the atmosphere or source characteristics to human exposure among individuals or sample populations. Recent developments in exposure modeling are described in this subsection, and errors and uncertainties of these approaches are described in Section 3.8.6.2.

3.8.3.1. Time-Weighted Microenvironmental Models

An individual's exposure is dictated by his or her activity patterns, as modeled by f_o and f_i in Equation 3-5. A number of panel studies have tracked subject exposures using questionnaires, time-activity diaries, or global positioning systems(e.g., Cohen et al., 2009, 190639; Elgethun et al., 2003, 190640; Johnson et al., 2000, 001660; Olson and Burke, 2006, 189951; Wallace et al., 2006, 089190). In many cases, the time-activity tracking is performed in conjunction with personal exposure and/or indoor and outdoor PM concentration monitoring to estimate overall PM exposure. Wu (2005, 086397) described a microenvironmental model of total personal exposure:

$$E_T = f_{oh}C_o + f_{oa}C_a + f_iC_i$$

Equation 3-9

where f_{oh} = fraction of time spent outdoors at home, f_{oa} = fraction of time spent outdoors away from home, C_o = PM concentration outside the home, and C_i = indoor PM concentration. In Equation 3-9, E_T can be calculated based on time-activity diary data and time-resolved PM concentration measurements. E_T can be expressed as a time-resolved value or cumulatively over a time period of interest using this formulation. In this model, ambient and nonambient exposure cannot be separated because it incorporates indoor concentrations that are a function of both ambient and nonambient sources. Additionally, Equation 3-9 distinguishes ambient concentration measured at a monitor from that measured immediately outside the home. Liu et al. (2003, 073841) found that this model predicted elderly exposures adequately but was a poor predictor of $PM_{2.5}$ exposure for asthmatic children. Wu et al. (2005, 086397) point out that this may be due to lack of availability of the children's time-activity data in school where children spend a substantial portion of their day. In a study of school children's exposure patterns, DeCastro et al. (2007, 190996) computed odds ratios of a panel subject's location within a given microenvironment using multivariate logistic models of the indoor school, indoor home, and outdoor microenvironments. They found that (1) the city of residence was a significant predictor of being indoors at school; (2) having an afterschool job was a significant predictor of being indoors at home; and (3) age and having an afterschool job were significant predictors of being outdoors. The results of the DeCastro et al. (2007, 190996) study were designed to predict f_i and f_o in exposure modeling.

A second approach proposed by Wu et al. (2005, 086397) is similar in formulation to Equation 3-5 because it computes ambient PM exposure by considering the amount of outdoor PM infiltrated indoors. This version also incorporates C_o and C_a:

$$E_a = f_{oh}C_o + f_{oa}C_a + f_i F_{\text{inf}} C_o$$

Equation 3-10

Equation 3-10 differs from Equation 3-5 because it accounts for concentrations immediately outside the building rather than considering all outdoor exposures to be a function of that measured at a community monitor. Factors influencing the contribution of E_a to E_T may include sample population characteristics, location of a site for microenvironmental monitoring, seasonal trends in PM concentration, and regional differences affecting ambient concentration and infiltration.

Regression based approaches can also be incorporated into time-weighted microenvironmental modeling. Chang et al. (2003, 053789) used data from the Scripted Activity Study and the Older Adults Study, both conducted in Baltimore in 1998 and 1999, to compute total personal exposure based on time-weighted microenvironmental exposures for each panel subject:

$$E_T = ME_i\beta_i \sum_k f_k C_k + ME_o\beta_o \sum_k f_k C_k$$

Equation 3-11

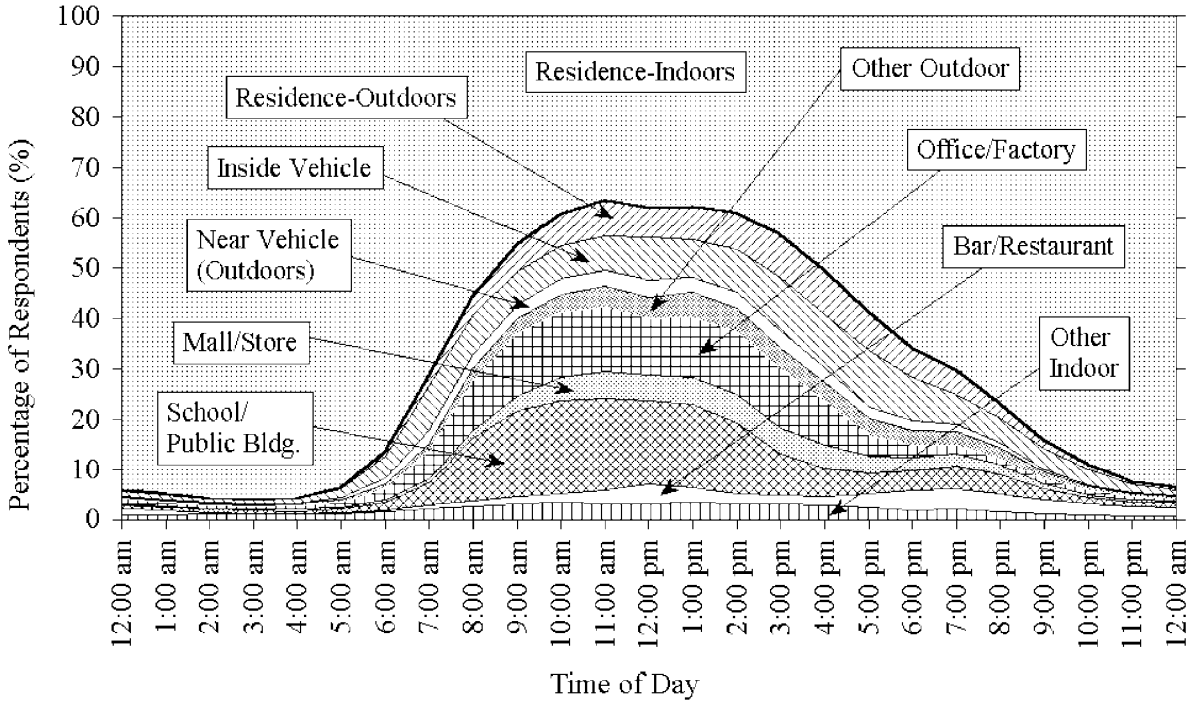
where ME = microenvironment (indoor or outdoor), β = regression coefficient reflecting the accuracy of the exposure estimate for a given microenvironment, f_k = fraction of time performing an activity k, and C_k = personal exposure while performing activity k. In this work, Chang et al. (2003, 053789) tested the models with hourly personal exposure data, hourly ambient concentration data, and daily ambient concentration data. The study found that time-activity data improved estimates of 24-h $PM_{2.5}$ exposure in comparison with using 24-h ambient $PM_{2.5}$ data, but the use of hourly ambient data was comparable to personal microenvironmental data in estimating exposure. When using ambient concentration data, β reflected infiltration for the indoor microenvironmental estimates for a sample population. Using a similar activity-based exposure modeling approach for a panel study in Seattle from 1999-2002, Allen et al. (2004, 190089) found that subjects' PM exposures were best represented by modeling ambient and nonambient exposures separately because ambient PM personal exposure was well correlated with PM concentration at central site monitors, while nonambient PM exposure was not.

3.8.3.2. Stochastic Population Exposure Models

Population-based methods, such as the Air Pollution Exposure (APEX), Stochastic Human Exposure and Dose Simulation (SHEDS), and EXPOLIS (exposure in polis, or cities) models, involve stochastic treatment of the model input factors (http://www.epa.gov/ttn/fera/human_apex.html; (Burke et al., 2001, 014050; Kruize et al., 2003, 156661). These are described in detail in Annex 3.7 of the 2008 NO_X ISA (U.S. EPA, 2008, 157073). Stochastic models utilize distributions of pollutant-related and individual-level variables, such as ambient and local PM concentration source contributions and breathing rate, respectively, to compute the distribution of individual exposures across the modeled population. Using distributions of input parameters in the model framework rather than point estimates allows the models to explicitly incorporate uncertainty and variability into exposure estimates (Zidek et al., 2007, 190076). These models estimate time-weighted exposure for modeled individuals by summing exposure in each microenvironment visited during the exposure period. The models also have the capability to estimate received dose through a dosimetry model. The initial set of input data for population exposure models is ambient air quality data, which may come from a monitoring network or model estimates. Estimates of concentrations in a set of microenvironments are generated either by mass balance methods or microenvironmental factors. Microenvironments modeled include residential indoor microenvironments; other indoor microenvironments, such as schools, offices, and public buildings; vehicles; and outdoor microenvironments. The sequence of microenvironments and exertion levels during the exposure period is determined from characteristics of each modeled individual. The APEX model does this by generating a profile for each simulated individual by sampling from distributions of demographic variables such as age, gender, and employment; physiological variables, such as height and weight; and situational variables, such as living in a house with a gas stove or air conditioning. Activity patterns from a database such as Consolidated Human Activity Database (CHAD) are assigned to the simulated individual using age, gender, and

biometric characteristics. Breathing rates are calculated for each activity based on exertion level, and the corresponding received dose is then computed. For APEX, the PM dosimetry algorithm is based on the International Commission on Radiological Protection's Human Respiratory Tract Model for Radiological Protection (ICRP, 1995, 006988), and calculates the rate of mass deposition of PM in the respiratory system (U.S. EPA, 2008, 191775). Summaries of individual- and population-level metrics are produced, such as maximum exposure or dose, number of individuals exceeding a specified exposure/dose threshold, and number of person-days at or above certain exposure levels. The models also consider the non-ambient contribution to total exposure. Nonambient source terms are added to the infiltration of ambient pollutants to calculate the total concentration in the microenvironment. Output from model runs with and without nonambient sources can be compared to estimate the ambient contribution to total exposure and dose.

Recent larger-scale human activity databases, such as those developed for CHAD or the National Human Activity Pattern Survey (NHAPS), have been designed to characterize exposure patterns among much larger population subsets than can be examined during individual panel studies (Klepeis et al., 2001, 002437; McCurdy et al., 2000, 000782). CHAD consists of a consolidation of human activity data obtained during several panel studies in which diary or retrospective activity data were obtained, while NHAPS acquired sample population time-activity data through surveys about human activity (Klepeis et al., 2001, 002437). The complex human activity patterns across the population (all ages) for NHAPS are illustrated in Figure 3-93 (Klepeis et al., 2001, 002437). This figure is presented to illustrate the diversity of daily activities among the entire population as well as the proportion of time spent in each microenvironment. Different patterns would be anticipated when breaking down activity patterns for subgroups, such as children or the elderly. With data for average PM concentrations in each microenvironment, population exposures can be estimated from this break-down of time-activity data.



Source: Reprinted with Permission of Nature Publishing Group from Klepeis et al. (2001, 002437).

Figure 3-93. Distribution of time sample population spends in various environments, from the National Human Activity Pattern Survey.

Stochastic and deterministic methods are often combined, as described below. Recently, SHEDS has been linked with the Modeling Environment for Total Risk Studies (MENTOR) model to expand population exposure assessment to individual risk assessment (Georgopoulos et al., 2005, 080269). In this formulation, CMAQ was used to predict initial concentrations at a coarse scale, and then a spatiotemporal random field method (Vyas and Christakos, 1997, 156142) was applied to interpolate the concentration to census tract scale in which exposure estimates are made. CHAD can also be incorporated into MENTOR so that estimates of exposure are related to dose and metabolic distributions to estimate risk of specific health impacts.

3.8.3.3. Dispersion Models

Dispersion models have been used both for direct estimation of exposure and as inputs for stochastic modeling systems, as described above. Location-based exposures have been predicted using models such as CALINE, AERMOD, CALPUFF, (all described in Section 3.6.2.3) or the Operational Street Pollution Model (OSPM) for estimation of street-level PM pollution coupled with infiltration models to represent indoor exposure to ambient levels (Gilliam et al., 2005, 056749; Mensink et al., 2008, 155980; Wilson and Zawar-Reza, 2006, 088292). For instance, CALPUFF was used to model transport and dispersion in lower Manhattan following the September 11, 2001 World Trade Center collapse to determine average location-based exposures (Gilliam et al., 2005, 056750). Wilson and Zawar-Reza (2006, 088292) used The Air Pollution Model (TAPM), which integrated an emissions model with a mesoscale meteorological driver, to assess PM_{10} dispersion and potential for exposure in Christchurch, New Zealand. Gulliver and Briggs (2005, 191079) used the Atmospheric Dispersion Modeling System (ADMS) to model dispersion of "line-source" traffic emissions in an urban environment. In a method similar to that employed by Georgopoulos et al. (Georgopoulos et al., 2005, 080269) with SHEDS, Wu et al. (2005, 058570) used CALINE to predict street-level concentrations of pollutants and input the results of that dispersion model into an individual exposure model that accounts for infiltration of specific building characteristics. Wu et al. (2005, 058570) employed CHAD to estimate the time-basis of exposures from the CALINE predictions. With an individualized exposure approach, the model is deterministic. However, population exposures can be estimated by performing repeated simulations using various housing characteristics and then computing a posterior probability distribution function for exposure. Isakov et al. (2009, 191192) developed a methodology to link a CTM (used to compute regional scale spatiotemporally-varying concentration in an urban area) with stochastic population exposure models to predict annual and seasonal variation in urban population exposure within urban microenvironments.

3.8.3.4. Land Use Regression and GIS-Based Models

LUR models have also been developed to describe pollution levels as a function of source characteristics (Briggs et al., 1997, 025950; Gilliland et al., 2005, 098820; Ryan and LeMasters, 2007, 156063). LUR is a regression derived from monitored concentration values as a function of data from a combination of factors (e.g., land use designation, traffic counts, home heating usage, point source strength, and population density). The regression is then computed for multiple locations based on the independent variables at locations without monitors. At the census tract level, a LUR is a multivariate description of pollution as a function of traffic, land use, and topographic variables (Briggs et al., 1997, 025950). Originally, LUR was used for NO_2 dispersion, but it was adapted for $PM_{2.5}$ exposure estimation by Brauer et al. (2003, 155702) for Stockholm, Sweden, Munich, Germany, and throughout The Netherlands. This study found a measure of traffic density to be the most significant variable predicting $PM_{2.5}$ exposure. Ryan et al. (2008, 156064) reported on a LUR model for childhood exposure to traffic-derived EC for the Cincinnati Allergy and Air Pollution Study and also found traffic to be the most important determinant of diesel exhaust particle exposure. In this case, wind direction was also factored into the model as a determinant of EC mixing. Like deterministic dispersion models, LUR can be performed over wide areas to develop a posterior probability distribution function of exposure at the urban scale. However, Hoek et al. (2008, 195851) warn of several limitations of LUR, including distinguishing real associations between pollutants and covariates from those of correlated copollutants, limitations in spatial resolution from monitor data, applicability of the LUR model under changing temporal conditions, and introduction of confounding factors when LUR is used in epidemiologic studies.

A GIS platform is typically used to organize the independent variable data and map the results. The GIS software creates numerous lattice points for the regression of concentration as a function of the covariates. For instance, Krewski et al. (2009, 191193) computed $PM_{2.5}$ concentrations for the New York City and Los Angeles metropolitan areas. For the Los Angeles analysis, the LUR was applied at 18,000 points in the simulation domain, and an inverse distance weighting kriging method was applied to interpolate the predicted concentration. In New York City, the LUR was applied at 49 monitors for a 3-yr model and 36 monitors for a model of winter 2000; kriging was employed only for the purpose of visualizing the concentration between monitors. The models explained 69% and 66% of the variation in $PM_{2.5}$ in Los Angeles and New York City, respectively.

GIS-based spatial smoothing models can be used to estimate PM concentration levels where monitors are not located. Yanosky et al. (2008, 099467) described an approach to estimate concentrations using a combination of reported AQS data and GIS-based and meteorological covariates. Temporally stationary covariates included distance to nearest road for different PM size fractions, urban land use, population density, point source emissions within 1 and 10 km buffers, and elevation above sea level. Time-varying covariates included area source emissions, precipitation, and wind speed. In this analysis, the GIS-based covariates were temporally stationary, while the meteorological and PM monitored concentration inputs were time-varying. This approach was applied to estimate $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10} exposures for the Nurse's Health Study and provided estimates of concentration at approximately 70,000 nodes with $PM_{2.5}$ and/or PM_{10} data input from more than 900 AQS sites with good validation of the $PM_{2.5}$ and PM_{10} models (Paciorek et al., 2009, 190090; Yanosky et al., 2008, 099467; Yanosky et al., 2009, 190114).

GIS-based methods can also be applied to integrate exposures over different microenvironments. For example, Gulliver and Briggs (2005, 191079) described development of the Space-Time Exposure Modeling System (STEMS) to model PM_{10} concentration. STEMS is a multipronged model that links traffic emissions estimates, dispersion, background PM estimates, and time-activity data within a GIS framework to create exposure estimates. Traffic emissions estimates and meteorological parameters are input into the ADMS dispersion model, which along with background PM measurements, are used to create hourly point estimates of PM concentration. Based on the time-activity data, the concentration estimates were then used to calculate exposures to traffic-related PM_{10} along a commuting path while an individual is in transit. PM_{10} was used by Gulliver and Briggs (2005, 191079) because ADMS had not yet been validated for smaller PM size fractions. In an analysis of the sensitivity of included variables, Gulliver and Briggs (2005, 191079) showed the model to be most sensitive to fluctuations in local meteorology followed by sudden vehicle speed reductions of 10 km/h. The STEMS model was primarily designed to model exposures during transit, but the authors state that this technique can be applied to modeling other microenvironmental exposures.

Source proximity is sometimes used as a covariate in GIS-based regression models. For instance, Baxter et al. (2007, 092725) predicted indoor exposure to $PM_{2.5}$, EC, and NO_x based on distance to roadways, indoor source characteristics, window opening, and ambient concentrations in the Boston metropolitan area. In this effort, Baxter et al. examined a variety of factors estimated using GIS including roadway density, roadway length, average daily traffic, and population density to determine which variables were significant predictors. They found that point estimates of $PM_{2.5}$ were largely influenced by regional ambient $PM_{2.5}$ while EC estimates were more influenced by local mobile sources. However, Baxter et al. (2008, 191194) found no association between distance to a bridge toll booth station and indoor EC concentration in Detroit homes when studying the impact of diesel emissions from traffic on the Ambassador Bridge as part of the Detroit Exposure and Aerosol Research Study (DEARS). Being located downwind of the booth, however, was a significant predictor of indoor EC concentration. Corburn (2007, 155738) tested two distinct modeling approaches, the cumulative air toxics surface (CATS) and the U.S. EPA's National Air Toxics Assessment (NATA) to determine how these approaches can yield estimates of human exposure to diesel exhaust and 33 air toxics for environmental impact assessment. The CATS approach included an exposure term incorporating source density and distance to source, and the sources include traffic as well as bus depots and transfer stations, airports, and industrial point sources. Corburn's results demonstrated that robust land use data can provide an approximation for urban exposures, although he cautioned that such estimates should not supersede environmental monitoring. In using these approaches, Huang and Batterman (2000, 156572) warn that geographic divisions must be sufficiently small to avoid inter-zone variability in source and exposure characteristics. Moreover, the HEI Report on Traffic Related Health Effects (2009, 191009)

discourages use of source proximity as a surrogate for traffic exposure in epidemiologic studies because it is not specific to particular pollutants and can be subject to confounding factors such as SES.

3.8.4. Exposure Assessment Studies

Table A-61 in Annex A lists exposure assessment studies performed in the U.S. by region of the country with personal, microenvironmental, and ambient mass concentrations presented (note that chemical speciation data, where available, are discussed below). The majority of urban-scale studies focus on $PM_{2.5}$ because $PM_{2.5}$ concentrations are more homogeneously distributed. Studies of microscale to neighborhood scale dispersion more commonly include data on UF and thoracic coarse PM in addition to $PM_{2.5}$ because they travel over shorter distances from the site of generation, as described in Section 3.5. Some of these studies present the outdoor concentration measured outside the test building, while others use ambient concentration obtained from a community site monitor. As would be expected, there is considerable variability within and across regions of the country with respect to indoor exposures and ambient concentrations. Furthermore, some regions are represented by only one or two studies, while other regions have many studies. Most studies have been conducted in only one or two metropolitan areas. Thus, the results presented may not be broadly representative.

Results of these studies highlight the uncertainties surrounding various estimates of the ambient contribution to personal exposure. This variation can be attributed to a number of factors, including PM size distribution, scope and magnitude of microenvironmental sources, proximity to microenvironmental sources, ambient concentrations of PM, percentages of time spent in various microenvironments, the age and condition of indoor microenvironments, natural and urban topography, and outdoor meteorology. Errors in exposure estimation are linked to the spatial scale of concentration measurements because pollutant transport and dispersion varies over different spatial scales as a function of the many factors mentioned in the previous sentence. Findings related to identifying the ambient components of personal exposure and modes of PM infiltration indoors are discussed in the subsequent subsections with respect to multiple spatial scales.

3.8.4.1. Micro-to-Neighborhood Scale Ambient PM Exposure

Near-Road Exposures

Sections 3.3 and 3.5 describe the physical and chemical composition of traffic emissions as well as characterization of the plume away from roads. Table 3-24 contains data from recent studies comparing outdoor personal exposure to fixed site monitors. Only studies where samples were obtained outdoors and compared with a community-based ambient monitoring site were included because indoor microenvironments have penetration losses that affect the comparability of the results. Note that some of these studies included enclosed transportation microenvironments (e.g., cars, buses, subways), but all studies examined personal exposure in the outdoor microscale environment. Also note that studies must be reviewed cautiously because most used different instrumentation for personal, microenvironmental, and ambient measurements, and measurement artifacts related to each instrument may differ. The Violante et al. (2006, 156140) study showed that outdoor personal exposure to PM_{10} was significantly higher than fixed community-based ambient PM_{10} measurements in downtown Bologna, Italy. Likewise, the Kaur et al. (2005, 088175), Kaur et al. (2005, 086504), and Adams et al. (2001, 019350) studies showed $PM_{2.5}$ measurements to be significantly higher than fixed community-based ambient $PM_{2.5}$ monitoring site measurements in central London, U.K. Kinney et al. (2000, 001774) performed personal exposure monitoring on study volunteers on streets in Manhattan and showed that $PM_{2.5}$ concentrations were not significantly different from ambient $PM_{2.5}$ measurements; this is more consistent with the urban-scale homogeneity in concentration of $PM_{2.5}$.

Morwaska et al. (2008, 191006) stated that UFP number concentrations in the near-road environment were roughly 18 times higher than in a non-urban background environment, while measured concentrations in street canyons and tunnels were 27 and 64 times higher, respectively

than background. This suggests that trapping of sources in a semi-enclosed environment can lead to higher UFP exposures. Additionally, fresh emission of short-lived UFPs would explain substantially higher concentrations near the site of emission. By sampling UFP number concentrations at multiple sites in Los Angeles, Moore et al. (2009, 191004) demonstrated five- to seven-fold differences between concentrations measured directly next to a freeway and an oceanside site during morning rush hour with substantial variability among sites throughout the day. When comparing sampling campaign data for clear weather and rainy days next to the I-710 freeway in Los Angeles, Ntziachristos et al. (2007, 089164) found that particle number concentration obtained with a CPC was 2.4 times higher in clear weather than when raining; particle surface area was 3.7 times larger in clear weather; and, black carbon concentration was 1.7 times higher in clear weather. However, SMPS data reported for rainy day particle number concentrations were almost 29 times higher in this study. Likewise, Zhou and Levy (2007, 098633) noted in a meta-analysis of near-road studies that the concentrations are generally elevated within 300-400 m of a roadway for EC and UFPs. Kinney et al. (2000, 001774) showed EC to increase linearly with increasing traffic counts and large spatial variations in two sites that had concentrations significantly higher than ambient measurements. These observations suggest caution should be taken regarding the representativeness of community averaged monitoring data for assessing exposures.

Particle chemistry is also an important consideration, because exposure may differ among PM components. Farmer et al. (2003, 089017) found that exposure to particle-bound PAHs, including benzo[a]pyrene, can be 2-3 times higher among those routinely exposed to outdoor traffic emissions (e.g., police, bus drivers) compared with control subjects. Particle-bound PAH exposure can also vary with vehicle operation. For example, Kinsey et al. (2007, 190073) estimated from continuous idling and restart school bus operating conditions (without retrofitting) that over a 10-min period of waiting at a bus stop, continuous idling resulted in exposure to 33% more particle-bound PAH than in the case where the bus was restarted 2 min into the simulation and idled for 8 min. Continuous idling produced approximately 34 times more particle-bound PAH than in another scenario where the bus was off for 10 min then restarted.

Table 3-24. Examples of studies comparing near-road personal exposures with fixed site ambient concentrations.

Reference and Site	Ambient monitors	Personal monitors	Microenvironment, other variables	Ambient v. Personal Association	Primary Findings
Violante et al. (2006, 156140) Bologna, Italy	Fixed PM_{10} and benzene monitoring station (method not specified).	Active pump with PM_{10} PEM, passive sample for benzene desorbed and analyzed by GC-MS.	Localized traffic density (vehicles/h); Meteorology (wind speed, wind direction, visibility, relative humidity).	Personal: 185.10 ± 38.52 µg/m^3 Fixed: 43.56 ± 24.10 µg/m^3 ($p<0.0001$)	Fixed PM_{10} correlated with multivariate model of traffic and meteorology, but not personal PM_{10}; relationship between benzene and PM_{10} not explored.
Kaur et al. (2005, 086504) London, U.K.	Fixed TEOM for $PM_{2.5}$ and fixed CO monitor at ambient and curbside sites.	High flow personal samplers for $PM_{2.5}$, P-Trak monitors for UFP, Langan T15 and T15v for CO.	Exposures stratified by mode of transport (walk, cycle, bus, car, taxi).	Average $PM_{2.5}$ sampled by TEOM was 3 times lower than average personal $PM_{2.5}$ sample, and 8 times lower than maximum personal $PM_{2.5}$ sample.	$PM_{2.5}$ exposures during walking significantly lower than during car and taxi rides, UFP exposures during walking significantly lower than bus and car rides, cycling exposures to $PM_{2.5}$ and UFP not significantly different from those on bus, car, or taxi.
Kaur et al. (2005, 088175) London, U.K.	Fixed TEOM for $PM_{2.5}$ and fixed CO monitor at ambient and curbside sites.	High flow personal samplers for $PM_{2.5}$ analyzed post-sample for reflectance for EC, P-Trak monitors for UFP, Langan T15 and T15v for CO.	Volunteers walking at set times and directions along Marylebone Rd in London.	Fixed vs. personal $PM_{2.5}$: slope = 0.29, R = 0.6; personal $PM_{2.5}$ measurements were >2 times background levels and more than 15 µg/m^3 greater than curbside measurements.	Pedestrian exposures were significantly higher than fixed site curbside or ambient measurements. Results indicate that exposure declined up to 10% from curbside to building edge within a street canyon.
Adams et al. (2001, 019350) London, U.K.	Fixed TEOM for $PM_{2.5}$ and fixed CO monitor at ambient and curbside sites.	High flow personal samplers for $PM_{2.5}$.	Exposures stratified by mode of transport (cycle, bus, car, subway).	Median values: (µg/m^3) Cycle: Summer 34.5, Winter 23.5 Bus: 39.0, 38.9 Car: 37.7, 33.7 Subway: 247.2, 157.3 Fixed: 15, 13 Curb: 24, 37	Exposures were 2.3-16.5 times higher than ambient and 1.4-10.3 times higher than curbside during summer. During winter, only subway exposures were appreciably higher (4.3 times) than curbside.
Kinney et al. (2000, 001774) New York City, NY (Harlem)	Ambient site filter in greased impactor with pump for $PM_{2.5}$; absorbance testing on filter for EC.	Three high traffic sites filter in greased impactor with pump; absorbance testing on filter for EC.	Localized traffic density (vehicles/h).	Mean values: (µg/m^3) $PM_{2.5}$ / EC Site 1: 45.7 (10.1) / 6.2 (1.9) Site 2: 47.1 (16.4) / 3.7 (0.6) Site 3: 36.6 (10.8) / 2.3 (0.9) Ambient: 38.7 (10.9) / 1.5 (0.5)	$PM_{2.5}$ at high traffic sites was not significantly higher than ambient; EC was significantly higher than ambient at 2 sites. EC increased linearly with traffic counts.

In-Vehicle and In-Transit Exposures

In-vehicle pollution has been identified in various studies as a source of exposure to $PM_{2.5}$, PM_{10}, and UFPs (Briggs et al., 2008, 156294; Diapouli et al., 2007, 156397; Fruin et al., 2008, 097183; Gómez-Perales et al., 2004, 054418; Gómez-Perales et al., 2007, 138816; Gulliver and Briggs, 2004, 053238; Gulliver and Briggs, 2007, 155814; Rossner et al., 2008, 156927; Sabin et al., 2005, 087728). Results from recent studies are provided in Table A-60 of Annex A. In many of these studies, in-vehicle exposures are shown to be comparable to or less than that of walkers on the same route. Typically, in-vehicle exposures were also higher than community-based ambient monitor concentrations for TSP and PM_{10} (Diapouli et al., 2008, 190119). Curbside measurements of UFPs and $PM_{2.5}$ obtained at a fixed site in the Kaur et al. (2005, 088175; 2005, 086504) studies were generally lower than exposures during transit, including during walking and cycling. In contrast, the Adams et al. (2001, 019350) study demonstrated that fixed site $PM_{2.5}$ concentrations were higher than curbside during the summer and lower than curbside during the winter. As particle size decreased to the fine and UF range, less difference between in-vehicle and ambient concentrations was observed for PM mass or count, with the exception of the Diapouli et al. (2008, 190119) study where in-bus UFP concentrations were several times higher than indoor or outdoor residential and school concentrations.

Fruin et al. (2008, 097183) and Westerdahl et al. (2005, 086502) observed that in-vehicle UFP concentrations increased for freeways in comparison with arterial roads. They estimated that 36% of exposure to UFPs occurred during a total daily commuting time of 1.5 h (6% of the day) in Los Angeles; 22% of total exposure occurred during 0.5 h spent on freeways. Gong et al. (2009, 190124) demonstrated that UFP deposition rate increased with decreasing particle size (down to ~30 nm) and increasing surface area inside the vehicle, where deposited PM on the seats and dashboard can be resuspended and then inhaled or ingested. UFP deposition rate also rose slightly with increased number of passengers. Zhu et al. (2007, 179919) found that in-vehicle UFP counts were 85% lower than outdoors when the fan was operating in recirculation mode. They estimated that a 1-h commute (4% of the day) accounts for 10-50% of daily exposure to UFPs generated by traffic. Based on the American Time Use Survey estimation of an average of 70.2 min spent in vehicles per person each day (U.S. Bureau of Labor Statistics http://www.bls.gov/tus/), cumulative in-vehicle exposure can become important.

In a study of $PM_{2.5}$ exposure on school buses, Adar et al. (2008, 191200) found that $PM_{2.5}$ on school buses was 2 times higher than on-road levels and 4 times higher than central site measurements. Sabin et al. (2005, 087728) demonstrated for school buses that emission control technologies had a significant impact on in-bus concentrations of black carbon mass, and Hammond et al. (2007, 190135) demonstrated significant reductions of particle number concentration measured for 0.02-1 μm particles when comparing buses using clean diesel or retrofits compared with non-retrofitted buses. Although not tested here for other vehicle types with respect to PM, these findings suggest that a portion of in-vehicle concentrations are due to self-pollution, defined by Behrentz et al. (2004, 155682) as the fraction of a vehicle's own exhaust entering the vehicle microenvironment. Behrentz et al. (2004, 155682) tested self-pollution with school buses using SF_6 tracer gas and demonstrated that 0.3% of in-vehicle air comes from self-pollution, and that this number was roughly 10 times greater than in-vehicle concentrations related to self-pollution on newer buses. The Behrentz et al. (2004, 155682) study also measured EC and particle-bound PAH and found that 25% of the variability in EC concentration was related to self-pollution. Adar et al. (2008, 191200) estimated that 35.5% of $PM_{2.5}$ mass on school buses was from self-pollution. These findings are important for exposure estimation when partitioning local and ambient sources of pollution during transport in vehicles.

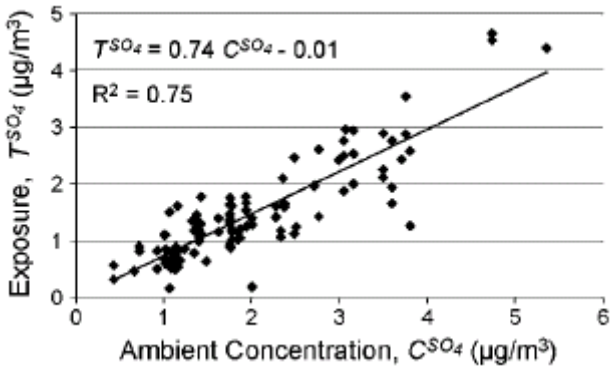
3.8.4.2. Ambient PM Exposure Estimates from Central Site Monitoring Data

The following paragraphs describe studies that estimate personal exposure to ambient PM from central site monitoring data. As shown in Figure 3-93, the large majority of an individual's time is spent indoors. Although calculation of infiltration and indoor personal exposure is an important part of this assessment, such exposures are described with respect to central site monitors. Assessing population-level exposure at the urban scale is particularly relevant for epidemiologic studies, which typically provide information on the relationship between health effects and community-averaged, rather than individual, exposure.

Indoor or other nonambient sources could significantly affect assessment of a person's total exposure to many pollutants. For this reason, many studies use PM components to estimate infiltration of ambient PM to indoor environments. Wilson et al. (2000, 010288) first proposed that SO_4^{2-} could be used as a tracer of the ambient $PM_{2.5}$ infiltration rate. Sarnat et al. (2002, 037056) also noted that it is reasonable to assume that the size distribution of ambient SO_4^{2-} particles is sufficiently similar to the size distribution of ambient $PM_{2.5}$, and therefore that the ambient SO_4^{2-} to personal SO_4^{2-} ratio is an acceptable surrogate for the ratio of the ambient $PM_{2.5}$ exposure to the ambient $PM_{2.5}$ concentration. Sulfate has been used this way in several studies, including Ebelt et al. (2005, 056907), Wallace and Williams (2005, 057485; 2006, 089190) and Wilson and Brauer (2006, 088933). For this method to be successful, indoor or other nonambient sources of the tracer must be small compared to ambient sources over the period of sampling. Wilson and Brauer (2006, 088933) noted that environmental tobacco smoke and tap water used in showers or humidifiers are indoor sources of SO_4^{2-}. Other concerns in using SO_4^{2-} as a tracer for $PM_{2.5}$ arise because SO_4^{2-} tends to be concentrated in the accumulation mode and thus it might not capture any coarse PM found in the upper end of the $PM_{2.5}$ distribution, which can include larger particles in the tail end of the coarse mode (Wallace and Williams, 2005, 057485). Strand et al. (2007, 157018) suggested that Fe be used as an additional tracer to correct for the infiltration of larger $PM_{2.5}$ particles. Their study took place in Denver, where indoor sources of Fe were small. However, there could be more substantial

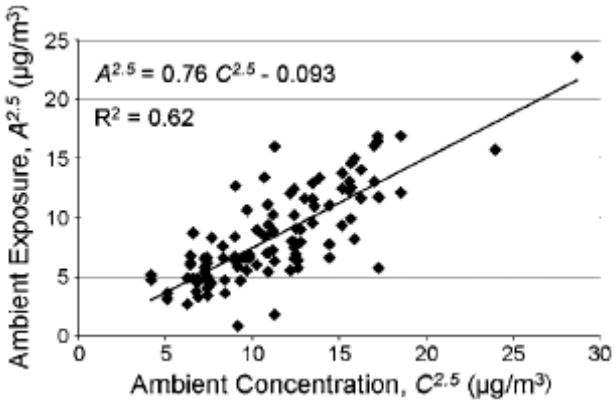
contributions from tracking iron in soil indoors in other locations. The spatial variability of Fe is also larger than that of $PM_{2.5}$ across urban areas. Volatilization of nitrate or organic compounds after infiltration of $PM_{2.5}$ indoors could lead to bias in exposure estimates (Sarnat et al., 2006, 089166). This could be a large problem in areas in which PM contains a large semi-volatile component.

Figure 3-94 shows total exposure to SO_4^{2-} as a function of measured ambient SO_4^{2-} concentration. Figure 3-95 shows estimated ambient exposure to $PM_{2.5}$ as a function of measured ambient $PM_{2.5}$ concentration, where ambient personal exposure is calculated from the ambient exposure factor for SO_4^{2-}. Close agreement between these figures can be observed. Figure 3-96 shows total exposure to $PM_{2.5}$ as a function of measured ambient $PM_{2.5}$ concentration. However, the total exposure to $PM_{2.5}$ shows virtually no association with ambient $PM_{2.5}$ because it contains nonambient contributions to $PM_{2.5}$.



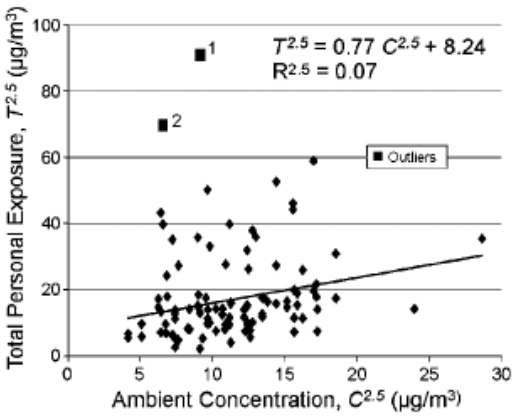
Source: Reprinted with Permission of Nature Publishing Group from Wilson and Brauer (2006, 088933)

Figure 3-94. Total exposure to SO_4^{2-} as a function of measured ambient SO_4^{2-} concentration, from the Vancouver study. Vancouver British Columbia, April-September 1998, with 16 non-smoking subjects aged 54-86 yr.



Source: Reprinted with Permission of Nature Publishing Group from Wilson and Brauer (2006, 088933)

Figure 3-95. Estimated ambient exposure to $PM_{2.5}$ as a function of measured ambient $PM_{2.5}$ concentration, from the Vancouver study (Vancouver, British Columbia, April-September 1998, with 16 non-smoking subjects aged 54-86 yr).



Source: Reprinted with Permission of Nature Publishing Group from Wilson and Brauer (2006, 088933)

Figure 3-96. Total exposure to $PM_{2.5}$ as a function of measured ambient $PM_{2.5}$ concentration, from the Vancouver study. Vancouver, British Columbia, April-September 1998, with 16 non-smoking subjects aged 54-86 yr.

The estimated ambient exposure to $PM_{2.5}$ is well correlated with measured ambient $PM_{2.5}$ concentration with zero intercept, implying that nonambient sources were minor. This technique works well in areas where SO_4^{2-} is a regional pollutant, because its spatial variability is small(Kim et al., 2005, 083181; U.S. EPA, 2004, 056905). Wilson and Brauer (2006, 088933) reported that the pooled Pearson correlation coefficient was 0.79 for personal ambient exposures (estimated by the tracer element method) vs. ambient concentrations of $PM_{2.5}$, and it was 0.001 for personal nonambient $PM_{2.5}$ exposure vs. ambient concentrations. Strand et al. (2006, 089203) conducted an exposure study in Denver (2002-2004) for 6-12 year-old school children. Up to 10 personal exposure samples were collected on each day, and ambient concentrations were measured simultaneously at a fixed site located at the school. The daily average personal SO_4^{2-} exposure was strongly associated with ambient SO_4^{2-} concentration ($r = 0.96$, $120 > N > 100$). Koutrakis et al. (2005, 095800) reported the median Spearman correlation coefficients between personal SO_4^{2-} exposure and ambient SO_4^{2-} concentration were above 0.60 during both winter and summer in Boston and Baltimore (15 subjects with 12 consecutive measurements during each season in both Boston and Baltimore). For another Baltimore cohort (15 senior subjects with up to 23 consecutive measurements for each person), Hopke et al. (2003, 095544) reported that the median Pearson correlation coefficient between personal exposure to the SO_4^{2-} factor and the ambient SO_4^{2-} factor was 0.93 (ranging from 0.56 to 0.98 for different subjects), while the median Pearson correlation coefficients were 0.25 for the crustal factor (ranging from -0.46 to 0.66) and 0.22 for a factor whose origin was not identified (ranging from -0.19 to 0.88). The inferences drawn from using the SO_4^{2-} component of $PM_{2.5}$ as an indicator for personal exposure to ambient $PM_{2.5}$ may apply in areas where SO_4^{2-} is a minor component of $PM_{2.5}$ or in the absence of significant nonambient sources of SO_4^{2-} (Sarnat et al., 2001, 019401).

Source apportionment techniques could also be used, in principle, to derive ambient personal $PM_{2.5}$ exposures. They would be especially useful in areas where the application of a tracer method might be problematic. Hopke et al. (2003, 095544) noted that four outdoor factors ($NH_4NO_3^-$ and $(NH_4)_2SO_4$, secondary SO_4^{2-}, OC, motor vehicle exhaust) would constitute an estimate of the personal ambient $PM_{2.5}$ concentration. However, the data used in this portion of the analysis were obtained only with fixed monitors and did not include measurements made by PEMs. They also used the Multilinear Engine to derive factors that were required to contribute jointly to central indoor and outdoor, individual apartment, and PEM samples of a panel of residents. Hopke et al. (2003, 095544) used PMF to derive source contributions to community, outdoor, and indoor PM exposures at a retirement facility in Towson, MD. Hopke et al. (2003, 095544) found three sources: SO_4^{2-}, unknown (perhaps combustion related, according to the authors), and soil, jointly contributing 46%, 13%, and 4% of $PM_{2.5}$ to the PEM samples, respectively. Further source resolution was not possible because there was a lack of data for a number of components in the PEM samples. The largest and most clearly identified contribution to personal exposure was from the SO_4^{2-} factor. This study also

determined that a few minor indoor and personal activity sources contributed <10% of the ambient SO_4^{2-} source to personal exposures.

Wilson and Brauer (2006, 088933) presented an adaptation of the SO_4^{2-} method for estimating exposure to $PM_{10-2.5}$. α is computed based on the SO_4^{2-} method as the ratio of exposure to ambient SO_4^{2-} (as measured by a personal monitor) to ambient SO_4^{2-} concentration. Then, knowing an individual subjects' time diary and the penetration and loss properties of SO_4^{2-}, the air exchange rate for an individual location can be calculated from Equation 3-5 and Equation 3-7. Finally, the penetration and loss rates of $PM_{10-2.5}$ from the PTEAM database (Ozkaynak et al., 1996, 073986) can be input into the individual exposure model along with the individual activity pattern and residential air exchange rate to compute the ambient $PM_{10-2.5}$ exposure factor and the ambient $PM_{10-2.5}$ exposure if $PM_{10-2.5}$ concentration is measured; in the Wilson and Brauer (2006, 088933) paper, $PM_{10-2.5}$ was estimated from ambient PM_{10} and $PM_{2.5}$ concentrations. Given that $PM_{10-2.5}$ deposits more readily and therefore disperses over a shorter distance than $PM_{2.5}$, it is possible that use of ambient $PM_{10-2.5}$ concentration may incur more error than in using this method for $PM_{2.5}$. Ebelt et al. (2005, 056907) observed in a Vancouver, Canada panel study that the correlation between ambient $PM_{10-2.5}$ exposure and ambient PM_{10} exposure ($r = 0.72$) was lower than the correlation between ambient $PM_{2.5}$ exposure and ambient PM_{10} exposure ($r = 0.92$). This is attributed to both a smaller F_{inf} for $PM_{10-2.5}$ and $PM_{2.5}$ comprising a greater fraction of the PM_{10} for the Vancouver study. In this study, $PM_{10-2.5}$ mass concentration was calculated from the difference between ambient PM_{10} and $PM_{2.5}$ mass concentration.

Wilson and Brauer (2006, 088933) state that their methodology for computing the ambient exposure factor based on the $PM_{2.5}$ SO_4^{2-} method can be applied to PM in the 0.1-0.5 µm size range. Little SO_4^{2-} mass is found below 0.1 µm, so the SO_4^{2-} tracer method would not be applicable for UFPs. Given the short atmospheric lifetime of UFPs resulting from particle growth and evaporation processes, primary UFPs are most prevalent at microscale rather than at an urban spatial scale (Sioutas et al., 2005, 088428). Moore et al. (2009, 191004) found substantial spatial, hourly, and daily variability in UFP concentration in a saturation study of Los Angeles. Moore et al. (2009, 191004) and Harrison and Jones (2005, 191005) also found that UFPs and $PM_{2.5}$ measurements were poorly correlated at the monitoring sites.

3.8.4.3. Infiltration

F_{inf} varies substantially given a vast array of conditions, and it can best be modeled dynamically based on a distribution of air exchange and deposition or other UF, accumulation mode, fine, and coarse PM loss rates rather than a single value (Bennett and Koutrakis, 2006, 089184; Wallace et al., 2006, 089190). Given that air exchange rates within a building vary as a function of ambient temperature and pressure, F_{inf} is subject to seasonal and regional changes (Meng et al., 2005, 058595; Sarnat et al., 2006, 089166; Wallace and Williams, 2005, 057485). These factors make F_{inf} a more accurate descriptor of infiltration than a simple I/O ratio because the I/O ratio also includes contributions from indoor sources in addition to PM that infiltrates from outdoors. Wallace et al. (2006, 089190) identified several significant factors affecting F_{inf}, including window opening, age of an indoor microenvironment, number of occupants, location on a dirt road, dryer usage, and air conditioning usage. This term becomes even more complex when one considers transformation of the size distribution and chemical composition of the PM through chemical reactions on the particle surface, agglomeration, growth, and evaporation given that F_{inf} depends on particle size (Keller and Siegmann, 2001, 025881). F_{inf} for PM is influenced by physical mechanisms, such as Brownian diffusion, thermophoresis, and impaction, all of which are functions of particle size (Bennett and Koutrakis, 2006, 089184; Tung et al., 1999, 049003). These differential effects are summarized below. Recent studies on infiltration are summarized in Table A-64 of Annex A. F_{inf} and I/O are listed where available, although it is recognized that I/O is not as meaningful a descriptor but provides an approximation of F_{inf}.

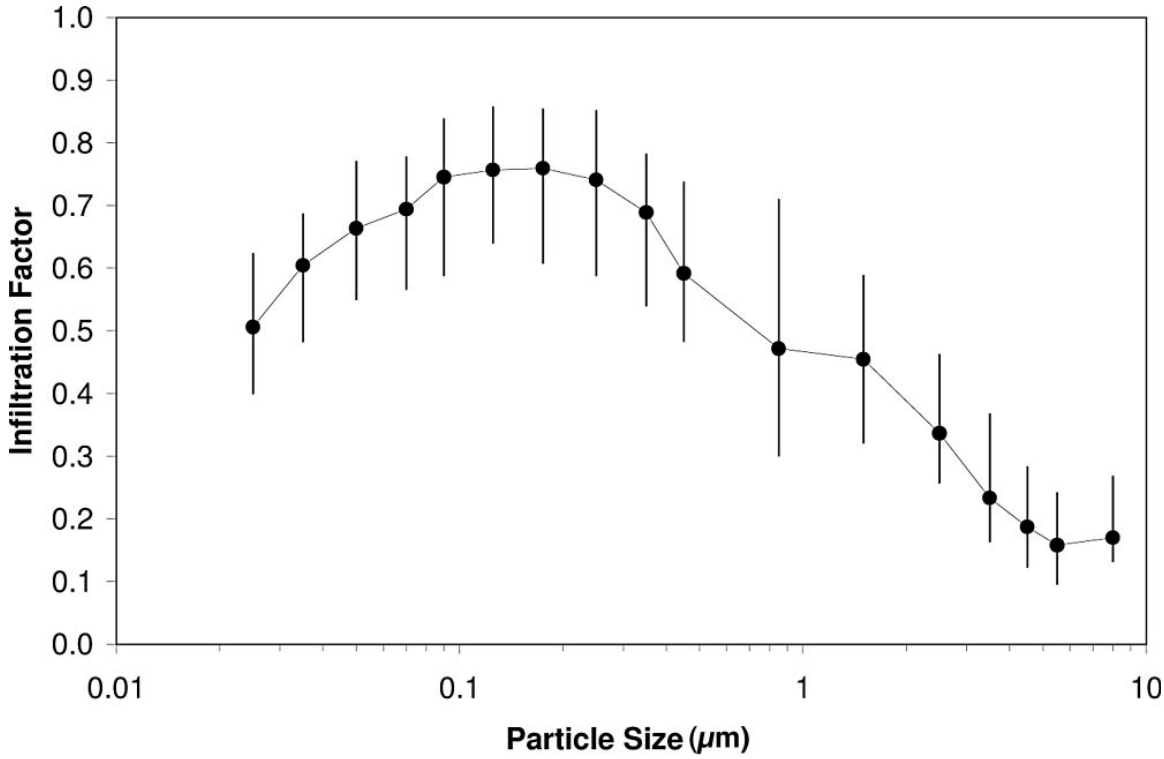
A number of studies have examined the impact of season on PM infiltration. Season is important because it affects the ventilation practices used (e.g., open windows, air conditioning or heating use) and ambient temperature and humidity conditions influence the transport, dispersion, and size distribution of the PM. Pandian et al. (1998, 090552) found that nationwide residential air exchange rates vary by season as: summer > spring > winter > fall with summer air exchange roughly 1.5-2 times greater than average air exchange rate for the entire year because the rates are driven by home air conditioning and heating usage. Allen (2003, 053578) provided information on

the range and distribution of F_{inf} for $PM_{2.5}$ at 44 residences in Seattle. The mean F_{inf} was calculated using light scattering measurements in a recursive mass balance method with no species data. For all sampling days, F_{inf} (± SD) was 0.65 ± 0.21. Differences in infiltration were observed for the heating season (0.53 ± 0.16), when windows would be expected to be closed, and for the non-heating season (0.79 ± 0.18). Residences with open windows had a mean F_{inf} of 0.69 vs. 0.58 for residences with closed windows. The authors combined the light scattering results with indoor and outdoor sulfur measurements to estimate that 79 ± 17% of indoor $PM_{2.5}$ was generated outdoors. This study provides important data on the distribution of residential F_{inf} values and illustrates the magnitude of the effect of season and window position on infiltration rates. Barn et al. (2008, 156252) and Baxter et al. (2007, 092725) also noted that window opening was an important variable. Barn et al. (2008, 156252) found F_{inf} of 0.61 ± 0.27 for 13 homes during summer and 0.27 ± 0.18 for 19 homes during winter in Canada for $PM_{2.5}$ from forest fires and wood smoke.

Likewise, location could impact residential ventilation practices and infiltration. Using the SO_4^{2-} method for estimating $PM_{2.5}$ infiltration, Cohen et al. (2009, 190639) noted differences in median infiltration among eight areas (including three comprising the Los Angeles region and two comprising the New York City region). Indoor-outdoor SO_4^{2-} ratio was noted to be highest in New York City (median: 0.85) and Los Angeles (median: 0.84) and lowest in St. Paul (median: 0.54). Pandian et al. (1998, 090552) observed that residential air exchange rates vary by region as: southwest > southeast > northeast > northwest, which reflects regional use of air conditioning. Sarnat et al. (2006, 089166) noted differences in $PM_{2.5}$ infiltration between coastal and inland residences, although these differences were not statistically significant.

Differential Infiltration Related to PM Size

Differential infiltration as a function of particle size has been observed to occur. Infiltration factors for particle diameters ranging from 20 nm to 10 μm were measured using continuous SMPS-APS monitoring in Boston by Long et al. (2001, 011526) during summer and fall for nighttime periods, when personal activity patterns would be less likely to generate indoor PM. The maximum infiltration factor was reported for particles between 80 and 500 nm to range from 0.8 to 1.0. Summer values were uniformly higher than fall values, consistent with higher observed air exchange rates. The infiltration factor decreased with size above 500 nm, reaching 0.1-0.2 for 6-10 μm particles. Particles smaller than 80 nm also were reported to have lower infiltration factors. This demonstrates the size dependence of PM infiltration, which has been further studied by recent investigators. Sarnat et al. (2006, 089166) examined infiltration as a function of particle size and found that I/O varies by particle diameter, as measured by a SMPS-APS system. Figure 3-97 presents I/O values for size fractions ranging from 0.02 to 10 μm. The maximum infiltration was observed around the accumulation mode (0.1-0.5 μm), with I/O = 0.7-0.8. Reduced infiltration was observed for coarse-mode PM (0.1-0.2 for D_p = 5-10 μm) and, to a lesser extent, UFPs (0.5-0.7 for D_p = 0.02-0.1 μm). This is consistent with increased removal mechanisms for those size fractions. Deposition is caused by settling for coarse-mode particles. Deposition of UFP can occur by diffusion leading to agglomeration into larger particles and subsequent settling, as well as losses to walls.



Source: Reprinted with Permission of Air & Waste Management Association from Sarnat et al. (2006, 089166).

Figure 3-97. F_{inf} as a function of particle size.

3.8.5. Multicomponent and Multipollutant PM Exposures

3.8.5.1. Exposure Issues Related to PM Composition

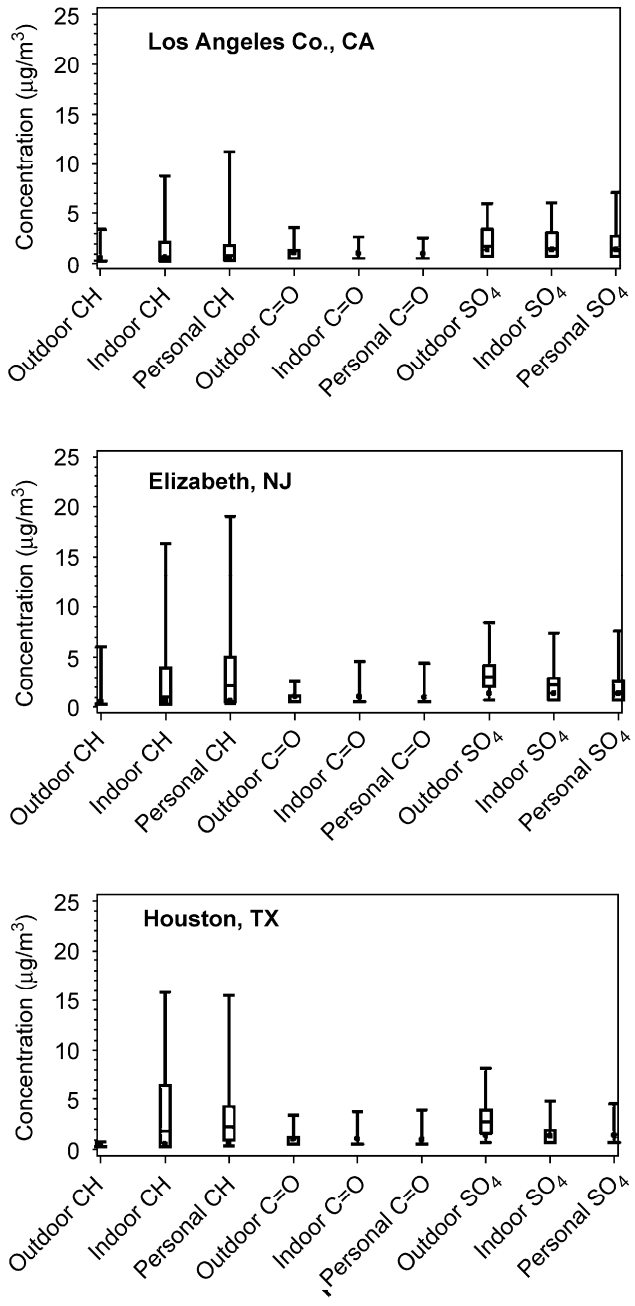
Annex A presents exposure studies that include chemical speciation data in Table A-62. Some of these studies focused on SO_4^{2-}, NO_3^-, or carbonaceous aerosols (EC, OC, particle-bound PAHs), while others measured concentrations of trace elements from crustal (Ca, Fe, Mn, K, Al, S, Cl in salt), mobile (Al, Ca, Fe, K, Mg, Na, Ba, Cr, Cu, Mn, Ni, Pb, S, Ti, V, and Zn), or industrial (particle-bound Hg, Cl, V, Zn, Ti, Cu, Pb) sources. A number of source apportionment studies have been performed over the last five years to determine the contribution of outdoor sources to indoor and personal PM constituents.

Source apportionment studies by Kim et al. (2005, 083181), Hopke et al. (2003, 095544) and Zhao et al. (2006, 156181) have shown that secondary SO_4^{2-} provides the largest ambient contribution to personal and indoor exposures. These studies took place in Baltimore, MD and Raleigh/Chapel Hill, NC. In a source apportionment study in Seattle, vegetative burning was the most significant source of outdoor origin (Larson et al., 2004, 098145). Zhao et al. (2007, 156182) performed a source apportionment study of personal exposure to $PM_{2.5}$ among residents in Denver and also observed lower contributions from secondary SO_4^{2-} in comparison with motor vehicle emissions and secondary NO_3^-. This suggests that personal exposure to SO_4^{2-} in parts of the West is lower than in the Mid-Atlantic. These observations are consistent with the composition distribution shown in Figure 3-17 and Figure 3-18. Viana et al. (2008, 156135) selected 4 sites of varying population density to represent exposures of pregnant subjects in an early childhood epidemiologic study. Viana et al. (2008, 156135) analyzed $PM_{2.5}$ and PM_{10} samples for several species along urban-to-rural gradients centered in Valencia, Spain and found gradients for both size fractions in anthropogenically-generated SO_4^{2-}, OC, EC, NO_3^-, Fe, and NH_4^+, but not in mineral species.

Combined, these findings suggest urban- and regional-scale variation in species composition can influence exposure estimates. Personal PM exposure studies including source apportionment analysis along with chemical speciation are presented in Annex A, Table A-63.

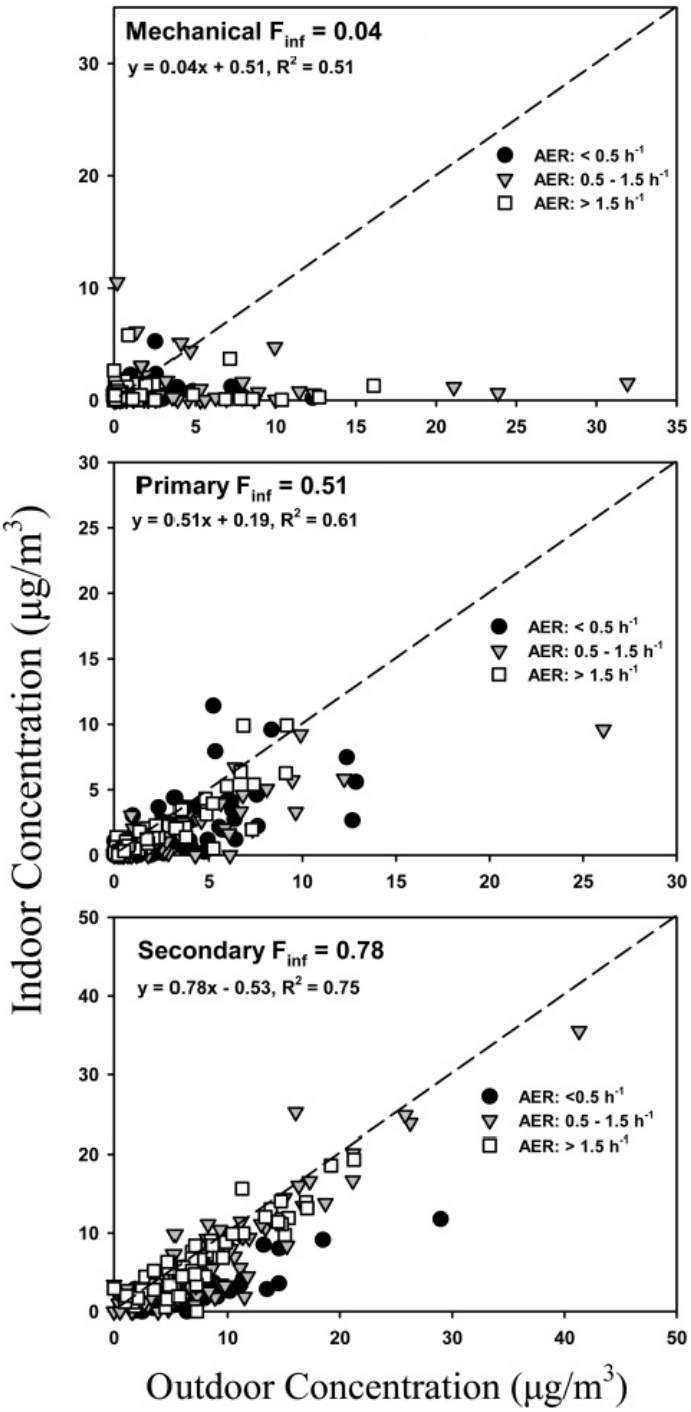
Source apportionment for carbonaceous aerosols is complicated by the fact that they can be derived from indoor and outdoor combustion sources. Carbonaceous aerosols are difficult to trace to specific indoor and outdoor sources because combustion is widespread. Sørensen et al. (2005, 089428), Ho et al. (2004, 056804), Larson et al. (2004, 098145), and Jansen et al. (2005, 082236) all found that personal and microenvironmental exposure to total carbon or BC was lower than that measured outdoors, while Sarnat et al. (2006, 089166) showed significant associations between personal and ambient measurements of EC for measurements taken during the fall for low and high ventilation conditions (slope = 0.66-0.73) and during the summer for high ventilation conditions (slope = 0.41). Wu et al. (2006, 179950), Delfino et al. (2006, 090745), Olson and Norris (2005, 156005) and Turpin et al. (2007, 157062) all demonstrated much higher levels of OC compared with EC in personal samples, possibly due to indoor sources of OC from cooking and home heating. Reff et al. (2007, 156045) and Meng et al. (2007, 194618) both reported findings from the Relationships between Indoor, Outdoor, and Personal Air (RIOPA) study in Los Angeles, Houston, and Elizabeth, NJ. Results from Reff et al. (2007, 156045) reveal significantly higher detection of aliphatic C-H functional groups indoors and in personal samples compared with outdoors (Figure 3-98). This information may help to distinguish carbonaceous compounds of indoor and outdoor origin in future source apportionment studies of PM exposure. Little regional variation in the aliphatic, carbonyl, or SO_4^{2-} groups tested were reported in this study. In Meng et al. (2007, 194618), indoor exposures were shown to decrease for secondary formation aerosols including SO_4^{2-} but not NO_3^- (not tested) when compared with outdoor concentrations. In this study, indoor exposures to mechanically generated aerosols decreased in comparison with outdoors (Figure 3-99).

Trace metal studies have shown variable results regarding personal exposure to ambient constituents. For instance, Molnár et al. (2006, 156773) found that personal exposure was higher than outdoor and ambient concentrations for mostly crustal Cl, K, Ca, Ti, Fe, and Cu. However, Adgate et al. (2007, 156196) found that personal exposures were higher than ambient for Fe, Mg, K, Zn, Cu, Pb, and Mn but lower than ambient for Al, Na, and Ti. Larson et al. (2004, 098145) found that personal exposure to Ca and Cl were higher than concentrations measured at ambient (central site) and residential outdoor monitors, lower for Fe, K, Mn, and As and the same for Al, Br, Cr, and Cu. Source apportionment for trace metals can vary significantly among cities and over seasons. For instance, in a Baltimore source apportionment study, exposure to Mn could be attributed nearly equally to the Quebec wildfires, roadway wear, and soil, while Pb exposure was largely found to be due to a local incinerator (Ogulei et al., 2006, 119973). In this case, the Quebec wildfires were a transient episodic source, while roadway wear and incineration were continuous. However, in Larson et al. (2004, 098145), Mn and Pb exposures in Seattle were largely attributable to mobile source and stationary source emissions. For this reason, source composition behavior cannot be generalized for characterizing exposures and resulting health effects across multiple locations or times.



Source: Reprinted with Permission of Elsevier Ltd. from Reff et al. (2007, 156045)

Figure 3-98. Apportionment of aliphatic carbon, carbonyl, and SO_4^{2-} components of outdoor, indoor, and personal $PM_{2.5}$ samples, for Los Angeles (top), Elizabeth (center), and Houston (bottom).

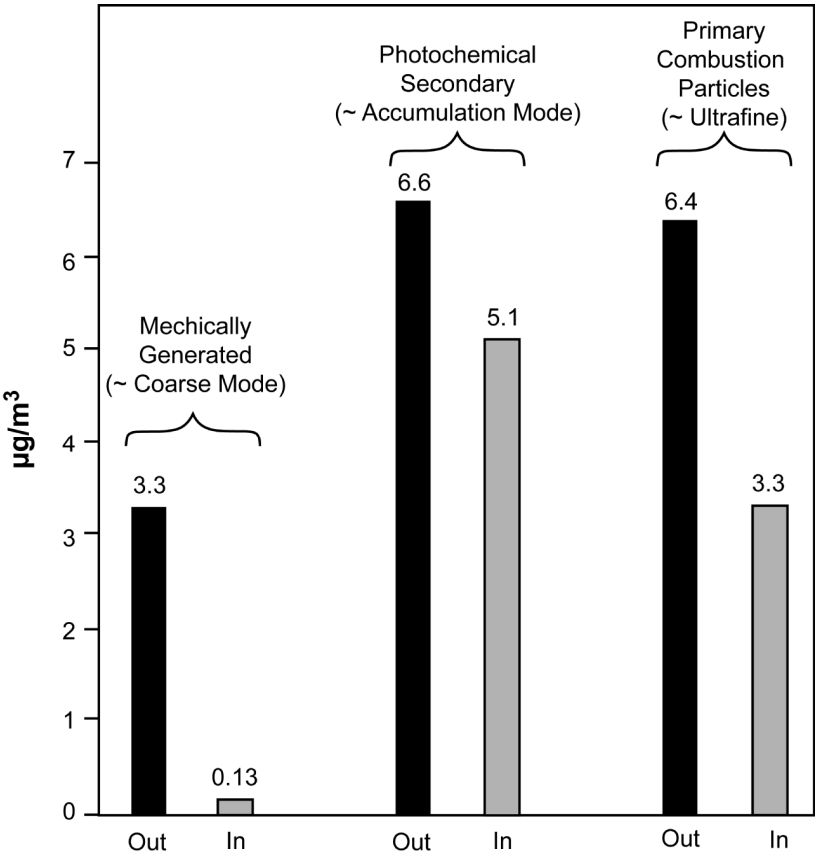


Source: Reprinted with Permission of ACS from Meng et al. (2007, 194618).

Figure 3-99. Apportionment of infiltrated PM from mechanical generation (top), primary combustion (center), and secondary combustion (bottom).

Differential Infiltration Related to PM Composition

A number of chemical factors influence the tendency for differential infiltration in PM. Lunden et al. (2003, 156718) studied infiltration of BC and OC aerosols and found that F_{inf} can vary substantially as a function of gas transport properties with differing air exchange rates. This study and Sarnat et al. (2006, 089166) also showed that BC aerosol infiltration is considerably higher than infiltration of OC, and that carbonaceous aerosol infiltration differed substantially from NO_3^- and SO_4^{2-} aerosols under the same building air exchange conditions. These disparities are likely related to differences in the particle size distribution of PM components, as described in Section 3.8.4.3. As shown in Figure 3-100, the composition of indoor PM that has infiltrated from outdoors is different from that of outdoor PM (Meng et al., 2007, 194618). In this case, the particles containing photochemical products (primarily accumulation mode) have a higher infiltration rate than the larger (primarily coarse mode) mechanically generated particles or the smaller primary combustion particles (likely to consist mostly of UFPs in the nucleation or Aitken nuclei mode).



Source: Reprinted with Permission of ACS from Meng et al. (2007, 194618).

Figure 3-100. Results of the positive matrix factorization model showing differences in the mass of outdoor PM and PM that has infiltrated indoors based on source category.

PM species enriched in the accumulation mode, such as SO_4^{2-}, will infiltrate more efficiently than components with larger size distributions, such as iron (Strand et al., 2007, 157018). Lunden et al. (2008, 155949) also compared I/O ratios for $PM_{2.5}$, total carbon, OC, and BC in an unoccupied house and found the lowest ratio for $PM_{2.5}$ (0.41 ± 0.2), the highest for BC (0.61 ± 0.2), and intermediate values for total carbon (0.50 ± 0.2) and OC (0.47 ± 0.2). The authors attributed the

lower $PM_{2.5}$ I/O ratio to indoor loss of NH_4NO_3 aerosol. The authors note that their BC I/O of 0.6 is somewhat lower than BC ratios measured in occupied spaces (Polidori et al., 2007, 156877). Conversely, indoor sources in occupied residences contribute to observed OC I/O ratios greater than 1 in other studies (Polidori et al., 2006, 156876; Sawant et al., 2004, 056798). Analytical results for $PM_{2.5}$ components from the Baxter et al. (2007, 092726) study found F_{inf} of 0.95 ± 0.07 for S and 0.60 ± 0.04 for V, the two components identified as having no indoor sources and which had I/O ratios significantly less than 1 (Baxter et al., 2007, 092726). It is possible that association of V with larger particles of lower penetration efficiency could contribute to a lower infiltration rate. Meng et al. (2005, 058595) also noted that the lack of indoor sources of S and V result in much lower variability in penetration and loss rates.

Volatilization of PM during infiltration can cause differences between the composition of indoor and outdoor PM. NO_3^-, a prevalent PM component year-round in the western U.S. and during winter throughout the mid-western and northeastern states, has a decreased F_{inf} due to volatilization of NO_3^- indoors. Sarnat et al. (2006, 089166) calculated F_{inf} values for NO_3^-, $PM_{2.5}$, and BC, and found the values to increase in that order. NO_3^- was low (median = 0.18, IQR = 0.12-0.33), while BC was high (median = 0.84, IQR = 0.70-0.96); the intermediate value of $PM_{2.5}$ (median = 0.48, IQR = 0.39-0.57) reflected its composition as a mixture of those two components (among others). Indoor volatilization of NO_3^- enriches indoor ambient PM in other components, creating differences in toxicity between indoor and outdoor ambient PM. The high infiltration of non-volatile BC creates additional sorption sites for organics, including indoor-generated compounds. Meng et al. (2007, 194618) found that secondary formation accounts for 55% of indoor PM of outdoor origin, while primary combustion accounts for 43%, and mechanical generation accounts for 2%. Meng et al. (2007, 194618) noted that secondary formation processes often result in more accumulation mode particles, so that diffusion losses are not as great as for primary combustion particles that are composed primarily of nucleation and condensation size modes (Figure 3-100). Likewise, Polidori et al. (2007, 156877) suggest that similarities in the EC and OC size distributions and infiltration factors reflect low vapor pressure secondary organic aerosols in the OC component. Sioutas et al. (2005, 088428) suggest that volatilization of UFPs while crossing the building envelope may impede infiltration in this size range. Variations in the presence of outdoor PM indoors, and resulting changes in removal behavior once indoors, relate to the species composition of PM.

3.8.5.2. Exposure to PM and Copollutants

Analysis of personal exposure to multipollutant mixtures is an area of growing research. Several multipollutant studies involving UF, fine, and coarse PM are presented in Table A-65. Sarnat et al. (2001, 019401) found significant associations between personal exposure to $PM_{2.5}$ and ambient concentrations of O_3, NO_2, CO (significant only for winter), and SO_2 in a panel study conducted in Baltimore. Personal exposures to $PM_{2.5}$ and personal exposures to the gases were not correlated in this study. This result may have arisen in part because personal exposures to the gases were often beneath detection limits of the personal monitoring devices. Schwartz et al. (2007, 090220) also used data from the Baltimore panel study to simulate distributions of personal exposures and ambient concentrations of $PM_{2.5}$, PM_{10}, SO_4^{2-}, NO_2, and O_3. They found that personal exposure to ambient $PM_{2.5}$ was significantly associated with ambient concentrations of $PM_{2.5}$, NO_2, and O_3 (O_3 in an inverse relationship). They also reported that personal exposure to SO_4^{2-} was significantly positively associated with ambient $PM_{2.5}$ and O_3 concentrations.

There is evidence that associations between ambient gases and personal exposure to $PM_{2.5}$ of ambient origin exist but are complex and vary by season and region. Seasonality of the associations could be a result of seasonal variability in photochemistry, source generation, and building ventilation. Sarnat et al. (2005, 087531) observed associations between personal exposure to total $PM_{2.5}$ and ambient concentrations of O_3, NO_2, and SO_2 measured at community-based monitors for groups of healthy senior citizens and school children in Boston during the summer. In this study, significant associations between personal exposure to ambient $PM_{2.5}$ and personal O_3 exposures were observed in summer and between personal $PM_{2.5}$ and personal NO_2 in winter and summer, unlike the Baltimore study in which only summertime personal $PM_{2.5}$ and personal NO_2 were associated (Sarnat et al., 2001, 019401). In their study of personal exposure to ambient air pollutants in Steubenville, OH, Sarnat et al. (2006, 090489) found low but significant associations for ambient O_3 with personal $PM_{2.5}$, SO_4^{2-}, and EC in the summer. Low but significant associations between ambient SO_2 and personal $PM_{2.5}$, and between ambient NO_2 and personal EC, were also observed. In the fall,

ambient O_3 had a weak but significant association with personal EC, and SO_2 had a weak but significant association with personal SO_4^{2-}. Ambient NO_2 was also significantly associated with personal $PM_{2.5}$, SO_4^{2-}, and EC with somewhat higher coefficient of determination (R^2 = 0.25-0.49) in the fall.

3.8.6. Implications of Exposure Assessment Issues for Interpretation of Epidemiologic Studies

Environmental epidemiologic study designs vary by many factors, including study sample size, measurement time interval, study duration, monitor type, and spatial distribution of the study sample. A panel epidemiology study consists of a relatively small sample (typically tens) of study participants followed over a period of days to months. Time-activity diary studies are examples of panel studies (e.g., Cohen et al., 2009, 190639; Elgethun et al., 2003, 190640; Johnson et al., 2000, 001660; Olson and Burke, 2006, 189951), and a microenvironmental model might be applied to represent exposure in this case. Community time-series studies may involve millions of people whose exposure and health status is estimated over the course of a few years using a short monitoring interval (hours to days). Because so many people are involved, community-averaged concentration is typically used as a surrogate for exposure in community time-series studies. Exposures and health effects are spatially aggregated over the time intervals of interest because they are designed to examine health effects and their potential causes at the community level (e.g., Dominici et al., 2000, 005828; Peng et al., 2005, 087463). A longitudinal cohort epidemiology study typically involves hundreds or thousands of subjects followed over several years or decades. Concentrations are generally aggregated over time and by community to estimate exposures (e.g., Dockery et al., 1993, 044457; Krewski et al., 2000, 012281). The importance of exposure misclassification varies with study design based on the spatial and temporal aspects of the design. Other factors that could influence exposure estimates in PM epidemiologic studies include source characteristics, particle size distribution, and particle composition. Potential issues that could influence estimates of PM exposure include measurement, modeling, spatial variability, temporal variability, use of surrogates for PM exposure, and compositional differences. These are described in detail in the following sections.

3.8.6.1. Measurement Error

Measurement Error at Community-Based Ambient Monitors and Exposure Assessment

Community-based ambient monitors are employed for time-series and longitudinal studies, although they can be used for panel studies as well. Section 3.4 discusses potential errors in measuring ambient PM in detail. Because there will likely be some random component to instrumental measurement error, the correlation of the measured PM mass with the true PM mass is expected to be <1. Sheppard et al. (2005, 079176) indicate that instrument error in the hourly or daily average concentrations has "the effect of attenuating the estimate of α." Zeger et al. (2000, 001949) suggest that in order for this error to cause substantial bias in later estimation of a health outcome, the measurement error must be strongly correlated with the measured concentrations. Positive and negative artifacts resulting from sampling volatile PM may therefore lead to lack of association with health endpoints in time-series and longitudinal studies. In multicity longitudinal studies, where PM composition and associated artifacts may vary across cities, the cumulative influence of such artifacts on exposure estimates is more difficult to predict.

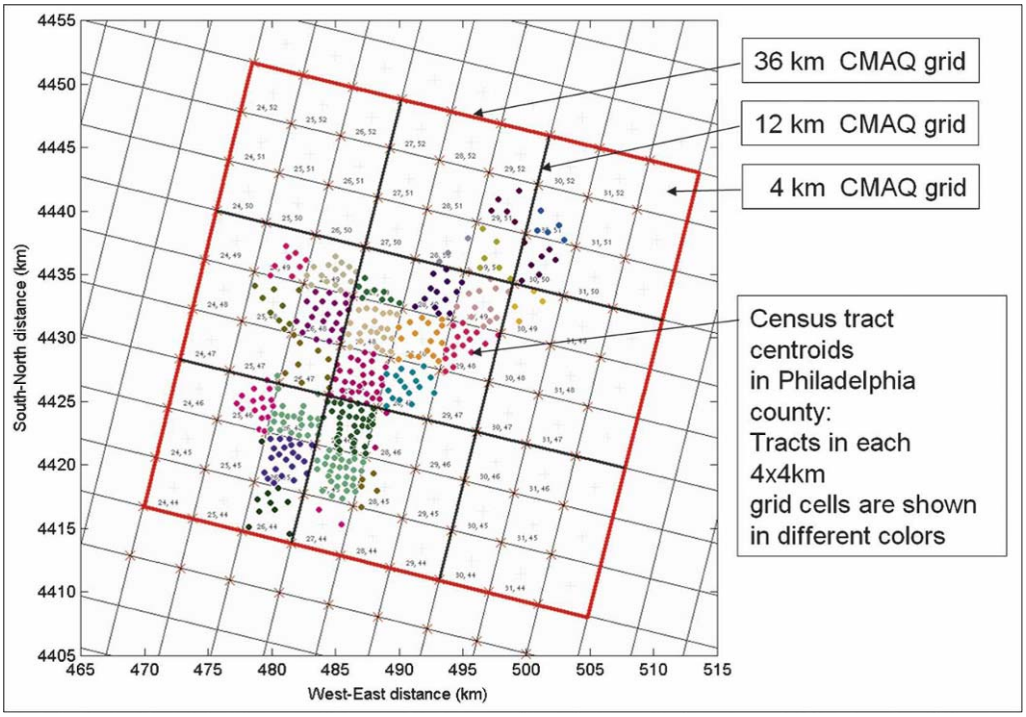
Measurement Error for Personal Exposure Monitors

PEMs are primarily used in panel exposure studies to measure total exposure to PM (e.g., Cohen et al., 2009, 190639; Elgethun et al., 2003, 190640; Johnson et al., 2000, 001660; Olson and Burke, 2006, 189951). PEMs are specialized monitors that, because people must carry them, have to

be small, light, quiet, and battery operated or passive. As a result, they may have lower face velocities across the filter and lower pressure drops than ambient-based filter measurements of PM, which typically sample at much higher flow rates, and consequently at much higher face velocities. Light scattering measurements are biased when relative humidity is high and are sensitive to size distribution (Lowenthal et al., 1995, 045134; Sioutas et al., 2000, 025223). Positive artifacts resulting from adsorption of vapor-phase organic compounds and negative artifacts from evaporation of semi-volatile PM also create challenges for interpreting personal exposure monitoring data (e.g., Pang et al., 2002, 030353). Olson and Norris (2005, 156005) attributed more OC particle mass collection to face velocity differences when using PEMS compared with FRMs. Data quality of PEMs is described in much greater detail in the 2004 PM AQCD (U.S. EPA, 2004, 056905). The artifacts listed here could result in either negative or positive sampling bias.

3.8.6.2. Model-Related Errors

When models are used in lieu of or to supplement measurements of ambient PM exposure or community-based ambient PM concentration, it is important to identify errors and uncertainties that could affect estimates of PM-related health effects. Model-related errors are determined by four factors: representativeness of the mathematical model, accuracy of model inputs, scale of model resolution, and model sensitivity. If verification errors related to these four factors are minimized, then the model can be evaluated against physical data to determine how well the model truly captures a real situation (Roache, 1998, 156915). Detail of the model design and inputs can have significant impact on validation, as observed in Meng et al.(2005, 058595) and Hering (2007, 155839). Meng et al. (2005, 058595) demonstrated how use of an increasingly more detailed mathematical model decreases the variability of the results with respect to modeled indoor $PM_{2.5}$ concentration of outdoor origin and to modeled infiltration factor. Hering (2007, 155839) compared infiltration model results for PM-based EC, NO_3^-, and SO_4^{2-}. Model inputs were from a central site monitor only, central site monitor with air exchange data, and detailed inputs related to initial outdoor (outside test building) and indoor concentrations. Use of more detailed inputs resulted in significant reductions in error for indoor EC concentration, smaller improvements for indoor SO_4^{2-}, and negligible improvement in model results for indoor NO_3^-. This illustrates the impact of differential infiltration discussed in Sections 3.8.4 and 3.8.5.



Source: Reprinted with Permission of ACS from Isakov et al.(2007, 195880).

Figure 3-101. Grid resolution of the CMAQ model in Philadelphia compared with distribution of census tracts in which exposure assessment is performed.

For any spatial interpolation models, grid resolution is another source of error. Isakov et al. (2007, 195880) linked CMAQ with the Hazardous Air Pollutant Exposure Model for exposure assessment in Philadelphia. Their simulation was implemented on a 4 km nested grid within 12 km and 36 km grids to bring the scale of their model from national to urban. However, the census tracts in which Isakov et al. (2007, 195880) sought to describe exposure were distributed on a much finer scale (Figure 3-101). They supplemented the CMAQ model with an Industrial Source Complex Short Term (ISCST) dispersion model to resolve the subgrid scale behavior. If concentrations were averaged across the cell in lieu of a more detailed subgrid representation, Isakov et al. (2007, 195880) found that exposures were overestimated by a factor of 2. Appel et al. (2008, 155660) noted that their 36 km simulations provided a closer estimate of SO_4^{2-} aerosol concentration than did their 12 km nested simulation, which overestimated concentrations. Hogrefe et al. (2007, 156561) also noted overestimation of the CMAQ model at the 12 km scale, where multiple point interpolation was used to obtain subgrid estimates. Model convergence theory would suggest that the 36 km simulation is not actually more accurate but coincidentally closer to the observed concentrations (Roache, 1998, 156915). It is possible that if secondary pollutants are more regionally dispersed, lower spatial resolution would be required to attain a converged solution of the spatial concentration field. However, higher spatial resolution in the simulation should produce very similar results if the solution is convergent.

Use of geospatial statistical methods for grid interpolation, as performed in the SHEDS/MENTOR simulation by Georgopoulos et al. (2005, 080269), provides another methodology for grid interpolation. Similar to Isakov et al.(2007, 195880), Georgopoulos et al. (2005, 080269) linked CMAQ with an exposure model for estimation of neighborhood-scale exposures using a 4 km resolution grid nested within 12 km and 36 km grids. The authors found that CMAQ underestimated $PM_{2.5}$ concentration at many times during the simulation. Kim et al. (2009, 188446) compared results from an exposure model using six different levels of spatial resolution. The model predicted $PM_{2.5}$ at monitor locations as a function of the mean concentration and spatial and random errors. The 6 levels of spatial resolution were simulated through assignment of the spatial and random error terms and by defining the distance over which spatial errors are correlated.

Between monitors, Kim et al. (2009, 188446) compared results from assigning nearest monitor values and from kriging. They found that model prediction error and bias in health effects estimates decreased with increased spatial resolution of the error terms, as well as with kriging over a nearest monitor scheme.

For GIS-based models designed to improve spatial resolution of exposure estimates, Yanosky et al. (2008, 099467) described three sources from which they derived an estimate of total model uncertainty: transient model components, stationary model components, and residual spatial and temporal components of variance. When analyzing relative contributions to uncertainty, they found that unexplained local spatial variability was the largest contributor. With model inputs from PM_{10} monitors for this study, poor model performance and high uncertainty were observed where monitors were sparsely located. High uncertainties were also calculated in a few select urban areas (New York City, Detroit, Cleveland, and Pittsburgh) where concentrations tend to be higher, although the latter may have been related to the Taylor series approximation used for the residual uncertainty term. Spatial and temporal uncertainties were also reduced when temporal resolution was increased in the model implementation.

In his review of various exposure assessment modeling techniques, Jerrett et al. (2005, 092864) reviewed source proximity and LUR for application to exposure assessment. The literature contains mixed evidence of the association between health effects and source proximity (e.g., Langholz et al., 2002, 191771; Maheswaran and Elliott, 2003, 125271; Venn et al., 2000, 007895; Venn et al., 2001, 023644). Jerrett et al. (2005, 092864) contend that source proximity modeling is limited because other confounding covariates, such as SES, may be related to source proximity. Additionally, subjects' time-activity patterns may vary from locations modeled through source proximity. Wind direction and topography may bring PM plumes away from a site located even in very close proximity to the source, so that high concentrations would be found at distances far downwind of a source. Jerrett et al. (2005, 092864) state that LUR is an adaptable framework allowing adaptation to localized conditions, but they caution that LUR is limited to fairly homogeneous spatial regions. They point to Briggs' (2000, 191772) simulation of Amsterdam as an example of LUR surfaces produced with little spatial variability.

LUR and kriging were both used in the ACS data reanalysis by Krewski et al. (2009, 191193) to study mortality as a function of spatial variability in $PM_{2.5}$ in New York and Los Angeles, as described in Section 3.8.3.4. The LUR solution produced some observed overpredictions near freeways. Kriged results were compared with LUR for both cities. For New York City, kriging produced slightly attenuated mortality risk estimates, while for Los Angeles, kriging did not exhibit as much spatial variability as LUR. The latter may be due to the fact that the monitoring network in Los Angeles was not situated to capture spatial variability in $PM_{2.5}$ concentration occurring near areas of high traffic. Despite similarities in the LUR performance, health effects predictions were quite different for New York City and Los Angeles, with increased hazard ratios of 1.56 and 1.39, respectively using the same LUR covariates. Krewski et al. (2009, 191193) noted that in New York City, the healthiest (and wealthiest) segment of the population lived in the most polluted areas, while in Los Angeles, there was a strong association between pollution and mortality. This finding implies that, because geographic regions may differ by multiple factors, such as building and power plant fuel use, roadway design, traffic patterns, and building design, significant variables in an LUR analysis may also differ by region.

3.8.6.3. Spatial Variability

For PM, spatial and temporal distribution as a function of particle size and composition also plays a large role in the selection of an exposure model. For instance, use of Equation 3-6 might be employed for a study of ambient $PM_{2.5}$ exposure because spatial variability in $PM_{2.5}$ concentration can be low over urban to regional scales in comparison with more spatially variable $PM_{10-2.5}$ and UFPs, as described in Section 3.8.4. Spatial issues leading to exposure misclassification are discussed below.

In panel studies, exposure error will be introduced if the ambient PM concentration measured at the central site monitor is used as an exposure surrogate and differs from the actual ambient PM concentration outside a subject's residence and/or worksite. Filleul et al. (2006, 089862) computed exposure based on varying contributions of community-based ambient monitors (deemed background) and proximal monitors (to represent a receptor) in Le Havre, France for black smoke measurements. They found that using a weighted mean with increasing weight for proximal monitors

resulted in non-significant but increased mean exposure estimates. Moore et al.'s (2009, 191004) finding of high variability in UFPs across Los Angeles also suggests that exposure error would occur from using one or a few UFP monitors. In an example using AQS data, PM_{10} monitors in the Chicago CSA are south of the most populated areas within Chicago (Figure A-8 in Annex A), where intersampler correlations for urban scale PM_{10} data for several monitor pairs are below 0.4 (Table A-23 in Annex A). In another example from AQS data, $PM_{2.5}$ and PM_{10} monitor locations in the Riverside CBSA are shown to correspond more closely with higher population density areas (Figures A-25 and A-26 in Annex A), where urban scale intersampler correlations for both $PM_{2.5}$ and PM_{10} are below 0.4 for several monitor pairs. For most cities, intersampler correlation is much higher for $PM_{2.5}$ than for PM_{10}. This is in accord with the findings of Sarnat et al. (2009, 180084) where, in an Atlanta time-series study of the effect of spatial variation in concentration on epidemiologic associations, spatially homogeneous $PM_{2.5}$ and O_3 were found to be consistently associated with emergency room visits using any monitor within the study area, while associations were less consistent across monitors for spatially heterogeneous CO and NO_2 among the entire population studied. Considering results reported in the literature along with inter-sampler correlations (reported in Annex A, Section A.2 for $PM_{2.5}$ and PM_{10}, and their corresponding monitor locations shown in Annex A, Section A.1), the magnitude of spatial exposure error likely depends on particle size as well as monitor location, source location, and characteristics such as urban and natural topography and meteorological trends.

Spatial variability among various studies further suggests that use of a single or small number of ambient monitors introduces uncertainty in exposure assessment panel studies. Violante et al. (2006, 156140) studied personal exposures to traffic of parking police in Bologna, Italy to determine how personal exposure to outdoor PM_{10} and benzene compares with that measured at a community-based monitor. This study found that personal exposures to PM_{10} were significantly higher than at the community-based monitor, although the authors were not able to demonstrate significant effects of meteorology or traffic on those exposures. Nerriere et al. (2007, 156801) observed spatial heterogeneity of personal exposures to metals in $PM_{2.5}$ and PM_{10}, with higher levels found near high-traffic and industrial areas. In a Bayesian hierarchical model analysis of personal exposure and ambient $PM_{2.5}$ data from the pilot Baltimore Epidemiology-Exposure Panel Study of 16 subjects, McBride et al. (2007, 124058) showed that community monitors overestimated personal exposures for the panel subjects, and that these results were not sensitive to model selection.

For community time-series epidemiology, the community-average concentration, not the concentration at each fixed monitoring site, is the concentration variable of concern (Zeger et al., 2000, 001949). Because variation in trends is of interest, bias in the central site monitor data will not affect health effects estimates unless the central site monitor is not correlated with the community-average concentration. The latter condition will cause the health effect estimate to be biased towards the null (Sheppard et al., 2005, 079176). The correlation between the concentration at a central community ambient monitor and the community-average concentration depends on homogeneity of the spatial distribution and representativeness of the central-site monitor location. Kim et al. (2005, 083181) noted that spatial variability among PM species can add uncertainty to exposure estimates in community time-series epidemiology studies exploring source contributions to health effects. The monitoring site is selected to represent the community average of the PM characteristic (mass and/or species) of interest. If the selected site is far from PM sources, then the average measurement may be lower than actual ambient PM concentrations. Likewise, if the site is selected to measure a "hot spot" or pollution from a nearby source, exposure estimates across the community could be skewed upwards.

Intra-urban spatial heterogeneity could affect health effects estimates derived from community time-series studies if a community is divided by urban or natural topographic features or by source locations into several sub-communities that differ in the temporal pattern of pollution. Intra-urban spatial heterogeneity is discussed in detail in Section 3.5. Community exposure may not be well-represented when monitors cover large areas with several sub-communities having different sources and topographies. This point is illustrated for Los Angeles in Figure 3-27 and Figure 3-37 where intersampler correlation decreases with respect to distance moreso than for other cities shown. Using zip code classified mortality data in a study of SES and acute cardiovascular mortality in Phoenix, high risk ratios were computed when a small area near the monitoring site was studied (Mar et al., 2003, 042841; Wilson et al., 2007, 157149), while use of larger-area county-wide data produced non-significant associations (Moolgavkar, 2000, 010305; Smith et al., 2000, 010335). At least part of the heterogeneity found between cities in multicity studies may be due to the use of a large

geographic area that is composed of several sub-communities that differ in the spatiotemporal distribution of air pollutants. Note that when zip codes cover large areas (e.g., in western mountain states) or when counties cover small areas (e.g., in the northeast), then assumptions change regarding use of zip code- or county-level data for epidemiologic studies. For all metropolitan areas investigated in this assessment, the PM_{10} data have significantly more scatter than $PM_{2.5}$. This suggests that the uncertainty of the community average concentration would increase in the coarse PM range. Metrics have been developed and used to compare the spatial variability of air pollutants (Wongphatarakul et al., 1998, 049281). These metrics are useful in assessing the potential for exposure error in the epidemiologic studies, especially when different monitors are used on different days to construct city-wide averages.

Epidemiologic studies of long-term exposure rely on differences among communities in long-term average ambient concentrations. If exposure errors are different in the different communities, the differences in long-term ambient concentrations among communities may not represent the differences in long-term average exposures (Dockery et al., 1993, 044457). Thus, in a regression of health effects against average concentration as an indicator for average exposure, there could be a different magnitude and direction of error in the exposure indicator for each spatial area. This could bias the slope up or down. The following epidemiologic studies, described in detail in Section 7.6, are cited here to illustrate the effect of spatial exposure error on health effects estimates. The Harvard Six-City Study dealt with this issue by design, where the members of the cohort in each city were located in a relatively small area near the monitor (Dockery et al., 1993, 044457). In the ACS study, the spatial area was the Metropolitan Statistical Area (MSA) (Krewski et al., 2000, 012281); other studies have used counties as the spatial area (Enstrom, 2005, 087356; Lipfert et al., 2000, 004087). In a comparison of several of the larger long-term cohort studies, those using county level spatial areas (Enstrom, 2005, 087356; Lipfert et al., 2000, 004087) sometimes did not find significant associations, whereas those using MSAs (Pope et al., 1995, 045159; Pope et al., 2002, 024689) or cities (Dockery et al., 1993, 044457) did find significant associations. Jerrett et al. (2005, 087600) used smaller zip code areas within Los Angeles County and found effects that were both significant and largest in magnitude compared to those reported for other long-term cohort studies. Krewski et al. (2009, 191193) suggested that significant associations between cardiovascular health effects estimates and $PM_{2.5}$ observed in Los Angeles but not in New York City were related to spatial homogeneity of $PM_{2.5}$ concentration in New York City. The Nurses' Health Study examined associations of mortality with PM_{10} and found higher and more significant associations when using estimated concentrations at subjects' individual residences (Puett et al., 2008, 156891) in lieu of county-level concentrations (Fuentes et al., 2006, 097647). These considerations suggest that studies that include large U.S. counties as spatial areas and find no significant associations of health effects with pollution cannot be considered definitive, because the likelihood of exposure error increases in this situation. Reducing the exposure error by using concentrations based on residence address or small zip code areas is associated with larger relative risk than those obtained with county-wide averages of concentrations.

3.8.6.4. Temporal Variability

Temporal Correlation

Concentration time series analyzed for community time-series epidemiologic studies can include those averaged over several monitors, a single monitor used as an estimate of the true community average exposure, or a monitor used to represent nearby exposures. Within a city, lack of correlation of relevant time series at various sites results in smoothing the exposure surrogate concentration function over time and resulting loss of peak structure from the data series. Burnett and Goldberg (2003, 042798) found that community time-series epidemiology results reflect actual population dynamics only when five conditions are met: environmental covariates are fixed spatially but vary temporally; the probability of the health effect estimate is small at any given time; each member of the population has the same probability of the health effect estimate at any given time after adjusting for risk factors; each member of the population is equally affected by environmental covariates; and, if risk factors are averaged across members of the population, they will exhibit smooth temporal variation. For this study, mortality was examined, but the temporal considerations

are generalizable to other health outcomes. Dominici et al. (2000, 005828) note that ensuring correlation between ambient and community-average exposure time series is made difficult by limitations in availability and duration of detailed ambient concentration and exposure time series data and, as a result, is often a source of uncertainty. Sheppard et al. (2005, 079176) also add that the health effect estimate can be biased by time-dependent error in α in a time-series study if the spatial variation in PM concentration is not significant. The direction of bias is related to seasonal correlation between α and C_a.

Seasonality

Community time-series studies can be designed to investigate seasonal effects by incorporating seasonal interaction terms for the exposure surrogate and/or meteorology (e.g., Dominici et al., 2000, 005828). Studies from Section 6.5 are briefly mentioned here to illustrate how seasonal exposures can influence health effect estimates. Bell et al. (2008, 156266) and Peng et al. (2005, 087463) observed higher health effect estimates and stronger seasonal dependence in the northeast than in the rest of the country for $PM_{2.5}$ and PM_{10}, respectively. Peng et al. (2005, 087463) stated that these results generated three hypotheses. First, the PM composition and resulting toxicity might vary with season. Bell et al. (2008, 156266) showed seasonal differences between respiratory and cardiovascular effect estimates that the authors hypothesized related to seasonal differences in dominance of a given PM species. Second, Peng et al. (2005, 087463) suggested that less seasonality in regions other than the northeast may reflect regional tendencies for spending more or less time outdoors. Exposure estimates for time spent outdoors may be less subject to exposure error because uncertainties related to infiltration are not a factor during that time. At the same time, air conditioning usage, which is more common in the summer and in warm climates (Pandian et al., 1998, 090552), has been associated with decreased association between $PM_{2.5}$ and cardiovascular morbidity (Bell et al., 2009, 191007). Third, infectious diseases are more prevalent during winter and so may influence health outcomes. However, it would be expected that regions other than the northeast would be affected by influenza in winter. Uncertainty in sources of seasonal bias may also indicate other unknown factors.

Data Frequency

Most panel and many time-series studies examine the associations of health outcomes only with exposure (or exposure surrogates) on the day of exposure (lag 0). Zanobetti et al. (2000, 004133) and Lokken et al. (2009, 186774) suggest that health effects may not occur until subsequent days or be distributed over several days. When PM measurements are obtained every three or six days, it is difficult to refine the study lag structure down to the day-level. In studies of the effects of short-term $PM_{2.5}$ exposure on cardiovascular and respiratory hospitalization in >200 urban U.S. counties, Bell et al. (2008, 156266) and Dominici et al. (2006, 088398) worked with a combination of air quality measurements obtained daily, those obtained every 3 days, and daily hospitalization data. Time lags of 0, 1, and 2 days were applied, such that $PM_{2.5}$ data obtained only on day 0 would be applied as lag 0 for the corresponding day's hospitalization record, as lag 1 for the next day's hospitalization, and as lag 2 for the following day. No lag 0 data would be available for day 1, and no lag 0 or 1 data would be available for day 2 in this example. This analysis could be performed with sufficient statistical power despite the reduction in days of PM data because a large number of counties were analyzed. Single city studies using data obtained every three or six days could employ the same approach but would lose statistical power compared with daily data because fewer data points would exist for each lag. Likewise, Dominici et al. (2006, 088398) only applied distributed lag analysis to the daily hospitalization data where daily $PM_{2.5}$ concentration data were also available.

3.8.6.5. Use of Surrogates for PM Exposure

Surrogates for Infiltration Tracers

In panel studies, a tracer can be used for PM that infiltrates indoors, such as sulfate as a surrogate for $PM_{2.5}$, as described in Section 3.8.4. For this method to be successful, indoor or other nonambient sources of the tracer must be small compared to ambient sources over the period of sampling. Wallace and Williams (2005, 057485) observed that, because SO_4^{2-} particles are typically smaller than other PM contributing to measurable $PM_{2.5}$ mass, F_{inf} may be biased by using this term to describe $PM_{2.5}$ infiltration. Other concerns in using SO_4^{2-} as a tracer for $PM_{2.5}$ arise because SO_4^{2-} tends to be concentrated in smaller particles and thus it might be a better tracer for fine mode particles than for the coarse fraction at the upper tail of the $PM_{2.5}$ particle size distribution. Volatilization of ammonium nitrate or organic compounds after infiltration of $PM_{2.5}$ indoors results in these components being poor surrogates for ambient PM in exposure estimates (Lunden et al., 2003, 081201).

Use of Ambient PM Concentration in Lieu of Ambient PM Exposure

Ambient PM concentration is often used as a surrogate for exposure to ambient PM in epidemiologic studies. The ambient concentration may be based on measurements made just outside the primary microenvironment, at the nearest community monitor, at a single community monitor, or as the average of several community monitors. Based on the information presented in Section 3.8.4 related to urban-scale PM distribution, there is less exposure error for accumulation mode PM because it has a more homogeneous spatial distribution and higher infiltration indoors, compared with coarse or UFPs. If appropriate measurements are made, it is also possible to estimate the ambient and nonambient components of total personal exposure and use four exposure surrogates in panel epidemiologic studies: C_a, E_T, E_a, and E_{na} (Ebelt et al., 2005, 056907; Koenig et al., 2005, 087384; Strand et al., 2006, 089203; Wilson and Brauer, 2006, 088933). Results from Wilson and Brauer (2006, 088933) showed that exposure error is introduced by 1) using C_a instead of E_a and 2) assuming E_a and E_{na} have the same effects on health outcomes. There was essentially no association of the effect with E_T or E_{na}. Wilson and Brauer (2006, 088933) noted that exposure to nonambient PM will not affect the relationship between C_a and E_a, but "the difference between ambient concentration and ambient exposure will bias the relative risk derived from epidemiologic studies." Strand et al. (2006, 089203) also noted that inclusion of nonambient $PM_{2.5}$ would not be expected to change health effect estimates because ambient and nonambient $PM_{2.5}$ calculations were not correlated.

Zeger et al. (2000, 001949) pointed out that for community time-series epidemiology, it is the correlation of the daily community-average personal exposure to the ambient concentration with daily community-average concentration that is important, not the correlation of each individual's daily exposure with the daily community-average concentration. Thus, the low correlation of individual daily exposure with the daily community-average concentration, as frequently found in pooled panel exposure studies, is not relevant to error in community time-series epidemiologic analysis. Sheppard et al. (2005, 079176) also notes that an insufficient number of total personal exposure samples used in a time-series design would introduce large classical measurement errors related to high variability in E_{na}. Sheppard et al. (2005, 079176) further maintain that these errors can be minimized by using the average concentration measured at community-based ambient monitors. However, overestimation of the community-average exposure by substituting C_a for E_a leads to underestimation of the effect estimate per unit mass of ambient PM. City-to-city variations in the indoor air exchange rate, related to differences in climate or housing stock, will cause city-to-city differences in the health effect endpoint estimate obtained from the study using C_a even if the endpoint remained the same using the community-average exposure.

Relationship between PM and Copollutants

Uncertainties in the composition of multipollutant mixtures of gases and PM to which the population is exposed can introduce uncertainties in health effects estimates. When copollutant associations exist, as described in Section 3.8.5, the potential for one pollutant to act as a surrogate for another pollutant or mix of pollutants introduces uncertainty into epidemiologic models (Sarnat et al., 2001, 019401). For example, O_3 may be an indicator of photochemical oxidation products including organic PM. SO_2 may be an indicator of Ni emissions from smelters, V from oil fired power plants, or As, Se or Hg from coal-fired power plants. In another example, the HEI Report on traffic-related health effects (2009, 191009) lists CO, NO_2, $PM_{2.5}$ and PM_{10} mass, UFP count, EC, benzene, and traffic metrics (e.g., count, fuel consumption) all as potential surrogates for traffic or for the mix of all PM and gaseous pollutants in traffic because all of these pollutants are found in mobile source emissions. Furthermore, in a multipollutant model, transfer of association can occur by an increase in the slope of a confounding copollutant and a concurrent decrease in the slope of the truly causal covariate. This can occur when copollutants are highly correlated with larger error for the true copollutant, smaller error for the confounder, and correlation between the copollutant measurement errors (U.S. EPA, 2004, 056905; Zeger et al., 2000, 001949; Zidek et al., 1996, 051879). For these reasons, this is an important area of uncertainty for interpretation of the multipollutant models discussed in Chapter 6.

3.8.6.6. Compositional Differences

Differences between the composition of ambient PM and the ambient PM that has infiltrated indoors may affect exposure estimates. Numerous differential infiltration studies related to indoor-outdoor changes in size distribution and chemical composition are cited in Sections 3.8.4 and 3.8.5, respectively. If differential infiltration results in differences in PM size distribution and chemical composition between indoor-ambient PM and outdoor-ambient PM, then use of outdoor-ambient PM could bias health effects estimates related to particular species. Baxter et al. (2007, 092726) showed that V tends to have lower F_{inf}, perhaps because metals exist more in the coarse range, while S has F_{inf} close to unity. Epidemiologic studies cited in Section 6.6 indicate that significant associations between health effects estimates and PM trace metal exposures exist and may be modified by season. Trace metal penetration efficiency estimates are thus relevant to those findings. Section 6.6 also discusses significant associations between health effects endpoints and exposure to EC and OC in PM. After initial emission, traffic-related PM is generally in the accumulation mode with volatile components; accumulation mode PM tends to have the highest infiltration factors, but volatile components may be lost during infiltration (Sarnat et al., 2006, 089166). If outdoor residential or central-site measurements are used for an exposure surrogate, differences in indoor and outdoor PM composition related to infiltration could introduce uncertainty into effects estimates.

Ebelt et al. (2005, 056907) illustrated that exposure error occurs when the PM on one or more days is not representative of the normal community PM. Section 6.3.2.1 discusses this COPD panel study of the association between respiratory and cardiovascular measures (i.e., lung function, blood pressure, heart rate, HRV, and ectopic beats) and $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10}. In their analysis, one day of dust from the Gobi Desert caused an increase in the concentration of fine and coarse PM. When this day was deleted from the analysis, the associations of health effects estimates with PM_{10} and especially with $PM_{10-2.5}$ became larger and more significant. Similar peaks in PM_{10} concentration have been observed on the Iberian Peninsula as a result of high transport events carrying dust from the Sahara Desert that could affect epidemiologic associations on given days (Artinano et al., 2001, 190099).

3.8.6.7. Conclusions

This section presents considerations for exposure assessment and the exposure misclassification issues that can potentially affect health effects estimates. These issues can be categorized into six areas: measurement, modeling, spatial variability, temporal variability, use of surrogates for PM exposure, and compositional differences. Potential influences of each of these sources on health effects estimates derived from panel, time-series, and longitudinal epidemiologic studies are described above. Additionally, error sources often interact with each other and are driven

by particle size distribution. For example, fresh diesel-generated PM is characterized by UFPs that dynamically grow and change in chemical composition over short time and spatial scales, and lack of spatial and temporal resolution in measurements or models can result in misclassifying this exposure (Moore et al., 2009, 191004). For this reason, conclusions regarding UFP exposure cannot be drawn from $PM_{2.5}$ concentration data, in part because $PM_{2.5}$ concentration is more spatially homogeneous across a city. In most circumstances, exposure error tends to bias a health effect estimate downward (Sheppard et al., 2005, 079176; Zeger et al., 2000, 001949). Insufficient spatial or temporal resolution to capture true variability and correlation of PM with copollutants are examples of sources of uncertainty that could widen confidence intervals and so potentially reduce the significance of health effects estimates.

3.9. Summary and Conclusions

3.9.1. Concentrations and Sources of Atmospheric PM

This section summarizes sources and concentrations of atmospheric PM. The following summaries cover source characteristics from Section 3.3, measurement techniques from Section 3.4, spacial and temporal variability and copollutant correlations from Section 3.5, source contributions from Section 3.6 and policy relevant background concentrations from Section 3.7.

3.9.1.1. PM Source Characteristics

PM in the atmosphere contains both primary (i.e., emitted directly by sources) and secondary components, which can be anthropogenic or natural in origin. Secondary components are produced by the oxidation of precursor gases such as SO_2 and NO_X and reactions of acidic products with NH_3 and organic compounds. Developments in the chemistry of formation of SOA indicate that oligomers are likely a major component of OC in aerosol samples. Recent observations suggest that small, but still significant quantities of SOA are formed from isoprene oxidation. Gasoline engines have been found to emit a mix of OC, EC, and nucleation-mode heavy and large polycyclic aromatic hydrocarbons on which unspent fuel and trace metals condense, while diesel particles are composed of a soot nucleus on which SO_4^{2-} and hydrocarbons condense. Data from standard emissions tests in which there is insufficient dilution of fresh exhaust from combustion sources tend to overestimate the primary component of organic aerosol at the expense of the semi-volatile components. These semi-volatile components are precursors to secondary organic aerosol formation and their oxidation results in more oxidized forms of SOA than previously considered, both in near source urban environments and further downwind.

3.9.1.2. Measurement Techniques

The federal reference methods for $PM_{2.5}$ and PM_{10} are based on criteria outlined in the CFR. They are, however, subject to several limitations that should be kept in mind when using compliance monitoring data for health outcome studies. FRM methods are subject to the loss of semi-volatile species such as organic compounds and ammonium nitrate (especially in the West). Since FRM gravimetric methods involve 24-h integrated filter samples, no information is available for variations over shorter averaging times. However, methods have been developed to measure real-time $PM_{2.5}$ or PM_{10} mass concentrations (e.g., FDMS-TEOM). New FRMs and FEMs are available for $PM_{10-2.5}$ and various methods (dichotomous samplers, cascade impactors, and passive sampling techniques) are under evaluation to improve $PM_{10-2.5}$ measurements. Techniques are available to characterize UFP mass, surface area, and number concentrations. Continuous and semi-continuous measurement techniques are also available for PM species, such as PILS for multiple ion analysis and AMS for multiple component analysis. Advances have also been achieved in PM organic speciation (e.g., TD-GC/MS).

3.9.1.3. Ambient PM Variability and Correlations

Advances in understanding the spatiotemporal distribution of PM mass and constituents have recently been made, particularly with regard to $PM_{2.5}$ mass and chemical composition and UFP concentrations. Emphasis in this ISA was on the period 2005-2007 so that the most recent validated EPA Air Quality System (AQS) data were used. Note, however, that a majority of U.S. counties were not represented by AQS data since their population fell below the regulatory monitoring threshold for PM. Moreover, monitors reporting to AQS were not uniformly distributed across the U.S. or within counties, and conclusions drawn from AQS data may not apply equally to all parts of a geographic region. Furthermore, biases can exist for some PM constituents (and hence total mass) owing to volatilization losses of nitrates and other semi-volatile compounds, and, conversely, to retention of particle-bound water by hygroscopic species. The degree of spatial variability in PM is likely to be region-specific and strongly influenced by region-specific sources and meteorological and topographic conditions.

Spatial Variability across the U.S.

County-scale, 24-h avg concentration data for $PM_{2.5}$ between 2005-2007 showed considerable variability across the U.S.. The highest reported 3-yr avg concentrations were for six counties within the San Joaquin Valley and inland southern California, as well as Jefferson County, AL (containing Birmingham) and Allegheny County, PA (containing Pittsburgh). The lowest reported annual average $PM_{2.5}$ concentrations were contained within 237 counties distributed throughout many western and northern states as well as Florida and the Carolinas. Of the 15 individual CSAs/CBSAs selected for detailed investigation based on their geographic distribution and importance in recent health effect studies, the highest mean 24-h $PM_{2.5}$ concentrations were reported for Riverside (17 $\mu g/m^3$), Birmingham (16 $\mu g/m^3$) and Pittsburgh (16 $\mu g/m^3$); the lowest were reported for Denver (9 $\mu g/m^3$) and Seattle (9 $\mu g/m^3$).

Since $PM_{10-2.5}$ is not routinely measured and reported to AQS, co-located low-volume PM_{10} and $PM_{2.5}$ measurements from the AQS network were used to investigate the spatial distribution in $PM_{10-2.5}$. Current data coverage (see Figure 3-10) and measurement errors limit the ability to draw any meaningful conclusions regarding the large-scale spatial distribution of $PM_{10-2.5}$ in urban areas. Only 6 of the 15 CSAs/CBSAs chosen for closer investigation had sufficient data for calculating $PM_{10-2.5}$. In general, in the eastern metropolitan areas including Atlanta, Boston, Chicago and New York, most of the mass of PM_{10} was in the $PM_{2.5}$ size fraction, with the highest ratio of $PM_{2.5}$ to $PM_{10-2.5}$ in Chicago (14 $\mu g/m^3$ $PM_{2.5,}$ 5 $\mu g/m^3$ $PM_{10-2.5,}$ ratio = 2.8). In contrast, Denver (9 $\mu g/m^3$ $PM_{2.5}$, 20 $\mu g/m^3$ $PM_{10-2.5}$, ratio = 0.45) and Phoenix (10 $\mu g/m^3$ $PM_{2.5}$, 22 $\mu g/m^3$ $PM_{10-2.5}$, ratio = 0.45) contained most of PM_{10} in the thoracic coarse mode.

Given the limited information available from AQS for $PM_{10-2.5}$ and the current National Ambient Air Quality Standard for PM_{10}, analyses were performed on the more prevalent PM_{10} data acknowledging that PM_{10} incorporates both thoracic coarse and fine particles. The highest reported 3-yr avg PM_{10} concentrations (>51 $\mu g/m^3$) occurred in two counties in southern California and five counties in southern Arizona and central New Mexico. The lowest reported annual average PM_{10} concentrations ($\leq$ 20 $\mu g/m^3$) were within 114 counties distributed fairly uniformly across the U.S. Of the 15 CSAs/CBSAs investigated, the highest mean 24-h PM_{10} concentrations was reported for Phoenix (52 $\mu g/m^3$), considerably higher than the means for the other CSAs/CBSAs investigated. The lowest was reported for Boston (17 $\mu g/m^3$) with New York, Philadelphia and Seattle only slightly higher (19 $\mu g/m^3$).

Spatial variability in $PM_{2.5}$ components obtained from the CSN varied considerably by species. The highest annual average OC concentrations (>5 $\mu g/m^3$) were observed in the western and southeastern U.S. Concentrations in the West peaked in the fall and winter, while concentrations in the Southeast peaked anytime between spring and fall. Of the 15 CSAs/CBSAs investigated, OC was the dominant $PM_{2.5}$ component on an annual basis in the western cities, ranging from 34% of $PM_{2.5}$ mass in Los Angeles to 58% in Seattle. EC exhibited less seasonal variability than OC and was particularly stable in the eastern half of the U.S. Annual average EC concentrations greater than 1.5 $\mu g/m^3$ were present in Los Angeles, Pittsburgh, New York and El Paso. Concentrations of SO_4^{2-} were higher in the eastern U.S. resulting from higher SO_2 emissions in the East compared with the West. There is also considerable seasonal variability with higher SO_4^{2-} concentrations in the summer months when the oxidation of SO_2 proceeds at a faster rate than during the winter. Of the 15

CSAs/CBSAs selected, sulfate was the dominant $PM_{2.5}$ component on an annual basis in the eastern cities, ranging from 42% of $PM_{2.5}$ mass in Chicago to 56% in Pittsburgh. NO_3^- concentrations were highest in California, with annual averages >4 $\mu g/m^3$ at many monitoring locations. There were also elevated concentrations of NO_3^- in the Midwest (>2 $\mu g/m^3$), with wintertime concentrations exceeding 4 $\mu g/m^3$. In general, NO_3^- was higher in the winter across the country, resulting from a number of factors including: (1) lower temperatures which favor partitioning into particles; (2) higher relative humidity, mainly in dry areas; (3) lower sulfate, allowing higher uptake of NO_3^-; and (4) residential wood burning in specific areas of the U.S., especially in the Northwest. Exceptions existed in Los Angeles and Riverside, where high NO_3^- readings appeared year-round. Crustal material constituted a substantial fraction of $PM_{2.5}$ year-round in Phoenix (28%) and Denver (16%), and during the summer in Houston (26%).

Clearly there are variations in both $PM_{2.5}$ mass and composition by city resulting from numerous controlling variables (e.g., meteorology, the nature of sources, proximity to sources, topography). These variables are frequently poorly characterized on a broad scale, making it difficult to draw general conclusions regarding $PM_{2.5}$ mass and composition across all cities within a given geographic region.

Spatial Variability on the Urban and Neighborhood Scales

In general, $PM_{2.5}$ has a longer atmospheric lifetime than $PM_{10-2.5}$ because larger particles have a higher gravitational settling velocity. For $PM_{2.5}$, most metropolitan areas exhibited high correlations (generally >0.75) between monitoring sites out to a distance of 100 km. Notable exceptions were Denver, Los Angeles and Riverside where correlations dropped below 0.75 somewhere between 20 and 50 km. Insufficient data were available in the 15 metropolitan areas to perform similar analyses for $PM_{10-2.5}$ using co-located, low volume FRM monitors. More abundant PM_{10} data, however, showed larger declines in inter-monitor correlations as a function of distance relative to $PM_{2.5}$. Atlanta, Boston, Denver, Los Angeles, New York City, Philadelphia, Phoenix, Pittsburgh and Riverside all showed an average correlation of 0.75 at 40 km or greater monitor separation while Birmingham, Chicago, Detroit, Houston and St. Louis had correlations that dropped off much more quickly with distance (average correlation of 0.75 at 6 km or less monitor separation). Furthermore, correlations between PM_{10} concentrations exhibited substantially more scatter relative to $PM_{2.5}$. Shorter atmospheric lifetimes for PM_{10} can result in local emission sources dominating PM_{10} annual average mass concentrations at particular monitors. Although the general understanding of PM differential settling leads to an expectation of greater spatial heterogeneity in the $PM_{10-2.5}$ fraction relative to the $PM_{2.5}$ fraction in urban areas, deposition of particles as a function of size depends strongly on local meteorological conditions, in particular on the degree of turbulence in the mixing layer. Therefore, the findings from these 15 CSAs/CBSAs may not apply to all locations or at all times.

Population density and associated building density are also important determinants of the spatial distribution of PM concentrations. Inter-sampler correlations as a function of distance between monitors obtained for sampler pairs located less than 4 km apart (i.e., on a neighborhood scale) showed a shallower slope for $PM_{2.5}$ than for PM_{10}. The average correlation was 0.93 for $PM_{2.5}$, but it dropped to 0.70 for PM_{10}.

Few studies have performed direct comparisons of UFP measurements at multiple locations within an urban area. A decrease in the number of UFPs was demonstrated with shifts from a dominant mode at around 10 nm within 20 m of a freeway to a flattened dominant mode at around 50 nm at a distance of roughly 100-150 m. At the same time, accumulation mode particle number concentration remained relatively constant to within ~300 m from the freeway. These findings suggest a high degree of spatial heterogeneity in UFPs compared with accumulation mode particles on the urban scale.

3.9.1.4. Temporal Variability

A steady decrease in $PM_{2.5}$ concentrations from 1999 (the beginning of nationwide monitoring for $PM_{2.5}$) to 2007 was observed in all 10 EPA Regions, with the 3-yr avg of the 98th percentile of 24-h $PM_{2.5}$ concentrations dropping 10% over this time period. Similar trends in PM_{10} concentrations show a steady decline from 1988 to 2007 in all 10 EPA Regions.

Using hourly PM observations in the 15 metropolitan areas, diel variation showed peaks that differ by PM size fraction and region. For $PM_{2.5}$, a morning peak was observed starting at approximately 6:00 a.m., corresponding with the start of morning rush hour. There was also an evening $PM_{2.5}$ concentration peak that was broader than the morning peak and extended into the overnight period, likely reflecting a combination of evening rush hour and the concentration increase caused by the usual collapse of the mixed layer after sundown. $PM_{2.5}$ concentrations in Pittsburgh remained elevated throughout the night, obscuring the morning peak. For PM_{10}, all areas showed a morning and afternoon peak in mean concentrations. The magnitude and duration of this peak varied considerably by metropolitan area.

Studies indicate that UFPs in urban environments exhibit similar two-peaked diel patterns in Los Angeles and the San Joaquin Valley as well as in Kawasaki City, Japan and Copenhagen, Denmark. The afternoon peak in UFPs likely represents the combination of primary source emissions such as evening rush-hour traffic and photochemical formation of secondary organic aerosol and sulfate. Comparison between weekdays and Sundays as well as an urban street canyon site and an urban background site in this figure suggest traffic is a major source of UFPs within a street canyon during the morning rush hour. Any fluctuations or changes in the timing of the individual daily peaks during the 3-yr period would result in a broadening of the distribution shown in the diel plots.

3.9.1.5. Correlations between Copollutants

Correlations between PM size fractions and between PM and gaseous copollutants including SO_2, NO_2, CO and O_3 varied both seasonally and spatially between and within metropolitan areas. On average, PM_{10} and $PM_{2.5}$ were correlated with each other better than with the gaseous copollutants. Correlations between PM_{10} and $PM_{10\text{-}2.5}$ were greater in all locations than correlations between $PM_{2.5}$ and $PM_{10\text{-}2.5}$. Correlations between PM_{10} and $PM_{10\text{-}2.5}$ were particularly high in Denver and Phoenix ($r > 0.88$ in all seasons). There was relatively little seasonal variability in the mean correlation between PM in both size fractions and SO_2 and NO_2. CO, however, showed higher correlations with PM_{10} and $PM_{2.5}$ on average in the winter compared with the other seasons. This seasonality results in part because a larger fraction of PM is primary in origin during the winter. To the extent that this primary component of PM is associated with common sources of NO_2 and CO, then higher correlations with these gaseous copollutants are to be expected. Increased atmospheric stability in colder months would also reinforce these associations. The correlation between daily maximum 8-h avg O_3 and PM showed the highest degree of seasonal variability with positive correlations on average in the spring, summer and fall, and negative correlations on average in the winter. This situation arises as the result of seasonal differences in PM primary emissions and photochemical production of secondary $PM_{2.5}$ and O_3.

3.9.1.6. Source Contributions to PM

Results of receptor modeling calculations indicate that $PM_{2.5}$ is produced mainly by combustion of fossil fuel, either by stationary sources or by transportation. It is apparent that a relatively small number of source categories, compared to the total number of chemical species that typically are measured in ambient monitoring source receptor model studies, are needed to account for the majority of the observed mass of PM in these studies. Trying to be more specific about contributions from source categories could result in ambiguity. For example, quite different mobile sources (e.g., trucks and locomotives) rely on diesel power and ancillary data is required to resolve contributions from these sources. A compilation of study results shows that secondary sulfate (mainly from EGUs), nitrate (from the oxidation of NO_X emitted mainly from transportation and EGUs), and primary mobile source categories constitute most of $PM_{2.5}$ (and PM_{10}) in the East. Fugitive dust, found mainly in the $PM_{10\text{-}2.5}$ size range, represents the largest source of ambient PM_{10} in many locations in the western U.S. Quoted uncertainties in the source apportionment of constituents in ambient aerosol samples typically range from 10 to 50%. A comparison of source apportionment techniques indicated that the same major source categories of $PM_{2.5}$ were consistently identified by several independent groups working with the same data sets. Soil-, sulfate-, residual oil-, and salt-associated mass were most clearly identified by the groups. Other sources with more ambiguous signatures, such as vegetative burning and traffic-related emissions were less consistently identified.

Spatial variability in source contributions across urban areas is an important consideration in assessing the likelihood of exposure error in epidemiologic studies relating health endpoints to sources. Concepts similar to those for using ambient concentrations as surrogates for personal exposures apply here. Studies for $PM_{2.5}$ indicate that intra-urban variability increases in the following order: regional (e.g., secondary SO_4^{2-} from EGUs) < area (e.g., on-road mobile sources) < point (e.g., stacks) sources. Only one study was available for $PM_{10-2.5}$, indicating a similar ordering, but without a regional component (resulting from the short lifetime of $PM_{10-2.5}$ compared to transport times on the regional scale).

3.9.1.7. Policy-Relevant Background

The background concentrations of PM that are useful for risk and policy assessments informing decisions about the NAAQS are referred to as policy-relevant background (PRB) concentrations. PRB concentrations have historically been defined by EPA as those concentrations that would occur in the U.S. in the absence of anthropogenic emissions in continental North America defined here as the U.S., Canada, and Mexico. For this document, PRB concentrations include contributions from natural sources everywhere in the world and from anthropogenic sources outside continental North America. Background concentrations so defined facilitated separation of pollution that can be controlled by U.S. regulations or through international agreements with neighboring countries from those that were judged to be generally uncontrollable by the U.S. Over time consideration of potential broader ranging international agreements may lead to alternative determinations of which PM source contributions should be considered by EPA as part of PRB. Contributions to PRB concentrations of PM include both primary and secondary natural and anthropogenic components. For this document, PRB concentrations for the continental U.S. were estimated using EPA's CMAQ modeling system, a deterministic CTM and with GEOS-Chem, a global-scale model for CMAQ boundary conditions. PRB concentrations of $PM_{2.5}$ were estimated to be less than 1 $\mu g/m^3$ on an annual basis, with maximum daily average values in a range from 3.1 to 20 $\mu g/m^3$ and having a peak of 63 $\mu g/m^3$ at the nine national park sites across the U.S. used to evaluate model performance for this analysis. For further information on methods used in modeling of PRB concentrations see Section 3.6, and for further information on the results of calculation of PRB concentrations see Section 3.7.

3.9.2. Human Exposure

This section summarizes the findings from the recent exposure assessment literature, which include the assessment of exposure to ambient PM, infiltration of ambient PM to indoor environments, and source apportionment of PM exposure. This summary is intended to support the interpretation of the findings from epidemiologic studies. For more detailed explication see Section 3.8.

3.9.2.1. Characterizing Human Exposure

A number of techniques have been applied in the literature to model human exposure to PM. Several studies have used time-weighted microenvironmental models to define total or ambient PM exposure. Time-activity diaries or global positioning systems have been employed to capture the time-basis for those models. Stochastic population exposure models, such as APEX and SHEDS, are applied for PM exposure risk assessment among the population. Concentrations from chemistry transport models have also been used to provide input to the stochastic exposure models at particular locations. LUR models have been applied for individual exposures at the intra-urban scale to examine exposure to pollution surrogates, such as traffic counts, land use, or topographic variables. Source proximity and kriging have also been applied. GIS-based models have been used to model exposure over large regions (e.g., for the Nurse's Health Study) using spatial smoothing models of AQS data and incorporating GIS-based and meteorological covariates. GIS approaches have also been used for intra-urban scale exposure studies. These methods all have their own uses and caveats. LUR is an adaptable framework allowing adaptation to localized conditions but might best be applied in relatively spatially homogeneous areas. In a comparison of LUR with kriging, kriging produced slightly attenuated mortality risk estimates for New York City, while for Los Angeles,

kriging did not exhibit as much spatial variability as LUR. Source proximity modeling is relatively simple to apply but is limited because other confounding covariates, such as socioeconomic status, may be related to source proximity. Additionally, source proximity models do not incorporate time-activity data.

New advancements in personal and microenvironmental monitoring techniques have been reported. Personal monitoring developments include new models of cascade impactors and cyclones to sample in the UF size range and miniature monitors for species detection. Additionally, new work on microenvironmental modeling using mobile platforms and GPS technology has been reported. The reader is referred to the 2004 PM AQCD (U.S. EPA, 2004, 056905) for descriptions of most real-time and filter-based personal and microenvironmental PM monitors currently available.

3.9.2.2. Spatial Scales of PM Exposure Assessment

Assessing population-level exposure at the urban scale is particularly relevant for time-series epidemiologic studies, which provide information on the relationship between health effects and community-average exposure, rather than variations in individual exposure. The correlation between the PM concentration measured at a central-site community ambient monitor and the true community average concentration depends on the spatial distribution of the PM, location of the monitoring site chosen to represent the community average, and division of the community by terrain features or source locations into several sub-communities that differ in the temporal pattern of pollution. Concentrations of SO_4^{2-} and some components of SOA measured at central-site monitors are expected to be uniform in urban areas given the regional nature of their sources. However, this is not true for primary components like EC whose sources are strongly spatially variable in urban areas. Given that roughly 90% of an individual's day is spent indoors, assessment of exposure to infiltrated ambient SO_4^{2-}, whose formation and dispersion also occurs over urban-to-regional scales and whose size distribution is in the accumulation mode, is commonly used to assess ambient $PM_{2.5}$ exposure. This technique has also been applied to assess $PM_{10-2.5}$ exposure but likely with more error than for $PM_{2.5}$ because $PM_{10-2.5}$ is more highly spatially variable than $PM_{2.5}$. Source apportionment techniques have also been applied to assess urban-scale $PM_{2.5}$ exposures using community-based ambient monitoring, outdoor, and indoor samples.

At micro-to-neighborhood scales, heterogeneity of sources and topography may cause more variability in exposure. This is particularly true for $PM_{10-2.5}$ and for UFPs, both of which are more highly spatially variable than $PM_{2.5.}$ Particle chemistry and source behavior also contribute to spatial heterogeneity of PM concentration. Some studies, conducted mainly in Europe, have found personal $PM_{2.5}$ and PM_{10} exposures for pedestrians in street canyons to be higher than ambient concentrations measured by urban background ambient monitors. Likewise, microenvironmental UFP concentrations were observed to be substantially higher in near-road environments, street canyons, and tunnels when compared with other environments in urban areas. In-vehicle UFP exposures can also be important. As a result, ambient monitors located at background, central urban, road side, or near-residential sites might not reflect peak exposures to individuals who commute.

PM infiltration factors, F_{inf}, depend on particle size, chemical composition, season, and region of the country. Infiltration can best be modeled dynamically based on a distribution of air exchange and deposition PM loss rates rather than being represented by a single value. There is significant variability within and across regions of the country with respect to indoor exposures to ambient PM. Infiltrated ambient PM concentrations depend in part on the ventilation properties of the building or vehicle in which the person is exposed. Season is important to PM infiltration because it affects the ventilation practices used, and ambient temperature and humidity conditions affect the transport, dispersion, and size distribution of PM. Residential air exchange rates have been observed to be higher in summer for regions with low air conditioning usage, and regional differences in air exchange rates (Southwest < Southeast < Northeast < Northwest) also reflect ventilation practices. Differential infiltration occurs as a function of PM size and composition. PM infiltration is largest for accumulation mode particles, and decreases for UFPs lost to diffusion and for coarse PM lost through inertial impaction mechanisms. Differential infiltration by size fraction can affect exposure estimates if not properly characterized.

3.9.2.3. Multicomponent and Multipollutant PM Exposures

Emission inventories and source apportionment studies suggest that sources of PM exposure vary by region. Comparison of studies performed in the eastern U.S. with studies performed in the western U.S. suggest that the contribution of SO_4^{2-} to personal exposure is higher for the East (16-46%) compared with the West (~4%) and that motor vehicle emissions and secondary NO_3^- are larger sources of personal exposure for the West (~9%) as compared with the East (~4%). Results of source apportionment studies of personal exposure to SO_4^{2-} indicate that personal SO_4^{2-} exposures are mainly attributable to ambient sources. Source apportionment for OC and EC is difficult because they originate from both indoor and outdoor sources. Exposure to OC of indoor and outdoor origin can be distinguished by the presence of aliphatic C-H groups generated indoors, since outdoor concentrations of aliphatic C-H are low. Trace metal studies have shown variable results regarding personal exposure to ambient constituents with significant variation among cities and over seasons that can be related to incinerator operation, fossil fuel combustion, biomass combustion (wildfires), and presence of crustal materials in the built environment, among other sources. Differential infiltration is also affected by variations in particle composition and volatility. For example EC infiltrates more readily than OC. This can lead to outdoor-indoor differentials in PM toxicity.

A number of studies have examined whether gaseous copollutants could act as surrogates for exposure to ambient PM. Several studies have concluded that ambient concentrations of O_3, NO_2, and SO_2 are associated with the ambient component of personal exposure to total $PM_{2.5}$ as opposed to the ambient component of personal exposures to the gases. However, in some studies this result may have arisen in part because personal exposure to the gases was often beneath the detection limits of the personal monitoring devices. Thus, the evidence that ambient gases can be considered surrogates of $PM_{2.5}$ exposure is mixed. It is likely that associations between ambient gases and personal exposure to $PM_{2.5}$ of ambient origin exist, but they are complex and vary by season and location.

3.9.2.4. Implications for Epidemiologic Studies

The importance of exposure error varies with study design based on the spatial and temporal aspects of the design. For PM epidemiology studies, source characteristics, particle size distribution, and particle composition are also important factors in interpreting exposure error for an epidemiology study. Potential sources of error that could influence estimates of PM exposure include measurements, use of surrogates for PM exposure, modeling, spatial variability, temporal variability, and compositional differences.

PM exposure estimates are subject to monitoring and modeling errors. Ambient and personal exposure monitoring errors can bias health effects estimates if the error is strongly correlated with the measurements of concentration. This can be an issue for sampling semi-volatile organic compounds in PM, especially where PM exposures in cities with different PM composition are compared. Ambient monitor height also affects estimates of exposure because PM concentration varies as a function of height. Within a street canyon, changes in wind direction and speed cause significant variability over a small distance. Wind tunnel studies have shown street canyon effects exist for suburban settings as well as for heavily urbanized settings. Additionally, model-based exposure estimates are subject to errors related to the spatial resolution of the modeling technique and the measurement-based inputs used.

Variations in PM and its components could lead to errors in using ambient PM measures as surrogates for PM exposure. $PM_{2.5}$ concentrations are relatively well-correlated across monitors in the urban areas examined. Correlation coefficients tend to be lower, and concentration differences tend to be higher between PM_{10} monitoring sites than between $PM_{2.5}$ monitoring sites. Likewise, studies have shown UFPs to be more spatially variable across urban areas. Even if $PM_{2.5}$, $PM_{10-2.5}$, and UFP concentrations measured at sites within an urban area are highly correlated, significant differences in their concentrations can occur on any given day. The degree of urban-scale spatial variability in PM concentrations varies across the country and with size fraction. Current information suggests that UFPs, $PM_{10-2.5,}$ and many PM components are more spatially variable than $PM_{2.5}$. These factors should be considered in using data obtained from monitoring networks to estimate community-scale human exposure to ambient PM, and caution should be exercised in extrapolating conclusions obtained from one urban area to another.

Community time-series epidemiologic studies use the average community PM concentration as a surrogate for the average personal exposure to ambient PM. The resulting health effect risk estimate, based on the average community ambient concentration, differs from the risk that would be estimated if the average community ambient exposure were used in the epidemiologic study. However, the risk estimate based on the ambient concentration gives the change in health effects resulting from a change in ambient PM concentration and is, therefore, an appropriate measure for risk assessment and risk management. Variations in ambient concentrations across a community, variations in individual ambient exposures around the community average, and seasonal or daily variation in the ambient exposure estimate may increase standard errors of PM health effects estimates, making it more difficult to detect a true underlying association between the correct exposure metric and the health outcome studied. Likewise, sampling time interval and lag time selection both determine whether an epidemiologic model captures the phenomena of interest with sufficient resolution. The use of the community average ambient $PM_{2.5}$ concentration as a surrogate for the community average personal exposure to ambient $PM_{2.5}$ is not expected to change the principal conclusions from $PM_{2.5}$ epidemiologic studies that use community average health and pollution data. Several recent studies support this by showing how the ambient component of personal exposure to $PM_{2.5}$ could be estimated using various tracer and source apportionment techniques and that it is highly correlated with ambient concentrations of $PM_{2.5}$. These studies also show that the non-ambient component of personal exposure to $PM_{2.5}$ is basically uncorrelated with ambient $PM_{2.5}$ concentrations. For long-term studies that use differences in long-term community average ambient PM concentrations as an exposure metric, the effect of possible community-to-community differences in the average ambient exposure factor or in the average non-ambient exposure are less understood. For panel epidemiologic studies, the most appropriate exposure metric may depend on the health outcome measured. However, sufficient information should be obtained to enable determining the association of the health outcome with ambient concentration, ambient exposure, non-ambient exposure, and total personal exposure.

Exposure error may occur if a measured PM component acts as a surrogate for another PM constituent. Differences between composition of outdoor and indoor ambient PM may also cause error in exposure assessment related either to differential losses of UF or coarse PM from diffusion, evaporation of semi-volatile PM, or impaction. The resulting differences in PM size distribution and chemical composition between indoor-ambient PM and outdoor-ambient PM are expected to cause differences in toxicity that could affect health outcomes. Lack of information regarding these relationships adds uncertainty to the health effects estimate.

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Chapter 4. Dosimetry

4.1. Introduction

Particle dosimetry refers to the characterization of deposition, translocation, clearance, and retention of particles and their constituents within the respiratory tract and extrapulmonary tissues. This chapter summarizes basic concepts presented in dosimetry chapters of the 1996 and 2004 PM AQCDs (U.S. EPA, 1996, 079380; U.S. EPA, 2004, 056905), and updates the state of the science based upon new literature appearing since publication of these PM AQCDS. Although the basic understanding of the mechanisms governing deposition and clearance of inhaled particles has not changed, there is significant additional information on the role of certain biological determinants such as gender, age and lung disease on deposition and clearance. Additionally, new studies have further characterized the retention and translocation of ultrafine particles (UFPs; also commonly referred to as nanoparticles) following deposition in the respiratory tract.

The dose from inhaled particles deposited and retained in the respiratory tract is governed by a number of factors. These include exposure concentration and duration, activity and ventilatory parameters, and particle properties (e.g., particle size, hygroscopicity, and solubility in airway fluids and cellular components). The basic characteristics of particles as they relate to deposition and retention, as well as anatomical and physiological factors influencing particle deposition and retention, were discussed in depth in Chapter 10 of 1996 PM AQCD and updated in Chapter 6 of the 2004 PM AQCD. Species differences between humans and rats in particle exposures, deposition patterns, and pulmonary retention were also reviewed in Brown et al. (2005, 089308). The current review of PM dosimetry focuses mainly on issues that may affect the susceptibility of an individual to adverse effects as well as issues that affect our ability to extrapolate findings between studies (e.g., in vitro to in vivo) and between species. Other than a brief overview in this introductory section, the disposition (i.e., deposition, absorption, distribution, metabolism, and elimination) of fibers and unique nano-objects (viz., dots, hollow spheres, rods, fibers, tubes) is not reviewed herein. Substantial exposures to fibers and unique nano-objects generally occur in the occupational settings rather than the ambient environment.

The deposition by interception of micro-sized fibers was briefly discussed in the 1996 and 2004 PM AQCD, but fiber retention in the respiratory tract was not addressed. Airborne fibers (length/diameter ratio ≥ 3), can exceed 150 μm in length and appear to be relatively stable in air. This is because their aerodynamic size is determined predominantly by their diameter, not their length. Fibers longer than 10 μm can deposit by interception and when aligned with the direction of airflow may penetrate deep into the respiratory tract. Once deposited, macrophage mediated clearance is the primary mechanism of removing micro-sized particles from the pulmonary region. The length of fibers can, however, affect their phagocytosis and clearance. For example, fibers of >17 μm in length are too long to be fully engulfed by rat alveolar macrophages and can protrude from macrophages (i.e., macrophage frustration) (Zeidler-Erdely et al., 2006, 190967). Further discussion of the fiber disposition in the respiratory tract is beyond the scope of this chapter.

The term "ultrafine particle" has traditionally been used by the aerosol research and occupational and environmental health communities to describe airborne particles or other laboratory generated aerosols used in toxicological studies that are <100 nm in size (based on physical size, diffusivity, or electrical mobility). Generally consistent with the definition of an UFP, the International Organization for Standardization (ISO) recently defined a nanoparticle as an object with all 3 external dimensions in the nanoscale, i.e., from approximately 1 and 100 nm (ISO, 2008, 190066). The ISO also defined a nano-object as a material with one or more external dimensions in

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Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISA) and the Integrated Risk Information System (IRIS).

the nanoscale. The terms, nanoparticle and UFP, have been used rather synonymously in the recent literature. However, the terms nanoparticle and nano-object are more commonly associated with engineered materials that are created for consumer products and industrial applications. With the current interest in nanotechnologies, many nano-objects have been created by manipulating materials at the atomic or molecular scale for the purpose of forming new materials, structures, and devices that exploit the unique physical and chemical properties associated with their nanoscale. Toxicological studies are becoming available that evaluate in vivo translocation and heath effects unique of nano-objects (viz., dots, hollow spheres, rods, tubes). The in vivo disposition of these unique nano-objects is not, however, necessarily relevant to the behavior of UF aerosols in the urban environment that are created by combustion sources and photochemical formation of secondary organic aerosols. Therefore, the disposition of unique nano-objects (viz., dots, hollow spheres, rods, fibers, tubes) is not considered in this chapter.

4.1.1. Size Characterization of Inhaled Particles

Particle size is a major determinant of the fraction of inhaled particles depositing in and cleared from various regions of the respiratory tract. The distribution of particle sizes in an aerosol is typically described by the lognormal distribution (i.e., the situation in which the logarithms of particle diameter are distributed normally). The geometric mean is the median of the distribution, and the variability around the median is the geometric standard deviation (GSD or σ_g) and is given by:

$$GSD = \sigma_g = \frac{d_{84\%}}{d_{50\%}} = \frac{d_{50\%}}{d_{16\%}}$$

Equation 4-1

where: $d_{16\%}$, $d_{50\%}$, $d_{84\%}$ are the particle diameters associated with the 16th, 50th (i.e., the median), and the 84th percentiles from the cumulative frequency distribution of particle sizes. By definition, GSD must be greater than one. The particle size associated with any percentile of the distribution, d_i, is given by:

$$d_i = d_{50\%}\, \sigma_g^{z(P)}$$

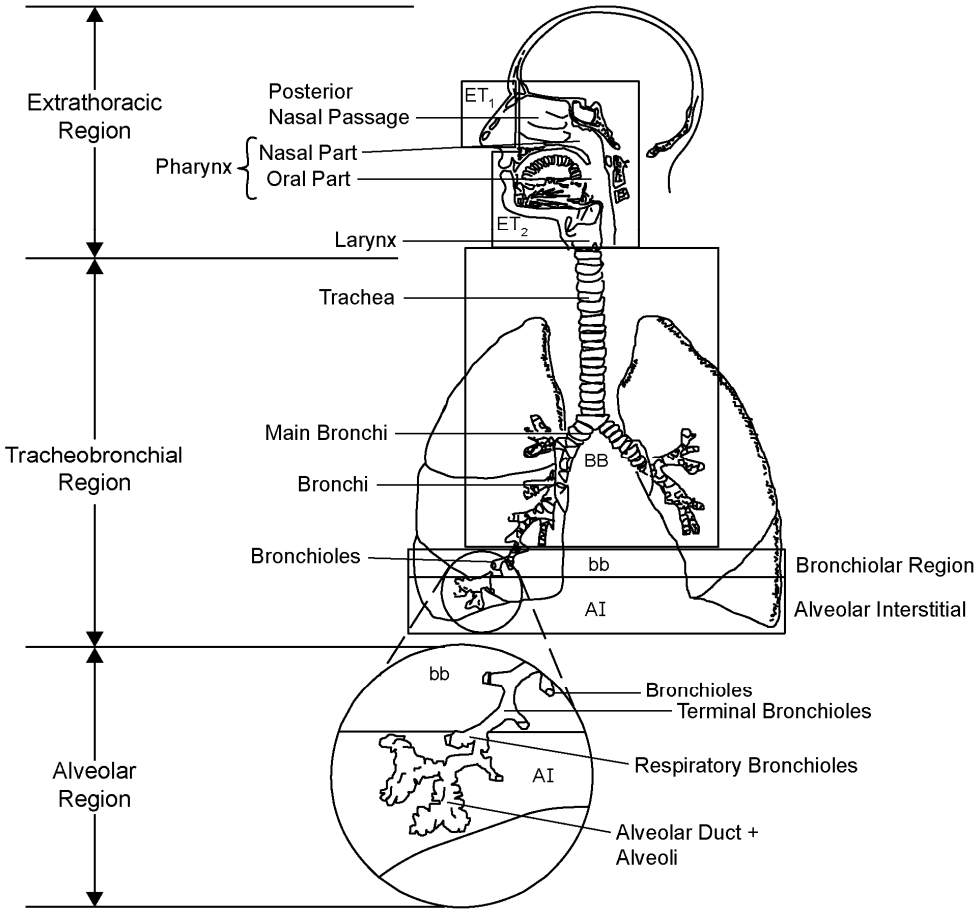
Equation 4-2

where: z(P) is the normal standard deviate for a given probability. In most cases, the aerosols to which people are naturally exposed are polydisperse. By contrast, most experimental studies of particle deposition and clearance in the lung use monodisperse particles (GSD <1.15). Ambient aerosols may also be composed of multiple size modes, each mode should be described by its specific median diameter and GSD.

Aerosol size distributions may be measured and described in various ways. When a distribution is described by counting particles, the median is called the count median diameter (CMD). On the other hand, the median of a distribution based on particle mass in an aerosol is the mass median diameter (MMD). Impaction and sedimentation of particles in the respiratory tract depend on a particle's aerodynamic diameter (d_{ae}), which is the size of a sphere of unit density that has the same terminal settling velocity as the particle of interest. The size distribution is frequently described in terms of d_{ae} as the mass median aerodynamic diameter (MMAD), which is the median of the distribution of mass with respect to aerodynamic equivalent diameter. Alternative descriptions should be used for particles with actual physical sizes below ≈ 0.5 μm because, for these sized particles, aerodynamic properties become less important and diffusion becomes ever more important. For these smaller particles, their physical diameter or CMD are typically used since diffusivity is not a function of particle density. For small irregular shaped particles and aggregates, the diameter of a spherical particle that has the same diffusion coefficient in air as the particle in question is appropriate.

4.1.2. Structure of the Respiratory Tract

The basic structure of the human respiratory tract is illustrated in Figure 4-1. In the literature, the terms extrathoracic (ET) region and upper airways are used synonymously. The term lower airways is used to refer to the intrathoracic airways, i.e., the combination of the tracheobronchial (TB) region which is the conducting airways and the alveolar region which is the functional part or parenchyma of the lung. A recent review of interspecies similarities and differences in the structure and function of the respiratory tract is provided by Phalen et al. (2008, 156865). Although the structure varies, the illustrated anatomic regions are common to all mammalian species with the exception of the respiratory bronchioles. Respiratory bronchioles, the transition region between ciliated and fully alveolated airways, are found in humans, dogs, ferrets, cats, and monkeys. Respiratory bronchioles are absent in rats and mice and abbreviated in hamsters, guinea pigs, oxen, sheep, and pigs. The branching structure of the ciliated bronchi and bronchioles also differs between species from being a rather symmetric and dichotomous branching network of airways in humans to a more monopodial branching network in other mammals.

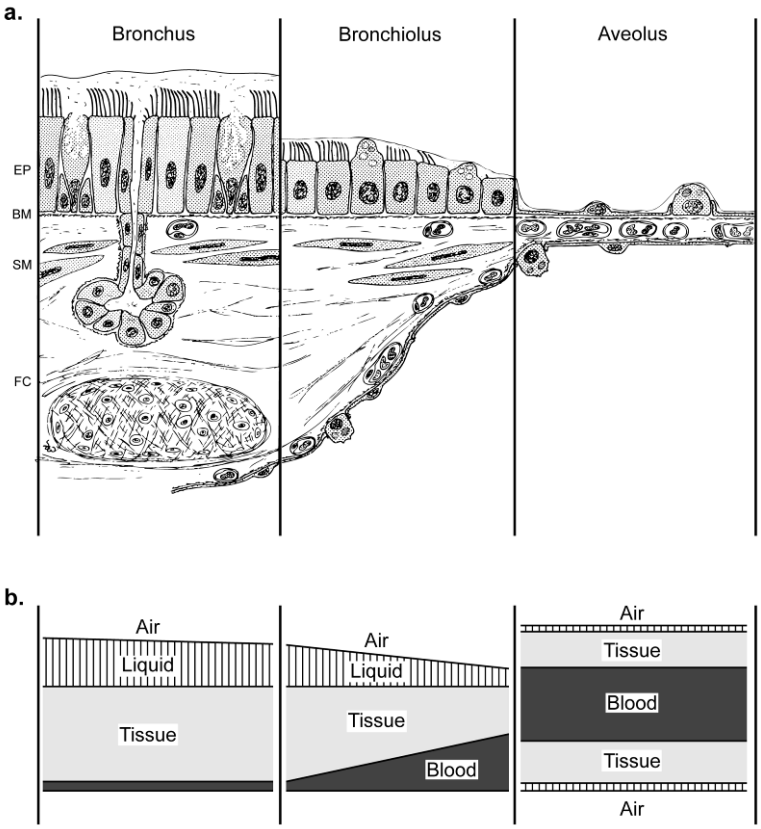


Source: Based on ICRP (1995, 006988).

Figure 4-1. Diagrammatic representation of respiratory tract regions in humans. Structures are anterior nasal passages, ET_1; oral airway and posterior nasal passages, ET_2; bronchial airways, BB; bronchioles, bb; and alveolar interstitial, AI.

Another species difference relevant to particle dosimetry is the route of breathing. For instance, rodents are obligate nose breathers, whereas most humans are oronasal breathers who breathe through the nose when at rest and increasingly through the mouth with increasing activity

level. There is inter-individual variability in the route by which people breathe. Most people, 87% (26 of 30) in the Niinimaa et al. (1981, 071758) study, breathed through their nose until an activity level was reached where they switched to oronasal breathing. Thirteen percent (4 of 30) of the subjects, however, were oronasal breathers even at rest. These two subject groups are commonly referred to in the literature (e.g. ICRP, 1995, 006988) as "normal augmenters" and "mouth breathers," respectively. In contrast to healthy subjects, Chadha et al. (1987, 037365) found that the majority (11 of 12) of patients with asthma or allergic rhinitis breathe oronasally even at rest.



Source: Panel (a) reprinted with permission from McGraw Hill (Fishman and Elias, 1980, 156436)

Figure 4-2. Structure of lower airways with progression from the large airways to the alveolus. Panel (a) illustrates basic airway anatomy. Structures are epithelial cells, EP; basement membrane, BM; smooth muscle cells, SM; and fibrocartilaginous coat, FC. Panel (b) illustrates the relative amounts of liquid, tissue, and blood with distal progression.

The site of particle deposition within the respiratory tract has implications related to lung retention and surface dose of particles as well as potential systemic distribution of particles or their constituents. Figure 4-2 illustrates the progressive change in airway anatomy with distal progression into the lower respiratory tract. In the bronchi there is a thick liquid lining and mucociliary clearance rapidly moves deposited particles toward the mouth. In general, in the bronchi, only highly soluble materials moving from the air into the liquid layer will have systemic access via the blood. With distal progression, the protective liquid lining diminishes and clearance rates slow. Soluble compounds and some poorly soluble UFPs may cross the air-liquid interface to enter the tissues and the blood especially in the alveolar region.

4.2. Particle Deposition

Inhaled particles may be either exhaled or deposited in the ET, TB, or alveolar region. A particle becomes deposited when it moves from the airway lumen to the wall of an airway. The deposition of particles in the respiratory tract depends primarily on inhaled particle size, route of breathing (nasal or oronasal), tidal volume (V_T), breathing frequency (f), and respiratory tract morphology. The distinction between air passing through the nose versus the mouth is important since the nasal passages more effectively remove inhaled particles than the oral passage. Respiratory tract morphology, which affects particle transport and deposition, varies between species, the size of an animal or human, and health status.

The fraction of inhaled aerosol becoming deposited in the human respiratory tract has been measured experimentally. Studies, using light scattering or particle counting techniques to quantify the amount of aerosol in inspired and expired breaths, have characterized total particle deposition for varied breathing conditions and particle sizes. The vast majority of in vivo data on the regional particle deposition has been obtained by scintigraphic methods where external monitors are used to measure gamma emissions from radiolabeled particles. These scintigraphic data have shown highly variable regional deposition with sites of highly localized deposition or "hot spots" in the obstructed lung relative to the healthy lung. Even in the healthy lung, "hot spots" occur in the region of airway bifurcations. Mathematical models aid in predicting the mixed effects of particle size, breathing conditions, and lung volume on total and regional deposition. Experimentally, however, there is considerable inter-individual variability in total and regional deposition even when inhaled particle size and breathing conditions are strictly controlled. Section 4.2.4 on Biological Factors Modulating Deposition provides more detailed information on factors affecting deposition among individuals.

In order to potentially become deposited in the respiratory tract, particles must first be inhaled. The inspirable particulate mass fraction of an aerosol is that fraction of the ambient airborne particles that can enter the uppermost respiratory tract compartment, i.e., the head (Soderholm, 1985, 156992). The American Conference of Governmental Industrial Hygienists (ACGIH) and the International Commission on Radiological Protection (ICRP) have established inhalability criteria for humans (ACGIH, 2005, 156188; ICRP, 1995, 006988). These criteria are indifferent to route of breathing and assume random orientation with respect to wind direction. They are based on experimental inhalability data for $d_{ae} \leq 100$ µm at wind speeds of between 1 and 8 m/s. For the ACGIH criterion, inhalability is 97% for an $d_{ae} = 1$ µm, 87% for an $d_{ae} = 5$ µm, 77% for an $d_{ae} = 10$ µm, and plateaus at 50% for d_{ae} above ~40 µm. The ICRP criterion, which also plateaus at 50% for very large d_{ae}, does not become of real importance until an $d_{ae} = 5$ µm where inhalability is 97%. Dai et al. (2006, 156377) reported slightly lower nasal particle inhalability in humans during moderate exercise than rest (e.g., 89.2 versus 98.1% for 13 µm particles, respectively). Nasal particle inhalability is similar between an adult and 7-year-old child (Hsu and Swift, 1999, 155855). Inhalability into the mouth from calm air in humans also becomes important for d_{ae} >10 µm (Anthony and Flynn, 2006, 155659; Brown, 2005, 156299). Unlike the inhalability from high wind speeds which plateaus at 50% for d_{ae} greater than ~40 µm, particle inhalability from calm air continues to decrease toward zero with increasing d_{ae}.

Inhalability data in laboratory animals, such as rats, are only available for breathing from relatively calm air (velocity ≤ 0.3 m/s). For nasal breathing, inhalability becomes an important consideration for d_{ae} of above 1 µm in rodents and 10 µm in humans (Ménache et al., 1995, 006533). The inhalability of particles having d_{ae} of 2.5, 5, and 10 µm is 80, 65, and 44% in rats, respectively, whereas it only decreases to 96% for an d_{ae} of 10 µm in humans during nasal breathing (Ménache et

al., 1995, 006533). Asgharian et al. (2003, 153068) suggested that an even more rapid decrease in inhalability with increasing d_{ae} may occur in rats. Inhalability is a particularly important consideration for rodent exposures. Section 4.2.3 provides additional discussion of interspecies patterns of particle deposition.

4.2.1. Mechanisms of Deposition

Particle deposition in the lung is predominantly governed by diffusion, impaction, and sedimentation. Most discussion herein focuses on these three dominant mechanisms of deposition. Simple interception, which is an important mechanism of fiber deposition, is not discussed in this chapter. Electrostatic and thermophoretic forces as mechanisms of deposition have not been thoroughly evaluated and receive limited discussion. Some generalizations with regard to deposition by these mechanisms follows, but should not be viewed as absolute rules. Both experimental studies and mathematical models have demonstrated that breathing patterns can dramatically alter regional and total deposition for all sized particles. The combined processes of aerodynamic and diffusive (or thermodynamic) deposition are important for particles in the range of 0.1 μm to 1 μm. Aerodynamic processes predominate above and thermodynamic processes predominate below this range.

Diffusive deposition, by the process of Brownian diffusion, is the primary mechanism of deposition for particles having physical diameters of less than 0.1 μm. For particles having physical diameters of roughly between 0.05 and 0.1 μm, diffusive deposition occurs mainly in the small distal bronchioles and the pulmonary region of the lung. However, with further decreases in particle diameter below ~0.05 μm, increases in particle diffusivity shift more deposition proximally to the bronchi and ET regions.

Governed by inertial or aerodynamic properties, impaction and sedimentation increase with d_{ae}. When a particle has sufficient inertia, it is unable to follow changes in flow direction and strikes a surface thus depositing by the process of impaction. Impaction occurs predominantly at bifurcations in the proximal airways, where linear velocities and secondary eddies are at their highest. Sedimentation, caused by the gravitational settling of a particle, is most important in the distal airways and pulmonary region of the lung. In these regions, residence time is the greatest and the distances that a particle must travel to reach the wall of an airway are minimal.

The electrical charge on some particles may result in an enhanced deposition over what would be expected based on size alone. With an estimated charge of 10-50 negative ions per 0.5 μm particle, Scheuch et al. (1990, 006948) found deposition in humans (V_T = 500 mL, f = 15 min^{-1}) to increase from 13.4% (no charge) to 17.8% (charged). This increase in deposition is thought to result from image charges induced on the surface of the airway by charged particles. Yu (1985, 006963) estimated a charge threshold level above which deposition fractions would be increased of about 12, 30, and 54% for 0.3, 0.6, and 1.0 μm diameter particles, respectively. Electrostatic deposition is generally considered negligible for particles below 0.01 μm because so few of these particles carry a charge at Boltzmann equilibrium. This mechanism is also thought to be a minor contributor to overall particle deposition, but it may be important in some laboratory studies due to specific aerosol generation techniques such as nebulization. Laboratory methods such as passage of aerosols through a Kr-85 charge neutralizer prior to inhalation are commonly used to mitigate this effect.

The National Radiological Protection Board (NRPB) recently evaluated the potential for corona discharges from high voltage power lines to charge particles and enhance particulate doses (NRPB, 2004, 156815). They concluded that electrostatic effects would be the most important for particles in the size range from about 0.1-1 μm, where deposition may theoretically increase by a factor of three to ten. However, given that only a small fraction of ambient particles would pass through the corona to become charged, the small range of relevant particle sizes (0.1-1 μm), and the subsequent required transport of charged particles to expose individuals; the NRPB concluded that effects, if any, of electric fields on particle deposition in the human respiratory tract would likely be minimal.

Thermophoretic forces on particles occur due to temperature differences between respired air and respiratory tract surfaces. Temperature gradients of around 20°C are thought to produce sufficient thermophoretic force to oppose diffusive and electrostatic deposition during inspiration and to perhaps augment deposition by these mechanisms during expiration (Jeffers, 2005, 156608). Thermophoresis is only relevant in the extrathoracic and large bronchi airways and reduces to zero as the temperature gradient decreases deeper in the lung. Theoretical analysis of thermophoresis has been done for smooth walled tubes and is important over distances that are several orders of

magnitude smaller than the diameter of the trachea. The alteration of the flow patterns by airway surface features such as cartilaginous rings may affect particle transport and deposition over far greater distances than thermophoretic force.

4.2.2. Deposition Patterns

Knowledge of sites where particles of different sizes deposit in the respiratory tract and the amount of deposition therein is necessary for understanding and interpreting the health effects associated with exposure to particles. Particles deposited in the various respiratory tract regions are subjected to large differences in clearance mechanisms and pathways and, consequently, retention times. Deposition patterns in the human respiratory tract were described in considerable detail in dosimetry chapters of prior PM AQCD (U.S. EPA, 1996, 079380; U.S. EPA, 2004, 056905); as such, they are only briefly described here.

Predicted total and regional deposition for an adult male during rest and light exercise are illustrated in Figure 4-3 and Figure 4-4, respectively. Note that a large proportion of inhaled coarse particles in the 3-6 μm (d_{ae}) range can reach and deposit in the lower respiratory tract, particularly the TB airways. Although these figures were provided in Chapter 6 of the 2004 PM AQCD, they are reproduced here to illustrate changes in deposition as a function of particle size and breathing conditions. The predictions were based on two publicly available particle deposition models, the ICRP (1995, 006988) and the Multi-Path Particle Dosimetry model (MPPD; Version 1.0, ©2002). The ICRP (1995, 006988) model was implemented by Lung Dose Evaluation Program (LUDEP; Version 2.07, June 2000). The MPPD[1] model was developed by the CIIT Centers for Health Research with support from the Dutch National Institute of Public Health and the Environment.

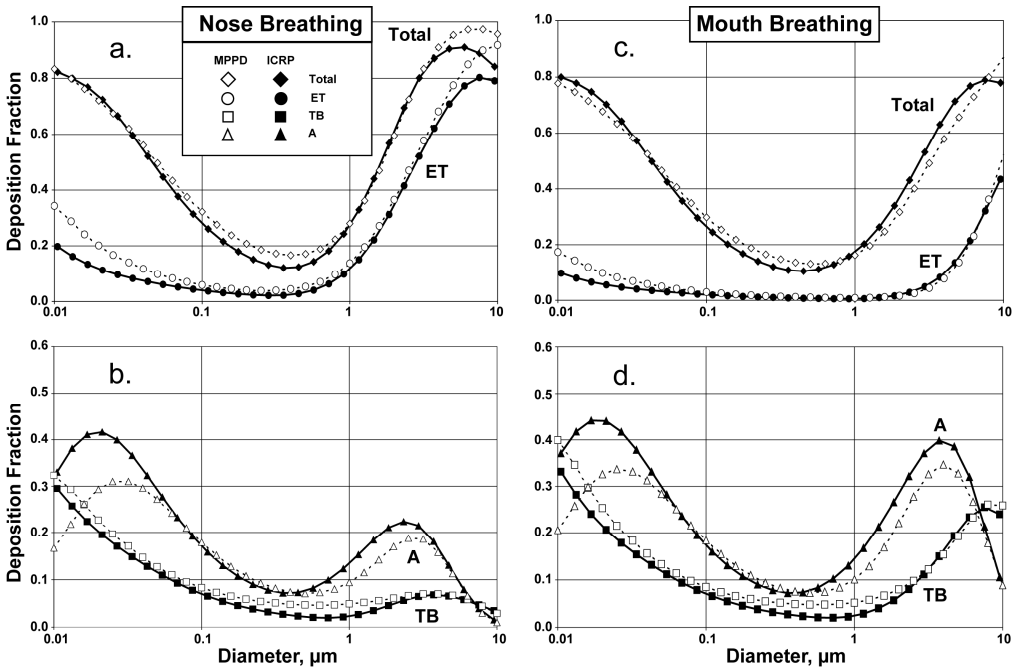


Figure 4-3. Comparison of total and regional deposition results from the ICRP and MPPD models for a resting breathing pattern (V_T = 625 mL, f = 12 min^{-1}) and corrected for particle inhalability. Regions are extrathoracic, ET; tracheobronchial, TB; and alveolar, A. Panels a-b are for nose breathing; panels c-d are for mouth breathing.

[1] For more information about this model, the reader is referred to: http://www.ara.com/products/mppd_capabilities.htm.

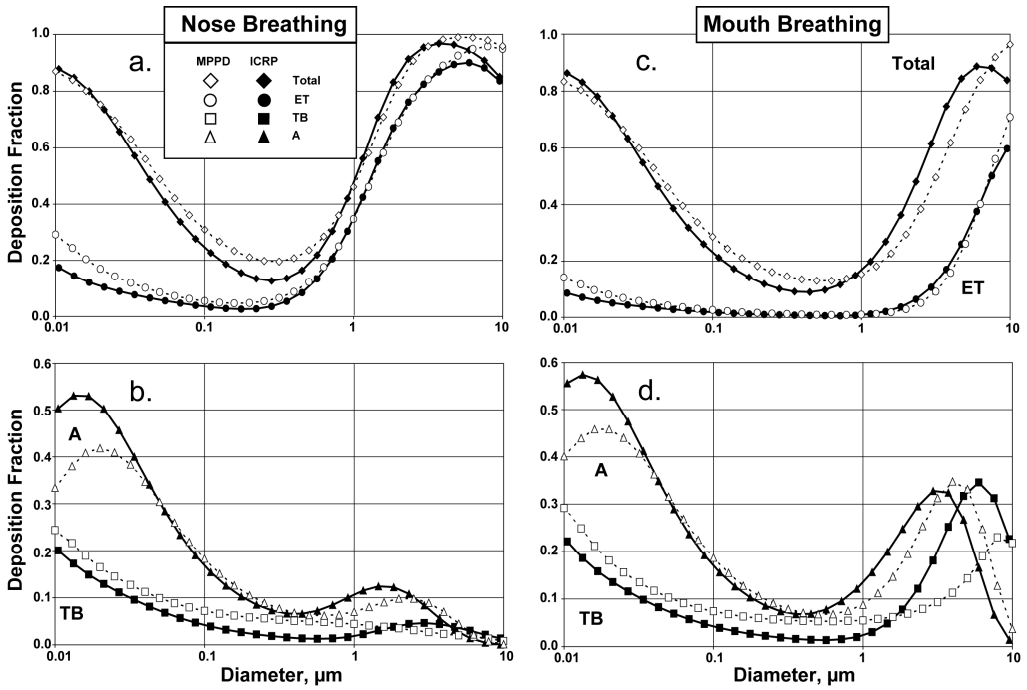
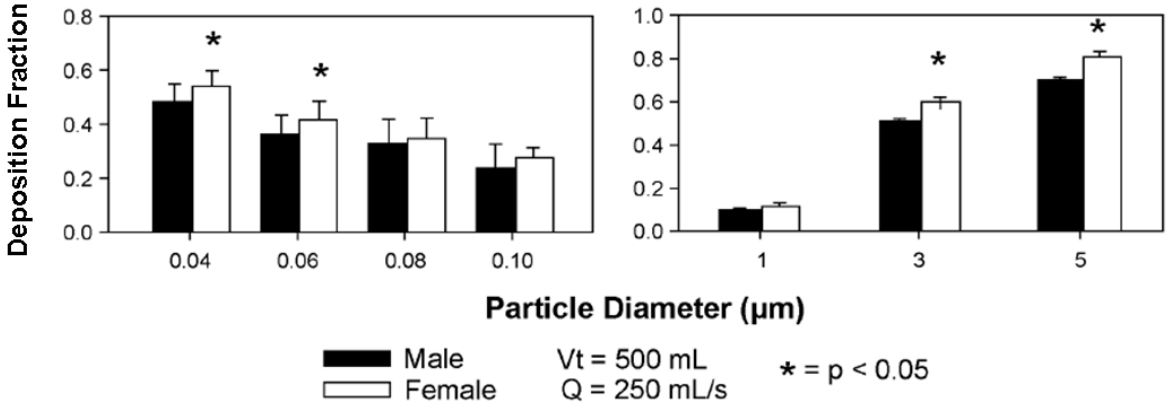


Figure 4-4. Comparison of total and regional deposition results from the ICRP and MPPD models for a light exercise breathing pattern (V_T = 1250 mL, f = 20 min^{-1}) and corrected for particle inhalability. Regions are extrathoracic, ET; tracheobronchial, TB; and alveolar, A. Panels a-b are for nose breathing; panels c-d are for mouth breathing.

4.2.2.1. Total Respiratory Tract Deposition

The efficiency of deposition in the respiratory tract may generally be described as a "U-shaped" curve on a plot of deposition efficiency versus the log of particle diameter. Total deposition shows a minimum for particle diameters in the range of 0.1 to 1.0 µm, where particles are small enough to have minimal sedimentation or impaction and sufficiently large so as to have minimal diffusive deposition. Total deposition does not decrease to zero for any sized particle, in part, because of mixing between particle laden tidal air and residual lung air. The particles mixed into residual air remain in the lung following a breath and are removed on subsequent breaths or gradually deposited. Total deposition approaches 100% for particles of roughly 0.01 µm (physical diameter) due to diffusive deposition and for particles of around 10 µm (d_{ae}) due to the efficiency of sedimentation and impaction.

Total human lung deposition, as a function of particle size, is depicted in Figure 4-5. These experimental data were obtained by using monodisperse spherical test particles in healthy adults during controlled breathing on a mouthpiece. Despite the control of inhaled particle size and breathing conditions, this figure illustrates variability in deposition efficiencies due to inter-individual differences in lung size and anatomical variability in airway dimensions and branching patterns.



Source: Data from Kim and Hu (1998, 086066) and Kim and Jaques (2000, 012811).

Figure 4-5. Total lung deposition measured in healthy adults (UF, 11 M, 11 F, 31 ± 4 yr; fine and coarse, 11 M, 11 F, 25 ± 4 yr) during controlled breathing on a mouthpiece. Deposition calculated from aerosol bolus measurements between 50 and 500 mL into a breath with 50 mL increments. Illustrated data are means and standard errors. Asterisk indicates significantly greater total deposition in females versus males.

4.2.2.2. Extrathoracic Region

The first line of defense for protecting the lower respiratory tract from inhaled particles is the nose and mouth. Particle deposition in the ET region, especially the nasal passages, reduces the amount available for deposition in the TB and alveolar regions. Recent data have become available, but are largely derived from computational fluid dynamics (CFD) modeling and experimental measurements in casts. As most of these studies do not substantially improve our understanding of deposition in the ET region they are not reviewed here.

For particles >1 µm d_{ae}, deposition efficiency in the oral and nasal passages has been generally described as a function of an impaction parameter (Stokes number) with the addition of a flow regime parameter (Reynolds number) for the oral passages (Finlay and Martin, 2008, 155776; Grgic et al., 2004, 155810; Kelly et al., 2005, 155894; Schroeter et al., 2006, 156076). For an adult male, the CFD simulations of Schroeter et al. (2006, 156076) predicted nasal deposition of 10 µm d_{ae} particles was 90%, and 100% for a V_E of 7.5 L/min (rest) and 15 L/min (light activity), respectively. Thus, relatively few large coarse particles will pass through the nasal passages into the lungs. Since the nasal passages are more efficient at removing inhaled particles than the oral passage, an individual's mode of breathing (i.e., oral versus nasal) influences the quantity of particles penetrating to the lung.

In limited studies, it has been shown that children tend to have more oral breathing both at rest and during exercise and also displayed more variability than adults (Becquemin et al., 1999, 155679; Bennett et al., 2008, 156269; James et al., 1997, 042422). In contrast to adults, there is little data on the uptake of particles for oral or nasal breathing in children. Theoretical calculations by Xu and Yu (1986, 072697) predict enhanced deposition of particles (>2 µm) in the head region for children when compared to adults. Studies of fine particle deposition in physical models of the nose, scaled to adult versus children sizes, predict that deposition efficiency in the nose is a function of pressure drop across the nose (Phalen et al., 1989, 156023). Consequently, these model analyses suggest that, when properly scaled physiological flows are used in the calculation of nasal deposition, children, who have higher nasal resistance than adults, should have higher nasal deposition compared to adults. Surprisingly, the few studies reporting measures of nasal deposition in children, found lower nasal deposition efficiencies for fine particles (1-3 µm d_{ae}) as compared to adults, despite their higher nasal resistances (Becquemin et al., 1991, 009187; Bennett et al., 2008, 156269). These findings of lesser nasal versus oral breathing and less efficient nasal deposition suggest that children's lower respiratory tract (i.e., the TB and alveolar regions) may receive a higher dose of

ambient PM compared to adults. Normalized to lung surface area, the dose rate to the lower airways of children versus adults is increased further because children breathe at higher minute ventilations relative to their lung volumes (see Section 4.2.4.2 on age as a factor modulating deposition).

4.2.2.3. Tracheobronchial and Alveolar Region

Inhaled particles passing the ET region enter and may become deposited in the lungs. For any given particle size, the pattern of particle deposition influences clearance by partitioning deposited material among lung regions. Deposition in the tracheobronchial airways and alveolar region cannot be directly measured in vivo. Much of the available deposition data for the TB and alveolar regions have been obtained from experiments with radioactively labeled, poorly soluble particles (U.S. EPA, 1996, 079380) or by use of aerosol bolus techniques (U.S. EPA, 2004, 056905). In general, the ability of these experimental data to define specific sites of particle deposition is limited to anatomically large regions of the respiratory tract such as the head, larynx, bronchi, bronchioles, and alveolar region. Mathematical modeling can provide more refined predictions of deposition sites. Comparisons of the modeling results obtained with two publicly available models were provided in Figure 4-3 and Figure 4-4. Highly localized sites of deposition within the bronchi are described in Section 4.2.2.4. Both experimental and modeling techniques are based on many assumptions that may be relatively good for the healthy lung but not for the diseased lung. For discussion of these issues, the reader is referred to Sections 4.2.4.4 and 4.2.4.5.

4.2.2.4. Localized Deposition Sites

From a toxicological perspective, it is important to realize that not all epithelial cells in an airway will receive the same dose of deposited particles. Localized deposition in the vicinity of airway bifurcations has been analyzed using experimental and mathematical modeling techniques. In the 1996 PM AQCD, experimental data were available illustrating the peak deposition of coarse particles (3, 5, and 7 μm d_{ae}) in daughter airways during inspiration and the parent airway during expiration, but always near the carinal ridge (Kim and Iglesias, 1989, 078539; Kim et al., 1989, 078538). In the 2004 PM AQCD, mathematical models predicted distinct "hot spots" of deposition in the vicinity of the carinal ridge for both coarse (10 μm) and UF (0.01 μm) particles (Heistracher and Hofmann, 1997, 047514; Hofmann et al., 1996, 047515). In a model of lung generations 4-5 during inspiration, hot spots occurred at the carinal ridge for 10 μm d_{ae} particles due to inertial impaction and for 0.01 μm particles due to secondary flow patterns formed at the bifurcation. During expiration, preferential sites of deposition for both particle sizes occurred 1) approaching the juncture of daughter airways on the walls forming and across the lumen from the carinal ridge; and 2) the top and bottom (visualizing the Y-shaped geometry laying horizontal) of the parent airway downstream of the bifurcation.

Recent studies further support these findings (Balashazy et al., 2003, 155671; Farkas and Balásházy, 2008, 157358; Farkas et al., 2006, 155771; Isaacs et al., 2006, 155861). Most of these studies quantified localized deposition in terms of an enhancement factor. Typically, the enhancement factor is the ratio of the deposition in a pre-specified surface area (e.g., 100 × 100 μm which corresponds to ~10 × 10 epithelial cells) to the average deposition density for the whole airway geometry. These enhancement factors are very sensitive to the size of the surface considered (Balashazy et al., 1999, 043201). The studies by Farkas et al. (2006, 155771) and Farkas and Balásházy (2008, 157358) investigated the phenomena of localized deposition down to 0.001 μm particles. The deposition of 0.001 μm was rather uniform, however, the deposition pattern became increasingly less uniform with increasing particle size. These studies indicate that, for particles greater than ~0.01 μm, some cells located near the carinal ridge of bronchial bifurcations may receive hundreds to thousands times the average dose (particles per unit surface area) of the parent and daughter airways. Furthermore, the inertial impaction of particles ≥ 1 μm d_{ae} at the carinal ridge of large bronchi will increase with increasing inspiratory flows. In a comparison of constricted versus healthy airways, Farkas et al. (2006, 155771) also reported that the overall deposition efficiency of 10 μm d_{ae} particles at bifurcations downstream of a constriction may be increased by 18 times. Given these considerations, Phalen and Oldham (2006, 156024) noted that substantial doses of particles (≥ 1 μm d_{ae}) may be justified for in vitro studies using tracheobronchial epithelial cell cultures.

4.2.3. Interspecies Patterns of Deposition

The primary purpose of this document is to assess the health effects of particles in humans. As such, human dosimetry studies have been stressed in this chapter. Such studies avoid the uncertainties associated with the extrapolation of dosimetric data from laboratory animals to humans. However, animal models have been and continue to be used in evaluating PM health effects because of ethical considerations regarding the types of studies that can be performed with human subjects. Thus, there is a considerable need to understand dosimetry in animals and dosimetric differences between animals and humans. Limited new data are becoming available. Similar deposition efficiencies have been reported in nasal casts of human and rhesus monkey for 1-10 μm d_{ae} for inspiratory flows mimicking resting breathing patterns (Kelly et al., 2005, 155894). Oldham and Robinson (2007, 156003) recently provided morphological data and predicted particle deposition in an asthma mouse model.

Interspecies similarities and differences in deposition were described in detail in the last two PM AQCDs (U.S. EPA, 1996, 079380; U.S. EPA, 2004, 056905). It was concluded that the general pattern of total particle deposition efficiency was similar between laboratory animals and humans: deposition increases on both sides of a minimum that occurs for particles of 0.2-1 μm. There are, however, marked interspecies differences in uptake into the respiratory tract and regional deposition. For instance, the nasal inhalability of 10 μm d_{ae} particles is predicted to be 96% in humans, whereas it is only 44% in rats (Ménache et al., 1995, 006533). In most laboratory animal species (rat, mouse, hamster, guinea pig, and dogs), deposition in the ET region is near 100% for particles >5 μm d_{ae} (Raabe et al., 1988, 001439), indicating greater efficiency than that seen in humans. Detailed presentation of dosimetric difference between rats and humans are available elsewhere (Brown et al., 2005, 089308; Jarabek et al., 2005, 056756).

Brown et al. (2005, 089308) conducted a thorough evaluation of extrapolations between rats and humans in relation to PM exposures. One of many factors they considered was the choice of a dose metric appropriate for comparison between species. For example, deposited mass may be an appropriate PM indicator for health effects associated with soluble PM constituents. For health effects associated with insoluble PM, the particle number, surface area, or mass may be appropriate indicators. Given interspecies differences in deposition patterns and clearance rates, the question of retained versus deposited dose was also discussed. It was concluded that for acute effects, the incremental dose may be the appropriate type of dose metric. For chronic effects, long-term burden may be more appropriate. For various dose metrics, estimates of particle concentration and exposure duration required for a rat to receive the same dose as received by a human were obtained with consideration of activity levels, mode of breathing, and particle size distributions. It was noted that high PM exposures over the period of months can lead to particle overload in rats (see Section 4.3.4.4). Exposure regimes were derived as a function of particle size and exposure duration that should avoid overwhelming macrophage mediated clearance achieving particle overload in rats (see Table 12 in Brown et al., 2005, 089308). The dosimetric calculations indicated that to achieve nominally similar acute doses per surface area in rats, relative to humans undergoing moderate to high exertion, PM exposure concentrations for rats would need to be somewhat higher than for humans. Since particle clearance from the lungs of rats is faster than humans, much higher exposure concentrations are required for the rat to simulate retained burdens of humans. Illustrating the complexity of such analyses, in some cases, rats were found to require lower exposures than humans to have comparable doses (generally when considering a scenario of humans at rest).

4.2.4. Biological Factors Modulating Deposition

Evaluation of factors affecting particle deposition is important to help understand potentially susceptible subpopulations. Differences in biological response following pollutant exposure may be caused by dosimetry differences as well as by differences in innate sensitivity. The effects of different biological factors on deposition were discussed in the 2004 PM AQCD (U.S. EPA, 2004, 056905) and are summarized briefly here.

4.2.4.1. Physical Activity

The activity level of an individual is well recognized to affect their minute ventilation and route of breathing. Changes in minute ventilation during exercise are accomplished by increasing both V_T and f (Table 4-1). Humans are oronasal breathers tending to breathe through the nose when at rest and increasingly through the mouth with increasing activity level. There is considerable inter-individual variability in both the route by which people breathe and the way breathing pattern changes occur.

Table 4-1. Breathing patterns with activity level in adult human male.

Activity	Awake Rest [a]	Slow Walk [a]	Light Exertion [a]	Moderate Exertion [a]	Heavy Exertion [b]
Breaths/min	12	16	19	28	26
Tidal volume, mL	625	813	1000	1429	1923
Minute ventilation, L/min	7.5	13	19	40	50

Sources: [a]Winter-Sorkina and Cassee (2002, 043670); [b]ICRP (1995, 006988)

Individuals typically breathe through their nose while at rest, switching to oronasal breathing as ventilation increases (Bennett et al., 2003, 191977; Niinimaa et al., 1981, 071758). The role of the nose in filtering particles is diminished as airflow is diverted from the nose to the mouth during exercise, bringing more particles to the lower respiratory tract. A recent study in adults (Bennett et al., 2003, 191977) found that nasal ventilation during exercise varied as a function of both race and gender. African-Americans possessed a greater nasal contribution to breathing during exercise than Caucasians. At similar exercise efforts (i.e., normalized to a % maximum work capacity) the females also had a greater nasal contribution to breathing during exercise than males.

In addition, when individuals increase their ventilation with activity the total number of particles inhaled per unit time (i.e., exposure rate) increases, but the fractional deposition of particles in each breath also changes with breathing pattern. Figure 4-3 and Figure 4-4 illustrate predicted deposition fractions in the respiratory tract during rest versus light exercise, respectively. During exercise, both V_T and f increase. Fractional deposition for all particles increases with increased V_T. Increasing the f, however, decreases the fractional deposition of fine and UFPs due to decreased time for gravitational and diffusive deposition. For particles larger than a d_{ae} of roughly 3 μm, increasing f can increase the deposition fraction due to increased impaction in the extrathoracic and TB airways. Thus, it should be expected that the change in deposition fraction with activity will vary among individuals depending on the relative influences of these two variables (i.e., V_T and f) in a given subject and the particle size to which they are exposed. Experimentally, the lung deposition fractions of fine particles during moderate exercise and mouth breathing are unchanged between rest and exercise (Bennett et al., 1985, 190034; Morgan et al., 1984, 190035). Kim (2000, 013112) evaluated differences in deposition of 1, 3, and 5 μm (MMAD) particles under varying breathing patterns (simulating breathing conditions of sleep, resting, and mild exercise). Total lung deposition increased with increasing V_T at a given flow rate and with increasing flow rate at a given breathing period. These experimental studies suggest that the total deposited dose rate (i.e., deposition per unit time) of particles will generally increase in direct proportion to the increase in minute ventilation associated with exercise.

The changes in ventilation, i.e., breathing pattern and flow rate, may also alter the regional deposition of particles. Coarse particle deposition increases in the TB and ET regions during exercise due to the increased flow rates and associated impaction. A rapid-shallow breathing pattern during exercise may result in more bronchial airway versus alveolar deposition, while a slow-deep pattern will shift deposition to deeper lung regions (Valberg et al., 1982, 190019). Bennett et al. (1985, 190034) showed for 2.6 μm particles that moderate exercise shifted deposition from the lung periphery towards ET and larger, bronchial airways. Similarly, Morgan et al. (1984, 190035) showed that even for fine particles (0.7 μm) TB deposition was enhanced with exercise. This shift in deposition toward the bronchial airways results in a much greater dose per unit surface area of tissue in those regions. Morgan et al. (1984, 190035) also found that the apical-to-basal distribution of fine

particles increased with exercise, i.e., a shift towards increased deposition in the lung apices. This shift may be less likely for larger particles, however, whose deposition in large airway bifurcations may preclude their transport to these more apical regions (Bennett et al., 1985, 190034).

4.2.4.2. Age

Airway structure and respiratory conditions vary with age, and these variations may alter the amount and site of particle deposition in the respiratory tract. It was concluded in the 2004 PM AQCD (U.S. EPA, 2004, 056905) that significant differences between adults and children had been predicted by mathematical models and observed in experimental studies. Studies generally indicated that ET and TB deposition was greater in children and that children received greater doses of particles per lung surface area than adults. Deposition studies in the elderly are still quite limited.

A few studies have attempted to measure oronasal breathing in children as compared to adults (Becquemin et al., 1999, 155679; Bennett et al., 2008, 156269; James et al., 1997, 042422). This is important since particles deposit with greater efficiency in the nose relative to the mouth, thereby affecting exposure of the lower respiratory tract. James et al. (1997, 042422) found that children (age 7-16 yr, n = 10) displayed more variability than adults with respect to their oronasal pattern of breathing with exercise. However, it was not possible to predict the pattern of the partitioning of ventilation during exercise based on age, gender, or nasal airway resistance. Further, in a limited number of children (age 8−16 yr, n = 10), Becquemin et al. (1999, 155679) found that the children tended to display more oral breathing both at rest and during exercise than the adults. The highest oral fractions were also found in the youngest children. None of these studies, however, was able to show a relationship between nasal resistance and the relative contribution of nasal breathing in children. Bennett et al. (2008, 156269) made preliminary measurements of the relative contributions of oral versus nasal breathing at rest and during incrementally graded submaximal exercise on the cycle ergometer for children (age 6-10 yr, n = 12) and adults (age 18-27 yr, n = 11). There was a trend for children to have a lesser nasal contribution to breathing at rest and during exercise, but the differences from adults were not statistically significant.

Breathing patterns are well recognized to change with increasing age, i.e., V_T increase and respiratory rates decrease (Tabachnik et al., 1981, 157036; Tobin et al., 1983, 156122). Bennett and Zeman (1998, 076182) measured the deposition fraction of inhaled, fine particles (2 μm d_{ae}) in children (age 7-14 yr, n=16) and adults (age 19-35 yr, n=12) as they breathed the aerosol with their natural, resting breathing pattern. Among the children, variation in deposition fractions, measured by photometry at the mouth, was highly dependent on intersubject variation in V_T. On the other hand, they found no difference in deposition fractions between children versus adults for these fine particles. This finding and the modeling predictions (Hofmann et al., 1989, 006922) are explained in part by the smaller V_T and faster breathing rate of children relative to adults for natural breathing conditions. Bennett et al. (2008, 156269) also recently reported measures of fine particle (1 and 2 μm d_{ae}) deposition at ventilation rates typical of light exercise in children (age 6-10 yr, n=12) and adults (age 18-27 yr, n=11) and showed that, like with resting breathing, deposition fractions were predicted by breathing pattern and did not differ or tended to be less in children compared to adults. On the other hand, because children breathe at higher minute ventilations relative to their lung volumes, the rate of deposition of fine particles normalized to lung surface area may be greater in children versus adults (Bennett and Zeman, 1998, 076182).

Bennett and Zeman (2004, 155686) expanded their measures of fine particle deposition during resting breathing to a larger group of healthy children (6-13 yr; 20 boys, 16 girls) and found again that the variation in total deposition was best predicted by V_T ($r = 0.79$, $p < 0.001$). But both V_T and resting minute ventilation increased with both height and body mass index (BMI) of the children. Interestingly, these data suggest that for a given height and age, children with higher BMI have larger minute ventilations and V_T at rest than those with lower BMI. These differences in breathing patterns as a function of BMI translated into increased deposition of fine particles in the heaviest children. The rate of deposition (i.e., particles depositing per unit time) in the overweight children was 2.8 times that of the leanest children ($p < 0.02$). Among all children, the rate of deposition was significantly correlated with BMI ($r = 0.46$, $p < 0.004$). Some of the increase in deposition fractions of heavier children may be due to their elevated V_T, which was well correlated with BMI ($r = 0.72$, $p < 0.001$).

In 62 healthy adults with normal lung function aged 18-80 yr, Bennett et al. (1996, 083284) showed there was no effect of age on the whole lung deposition fractions of 2-μm particles under

natural breathing conditions. Across all subjects, the deposition fractions were found to be independent of age, depending on breathing period ($r = 0.58$, $p < 0.001$) and airway resistance ($r = 0.46$, $p < 0.001$). In the same adults breathing with a fixed pattern (360 mL V_T, 3.4 sec breathing period), there was a mild decrease in deposition with increasing age, which could be attributed to increased peripheral airspace dimensions in the elderly.

4.2.4.3. Gender

Males and females differ in body size, conductive airway size, and ventilatory parameters; therefore, gender differences in deposition might be expected. In some of the controlled studies, however, the men and women were constrained to breathe at the same V_T and f. Since women are generally smaller than men, the increased minute ventilation of women compared to their normal ventilation could affect deposition patterns. This may help explain why gender related effects on deposition have been observed in some studies.

Kim and Hu (1998, 086066) assessed the regional deposition patterns of 1-, 3-, and 5-μm MMAD particles in healthy adult males and females using controlled breathing. The total fractional deposition in the lungs was similar for both genders with the 1-μm particle size, but was greater in women for the 3- and 5-μm particles. Deposition also appeared to be more localized in the lungs of females compared to those of males. Kim and Jaques (2000, 012811) measured deposition in healthy adults using sizes in the UF mode (0.04-0.1 μm). Total fractional lung deposition was greater in females than in males for 0.04- and 0.06-μm particles. The region of peak fractional deposition was shifted closer to the mouth and peak height was slightly greater for women than for men for all exposure conditions. The total lung deposition data from these studies are illustrated in Figure 4-5. These differences were generally attributed to the smaller size of the upper airways, particularly of the laryngeal structure, in females.

In another study (Bennett et al., 1996, 083284), the total respiratory tract deposition of 2-μm particles was examined in adult males and females aged 18-80 yr who breathed with a normal resting pattern. There was a tendency for greater deposition fractions in females compared to males. However, since males had greater minute ventilation, the deposition rate (i.e., deposition per unit time) was greater in males than in females. More recently, Bennett and Zeman (2004, 155686) found no difference in the deposition of 2-μm particles in boys versus girls aged 6-13 yr ($n = 36$).

4.2.4.4. Anatomical Variability

Anatomical variability, even in the absence of respiratory disease, can affect deposition throughout the respiratory tract. The ET region is the first exposed to inhaled particles and, therefore, deposition within this region would reduce the amount of particles available for deposition in the lungs. Variations in relative deposition within the ET region will, therefore, propagate through the rest of the respiratory tract, creating differences in calculated doses among individuals.

The influence of variations in nasal airway geometry on particle deposition has been investigated. Cheng et al. (1996, 047520) examined nasal airway deposition in healthy adults using particles ranging in size from 0.004 to 0.15 μm and at 2 constant inspiratory flow rates, 167 and 333 mL/s. Inter-individual variability in deposition was correlated with the wide variation of nasal dimensions; in that, greater surface area, smaller cross-sectional area, and increasing complexity of airway shape were all associated with enhanced deposition. Bennett and Zeman (2005, 155687) have also shown that nasal anatomy influences the efficiency of particle uptake in the noses of adults. For light exercise breathing conditions in adults, their study demonstrated that nasal deposition efficiencies for both 1- and 2-μm monodisperse particles were significantly less in African Americans versus Caucasians. The lesser nasal efficiencies in African-Americans were associated with both lower nasal resistance and less elliptical nostrils compared to Caucasians.

Within the lungs, the branching structure of the airways may also differ between individuals. Zhao et al. (2009, 157187) recently examined the bronchial anatomy of the left lung in patients (132 M, 84 W; mean age 47 yr) that underwent conventional thoracic computed tomography scans for various reasons. At the level of the segmental bronchus in the upper and lower lobes, a bifurcation occurred in the majority of patients. A trifurcation, however, was observed in 23% of the upper and 18% of the lower lobes. Other more unusual findings were also reported such as four bronchi arising from the left upper lobe bronchus. As described in Section 4.2.2.4, deposition can be highly localized near the carinal ridge of bifurcations. The effect of a bifurcation versus other

branching patterns on airflow patterns and particle deposition has not been described in the literature. Martonen et al. (1994, 000847) showed that a wide blunt carinal ridge shape dramatically affected the flow stream lines relative to a narrower and more rounded ridge shape. Specifically, there were high flow velocities across the entire area of the blunt carinal ridge versus a smoother division of the airstream in the case of the narrow rounded ridge shape. The implication may be that localized particle deposition on the carinal ridge would increase with ridge width. A similar situation might be expected for a trifurcation versus a bifurcation. These differences in branching patterns provide a clear example of anatomical variability among individuals that might affect both air flow patterns and sites of particle deposition.

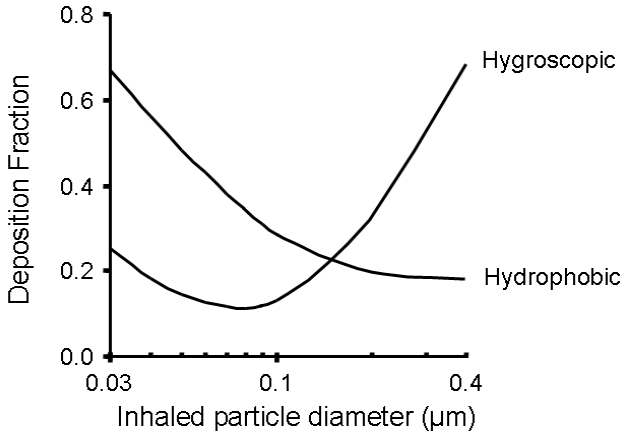
4.2.4.5. Respiratory Tract Disease

The presence of respiratory tract disease can affect airway structure and ventilatory parameters, thus altering deposition compared to that occurring in healthy individuals. The effect of airway diseases on deposition has been studied extensively, as described in the 1996 and 2004 PM AQCD (U.S. EPA, 1996, 079380; U.S. EPA, 2004, 056905). Studies described therein showed that people with chronic obstructive pulmonary disease (COPD) had very heterogeneous deposition patterns and differences in regional deposition compared to healthy individuals. People with obstructive pulmonary diseases tended to have greater deposition in the TB region than did healthy people. Furthermore, there tended to be an inverse relationship between bronchoconstriction and the extent of deposition in the alveolar region, whereas total respiratory tract deposition generally increased with increasing degrees of airway obstruction.

The vast majority of deposition studies in individuals with respiratory disease have been performed during controlled breathing, i.e., all subjects breathed with the same V_T and f. However, although resting V_T is similar or elevated in people with COPD compared to healthy individuals, the former tend to breathe at a faster rate, resulting in higher than normal tidal peak flow and resting minute ventilation. Thus, given that breathing patterns differ between healthy and obstructed individuals, particle deposition data for controlled breathing may not be appropriate for estimating respiratory doses from ambient PM exposures.

Bennett et al. (1997, 078839) measured the fractional deposition of insoluble 2-μm particles in moderate-to-severe COPD patients (n = 13; mean age 62 yr) and healthy older adults (n = 11; mean age 67 yr) during natural resting breathing. COPD patients had about a 50% greater deposition fraction and a 50% increase in resting minute ventilation relative to the healthy adults. As a result, the patients had an average deposition rate of about 2.5 times that of healthy adults. Similar to previously reviewed studies (U.S. EPA, 1996, 079380; U.S. EPA, 2004, 056905), these investigators observed an increase in deposition with an increase in airway resistance, suggesting that deposition increased with the severity of airway disease.

Brown et al. (2002, 043216) measured the deposition of an UF aerosol (CMD = 0.033 μm) during natural resting breathing in 10 patients with moderate-to-severe COPD (mean age 61 yr) and 9 healthy adults (mean age 53 yr). The COPD group consisted of 7 patients with chronic bronchitis and 3 patients with emphysema. The total deposition fraction in the bronchitic patients (0.67) was significantly ($p < 0.02$) greater than in either the patients with emphysema (0.48) or the healthy subjects (0.54). Minute ventilation increased with disease severity (healthy, 5.8 L/min; chronic bronchitic, 6.9 L/min; emphysema, 11 L/min). Relative to the healthy subjects, the average dose rate was significantly ($p < 0.05$) increased by 1.5 times in the COPD patients, whereas the average deposition fraction only tended to be increased by 1.1 times. These data further demonstrate the need to consider dose rates (which depend on minute ventilation) rather than just deposition fractions when evaluating the effect of respiratory disease on particle deposition and dose.



Source:Data from Tu and Knutson (1984, 072870).

Figure 4-6. Total deposition of hygroscopic sodium chloride and hydrophobic aluminosilicate aerosols during oral breathing (V_T = 1.0 L; f = 15 min^{-1}).

4.2.4.6. Hygroscopicity of Aerosols

Experimental and modeling studies of hygroscopic aerosol growth and deposition in the lung were extensively discussed in Section 10.4.3.1 of the 1996 PM AQCD (U.S. EPA, 1996, 079380). Hygroscopic ambient aerosols include sulfates, nitrates, some organics, and aerosols laden with sodium or potassium. The high relative humidity in the lungs contributes to rapid growth of hygroscopic particles and dramatically alters the deposition characteristics of ambient hygroscopic aerosols relative to nonhygroscopic aerosols. Nonhygroscopic particles in the range of 0.3 μm have minimal intrinsic mobility and low total deposition in the lungs. However, a 0.3 μm salt particle (dry) will grow in vivo to nearly 2 μm and deposit to a far greater extent (Anselm et al., 1990, 156217). The hygroscopic growth of particles in the respiratory tract decreases diffusive deposition and increases aerodynamic deposition as illustrated in Figure 4-6.

4.2.5. Summary

Particle deposition in the respiratory tract occurs predominantly by diffusion, impaction, and sedimentation. Deposition is minimal for particle diameters in the range of 0.1 to 1.0 μm, where particles are small enough to have minimal sedimentation or impaction and sufficiently large so as to have minimal diffusive deposition. In humans, total respiratory tract deposition approaches 100% for particles of roughly 0.01 μm (physical diameter) due to diffusive deposition and for particles of around 10 μm d_{ae} due to the efficiency of sedimentation and impaction.

The first line of defense for protecting the lower respiratory tract from inhaled particles is the nose and mouth. Nasal deposition approaches 100% in the average human for 10 μm d_{ae} particles. Experimental studies show lower nasal particle deposition in children than adults. Relative to adults, children also tend to breathe more through their mouth which is less efficient for removing inhaled particles than the nose. These findings suggest that the lower respiratory tract of children may receive a higher dose of ambient PM compared to adults. Since children breathe at higher minute ventilations relative to their lung volumes, the rate of particle deposition normalized to lung surface area may be further increased relative to adults.

People with COPD generally have greater total deposition and more heterogeneous deposition patterns compared to healthy individuals. The observed increase in deposition correlates with increases in airway resistance, suggesting that deposition increases with the severity of airway disease. COPD patients also have an increased resting minute ventilation relative to the healthy adults. This demonstrates the need to consider dose rates (which depend on minute ventilation)

rather than just deposition fractions when evaluating the effect of respiratory disease on particle deposition and dose.

Modeling studies indicate that, for particles greater than ~0.01 μm, some cells located near the carinal ridge of bronchial bifurcations may receive hundreds to thousands times the average dose (particles per unit surface area) of the parent and daughter airways. The inertial impaction of particles ≥ 1 μm d_{ae} at the carinal ridge of large bronchi increases with increasing inspiratory flows. Airway constriction can further augment the overall deposition efficiency of coarse particles at downstream bifurcations. These findings suggest that substantial doses of particles (≥ 1 μm d_{ae}) may be justified for in vitro studies using tracheobronchial epithelial cell cultures.

Our ability to extrapolate between species has not generally changed since the 2004 PM AQCD (U.S. EPA, 2004, 056905). However, some considerations related to coarse particles warrant comment. The inhalability of particles having d_{ae} of 2.5, 5, and 10 μm is 80, 65, and 44% in rats, respectively, whereas it remains near 100% for a d_{ae} of 10 μm in humans. In most laboratory animal species (rat, mouse, hamster, guinea pig, and dogs), deposition in the extrathoracic region is near 100% for particles greater than 5 μm d_{ae}. By contrast, in humans nasal deposition approaches 100% for 10 μm d_{ae}. Oronasal breathing versus obligate nasal breathing further contributes to greater penetration of coarse particles into the lower respiratory tract of humans than rodents.

4.3. Clearance of Poorly Soluble Particles

This section discusses the clearance and translocation of poorly soluble particles that have deposited in the respiratory tract. The term "clearance" is used here to refer to the processes by which deposited particles are removed by mucociliary action or phagocytosis from the respiratory tract. "Translocation" is used here mainly to refer to the movement of free particles across cell membranes and to extrapulmonary sites. In the literature, translocation may also refer to the extra- and intracellular dissolution of particles and the subsequent transfer of dissociated material to the blood through extra- and intracellular fluids and across the various cell membranes and lung tissues. The clearance and distribution of soluble particles and soluble constituents of particles are discussed in Section 4.4.

A basic overview of biological mechanisms and clearance pathways from various regions of the respiratory tract are presented in the following sections. Then regional kinetics of particle clearance are addressed. Subsequently, an update on interspecies patterns and rates of particle clearance is provided. The translocation of UFPs is also discussed. Finally, information on biological factors that may modulate clearance is presented.

4.3.1. Clearance Mechanisms and Kinetics

For any given particle size, the deposition pattern of poorly soluble particles influences clearance by partitioning deposited material between lung regions. Tracheobronchial clearance of poorly soluble particles in humans, with some exceptions, is thought (in general) to be complete within 24-48 h through the action of the mucociliary escalator. Clearance of poorly soluble particles from the alveolar region is a much slower process which may continue from months to years.

4.3.1.1. Extrathoracic Region

Particles deposited in either the nasal or oral passages are cleared by several mechanisms. Particles depositing in the mouth may generally be assumed to be swallowed or removed by expectoration. Particles deposited in the posterior portions of the nasal passages are moved via mucociliary transport towards the nasopharynx and swallowed. Mucus flow in the most anterior portion of the nasal passages is forward, toward the vestibular region where removal occurs by sneezing, wiping, or nose blowing.

4.3.1.2. Tracheobronchial Region

Mucociliary clearance in the TB region has generally been considered to be a rapid process that is relatively complete by 24-48 h post-inhalation in humans. Mucociliary clearance is frequently modeled as a series of "escalators" moving material proximally from one generation to the next. As such, the removal rate of particles from an airway generation increases with increasing tracheal mucus velocity. Assuming continuity in the amount of mucus between airway generations, mucus velocities decrease and transit times within an airway generation increase with distal progression. Although clearance from the TB region is generally rapid, experimental evidence discussed in the 1996 and 2004 PM AQCD (U.S. EPA, 1996, 079380; U.S. EPA, 2004, 056905) showed that a fraction of material deposited in the TB region is retained much longer.

The slow-cleared TB fraction (i.e., the fraction of particles deposited in the TB region that are subject to slow clearance) was thought to increase with decreasing particle size. For instance, Roth et al. (1993, 156928) showed approximately 93% retention of UFPs (30 nm median diameter) thought to be deposited in the TB region at 24 h post-inhalation. The slow phase clearance of these UFPs continued with an estimated half-time ($t_{1/2}$) of around 40 days. Using a technique to target inhaled particles (monodisperse 4.2 μm MMAD) to the conducting airways, Möller et al. (2004, 155987) observed that 49 ± 9% of particles cleared rapidly ($t_{1/2}$ of 3.0 ± 1.6 h), whereas the remaining fraction cleared considerably slower ($t_{1/2}$ of 109 ± 78 days). The ICRP (1995, 006988) human respiratory tract model assumes particles ≤ 2.5 μm (physical diameter) to have a slow-cleared TB fraction of 50%. The slow-cleared fraction assumed by the ICRP (1995, 006988) decreases with increasing particle size to <1% for 9 μm particles. Considering the UF data of Roth et al. (1993, 156928) in addition to data considered by the ICRP (1995, 006988), Bailey et al. (1995, 190057) estimated a slow-cleared TB fraction of 75% for UFPs. At that time, they (Bailey et al. 1995) also estimated the slow-cleared fraction to decrease with increasing particle size to 0% for particles ≥ 6 μm. Recent experimental evidence from the same group (Smith et al., 2008, 190037) showed no difference in TB clearance among humans for particles with geometric sizes of 1.2 versus 5 μm, but the same d_{ae} (5 μm) so as to deposit similarly in the TB airways. For at least micron-sized particles, these recent findings do not support the particle size dependence of a slow-cleared TB fraction. As discussed further below, much of the apparent slow-cleared TB fraction may be accounted for by differences in deposition patterns, i.e., greater deposition in the alveolar region than expected.

A portion of the slow cleared fraction from the TB region appears to be associated with small bronchioles. For large particles (d_{ae} = 6.2 μm) inhaled at a very slow rate to theoretically deposit mainly in small ciliated airways, 50% had cleared by 24 h post-inhalation. Of the remaining particles, 20% cleared with a $t_{1/2}$ of 2.0 days and 80% with a $t_{1/2}$ of 50 days (Falk et al., 1997, 086080). Using the same techniques, Svartengren et al. (2005, 157034) also reported the existence of long-term clearance in humans from the small airways. It should be noted that the clearance rates for the slow-cleared TB fraction still exceeds the clearance rate of the alveolar region in humans. Kreyling et al. (1999, 039175) targeted inhaled particle (d_{ae} = 2.2 and 2.5 μm) deposition to the TB airways of adult beagle dogs and subsequently quantified particle retention using scintigraphic and morphometric analyses. Despite the use of shallow aerosol bolus inhalation to a volumetric lung depth of less than the anatomic dead space, 2.5-25% of inhaled particles deposited in alveoli. At 24 and 96 h post-inhalation, more than 50% of the retained particles were in alveoli. However, 40% of particles present at 24 and 96 h were localized to small TB airways of between 0.3 and 1 mm in diameter. Collectively, these studies suggest that although mucociliary clearance is fast and effective in healthy large airways, it is less effective and sites of longer retention exist in the smaller TB airways.

The underlying sites and mechanisms of long-term TB retention in the smaller airways remain largely unknown. Several factors may contribute to the existence or experimental artifact of slow clearance from the smaller TB airways. Even when inhaled to very shallow lung volumes, some particles reach the alveolar region (Kreyling et al., 1999, 039175). Therefore, experiments utilizing bolus techniques to target inhaled particle deposition to the TB airways may have had some deposition in the alveolar region. This may occur due to variability in path length and the number of generations to the alveoli (Asgharian et al., 2001, 017025) and/or differences in regional ventilation (Brown and Bennett, 2004, 190032). Nonetheless, the experimentally measured clearance rates measured for the slow cleared TB fraction are faster than that of the alveolar region in both humans and canines. Thus, although experimental artifacts likely occur, they do not discount the existence of a slow cleared TB fraction. To some extent, it is possible that the slow cleared TB fraction may be due to bronchioles that do not have a continuous ciliated epithelium as in the larger bronchi. Neither

path length, ventilation distribution, nor a discontinuous ciliated epithelium explains an apparently slow cleared TB fraction with decreasing particle size below 0.1 μm. As discussed in Section 4.3.3 on Particle Translocation, UFPs cross cell membranes by mechanisms different from larger (~1 μm) particles. Based on that body of literature, particles smaller than a micron may enter epithelial cells resulting in their prolonged retention, particularly in the bronchioles where the residence time is longer and distances necessary to reach the epithelium are shorter compared to that in the bronchi.

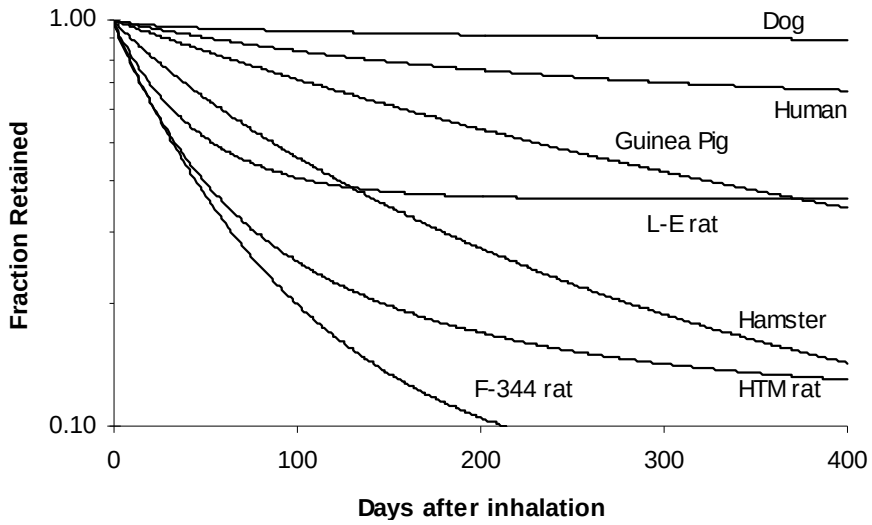
4.3.1.3. Alveolar Region

The primary alveolar clearance mechanism is macrophage phagocytosis and migration to terminal bronchioles where the cells are cleared by the mucociliary escalator. Alveolar macrophages originate from bone marrow, circulate briefly as monocytes in the blood, and then become pulmonary interstitial macrophages before migrating to the luminal surfaces. Under normal conditions, a small fraction of ingested particles may also be cleared through the lymphatic system. This may occur by transepithelial migration of alveolar macrophage following particle ingestion or free particle translocation with subsequent uptake by interstitial macrophages. Snipes et al. (1997, 156092) have also demonstrated the importance of neutrophil phagocytosis in clearance of particles from the alveolar region. Rates of alveolar clearance of poorly soluble particles vary between species and are briefly discussed in Section 4.3.2. The translocation of particles from their site of deposition is discussed in Section 4.3.3.

The efficiency of macrophage phagocytosis is thought to be greatest for particles between 1.5 and 3 μm (Oberdörster, 1988, 006857). The decreased efficiency of alveolar macrophage for engulfing UFPs increases the time available for these particles to be taken up by epithelial cells and moved into the interstitium (Ferin et al., 1992, 044401). Consistent with this supposition (i.e., translocation increases with time), an increase in titanium dioxide (TiO_2) particle transport to lymph nodes has been reported following inhalation of a cytotoxin to macrophages (Greenspan et al., 1988, 045031). Interestingly, the long-term clearance kinetics of the poorly soluble UF (15-20 nm CMD) iridium (Ir) particles were found to be similar to the kinetics reported in the literature for micrometer-sized particles (Semmler et al., 2004, 055641; Semmler-Behnke et al., 2007, 156080). Semmler-Behnke et al. (2007, 156080) concluded that UF Ir particles are less phagocytized by alveolar macrophage than larger particles, but are effectively removed from the airway surface into the interstitium. Particles are then engulfed by interstitial macrophages which then migrate to the airway lumen and are removed by mucociliary clearance to the larynx. The major role of macrophage-mediated clearance was supported by lavage of relatively few free particles versus predominantly phagocytized particles at time-points of up to 6 mo. It is also possible that some free particles as well as particle-laden macrophages were carried from interstitial sites via the lymph flow to bronchial and bronchiolar sites, including bronchial-associated lymphatic tissue, where they were excreted again into the airway lumen.

4.3.2. Interspecies Patterns of Clearance and Retention

There are differences between species in both the rates of particle clearance from the lung and manner in which particles are retained in the lung. For instance, based on models of mucociliary clearance from un-diseased airways, >95% of particles deposited in the tracheobronchial airways of rats are predicted to be cleared by 5 h post deposition, whereas it takes nearly 40 h for comparable clearance in humans (Hofmann and Asgharian, 2003, 055579). As noted in Section 4.3.1.2, however, there is considerable evidence that a sizeable fraction of particles deposited at the bronchiolar level of the ciliated airways in humans (as well as canines) are cleared at a far slower rate. The slow cleared TB fraction appears to increase with decreasing particle size.



Source: Data from Kreyling and Scheuch (2000, 056281).

Figure 4-7. Retention of poorly soluble particles (0.5-5 µm) in the alveolar region of the lung over time in various mammalian species.

Figure 4-7 illustrates rates of alveolar clearance for 0.5-5 µm particles in various mammalian species. The alveolar clearance rate of particles smaller than 0.1 µm and larger than 5 µm is slower than that of particles in the 0.5-5 µm range. From interspecies comparisons of alveolar clearance, the path length from alveoli to ciliated terminal bronchioles may affect the particle transport rate (Kreyling and Scheuch, 2000, 056281). The average path length from alveoli to ciliated terminal bronchioli is longer in humans, monkeys, and dogs, than in sheep, rats, hamsters, and mice. Transport time and hence retention times may increase with path length. This hypothesis fits with all species in this comparison, except guinea pigs, which have a short path length yet particle retention that is nearly as long as in humans, monkeys, and dogs. However, sheep have a short path length and particle transport as fast as rodents. In general, alveolar clearance rates appear to increase with increasing path length from the alveoli to ciliated airways.

There are also distinct differences in the sites of particle retention between species. Large mammals retain particles in interstitial tissues under normal conditions, whereas rats retain particles in alveolar macrophages (Snipes, 1996, 076041). In rats with chronic high doses there is a shift in the pattern of dust accumulation and response from that observed at lower doses in the lungs (Snipes, 1996, 076041; Vincent and Donaldson, 1990, 002462). Rats chronically exposed to high concentrations of insoluble particles experience a reduction in their alveolar clearance rates and an accumulation of interstitial particle burden (Bermudez et al., 2002, 055578; Bermudez et al., 2004, 056707; Ferin et al., 1992, 044401; Oberdörster et al., 1994, 046203; Oberdörster et al., 1994, 056285; Warheit et al., 1997, 086055). The influence of exposure concentration on the pattern of particle retention in rats (exposed to diesel soot) and humans (exposed to coal dust) was examined by Nikula et al. (2001, 016641). In rats, the diesel particles were found to be primarily in the lumens of the alveolar duct and alveoli; whereas in humans, retained dust was found primarily in the interstitial tissue within the respiratory acini.

4.3.3. Particle Translocation

Mucociliary and macrophage mediated clearance of poorly soluble particles from the respiratory tract was discussed in Section 4.3.1. There is evidence that particles may cross cell membranes and move from their site of deposition by other mechanisms. The following subsections discuss the movement of particles from the luminal surfaces of the alveolar region and from the olfactory mucosa. The clearance and distribution of soluble particles and soluble constituents of particles are discussed in Section 4.4.

4.3.3.1. Alveolar Region

Numerous studies have examined the translocation of UFPs from their site of deposition in the lung. Traditionally viewed as a relatively inert particle type, UF TiO_2 has received the most study. At the time the 2004 PM AQCD was released, there were conflicting results regarding the rate and magnitude of UF carbon translocation from the human lung. Since that time, it has become well-established that the transport of UF carbon particles from the human lung is far slower than that of soluble materials. However, it has also been shown in animal studies (primarily of rats) that UFPs cross cell membranes by mechanisms different from larger (~1 μm) particles and that a small fraction of these particles enter capillaries and may distribute systemically. Described in brief below, details of selected new studies investigating the disposition of poorly soluble particles are provided in Annex B.

There has been some contention regarding ability of UF carbon particles to rapidly diffuse from the lungs into the systemic circulation. Based on their study of 5 healthy volunteers, Nemmar et al. (2002, 024914) suggested that UF carbon particles (<100 nm) pass rapidly into the systemic circulation. However, Brown et al. (2002, 043216) found that the majority of UF carbon particles (CMD, 33 ± 2 nm) were still in the lungs of healthy human adult volunteers (n = 9; aged 40-67 yr) and COPD patients (n = 10; 45-70 yr) at 24 h post-inhalation. Brown et al. (2002, 043216) and Burch (2002, 056754) contended that the findings reported by Nemmar et al. (2002, 024914) were consistent with soluble pertechnetate clearance, but not insoluble UF carbon particles. Highly soluble in normal saline, pertechnetate clears rapidly from the lung with a half-time of ~10 min and accumulates most notably in the bladder, stomach, thyroid, and salivary glands. Three recent studies have confirmed that the majority (>95%) of UF carbon particles deposited in the lungs of human volunteers are retained at 24 h post-inhalation (Mills et al., 2006, 088770; Wiebert et al., 2006, 157146; Wiebert et al., 2006, 156154). Wiebert et al. (2006, 157146) modified their aerosol generation system to reduce leaching of the ^{99m}Tc radiolabel from carbon particles. Except for a small amount of radiotracer leaching from particles (1.0 ± 0.6% of initially deposited activity in urine by 24 h), these investigators found negligible radiolabel and associated particle clearance from the lungs by 70 h. The available data show that there is not a rapid or significant amount of UF carbon particle migration into circulation (Brown et al., 2002, 043216; Burch, 2002, 056754; Mills et al., 2006, 088770; Möller et al., 2008, 156771; Wiebert et al., 2006, 157146; Wiebert et al., 2006, 156154).

Although human studies show that the vast majority of UF carbon particles are retained in the lungs until at least 24 h post-inhalation, both in vitro and in vivo studies support the rapid (≤ 1 h) translocation of free UF TiO_2 particles across pulmonary cell membranes (Churg et al., 1998, 085815; Ferin et al., 1992, 044401; Geiser et al., 2005, 087362). Peculiar to TiO_2 aerosols, there is evidence that particle aggregates may disassociate once deposited in the lungs. This disassociation makes inhaled aggregate size the determinant of deposition amount and site, but primary particle size the determinant of subsequent clearance (Bermudez et al., 2002, 055578; Ferin et al., 1992, 044401; Takenaka et al., 1986, 046210). Following disaggregation, the UF TiO_2 particles are cleared more slowly and cause a greater inflammatory response (neutrophil influx) than fine TiO_2 particles (Bermudez et al., 2002, 055578; Ferin et al., 1992, 044401; Oberdörster et al., 1994, 046203; Oberdörster et al., 1994, 056285; Oberdorster et al., 2000, 039014). The differences in inflammatory effects and possibly lymph burdens between fine and UF TiO_2 in many studies appear related to lung burden in terms of particle surface area and not particle mass or number (Oberdorster, 1996, 039852; Oberdörster et al., 1992, 045110; Oberdorster et al., 2000, 039014; Tran et al., 2000, 013071). More recently, others have noted that particle surface area is not an appropriate metric across all particle types (Warheit et al., 2006, 088436). Surface characteristics such as roughness can also affect protein binding and potentially clearance kinetics, with smoother TiO_2 surfaces being more hydrophobic (Sousa et al., 2004, 089866).

Geiser et al. (2005, 087362) conducted a detailed examination of the disposition of inhaled UF TiO_2 in 20 healthy adult rats. They found that distributions of particles among lung tissue compartments appeared to follow the volume fraction of the tissues and did not significantly differ between 1 and 24 h post-inhalation. Averaging 1- and 24-h data, 79.3 ± 7.6% of particles were on the luminal side of the airway surfaces, 4.6 ± 2.6% were in epithelial or endothelial cells, 4.8 ± 4.5% were in connective tissues, and 11.3 ± 3.9% were within capillaries. Particles within cells were not membrane bound. It is not clear why the fraction of particles identified in compartments such as the capillaries did not differ between 1 and 24 h post-inhalation. These findings were consistent with the smaller study of 5 rats by Kapp et al. (2004, 156624) who reported identifying TiO_2 aggregates in a

type II pneumocyte; a capillary close to the endothelial cells; and within the surface-lining layer close to the alveolar epithelium immediately following a 1-h exposure. These studies effectively demonstrate that some inhaled UF TiO_2 particles, once deposited on the pulmonary surfaces, can rapidly ($\leq$ 1 h) translocate beyond the epithelium and potentially into the vasculature.

Extrapulmonary translocation has also been described for poorly soluble UF gold and Ir particles. In male Wistar-Kyoto rats exposed to UF gold particles (5-8 nm), Takenaka et al. (2006, 156110) reported a low but significant fraction (0.03 to 0.06% of lung concentration) of gold in the blood from 1 to 7 days post-inhalation. Semmler et al. (2004, 055641) also found small but detectable amounts of poorly soluble Ir particle (15 and 20 nm CMD) translocation from the lungs of male Wistar-Kyoto rats to secondary target organs like the liver, spleen, brain, and kidneys. Each of these organs contained about 0.2% of deposited Ir. The peak levels in these organs were found 7 days post-inhalation. The translocated particles were largely cleared from extrapulmonary organs by 20 days and Ir levels were near background at 60 days post-inhalation. Particles may have been distributed systemically via the gastrointestinal tract. Immediately after the 6-h inhalation exposure, 18 ± 5% of the deposited Ir particles had already cleared into the gastrointestinal tract. After 3 wk, 31 ± 5% of the deposited particles were retained in the lung. By 2 and 6 mo post-inhalation, lung retention was 17 ± 3 and 7 ± 1%, respectively. The particles appeared to be cleared predominantly from the peripheral lung via the mucociliary escalator into the GI tract and were found in feces.

A few recent studies have characterized differences in the behavior of fine and UF particles in vitro. Geiser et al. (2005, 087362) found that both UF and fine (0.025 µm gold, 0.078 µm TiO_2, and 0.2 µm TiO_2) particles cross cellular membranes by non-endocytic (i.e., involving vesicle formation) mechanisms such as adhesive interactions and diffusion, whereas the phagocytosis of larger 1 µm TiO_2 particles is ligand-receptor mediated. Edetsberger et al. (2005, 155759) found that UFPs (0.020 µm polystyrene) translocated into cells by first measurement (~1 min after particle application). Intracellular agglomerates of 88-117 nm were seen by 15-20 min and of 253-675 nm by 50-60 min after particle application. These intracellular aggregates were thought to result from particle incorporation into endosomes or similar structures since Genistein or Cytochalasin treatment generally blocked aggregate formation. Interestingly, particles did not translocate into dead cells, rather they attached to the outside of the cell membrane. Amine- or carboxyl-modified surfaces (46 nm polystyrene) did not affect translocation across cultures of human bronchial epithelial cells with about 6% regardless of the surface characteristics (Geys et al., 2006, 155789).

4.3.3.2. Olfactory Region

Numerous studies have demonstrated the translocation of soluble and poorly soluble particles from the olfactory mucosa via the axons to the olfactory bulb of the brain. The vast majority of these studies were conducted in rodents. However, DeLorenzo (1970, 156391) observed the rapid (within 30-60 min) movement of 50 nm silver-coated colloidal gold particles instilled on the olfactory mucosa into the olfactory bulb of squirrel monkeys. The specifics of this and other key studies that have investigated the translocation of particles to the olfactory bulb are provided in Annex B.

Two recent studies reported the movement of UFPs deposited in the olfactory region of the nose along the olfactory nerve and into the olfactory bulb of the brain in rats. Oberdörster et al. (2004, 055639) exposed rats to UF carbon particles (36 nm CMD, 1.7 σ_g) containing ^{13}C in a whole-body chamber for 6 h. The distribution of ^{13}C was followed for 7 days postexposure. There was a significant increase in ^{13}C in the olfactory bulb on Day 1 with persistent and continued increase through Day 7. Elder et al. (2006, 089253) exposed rats to manganese (Mn) oxide (~30 nm equivalent sphere with 3-8 nm primary particles) via whole-body inhalation exposure for 12 days (6 h/day, 5 days/wk) with both nares open or Mn oxide for 2 days (6 h/day) with right nostril blocked. After the 12 days exposure via both nostrils, Mn in the olfactory bulb increased 3.5-fold. After the 2-day exposure with the right nostril blocked, Mn was found mainly in the left olfactory bulb (2.4-fold increase). These studies suggest the neuronal uptake and translocation of UFPs without particle dissolution and in the absence of mucosal injury.

Elder et al. (2006, 089253) also addressed the issue of whether solubilization of particles was requisite for translocation along the olfactory nerve and into the brain. Similar amounts of soluble manganese chloride ($MnCl_2$) and poorly soluble Mn oxide were instilled onto the left naris of anesthetized rats. At 24 h post-instillation, similar amounts of Mn were found in the left olfactory bulb of rats instilled with $MnCl_2$ (8.2 ± 3.6% of instilled) and Mn oxide (8.2 ± 0.7% of instilled). If solubilization were required for translocation, then a lower amount of Mn oxide than $MnCl_2$ should

have reached the olfactory bulb. Following 14 consecutive days of aerosol exposure, Dorman et al. (2001, 055433) demonstrated that more soluble Mn sulfate reaches the olfactory bulb and striatum of rat brains than the poorly soluble form of Mn tetroxide. Nonetheless, the Mn levels were statistically increased in both the olfactory bulb and striatum following exposure to Mn tetroxide relative to filtered air. In a subsequent 13-wk exposure study, Dorman et al. (2004, 155752) also demonstrated that more soluble manganese sulfate ($MnSO_4$) reached the olfactory bulb than was observed for the less soluble Mn form (hureaulite). Both the soluble and less soluble forms of Mn resulted in statistically increased levels of Mn in the olfactory bulb relative to air exposed controls. The soluble $MnSO_4$ was also observed to reach the striatum and cerebellum. In addition, Yu et al. (2003, 156171) demonstrated increased Mn levels in the brains of rats exposed to welding-fumes for 60 days, however, the role of transport via the blood is less clear in this study.

The translocation of zinc (Zn) and TiO_2 to the olfactory bulb has also been reported in the literature. Persson et al. (2003, 051846) observed the translocation of Zn to the olfactory bulbs following instillation in both rats and freshwater pike. Wang et al. (2007, 156146) reported the translocation of both fine (155 nm) and UF (21 and 71 nm) TiO_2 particles in mice. Interestingly, a qualitative analysis of the data showed that more of the fine TiO_2 than UF TiO_2 reached the olfactory bulb. Wang et al. (2007, 156146) suggested that a strong hydrophilic character and propensity for aggregation reduced the translocation of the UF TiO_2.

The importance of particle translocation to the brain is not yet understood. Translocation via the axon to the olfactory bulb has been observed for numerous compounds of varying composition, particle size, and solubility. Although the rate of translocation is rapid, perhaps less than an hour, the magnitude of transport remains poorly characterized. With regard to the magnitude of transport, Elder et al. (2006, 089253) found that as much as 8% of both soluble and insoluble forms of Mn were translocated to the olfactory bulb in rats following intranasal instillation. It is also still unclear to what extent translocation to the olfactory bulb and other brain regions may vary between species. The olfactory mucosa covers approximately 50% of the nasal epithelium in rodents versus only about 5% in primates (Aschner et al., 2005, 155663). Additionally, a greater portion of inhaled air passes through the olfactory region of rats relative to primates (Kimbell, 2006, 155902). These differences may predispose rats, more so than humans, to deposition of particles in the olfactory region with subsequent particle translocation to the olfactory bulb.

4.3.4. Factors Modulating Clearance

4.3.4.1. Age

It was previously concluded that there appeared to be no clear evidence for any age-related differences in clearance from the lung or total respiratory tract, either from child to adult, or young adult to elderly (U.S. EPA, 1996, 079380; U.S. EPA, 2004, 056905). Studies showed either no change or some slowing in mucus clearance with age after maturity. Although some differences in alveolar macrophage function were reported between mature and senescent mice, no age-related decline in macrophage function had been observed in humans. A comprehensive review of the recent and older literature supports a decrease in mucociliary clearance with increasing age beyond adulthood in humans and animals. Limited animal data also suggest macrophage-mediated alveolar clearance may also decrease with age.

Studies addressing the effects of age on respiratory tract clearance are provided in Annex B. Ho et al. (2001, 156549) demonstrated that nasal mucociliary clearance rates were about 40% lower in old (age >40-90 yr) versus young (age 11-40 yr) men and women. Tracheal mucus velocities in elderly (or aged) humans and beagle dogs are about 50% that of young adults (Goodman et al., 1978, 071130; Whaley et al., 1987, 156153). Several human studies have demonstrated decreasing rates of mucociliary particle clearance from the large and small bronchial airways with increasing age (Puchelle et al., 1979, 006863; Svartengren et al., 2005, 157034; Vastag et al., 1985, 157088). Linear fits to the data show that rapid clearance (within 1 h) from large bronchi and prolonged clearance (between 1-21 days) from the small bronchioles in an 80-year-old is only about 50% of that in a 20-year-old (Svartengren et al., 2005, 157034; Vastag et al., 1985, 157088). One study reported that alveolar particle clearance rates decreased by nearly 40% in old versus young rats (Muhle et al., 1990, 006853). Another study has reported that older rats have an increased susceptibility to

pulmonary infection due to altered alveolar macrophage function and slowed bacterial clearance (Antonini et al., 2001, 156219). Although data are somewhat limited, they consistently show a depression of clearance throughout the respiratory tract with increasing age from young adulthood in humans and laboratory animals.

4.3.4.2. Gender

Gender was not found to affect clearance rates in prior reviews (U.S. EPA, 1996, 079380; U.S. EPA, 2004, 056905). Studies not included in those reviews also show that human males and females have similar nasal mucus clearance rates (Ho et al., 2001, 156549), tracheal mucus velocities (Yeates et al., 1981, 095391), and large bronchial airway clearance rates (Vastag et al., 1985, 157088).

4.3.4.3. Respiratory Tract Disease

At the time of the last two reviews (U.S. EPA, 1996, 079380; U.S. EPA, 2004, 056905), it was well recognized that obstructive airways disease may influence both the site of initial deposition and the rate of mucociliary clearance from the airways. When deposition patterns are matched, mucociliary clearance rates are reduced in patients with COPD relative to healthy controls. The effects of acute bacterial/viral infections and cough on mucociliary clearance were briefly summarized in Section 10.4.2.5 (EPA, 1996, 079380) and Section 6.3.4.4 (EPA, 2004, 056905) of past reviews. While cough is generally a reaction to some inhaled stimulus, in some cases, especially respiratory disease, it can also serve to clear the upper bronchial airways of deposited substances by dislodging mucus from the airway surface. One of the difficulties in assessing effects on infection on mucociliary clearance is that spontaneous coughing increases during acute infections. Cough has been shown to supplement mucociliary clearance of secretions, especially in patients with obstructive lung disease and primary ciliary dyskinesia.

Using a bolus technique to target specific lung regions, Möller et al. (2008, 156771) examined particle clearance from the ciliated airways and alveolar region of healthy subjects, smokers, and patients with COPD. Airway retention after 1.5 hours was significantly lower in healthy subjects (89 ± 6%) than smokers (97 ± 3%) or COPD patients (96 ± 6%). At 24 and 48 h, retention remained significantly higher in COPD patients (86 ± 6% and 82 ± 6%, respectively) than healthy subjects (75 ± 10% and 70 ± 9%, respectively). However, these findings are confounded by the more central pattern of deposition in the healthy subjects than in the smokers and COPD patients. Alveolar retention of particles was similar between the groups at 48 h post-inhalation.

The effect of asthma on lung clearance of particles may depend on disease status. Lay et al. (2009, 190060) found significantly ($p < 0.01$) more rapid particle (0.22 μm) mucociliary clearance over a 2-h period post-inhalation in mild asthmatics than in healthy volunteers. Although the pattern of deposition tended to be more central in the asthmatics, there was not a statistically significant difference from healthy controls. In vivo uptake by airway macrophages in mild asthmatics was also enhanced relative to healthy volunteers ($p < 0.01$). In an ex vivo study, airway macrophages from individuals with more severe asthma had impaired phagocytic capacity relative to less severely affected asthmatics and healthy volunteers (Alexis et al., 2001, 190013). Lay et al. (2009, 190060) concluded that enhanced uptake and processing of particulate antigens could contribute to the pathogenesis and progression of allergic airways disease in asthmatics and may contribute to an increased risk of exacerbations with particulate exposure.

Chen et al. (2006, 147267) investigated the effect of endotoxin on the disposition of particles. Healthy rats and those pretreated with endotoxin (12 h before particle instillation) were instilled with UF (56.4 nm) or fine (202 nm) particles. In healthy rats, there were no marked differences in lung retention or systemic distribution between the UF and fine particles. In healthy animals, UFPs were primarily retained in lungs (72 ± 10% at 0.5-2 h; 65 ± 1% at 1 day; 62 ± 5% at 5 days). Particles were also detected in the blood (2 ± 1% at 0.5-2 h; 0.1 ± 0.1% at 5 days) and liver (3 ± 2% at 0.5-2 h; 1 ± 0.1% at 5 days) of the healthy animals. At 1 day post-instillation, about 13% of the particles were excreted in the urine or feces of the healthy animals. In rats pretreated with endotoxin, by 2 h post-instillation, the UFPs accessed the blood (5 versus 2%) and liver (11 versus 4%) to a significantly greater extent than fine particles. The endotoxin-treated rats also had significantly greater amounts of UFPs in the blood (5% versus 2%) and liver (11% versus 3%) relative to the

healthy control rats. This study demonstrates that acute pulmonary inflammation caused by endotoxin increases the migration of UFPs into systemic circulation.

Adamson and Preditis (1995, 189982) investigated the possibility that particle deposition into an already injured lung might affect particle retention and enhance the toxicity of "inert" particles. Bleomycin was instilled into mice to induce epithelial necrosis and subsequent pulmonary fibrosis. Instilled 3 days following bleomycin treatment, while epithelial permeability was compromised, carbon black particles in treated mice were translocated to the interstitium and showed increased pulmonary retention relative to untreated mice. When instilled 4 wk post-bleomycin treatment, after epithelial integrity was restored, carbon black particle retention was similar between treated and untreated mice with minimal translocation to the interstitium. The instillation of carbon particles did not appear to increase lung injury in the bleomycin treated mice at either time point. This study shows that integrity of the epithelium affects particle retention and translocation into interstitial tissues.

4.3.4.4. Particle Overload

Unlike other laboratory animals, rats appear susceptible to "particle overload" effects due to impaired macrophage-mediated alveolar clearance. Numerous reviews have discussed this phenomenon and the difficulties it poses for the extrapolation of chronic effects in rats to humans (International, 2000, 002892; Miller, 2000, 011822; Morrow, 1994, 006850; Oberdorster, 1995, 046596; Oberdorster, 2002, 021111). Large mammals have slow pulmonary particle clearance and retain particles in interstitial tissues under normal conditions, whereas rats have rapid pulmonary clearance and retain particles in alveolar macrophages (Snipes, 1996, 076041). With chronic high doses of PM there is a shift in the pattern of dust accumulation and response from that observed at lower doses in rat lungs (Snipes, 1996, 076041; Vincent and Donaldson, 1990, 002462). Rats chronically exposed to high concentrations of insoluble particles experience a reduction in their alveolar clearance rates and an accumulation of interstitial particle burden (Bermudez et al., 2002, 055578; Bermudez et al., 2004, 056707; Ferin et al., 1992, 044401; Oberdörster et al., 1994, 046203; Oberdörster et al., 1994, 056285; Warheit et al., 1997, 086055). With continued exposure, some rats eventually develop pulmonary fibrosis and both benign and malignant tumors(Lee et al., 1985, 067628; Lee et al., 1986, 067629; Warheit et al., 1997, 086055). Oberdörster (1996, 039852; 2002, 021111) proposed that high-dose effects observed in rats may be associated with two thresholds. The first threshold is the pulmonary dose that results in a reduction in macrophage-mediated clearance. The second threshold, occurring at a higher dose than the first, is the dose at which antioxidant defenses are overwhelmed and pulmonary tumors develop. Intrapulmonary tumors following TiO_2 exposures are exclusive to rats and are not found in mice or hamsters (Mauderly, 1997, 084631). Moreover, Lee et al. (1985, 067628) noted that the squamous cell carcinomas observed with prolonged high concentration TiO_2 exposures developed from the alveolar lining cells adjacent to the alveolar ducts, whereas squamous cell carcinomas in humans which are generally linked with cigarette smoking are thought to arise from basal cells of the bronchial epithelium. Quoting Lee et al. (1986, 067629), "Since the lung tumors were a unique type of experimentally induced tumor under exaggerated exposure conditions and have not usually been seen in man or animals, their relevance to man in questionable."

4.3.5. Summary

For any given particle size, the pattern of poorly soluble particle deposition influences clearance by partitioning deposited material between regions of the respiratory tract. Particles depositing in the mouth may generally be assumed to be swallowed or removed by expectoration. Particles deposited in the posterior portions of the nasal passages or the TB airways are moved via mucociliary transport towards the nasopharynx and swallowed. Although clearance from the TB region is generally rapid, there appears to be fraction of material deposited in the TB region of humans that is retained much longer. The underlying sites and mechanisms of long-term TB retention are not known. The primary alveolar clearance mechanism is macrophage phagocytosis and migration to terminal bronchioles where the cells are cleared by the mucociliary escalator. Clearance from both the TB and alveolar region is more rapid in rodents than humans. Mucociliary and macrophage-mediated clearance decreases with age beyond adulthood.

Human data show that there is not a rapid or significant amount of UF carbon particle migration into circulation. However, both in vitro and in vivo animal studies support the rapid (≤ 1 h) translocation of free UF TiO_2 particles across pulmonary cell membranes. Extrapulmonary translocation has also been described in rats for poorly soluble UF gold and Ir particles. A low, but statistically significant, fraction (0.03-0.06% of lung concentration) of UF gold particles has been observed in the blood of rats from 1 to 7 days post-inhalation. The translocation in detectable amounts (<1% of deposited material) of poorly soluble Ir particles (15 and 20 nm CMD) from the lungs of rats to secondary target organs like the liver, spleen, brain, and kidneys has also been reported. However, the systemic distribution of particles may have occurred via normal clearance from the lungs to the gastrointestinal tract.

Although the importance of particle translocation to the brain is not yet understood, translocation from the olfactory mucosa via the axon to the olfactory bulb has been reported in primates, rodents, and freshwater pike for numerous compounds of varying composition, particle size, and solubility. The rate of translocation is rapid, perhaps less than an hour. In rats, as much as 8% of material may become translocated to the olfactory bulb following intranasal instillation. It is unclear to what extent translocation to the olfactory bulb and other brain regions may vary between species. Interspecies differences may predispose rats, more so than humans, to the deposition of particles in the olfactory region with subsequent translocation to the olfactory bulb.

4.4. Clearance of Soluble Materials

Soluble particles and soluble constituents of particles may be absorbed through the epithelium and distributed systemically or retained in the lung. The rate of dissolution depends on a number of factors, including particle surface area and chemical structure. Some dissolved materials bind to proteins or other components in the airway surface liquid layer. In the ciliated airways, solutes are cleared by mucociliary transport and diffuse into underlying tissues and the blood. In the alveolar regions, the thin barrier between the air and blood allows for rapid transport of solutes into the blood. The movement of soluble materials depends on the site of deposition in the lung, the rate of material dissolution from particles, and the molecular weight of the solute. The rate of soluble material clearance from the lungs depends on epithelial permeability which may be affected by age, respiratory disease, and concurrent exposures. While enhanced clearance of insoluble particles acts to reduce dose to airway tissue, increased transport of soluble matter into the blood stream may enhance effects on extra-pulmonary organs.

4.4.1. Clearance Mechanisms and Kinetics

The rate of absorption across the epithelium for materials that dissolve in the airway or alveolar lining fluid is fairly rapid (minutes to hours) and is a function of their molecular size and their water or lipid solubility (Enna and Schanker, 1972, 155767; Huchon et al., 1987, 024923; Oberdörster, 1988, 006857; Schanker et al., 1986, 005100). Huchon et al. (1987, 024923) studied the clearance of a variety of aerosolized solutes from the lungs of dogs. Solute clearance was inversely related to molecular weight. Negligible clearance of the largest molecular weight solute (transferrin mol wt ~76,000 daltons) in their study was found over a 30-min observation period. At the other extreme, free pertechnetate (mol wt ~163 daltons) had a clearance rate of 6% per min. Clearance of hydrophilic solutes is diffusion limited by pore sizes associated with intercellular tight junctions (estimated at 0.6-1.5 nm). Absorption of lipophilic compounds that pass easily through cell membranes is perfusion limited and thus generally occurs very rapidly. However, if lipophilic materials are adsorbed onto insoluble particles their retention in the lung may be prolonged (Creasia et al., 1976, 059713). In addition to diffusion through intercellular junctions, transcellular transport of large solutes by pinocytosis into epithelial cells has also been observed (Chinard, 1980, 156341).

A portion of poorly soluble particles may become dissolved with subsequent solute clearance. More rapid dissolution of poorly soluble nano- or UF particles relative to micro-sized particles occurs due to an increasing surface-to-volume ratio with decreasing particle size. Kreyling et al. (2002, 037332) examined the dissolution of poorly soluble UF Ir particle agglomerates (15-80 nm CMD) composed of 5 nm primary particles. After 7 days, <1% of the particles were dissolved in buffered saline, whereas 6% dissolved in 1 N hydrochloric acid after 1 day. Thus, the high surface-

to-volume ratio of UFPs should not be misconstrued to imply rapid dissolution of poorly soluble particles following deposition in the respiratory tract. However, poorly soluble particles that become phagocytosed may slowly dissolve in the acidic (pH of 4.3-5.3) environment of the phagolysosome to be released in their solubilized form from the cell and potential move across the epithelium into the bloodstream. The dissolution rate is inversely related to particle size and directly related to specific surface area (Kreyling and Scheuch, 2000, 056281) and facilitated by the acidic environment of the macrophage (Kreyling, 1992, 067243).

There is considerable evidence that soluble particles depositing in the bronchial airways are cleared by dual mechanisms (Bennett and Ilowite, 1989, 000835; Lay et al., 2003, 155920; Matsui et al., 1998, 040405; Sakagami et al., 2002, 156936; Wagner and Foster, 2001, 156143). The relative contribution of their removal by transepithelial absorption versus mucociliary clearance is likely a function of both the molecular size and water or lipid solubility of the material (Enna and Schanker, 1972, 155767; Huchon et al., 1987, 024923; Oberdörster, 1988, 006857; Sakagami et al., 2002, 156936). Furthermore, the rate of mucociliary transport for soluble particles may be less than that of insoluble particles (Lay et al., 2003, 155920). Consequently, non-permeating hydrophilic solutes may remain in contact with the airway epithelium for a longer period than insoluble particles. This may be due to diffusion of a greater portion of the solute into the periciliary sol layer which may be transported less efficiently than the mucus layer during mucociliary clearance. Bronchial blood flow has also been shown to modulate airway retention of soluble particles (Wagner and Foster, 2001, 156143), i.e., decreasing blood flow increases airway retention of soluble particles.

As an example of how transport of soluble components of PM may clear the lung by transepithelial absorption, Wallenborn et al. (2007, 156144) measured elemental content of lungs, plasma, heart, and liver of healthy male WKY rats (12-15 wk old) 4 or 24 h following a single intratracheal (IT) instillation of saline or 8.33 mg/kg of oil combustion PM containing a variety of transition metals with differing water and acid solubility. Metals with high water solubility and relatively high concentration in oil combustion PM were increased in extrapulmonary organs. Elements with low water or acid solubility, like silicon and aluminum, were not detected in extrapulmonary tissues despite decreased levels in the lung suggesting they cleared the lung primarily by mucociliary clearance. Thus, PM-associated metals deposited in the lung may be released into systemic circulation at different rates depending on their water/acid solubility.

The amount and type of water soluble or leachable metals associated with PM varies with location and by source. Furthermore some metals such as Zn, Cu, and Fe are essential to body function while others such as vanadium and nickel are nonessential metals. Consequently the body and the lung have different ways of dealing with excesses in inhaled soluble metals associated with PM. Bioavailability, and potentially the toxicity, of leachable metals may be altered by protein binding within the lung and blood as well as the affinities of these binding sites. For example Zn is tightly regulated by a variety of metal binding proteins, including metallothionein and a family of Zn specific transporters. In the plasma, Zn binds to many proteins, including α2-macroglobulin and albumin. Zn is an example of a common abundant water soluble metal in ambient air that may contribute to increased respiratory and cardiovascular disease risk associated with PM exposure. Wallenborn et al. (2009, 191172) recently showed that soluble Zn sulfate (in the form of ^{70}Zn, a rare isotope of Zn) introduced into the lungs by instillation not only reaches, but accumulates in extrapulmonary organs, including the heart and liver, following pulmonary exposure. However, the retention of greater than 50% of ^{70}Zn in the lung at 4 h post-instillation suggested that the transepithelial absorption of soluble Zn was indeed slowed by binding to proteins in the lungs. While it could not be ascertained if ^{70}Zn measured in the heart was replacing endogenous Zn pools, any accumulation in cardiac Zn levels could lead to mitochondrial dysfunction and ion channel disruption, possibly explaining adverse cardiac effects from inhalation of Zn-rich PM. Effects of Zn instillation on epithelial integrity were not evaluated.

4.4.2. Factors Modulating Clearance

A number of studies have evaluated the epithelial permeability by measuring the clearance of ^{99m}Tc-diethylenetriaminepentaacetic acid (^{99m}Tc-DTPA), a small hydrophilic solute (492 daltons, 0.57 nm). These studies are the basis for much of the discussion in this section.

4.4.2.1. Age

In humans, the clearance of water-soluble particles (^{99m}Tc-DTPA) from the alveolar epithelium generally slows with increasing age (Braga et al., 1996, 156289; Pigorini et al., 1988, 156027). However, Tankersley et al. (2003, 096363) recently showed enhanced permeability of soluble particles (^{99m}Tc-DTPA) in terminally senescent mice just before death, suggesting that a disintegration of the epithelial barrier may be a feature of lung homeostatic loss during this period of terminal senescence.

4.4.2.2. Physical Activity

The transepithelial transport rates of soluble particles, ^{99m}Tc-DTPA, have also been found to increase during exercise (Hanel et al., 2003, 155826; Lorino et al., 1989, 155946; Meignan et al., 1986, 156752). This enhancement was linked to increases in V_T associated with exercise (Lorino et al., 1989, 155946). Regionally, this effect was dominated by increased apical lung clearance and attributed to an increase in apical blood flow (Meignan et al., 1986, 156752). The increased permeability with exercise appears to resolve to baseline after a short period post exercise, i.e., within a couple hours (Hanel et al., 2003, 155826).

4.4.2.3. Disease

Because the integrity of the epithelial surface lining of the lungs may be damaged from lung disease, particles (either insoluble or soluble) may gain greater access to the interstitium, lymph, and blood stream. Damage to the epithelial barrier is most likely to acutely affect transepithelial transport rates of soluble particles. From bronchial biopsies, Laitinen et al. (1985, 037521) found various degrees of epithelial damage, from loosening of tight junctions to complete denudation of the airway epithelium, in asthmatics. Consistent with these findings, Ilowite et al. (1989, 156584) found that asthmatics had increased permeability of the bronchial mucosa to the hydrophilic solute ^{99m}Tc-DTPA. On the other hand, a more recent study in a sheep model showed that the presence of bronchial edema could slow the uptake of soluble DTPA into the blood and enhanced retention in the airways, likely within the expanded interstitial barrier (Foster and Wagner, 2001, 155778). Both a leaky epithelial barrier and expanded interstitial barrier associated with asthma may result in enhanced exposure of submucosal immune and smooth muscle cells to xenobiotic substances.

Alveolar epithelial permeability was also shown to be affected by the presence of lung inflammation. The most common finding has been a clear increase in alveolar permeability induced by cigarette smoking (Jones et al., 1980, 155883). This effect appears to be dependent on the recent cigarette smoke exposure as indexed by carboxyhaemoglobin (Jones et al., 1983, 155884) and is rapidly reversible within a week of smoking cessation (Mason et al., 1983, 013169). In fact, Huchon et al. (1984, 156576) demonstrated that COPD patients who have stopped smoking have normal clearance of ^{99m}Tc-DTPA.

In general, increased alveolar permeability to ^{99m}Tc-DTPA has been found to be associated with any lung syndrome characterized by pulmonary edema. While the trans-alveolar transport of a small solute like DTPA is very sensitive to even mild acute lung injury (such as that associated with even mild cigarette smoking), increased transport rates of larger molecules (>100K daltons) across the alveolar epithelium require more severe damage like that seen in adult respiratory distress syndrome (ARDS) (Braude et al., 1986, 155701; Peterson et al., 1989, 024922). Interstitial lung disease and pulmonary fibrosis are also characterized by increased alveolar permeability (Antoniou et al., 2006, 156220; Bodolay et al., 2005, 156280; Watanabe et al., 2007, 157115). Interestingly, these recent studies have also shown that the increased permeability in these patients could be corrected with immunosuppressive/steroid treatments (Bodolay et al., 2005, 156280; Watanabe et al., 2007, 157115). Furthermore, studies of DTPA clearance in bleomycin injured dogs, a model of pulmonary fibrosis, suggest that the enhanced permeability is associated with the initial acute phase of the lung damage, with clearance rates returning to normal as chronic fibrosis developed over time (Suga et al., 2003, 157024).

Finally, as evidence of lung complications associated with non-insulin dependent diabetes (type 2), Lin et al. (2002, 155932) found impairment of alveolar integrity as shown by increased transport rates of both hydrophilic and lipophilic solutes from the lungs in these patients. By contrast, a number of other studies have found epithelial permeability reduced, i.e., slower transport

rates, in diabetes (Caner et al., 1994, 156320; Mousa et al., 2000, 156786; Ozsahin et al., 2006, 156833) that may be related to disease duration and metabolic control (Ozsahin et al., 2006, 156833) . These findings are consistent with thickening of alveolar basement membrane detected in autopsies of diabetes patients (Weynand et al., 1999, 157140).

4.4.2.4. Concurrent Exposures

The integrity of the alveolar epithelium may be disrupted by co-pollutants such that soluble components of inhaled particles can more easily enter the interstitium and blood stream. Like active cigarette smoking discussed previously, Beadsmoore et al. (2007, 156259) showed clearance half-times in healthy passive smokers to be shorter compared with healthy non-smokers but still longer than in healthy smokers. These findings show a progressive increase in epithelial permeability with exposure to cigarette smoke. Similarly, acute exposure of humans to 0.4 ppm ozone for 2 h with intermittent exercise has been shown to alter epithelial integrity and increase clearance of soluble hydrophilic particles from the alveolar surfaces of the lung (Kehrl et al., 1987, 040824). This effect persists to at least 24 h post-exposure even following lower exposure levels (0.24 ppm average for 130 min) of ozone (Foster and Stetkiewicz, 1996, 079920). Similarly, 0.8 ppm O_3 exposure for 2 h in rats caused increased permeability to macromolecules at all levels of the respiratory tract (Bhalla et al., 1986, 040407) that persisted in the alveolar region beyond 24 h post-exposure. Cohen et al. (1997, 009213) may have best illustrated the competing effects of mucociliary and transepithelial transport by showing that coexposure to ozone affected the retention of inhaled chromium in rats differently depending on its solubility. In its soluble potassium chromate form, ozone decreased the retention of chromium, but when chromium was inhaled as insoluble barium chromate, its retention in the lung was increased by ozone coexposure. Similarly, a study that showed decreased clearance of insoluble cesium oxide particles following influenza infection also showed a virus-induced enhancement of clearance for a soluble cesium chloride (Lundgren et al., 1978, 155950). Chang et al. (2005, 097776) also recently showed that UF carbon black acts through a reactive oxygen species (ROS) dependent pathway to increase epithelial permeability in mice.

Chronic exposure to other particulate or gaseous pollutants does not always led to increased epithelial permeability. Studying subjects with a variety of occupational exposures, Kaya et al. (2006, 156632) showed that nonsmoking welders actually have decreased epithelial permeability relative to nonsmoking control subjects, and occupational exposure of painters to isocyanates has no effect on bronchoalveolar epithelial permeability (Kaya et al., 2003, 156631).

4.4.3. Summary

The healthy airway and alveolar epithelium is generally impermeable to very large insoluble macromolecules and particles. Water and acid soluble particles may more rapidly move through the epithelium as they dissolve on the airway surface or within the phagolysomes of macrophages. The presence of airway inflammation in a variety of airway diseases (e.g., asthma, fibrosis, ARDS, pulmonary edema, inflammation from smoking) alters epithelial integrity to allow more rapid movement of these solutes into the bloodstream. While diabetics are another group recently shown to have increased susceptibility to particulate air pollution (Zanobetti and Schwartz, 2002, 034821), it is unclear whether transport of soluble particles across the epithelium is affected in these patients. In general, it appears that coexposure to irritant pollutants results in a disruption of epithelial integrity and macrophage function which, on the one hand, retards mucociliary and alveolar clearance, but also allows for a more rapid movement of soluble constituents across the epithelial surface into the interstitium and blood stream. Alterations in epithelial permeability by disease, pollutant exposure, or infection may partially explain increased susceptibility to PM associated with these co-conditions.

Chapter 4 References

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Chapter 5. Possible Pathways/ Modes of Action

The mechanisms underlying pulmonary effects of inhaled PM have been well-studied in the laboratory and there is general agreement regarding the key roles played by cellular injury and inflammation. These pathways are initiated following the deposition of inhaled particles on respiratory tract surfaces. Since most of these studies were conducted at concentrations of PM much higher than ambient levels, there is some question regarding the relevance of these responses and mechanisms to ambient exposures.

Interestingly, inhaled PM may also affect the cardiovascular, hematopoietic and other systems. Mechanisms underlying these extra-pulmonary effects are incompletely understood. However, pulmonary inflammation can lead to systemic inflammation and pulmonary reflexes can activate the autonomic nervous system (ANS). These latter responses may mediate cardiovascular and other systemic effects, as will be discussed below. In addition, it has been proposed that PM or soluble components of PM reach the circulation by translocating across the epithelial and endothelial barriers of the respiratory tract. In this way, PM or its components may interact directly with cells in the vasculature and blood and be transported to the heart and other organs. At this time, evidence clearly supports the translocation of small solutes following inhalation exposures and the translocation of soluble components of PM following some high dose exposures involving intratracheal (IT) instillation. However, there is insufficient evidence to support translocation of appreciable amounts of intact particles following inhalation exposures at lower concentrations (Section 4.3.3.1). Future studies will be required to resolve these issues.

The following sections discuss biological pathways which comprise proposed modes of action for the pulmonary and extra-pulmonary effects of inhaled PM. Overall themes are emphasized and supportive evidence from new in vitro and in vivo animal studies is cited. The characterization of evidence here is for PM in general, since most of the potential pathways or modes of action do not appear to be specific to a particular size class of PM. However, characteristics of ultrafine particles (UFPs) may allow for unique modes of action or effects disproportionate to their mass, as will be described below. Recent studies suggest an enhanced potential of this size class of PM to cause adverse effects; however evidence supporting this hypothesis is limited. Finally, a compilation of results from new inhalation studies which are relevant to ambient PM exposures and which confirm and extend these proposed mechanisms is found at the end of this chapter. Detailed descriptions of these key new studies are found in Chapters 6 and 7.

5.1. Pulmonary Effects

5.1.1. Reactive Oxygen Species

A great deal of research interest has focused on the role of reactive oxygen species (ROS) in the initiation of pulmonary injury and inflammation following exposure to PM. Numerous studies have demonstrated PM oxidative potential in in vitro and in vivo assay systems (Ayres et al., 2008, 155666; Cho et al., 2005, 087937; Shi et al., 2003, 088248; Tao et al., 2003, 156111). Both redox active surface components, such as metals and organic species, and the surface characteristics of crystal structures have been shown to contribute to oxidative potential (Jiang et al., 2008, 156609; Tao et al., 2003, 156111; Warheit et al., 2007, 090482). In this way, PM may be a direct source of ROS in the respiratory tract (Figure 5-1).

Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISA) and the Integrated Risk Information System (IRIS).

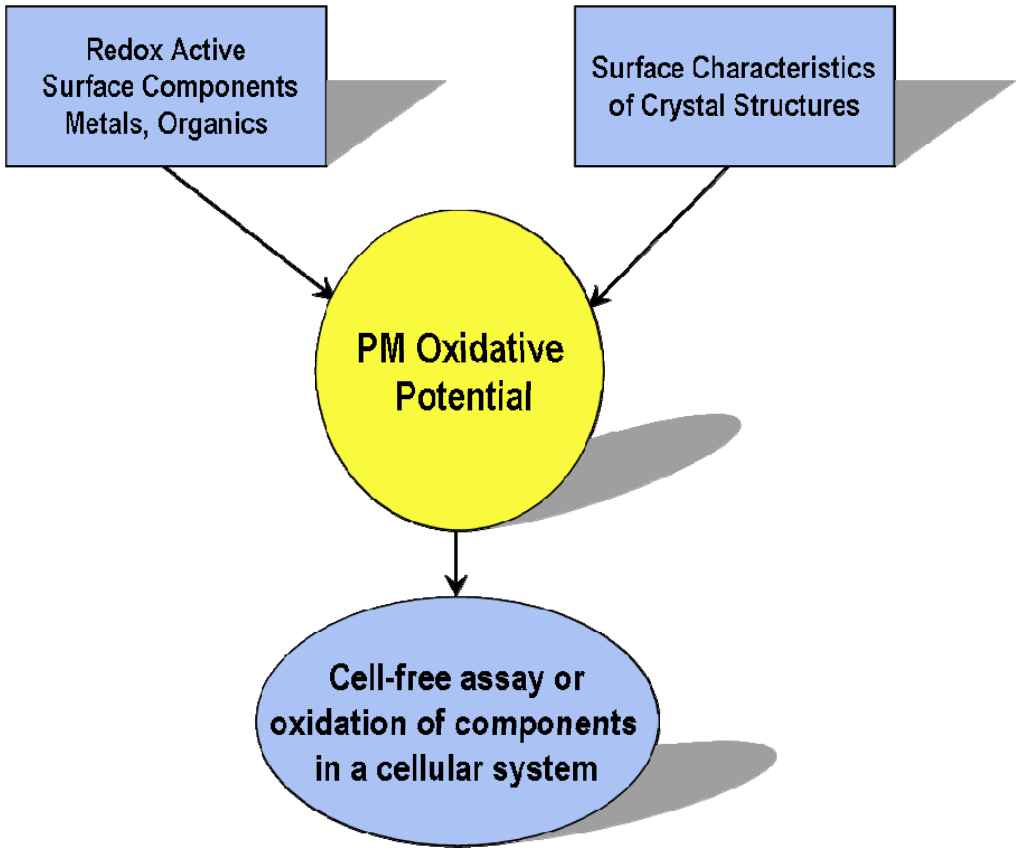

Figure 5-1. PM oxidative potential.

PM may also act as an indirect source of ROS in the respiratory tract by stimulating cells to produce ROS (Ayres et al., 2008, 155666; Tao et al., 2003, 156111) (Figure 5-2). This may explain the observation that the oxidative potential of isolated PM does not always correlate with cellular or tissue oxidative stress induced by PM exposure. Exposure to PM increases intracellular production of ROS by a variety of mechanisms. For example, PM interaction with cell surfaces results in stimulation of NADPH oxidase in macrophages (i.e., the respiratory burst) (Dostert et al., 2008, 155753) and in epithelial cells (Amara et al., 2007, 156212; Becher et al., 2007, 097125; Tamaoki et al., 2004, 157040). Absorption of PM soluble components (e.g., PAH, transition metals) by respiratory tract cells can occur (Penn et al., 2005, 088257) and be followed by microsomal transformation of PAHs to quinones or by redox cycling of transition metals with production of intracellular ROS (Molinelli et al., 2002, 035347; Xia et al., 2004, 087486). Disruption of intracellular iron homeostasis with the subsequent generation of ROS has also been demonstrated following PM exposure (Ghio and Cohen, 2005, 088272). In some cases, mitochondria serve as the source of ROS in response to PM (Huang et al., 2003, 156573; Risom and Loft, 2005, 089070; Soberanes et al., 2006, 156991; Soberanes et al., 2009, 190483). Furthermore, PM interaction with cells can lead to the induction of nitric oxide synthase (Becher et al., 2007, 097125; Lindbom et al., 2007, 155934; Xiao et al., 2005, 156164; Zhao et al., 2006, 100996) and the production of nitric oxide and other reactive nitrogen species (RNS).

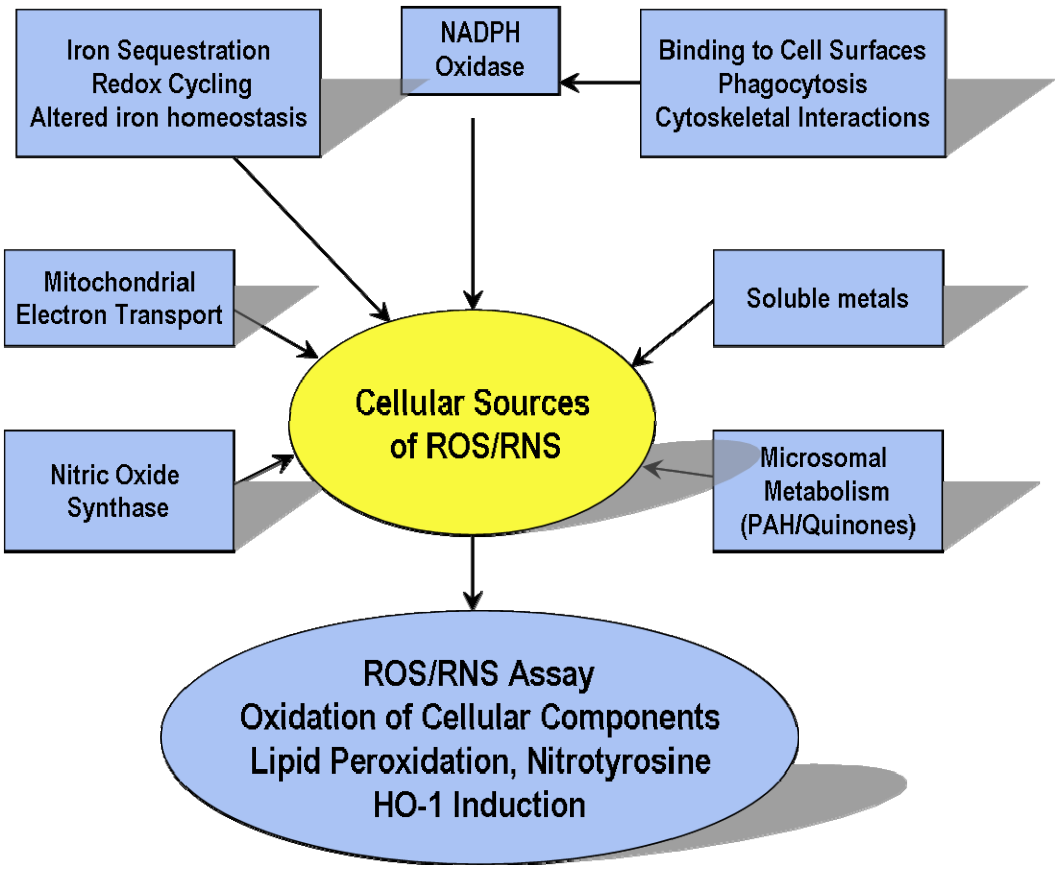

Figure 5-2 PM stimulates pulmonary cells to produce ROS/RNS.

Although all size fractions of PM may contribute to oxidative and nitrosative stress, UFPs may contribute disproportionately to their mass due to their large surface/volume ratio. The relative enrichment of redox active surface components, such as metals and organics, per unit mass may translate to a relatively greater oxidative potential of UFPs compared with larger particles with similar surface components. In addition, the greater surface per unit volume could potentially deliver relatively more adsorbed soluble components to cells. These components may undergo intracellular redox cycling following cellular uptake. Furthermore, per unit mass, UFPs may have more opportunity to interact with cell surfaces due to their greater surface area and their greater particle number compared with larger PM. These interactions with cell surfaces can lead to ROS generation, as described above. Recent studies have also demonstrated that UFPs have the capacity to cross cellular membranes by non-endocytotic mechanisms involving adhesive interactions and diffusion (Geiser et al., 2005, 087362), as described in Chapter 4. This may allow UFPs to interact with or penetrate intracellular organelles.

In general, high levels of intracellular ROS/RNS can lead to irreversible protein modifications, loss of cellular membrane integrity, DNA damage and cellular toxicity. Lower levels of ROS/RNS may cause reversible protein modifications that trigger intracellular signaling pathways and/or adaptive responses. Thus PM-dependent generation of ROS may be responsible for a continuum of responses from cell signaling to cellular injury.

5.1.2. Activation of Cell Signaling Pathways

Activation of cell signaling pathways by ROS/RNS has received increasing attention by numerous investigators over the years. An early example was provided by Kaul and Forman (1996, 155892) who demonstrated that respiratory burst-derived H_2O_2 activates the transcription factor

nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB). Numerous studies since then have demonstrated that PM, which serves as both a direct and indirect source of ROS/RNS, activates cell signaling pathways by this mechanism.

PM also has the potential to activate cell signaling by mechanisms that are independent of ROS/RNS. For example, PM delivers water-soluble components, such as endotoxin and zinc (Zn), to cell surfaces. Endotoxin binds to toll-like receptors on alveolar macrophages and other cells, resulting in the upregulation of cytokines (Becker et al., 2002, 052419). Zn, a transition metal which does not redox cycle, inhibits protein tyrosine phophatases in airway epithelial cells resulting in a cascade of cell signaling events (Tal et al., 2006, 108588). Similarly, PM-mediated delivery of lipid soluble components such as PAH results in binding and activation of the arylhydrocarbon receptor (AhR). AhR is a transcription factor responsible for the upregulation of CYP1A1, a cytochrome oxidase involved in PAH biotransformation to metabolites capable of forming DNA adducts or eliciting oxidative stress responses (Rouse et al., 2008, 156930). In addition, interaction of PM with cell surfaces may activate cell signaling by perturbation of the cytoskeleton, adherence, internalization, or receptor-mediated pathways.

Recent studies involving PM exposures have focused on intracellular pathways involving protein kinases, such as mitogen-activated protein kinase (MAPK) (Bayram et al., 2006, 088439; Lee et al., 2005, 156682; Roberts et al., 2003, 156051; Soberanes et al., 2009, 190483); AKT (Ahsan et al., 2005, 156200); src (Cao et al., 2007, 156322) and epidermal growth factor receptor (Blanchet et al., 2004, 087982; Cao et al., 2007, 156322; Tamaoki et al., 2004, 157040), as well as ras (Tamaoki et al., 2004, 157040), toll-like receptors (Becker et al., 2002, 052419; Becker et al., 2005, 088590), protein tyrosine phosphatases (Tal et al., 2006, 108588), phospholipases A_2 (Lee et al., 2003, 156678), calcium (Agopyan et al., 2003, 155649; Brown et al., 2004, 155705; Brown et al., 2004, 088663; Geng et al., 2005, 096689; 2006, 097026; Sakamoto et al., 2007, 096282), caspases (Soberanes et al., 2006, 156991; Zhang et al., 2007, 156179), poly (ADP-ribose) polymerase family member 1 (PARP-1) (Zhang et al., 2007, 156179) and histone acetylation (Gilmour et al., 2003, 096959). The transcription factors regulated by these pathways, including NF-κB (Bayram et al., 2006, 088439; Lee et al., 2005, 156682; Takizawa et al., 2003, 157039), activator protein 1 (AP-1) (Donaldson et al., 2003, 156408), signal transducers and activators of transcription protein (STAT) (Cao et al., 2007, 156322), antioxidant response element (ARE) (Li and Nel, 2006, 156694), and AhR (Rouse et al., 2008, 156930) have also been studied following PM exposures. Activation of these intracellular pathways and transcription factors leads to the upregulation of genes responsible for inflammatory, immune and acute phase responses as well as genes responsible for antioxidant defense and xenobiotic metabolism.

5.1.3. Pulmonary Inflammation

Following PM exposure, transcription factor activation in macrophages and epithelial cells stimulates the synthesis and release of soluble mediators involved in inflammatory and immune responses including cytokines, chemokines, proteases and eicosanoids (Figure 5-3). These substances play a role in recruiting inflammatory cells such as neutrophils, monocytes, mast cells and eosinophils to the lung. Interactions between macrophages and epithelial cells enhance these responses (Tao and Kobzik, 2002, 157044).

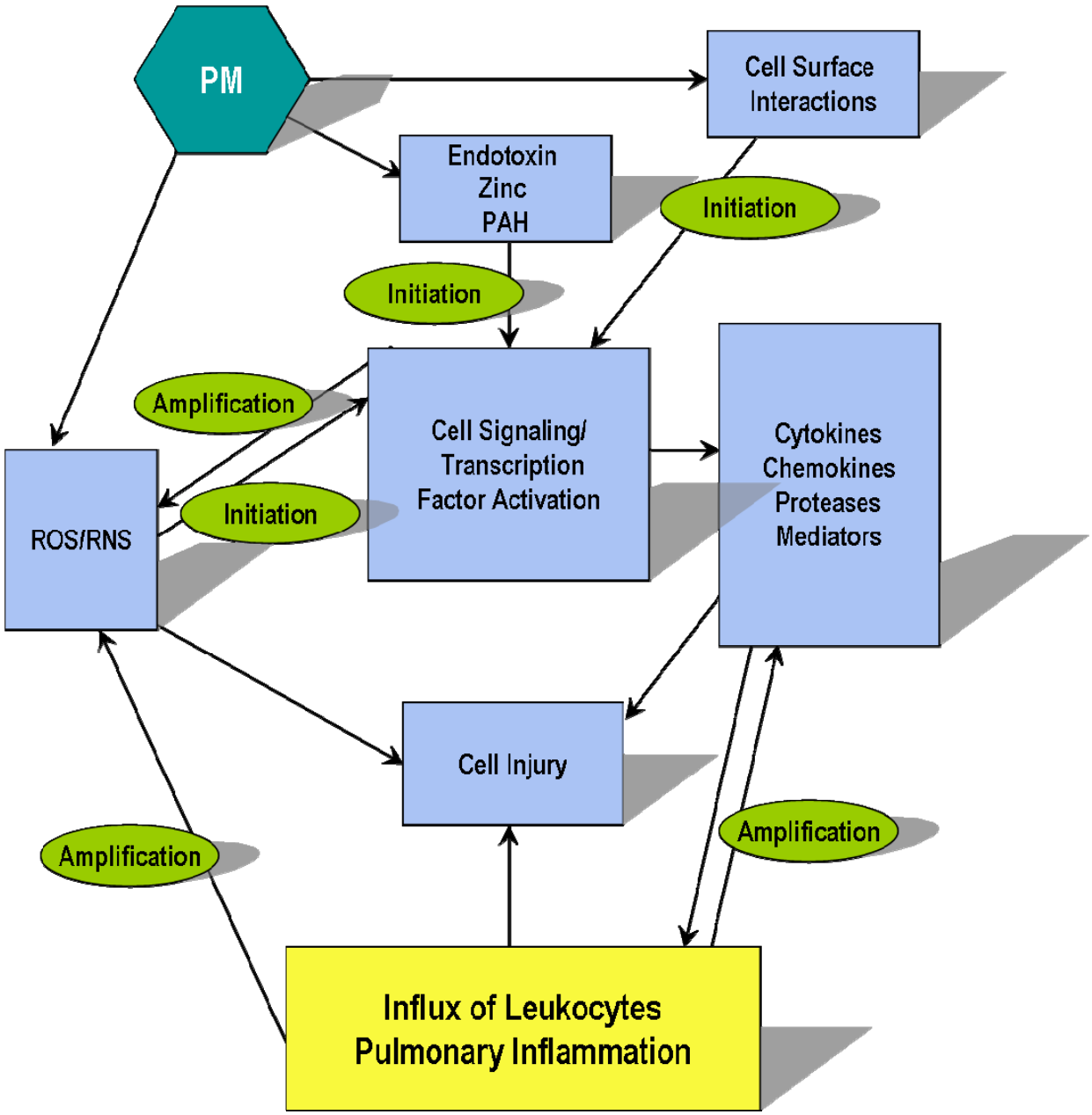

Figure 5-3. PM activates cell signaling pathways leading to pulmonary inflammation.

Inflammatory cells can serve as a source of extracellular ROS which, along with soluble mediators derived from the inflammatory cells, amplify the inflammatory response. Unchecked inflammation may cause cellular and tissue injury through the generation of excess amounts of ROS and soluble mediators. In some cases the oxidative potential of PM is well-correlated with the degree of inflammation (Dick et al., 2003, 036605), suggesting that the inflammation is a direct consequence of PM-generated ROS. However, in other cases the oxidative potential of PM is not well-correlated with the degree of inflammation (Beck-Speier et al., 2005, 156262), suggesting that the inflammation is a consequence of the ROS-independent mechanisms by which PM activates intracellular signaling pathways. Particle surface area has been identified as a key determinant of the extent of inflammation in the case of low-toxicity, low-solubility particles (Donaldson et al., 2008,

190217). Moreover, UFPs may cause inflammation disproportionately to their mass compared with PM of larger sizes given their large surface/volume ratio compared with other PM fractions.

PM exposure often results in neutrophilic inflammation in laboratory studies (Tao et al., 2003, 156111). Neutrophilic inflammation is also associated with acute lung injury in humans as well as chronic lung diseases such as COPD and certain forms of asthma (Barnes, 2007, 191139; Cowburn et al., 2008, 191142). Circulating neutrophils respond to chemotactic factors in the lung such as leukotriene B_4 and IL-8 (Barnes, 2007, 191139). They migrate into the lung parenchyma across the pulmonary capillary network and into the airways from the bronchial circulation (Cowburn et al., 2008, 191142). As a consequence of priming by inflammatory mediators or contact with extracellular matrix components, neutrophils become hyperresponsive to activating signals and insensitive to chemotactic signals (Cowburn et al., 2008, 191142). Activation results in neutrophil degranulation, respiratory burst responses and soluble mediator release (Cowburn et al., 2008, 191142). Neutrophils eventually undergo apoptosis and are phagocytized by inflammatory macrophages (Cowburn et al., 2008, 191142). This is accompanied by the release of anti-inflammatory mediators such as IL-10 and transforming growth factor-β (TGF- β) (Cowburn et al., 2008, 191142). These steps are key to the resolution of inflammation and prevent unregulated release of toxic neutrophil products such as neutrophil elastase (Cowburn et al., 2008, 191142). Thus, circumstances leading to the decreased ingestion of apoptotic neutrophils by macrophages may lead to tissue injury. Impairment of macrophage function may serve as an important mechanism by which PM contributes to disease.

5.1.4. Respiratory Tract Barrier Function

Epithelial injury can lead to an increase in permeability of the airway epithelial and alveolar-capillary barriers (Braude et al., 1986, 155701). Enhanced transport of soluble and possibly of insoluble PM components into the circulation may occur under these conditions. Increased epithelial permeability is also associated with enhanced immune responses to proteins, including allergens, on the epithelial surface, presumably due to the greater availability of antigens to underlying immune cells (Wan et al., 1999, 191903). Furthermore, endothelial injury can compromise the integrity of the alveolar-capillary barrier resulting in transvascular fluid and solute flux (Braude et al., 1986, 155701). Soluble mediators derived from inflammatory and lung cells (Chang et al., 2005, 097776) and peptides released by some nerve cells (Widdicombe and Lee, 2001, 019049) can increase the permeability of the alveolar-capillary barrier and result in alveolar edema. Compromised barrier function in the airways may lead to airway edema. Edema occurring secondarily to nerve cell stimulation is one component of the process termed neurogenic inflammation.

Given the small size of UFPs, modest changes in epithelial permeability may particularly affect the disposition of this fraction. Enhanced translocation to interstitial compartments or to the circulation may be important sequelae. A recent study described in Section 4.3.4.3 demonstrated greater translocation of UFPs compared with $PM_{2.5}$ into the circulation of rodents treated with endotoxin to induce acute lung injury prior to IT instillation of PM (Chen et al., 2006, 147267). Furthermore, epithelial injury in another model resulted in greater translocation of UFPs into the interstitial compartment (Adamson and Prieditis, 1995, 189982).

5.1.5. Antioxidant Defenses and Adaptive Responses

Antioxidant defenses and adaptive responses are important modulators of oxidative stress and other cellular stresses resulting from PM exposure. Antioxidants are present in the epithelial lining fluid in all regions of the respiratory tract. In addition, they are present in cells of the lung parenchyma and inflammatory cells found in airways and alveoli. Some antioxidants act directly against oxidant species (e.g., glutathione, ascorbate, superoxide dismutase) while others act indirectly (e.g., gamma-glutamylcysteine synthetase [γGCS], glutathione reductase). Furthermore, some antioxidants (e.g., Phase 2 enzymes heme oxygenase-1[HO-1], NADPH quinone oxidoreductase 1 [NQO1], glutathione-S-transferase [GST]) are inducible via activation of the nuclear factor (erythroid-derived 2)- related factor 2 (Nrf2)-ARE pathway, which occurs as an adaptive response to stress (Cho et al., 2006, 156345; Li and Nel, 2006, 156694). Antioxidants play

an important role in reducing the oxidative potential of those PM species that directly generate ROS. They also inhibit responses due to generation of intracellular ROS.

Recently a three-tier response to oxidative stress was proposed (Li and Nel, 2006, 156694). In this scheme, mild oxidative stress enhances antioxidant defenses by upregulating Phase 2 and other antioxidant enzymes (Tier 1). Further increase in oxidative stress induces inflammation (Tier 2) and cell death (Tier 3). Experimental evidence is supportive of this scheme. Numerous studies have demonstrated that enhancement of lung and cellular antioxidant defenses inhibits inflammation, cytotoxicity and other responses following exposure to PM (Ahsan et al., 2005, 156200; Bachoual et al., 2007, 155667; Bayram et al., 2006, 088439; Chang et al., 2005, 097776; Imrich et al., 2007, 155859; Koike and Kobayashi, 2005, 088303; Koike et al., 2004, 058555; Li et al., 2007, 155929; Ramage and Guy, 2004, 055640; Rhoden et al., 2004, 087969; Steerenberg et al., 2004, 087981; Takizawa et al., 2003, 157039; Tao et al., 2003, 156111; Upadhyay et al., 2003, 097370; Wan and Diaz-Sanchez, 2006, 097399; Wan and Diaz-Sanchez, 2007, 156145; Yin et al., 2004, 087983).

Cellular and tissue exposure to xenobiotics carried by PM can lead to induction of Phase 1 and Phase 2 detoxifying enzymes following the activation of cell signaling pathways and transcription factors AhR and ARE, respectively (Rengasamy et al., 2003, 156907; Rouse et al., 2008, 156930; Zhao et al., 2006, 100996).

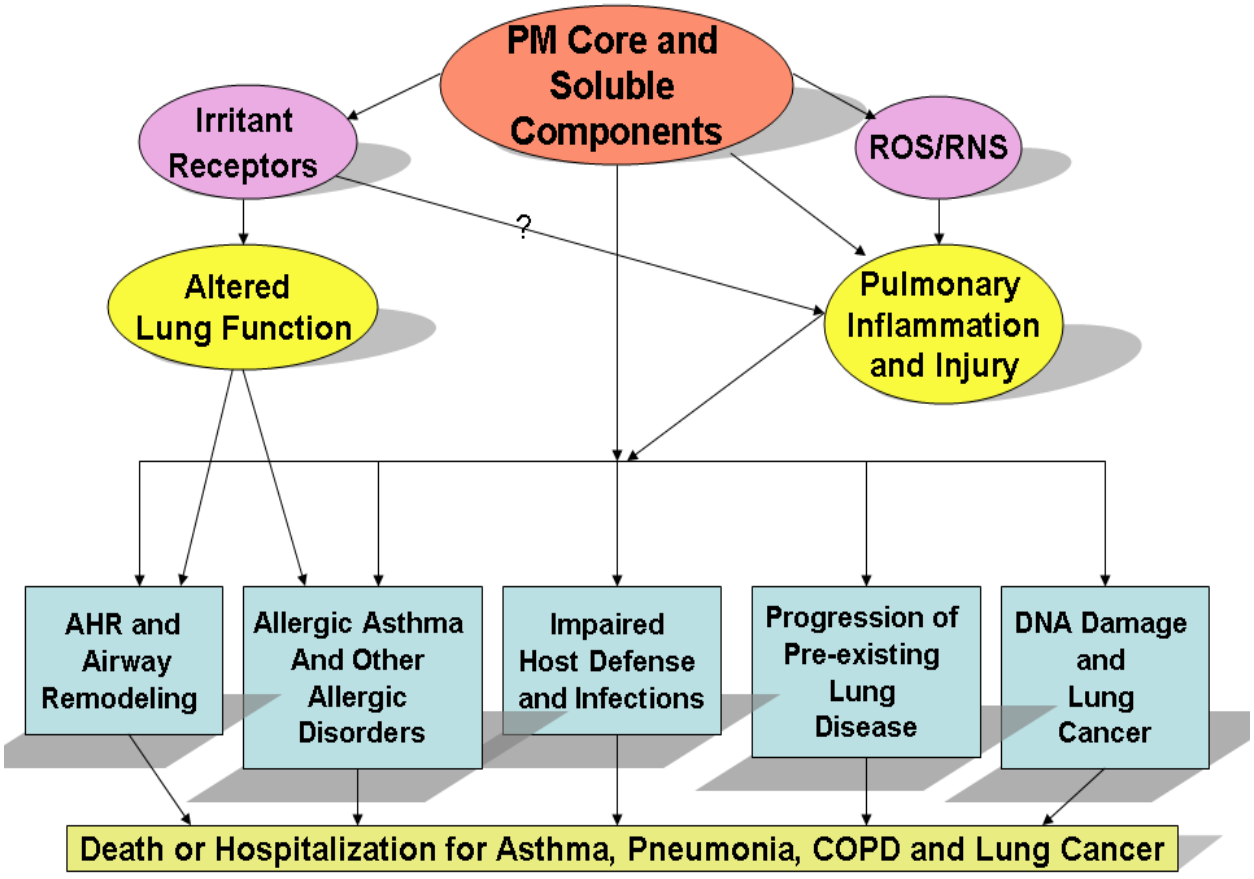

Figure 5-4. Potential pathways for the effects of PM on the respiratory system.

5.1.6. Pulmonary Function

PM exposure may alter pulmonary function by a variety of different mechanisms (Figure 5-4). In the short-term, airway hyperresponsiveness (AHR) may ensue due to the influence of inflammatory mediators. In the long-term, morphological changes may occur, in some cases leading to mucus hypersecretion and airway remodeling. Activation of irritant receptors and stimulation of the ANS in the respiratory tract is another mechanism by which PM exposure may alter pulmonary function (Section 5.4).

5.1.7. Allergic Disorders

PM exposure sometimes leads to the development of allergic immune responses (Figure 5-4). These responses are predominately mediated by T helper 2 cells (Th2). Th1 responses, characterized by IFN-γ and classical macrophage activation, are inflammatory; in excess they can lead to tissue damage. Alternatively, Th2 responses are associated with allergy and asthma and are characterized by IL-4, IL-5, IL-13, influx of eosinophils, B–lymphocyte production of IgE, and alternative macrophage activation. PM exposure can also lead to the exacerbation of airway allergic responses, such as antigen-specific IgE production and AHR.

Due to soluble mediators and immune cell trafficking, pulmonary exposure may result in systemic immune alterations. Not only do macrophages ingest PM, but they are also antigen presenting cells whose level of activation dictates costimulation and thus subsequent T cell responses. These cells are highly mobile and can transport PM to other sites such as lymph nodes. Dendritic cells (DC) also play a key role as antigen presenting cells and in modulating T and B cell activity. A cell culture model of the human epithelial airway wall was used to demonstrate that DC extended processes between epithelial cells through the tight junctions, collected particles in the lumenal space and transported them across the epithelium (Blank et al., 2007, 096521). DC also transmigrated through the epithelium to take up particles on the epithelial surface (Blank et al., 2007, 096521). Furthermore, DC interacted with particle-loaded macrophages on top of the epithelium and with other DC within or beneath the epithelium to transfer particles (Blank et al., 2007, 096521). In vitro studies also demonstrated that the adjuvant activity of diesel exhaust particles (DEPs) involved stimulation of immature monocyte-derived dendritic cells (iMDDC) to undergo maturation in response to an altered airway epithelial cell-derived microenvironment (Bleck et al., 2006, 096560). Additionally, DEP directly influenced the profile of cytokines secreted by DC and caused a predisposition toward Th2-mediated or allergic responses (Chan et al., 2006, 097468). Thus PM can negatively affect both innate immunity through effects on macrophage pathogen handling (Section 5.1.8) as well as adaptive immunity by altering macrophage or DC antigen presenting activity and subsequent T cell responses.

Moreover, recent studies have demonstrated that ambient PM can act as an adjuvant for allergic sensitization with UFPs having a greater effect than fine particles (de Haar et al., 2006, 144746; Li et al., 2009, 190457). This has been attributed to higher oxidative potential of the UFPs compared with the same mass of particles of larger size (Li et al., 2009, 190457), although the larger surface area and particle number per unit mass as well as the propensity of UFPs for trans-epithelial movement may also contribute to this effect.

5.1.8. Impaired Lung Defense Mechanisms

PM exposure may impair lung defense mechanisms and result in frequent or persistent infections (Figure 5-4). Potential targets include mucociliary transport, surfactant function and pathogen clearance. Pathogen clearance is dependent on the integrity of macrophages and their migration, phagocytosis and respiratory burst functions. PM-mediated cytotoxicity of macrophages with the concomitant release of lysosomal contents may affect pathogen clearance and cause damage to nearby cells and tissues. IT instillation and cell culture experiments have demonstrated PM-dependent impairment of lung defense mechanisms (Jaspers et al., 2005, 088115; Kaan and Hegele, 2003, 095753; Long et al., 2005, 087454; Moller et al., 2005, 156770; Monn et al., 2003, 052418; Roberts et al., 2007, 097623; Yin et al., 2004, 087983).

5.1.9. Resolution of Inflammation/Progression or Exacerbation of Disease

Resolution of pulmonary inflammation and injury has been demonstrated in many experimental models using higher than ambient concentrations of PM. Factors contributing to this complex process are likely to include the uptake and clearance of PM by macrophages; the retention of PM in parenchymal cells and tissues; the balance of pro/anti-inflammatory soluble mediators, oxidants/antioxidants and proteases/anti-proteases; and the presence of pre-existing disease. These factors may also influence the resolution of pulmonary responses to ambient PM exposures (Figure 5-4). The long-term consequences of prolonged inflammation are not likely to be beneficial and may lead to remodeling of the respiratory tract and to the progression or exacerbation of disease.

5.1.9.1. Factors Affecting the Retention of PM

Clearance of poorly soluble particles from ET, TB and alveolar regions is extensively discussed in Section 4.3. While clearance from ET and TB regions generally occurs over hours to days, clearance from the alveolar compartment is much slower, occurring over months to years depending on the species. Phagocytosis by alveolar macrophages and transport by the mucociliary escalator is the primary mechanism of clearance from the alveolar compartment although neutrophil phagocytosis also plays a role (Snipes et al., 1997, 156092). Pre-existing disease can alter the extent and localization of PM deposition as discussed in Section 4.2.4.5. In addition, mechanisms of clearance may be altered in cases of pre-existing disease as discussed in Section 4.3.4.3. While mild asthma was associated with enhanced mucociliary clearance, acute lung injury was associated with enhanced particle translocation to the circulation and the interstitial compartment. Whether retained particles are localized in alveolar macrophages or parenchymal tissue also differs according to species (Snipes, 1996, 076041).

UFPs may have a special propensity for retention given the decreased efficiency of alveolar macrophages for phagocytosis of this size particle (Oberdörster, 1988, 006857) and the demonstration that UFPs can readily cross cellular membranes (Geiser et al., 2005, 087362). Some studies suggest that UFPs are taken up by epithelial cells and move to the interstitum where they are cleared by other pathways (Semmler-Behnke et al., 2007, 156080); however clearance mechanisms are not entirely understood.

Enhanced deposition of particles in "hot spots" may influence retention. For example, deposition in the centriacinar or proximal alveolar region, where clearance is slow, may result in accumulated particle dose in this region and the potential for prolonged inflammation at the site leading to the development of pulmonary fibrosis or emphysema (Donaldson et al., 2008, 190217). A recent study suggests an important role for retained particles in the progression of disease. Complexation of endogenous iron by retained particles resulted in retained particles growing larger over time. The authors suggested that redox cycling of complexed iron may be responsible for disease progression (Ghio and Cohen, 2005, 088272; Ghio et al., 2004, 155790).

5.1.9.2. Factors Affecting the Balance of Pro/Anti-Inflammatory Mediators, Oxidants/Anti-Oxidants and Proteases/Anti-Proteases

Inflammation can be enhanced by pro-inflammatory mediators or dampened by anti-inflammatory mediators. Production of anti-inflammatory mediators normally occurs at several steps of the inflammation pathway, such as the release of IL-10 and TGF-β during phagocytosis of apoptotic neutrophils by macrophages (Cowburn et al., 2008, 191142). Dsyregulation of the inflammatory process may prevent the resolution of inflammation. PM exposure may result in the production of pro-inflammatory mediators as well as decrease the production of anti-inflammatory mediators by impairing macrophage function.

An unfavorable balance of oxidants to antioxidants in the lung is associated with inflammatory lung diseases including asthma and COPD (Rahman et al., 2006, 191165). PM is likely to contribute to an unfavorable balance through its oxidative potential and capacity to promote cellular production of ROS. Exacerbations of asthma and COPD resulting from bacterial and viral infections are also associated with increased oxidative stress (Barnes, 2007, 191139). Conversely, antioxidants may reduce neutrophilic inflammation associated with oxidative stress (Barnes, 2007, 191139).

Protease/anti-protease balance has long been tied to the pathogenesis of emphysema and other forms of COPD (Owen, 2008, 191162). Key steps include the release of proteinases by inflammatory cells which degrade the extracellular matrix components of alveolar walls. Destruction of alveolar walls and airspace enlargement ensues. Endogenous anti-protease defenses in the lung modulate this response but may be insufficient to prevent it during prolonged inflammation. Proteases also play a role in pathologies which lead to small airway fibrosis (Owen, 2008, 191162). Oxidative stress has been linked to both activation of proteases and inactivation of anti-proteases (Owen, 2008, 191162). PM may contribute to an unfavorable protease/anti-protease balance through the generation of ROS.

Although there are numerous inflammatory cell-derived proteases and lung anti-proteases, many recent studies have focused on matrix metalloproteinases (MMPs). MMPs are a family of Zn-containing enzymes normally found in an inactive pro-enzyme form. Activation involves proteolytic cleavage or oxidation of the "cysteine switch" (Pardo and Selman, 2005, 191163). Inhibitors include tissue inhibitors of metalloproteinases (TIMPs) (Pardo and Selman, 2005, 191163). In particular, MMP-1 is well-studied and found to play an important role in physiological processes such as development and wound repair as well as in diseases such as pulmonary emphysema, fibrosis, asthma and bronchial carcinoma (Li et al., 2009, 190424; Pardo and Selman, 2005, 191163). In addition to its activity in degrading collagenase, MMP-1 also acts on non-matrix substrates and cell surface molecules suggesting that it may influence cell signaling (Pardo and Selman, 2005, 191163). MMP-2 and MMP-9 are thought to be involved in the pathogenesis of disease through their gelatinase activity. Interestingly, recent in vitro studies have demonstrated upregulation of MMP-1 by hydrogen peroxide, cigarette smoke and DEPs (Amara et al., 2007, 156212; Li et al., 2009, 190424; Mercer et al., 2004, 191180), and up-regulation of MMP-12 following instillation of PM collected from the Paris subway (Bachoual et al., 2007, 155667). These considerations suggest that particulate air pollution may act via MMP to mediate progression or exacerbation of lung disease.

5.1.9.3. Pre-Existing Disease

In addition to its effects on deposition, retention and clearance of PM described above, pre-existing disease may also alter the balance of the aforementioned factors. For example, acute exacerbations of COPD are characterized by a rapid influx of neutrophils into the airways (Owen, 2008, 191162). However, clearance of apoptotic neutrophils by macrophages is impaired in COPD leading to greater release of neutrophil-derived inflammatory mediators, oxidants and proteases (Owen, 2008, 191162). Thus, exacerbation of disease may occur as a result of unchecked inflammation.

5.1.10. Pulmonary DNA Damage

Pulmonary DNA damage can occur primarily or secondarily to PM exposure. Primary effects include oxidative DNA injury or DNA adduct formation due directly to PM while secondary effects occur due to PM-mediated inflammation (De Kok et al., 2005, 088656; Gabelová et al., 2007, 156457; Gallagher et al., 2003, 140171; Schins and Knaapen, 2007, 156074). These responses may lead to chromosomal aberrations or DNA strand breaks. PM effects on cell cycle arrest, proliferation, apoptosis, and DNA repair mechanisms may also influence the genotoxic, mutagenic or carcinogenic potential of DNA damage as reviewed by Schins et al. (2007, 156074).

5.1.11. Epigenetic Changes

Epigenetic mechanisms regulate the transcription of genes without altering the nucleotide sequence of DNA. These mechanisms generally involve DNA methylation and histone modifications, leading to alterations which may have long-term consequences or are heritable (Jones and Baylin, 2007, 191153; Keverne and Curley, 2008, 191154). DNA methylation and histone modifications, which include methylation, acetylation, phosphorylation, ubiquitylation and sumoylation, are known to be linked (Hitchler and Domann, 2007, 191151; Jones and Baylin, 2007, 191153). Numerous studies have identified epigenetic processes in the control of cancer (Foley et al., 2009, 191144; Gopalakrishnan et al., 2008, 191147; Jones and Baylin, 2007, 191153; Valinluck et al., 2004, 191170), embryonic development (Foley et al., 2009, 191144; Gopalakrishnan et al., 2008,

191147; Keverne and Curley, 2008, 191154) and inflammation and other immune system functions (Adcock et al., 2007, 191178).

Epigenetic modifications resulting in decreased expression of tumor suppressor genes and increased expression of transforming genes have been observed in human tumors (Valinluck et al., 2004, 191170). In general, transcription repression is associated with DNA methylation in promoter regions of genes. Cytosine methylation in CpG dinucleotides has emerged as an important, heritable epigenetic modification which can result in chromatin remodeling and decreased gene expression (Valinluck et al., 2004, 191170). Global changes in DNA methylation are also seen in cancer and hypomethylation is associated with genomic instability (Gopalakrishnan et al., 2008, 191147).

Embryonic development is characterized by several phases of epigenetic modifications. DNA methylation is very dynamic following fertilization, with demethylation and re-methylation of egg and sperm genomes occurring immediately (Foley et al., 2009, 191144). Imprinted genes, however, retain the methylation profile of the parent of origin (Foley et al., 2009, 191144). Epigenetic changes accumulated through a life course may be passed from parent to offspring in the germline (i.e., germline transmission of epimutation) if they survive the epigenetic remodeling that occurs during gametogenesis and early embryogenesis (Foley et al., 2009, 191144). Early development is characterized by the process of cell differentiation, which produces different cell types and involves the selective activation of some sets of genes and the silencing of others in a temporal pattern (Foley et al., 2009, 191144; Gopalakrishnan et al., 2008, 191147). DNA methylation is postulated to provide a basis for cell differentiation (Gopalakrishnan et al., 2008, 191147).

In the lung, histone acetylation and methylation have been linked to inflammatory gene expression, T cell differentiation, and the regulation of macrophage function following pathogen challenge (Adcock et al., 2007, 191178). Furthermore, altered patterns of methylation and acetylation have been reported in inflammatory diseases (Adcock et al., 2007, 191178). Reduced expression and activity of histone deacetylase have been demonstrated in lung and inflammatory cells in COPD and asthma (Adcock et al., 2007, 191178; Barnes, 2007, 191139). Consequently, histone deacetylase has been identified as a potential therapeutic target for epigenetic therapy (Adcock et al., 2007, 191178; Jones and Baylin, 2007, 191153).

Epigenetic mechanisms have been identified as potential targets for gene-environment interactions and recent studies have demonstrated that diet, cigarette smoking, endocrine disrupters, heavy metals and bacterial infection can alter the epigenetic profile in animals and humans (Foley et al., 2009, 191144). A role for PM in promoting epigenetic changes has been proposed and new studies, discussed in later chapters, provide some evidence for this pathway (Baccarelli et al., 2009, 192155; Liu et al., 2008, 156709; Reed et al., 2008, 156903; Tarantini et al., 2009, 192010; Tarantini et al., 2009, 192153; Yauk et al., 2008, 157164).

Early life exposures may be especially important in this regard since periods of rapid cell division and epigenetic remodeling are likely to occur at this time (Foley et al., 2009, 191144; Keverne and Curley, 2008, 191154; Wright and Baccarelli, 2007, 191173). This may provide a basis for fetal origins of adult disease.

It has been suggested that DNA methylation is regulated by oxygen gradients and redox status (Hitchler and Domann, 2007, 191151). While this is of particular importance during development where oxygen gradients and redox status are linked to cellular differentiation, these processes are also important for cell signaling during all stages of life. A common metabolic precursor for both methylation reactions and glutathione availability (involved in redox status) is methionine (Hitchler and Domann, 2007, 191151). Methionine availability regulates the cell's ability to generate S-adenosyl methionine which is directly involved in DNA and histone methylation and the cell's ability to generate homocysteine/cysteine which is involved in glutathione biosynthesis (Hitchler and Domann, 2007, 191151). Furthermore, the folate cycle is a key determinant of methionine bioavailability (Hitchler and Domann, 2007, 191151). In this way, cellular intermediary metabolism is linked to epigenetic processes, with oxidative stress necessitating a metabolic shift resulting in decreased DNA methylation and increased glutathione production.

5.1.12. Lung Development

Lung development is a multi-step process which begins in embryogenesis and continues to adult life (Pinkerton and Joad, 2006, 091237). This allows for a long period of potential vulnerability to environmental and other stressors. Furthermore, enzymatic systems responsible for detoxification of xenobiotic compounds are not fully developed until the postnatal period (Pinkerton and Joad,

2006, 091237). Disruption of cell signaling during development could affect cellular differentiation, branching morphogenesis and overall lung growth, possibly leading to life-long consequences. Although very little is known about the effects of maternal exposure to PM on the fetus or the effects of exposure during childhood, recent animal studies demonstrate respiratory and immune system effects of perinatal exposure to sidestream cigarette smoke (Pinkerton and Joad, 2006, 091237; Wang and Pinkerton, 2007, 179975).

5.2. Systemic Inflammation

Pulmonary inflammation resulting from PM exposure may trigger systemic inflammation through the action of cytokines and other soluble mediators which leave the lung and enter the circulation (Figure 5-5). Epithelial permeability may exert an important influence on this process (Section 5.1.4). Cytokines released by alveolar macrophages can stimulate bone marrow production of leukocytes resulting in an increased number of total and immature leukocytes in the circulation (Van and Hogg, 2002, 088111; Van Eeden et al., 2001, 019018). They also can activate neutrophils and promote their sequestration in microvascular beds (Van Eeden et al., 2001, 019018). The time course of these responses varies according to the acute or chronic nature of the PM exposure (van Eeden et al., 2005, 157086).

Systemic inflammation is seen under conditions of mild pulmonary inflammation – and sometimes under conditions of no measurable pulmonary inflammation – following PM exposure. The time-dependent nature of pulmonary and systemic inflammatory responses may in part explain these findings since biomarkers of inflammation are frequently measured only at one time point. Furthermore, chronic exposures may lead to adaptive responses. In general, systemic inflammation is associated with changes in circulating white blood cells, the acute phase response, pro-coagulation effects, endothelial dysfunction and the development of atherosclerosis (Figure 5-5). Adverse effects on the cardiovascular and cerebrovascular systems such as thrombosis, plaque rupture, MI and stroke may result. Systemic inflammation may affect other organ systems such as the liver or the CNS.

One recent study demonstrated that alveolar macrophage-derived IL-6 mediated pro-coagulation effects in mice exposed by IT instillation to PM_{10} (Mutlu et al., 2007, 121441). This study provides a clear link between lung cytokines and systemic responses in one model system. Whether this mechanism or others account for the majority of extra-pulmonary effects following inhalation of PM at concentrations relevant to ambient exposures is not yet known.

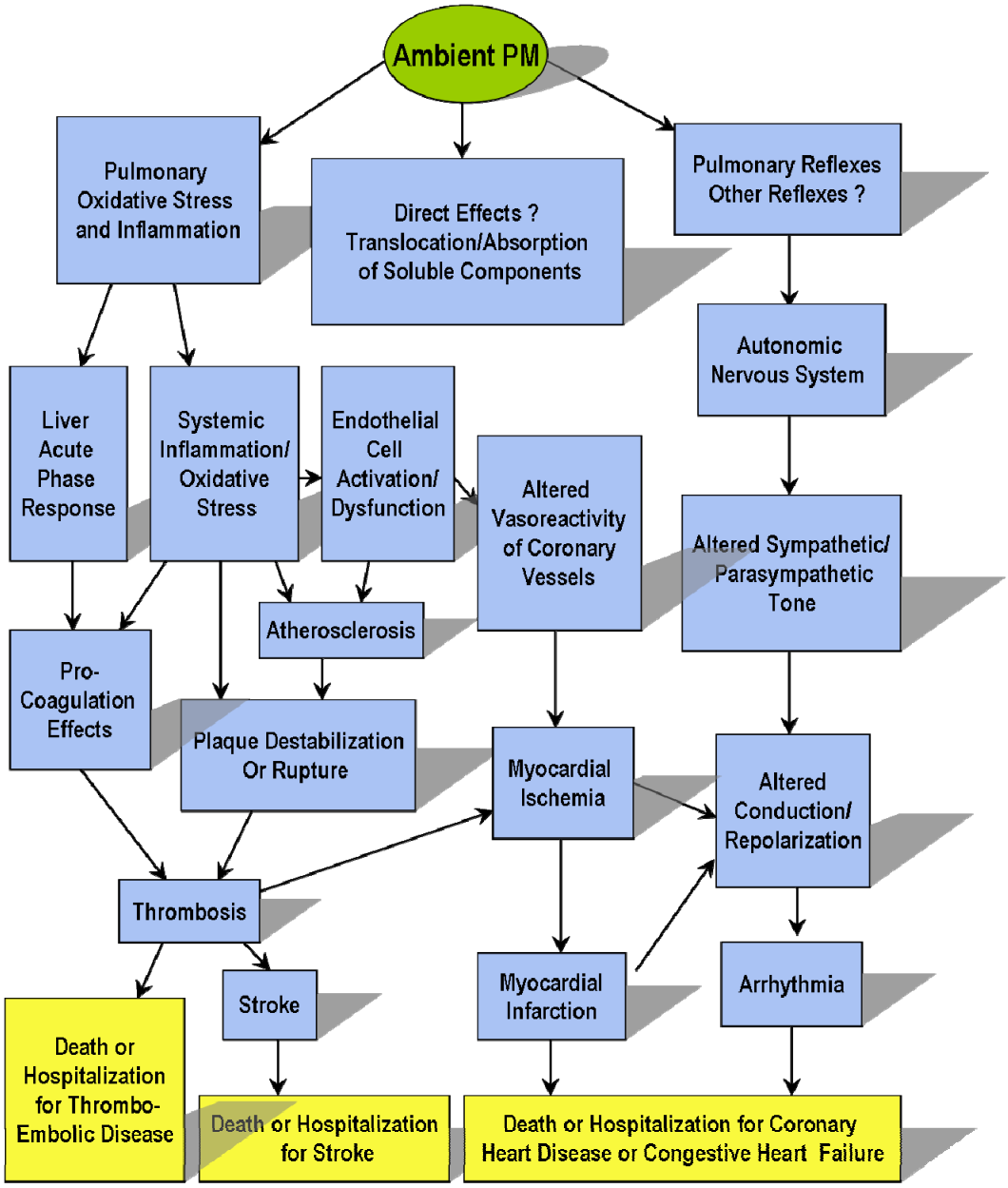

Figure 5-5. Potential pathways for the effects of PM on the cardiovascular system.

5.2.1. Endothelial Dysfunction and Altered Vasoreactivity

The lumenal surface of blood vessels is lined by endothelial cells which, in addition to providing a barrier function, are key regulators of vascular homeostasis. Endothelial cells synthesize and release vasodilators such as nitric oxide (NO) and prostacyclin and vasoconstrictors such as endothelin (ET), which act on neighboring smooth muscle cells. ET also stimulates endothelial NO synthesis through a feedback mechanism. Inhalation of high concentrations of PM has been reported to increase ET levels in the circulation (Thomson et al., 2005, 087554). ET has also been proposed to play a role in hypoxia-induced MI (Caligiuri et al., 1999, 157365). However, the role of ET in mediating cardiovascular effects following ambient PM exposures is unclear (Section 6.2.4.3).

Endothelial dysfunction can lead to or follow endothelial activation under conditions of systemic inflammation and/or vascular oxidative stress. Both systemic inflammation and vascular oxidative stress have been associated with PM exposure (Nurkiewicz et al., 2006, 088611; Van Eeden et al., 2001, 019018). Cytokines activate endothelial cells and upregulate endothelial cell adhesion molecules. They also promote the sequestration of neutrophils in microvascular beds. Neutrophil sequestration is sometimes associated with the deposition of myeloperoxidase (MPO) on endothelial cell surfaces (Nurkiewicz et al., 2006, 088611). ROS-derived from neutrophils, MPO, other adhered inflammatory cells and/or other sources can perturb the balance of vasodilator and vasoconstrictor species produced by endothelial cells. Oxidative stress can result in decreased synthesis of NO due to limitation of the redox-sensitive essential cofactor tetrahydrobiopterin and in decreased bioavailability of NO due to reaction with superoxide. Prostacyclin synthesis is also decreased by oxidative stress. Importantly, these processes can affect vasoreactivity such that blood vessels may be unable to respond to vasoconstrictor stimuli with compensatory vasodilation.

Loss of NO and prostacyclin synthesis due to PM-dependent vascular oxidative stress may have other consequences since both exert negative influences on platelet and neutrophil activation. While endothelial surfaces normally are anti-thrombotic, endothelial dysfunction can contribute to thrombus formation. Furthermore, inflammation and oxidative stress associated with endothelial dysfunction can contribute to the development or progression of atherosclerosis (van Eeden et al., 2005, 157086).

5.2.2. Activation of Coagulation and Acute Phase Response

The primary function of the coagulation cascade is to stop the loss of blood after vascular injury by forming a fibrin clot. However in some cases, activation of coagulation can promote intravascular thrombosis (Karoly et al., 2007, 155890). It has been proposed that air pollution-associated PM can activate clotting pathways and enhance the likelihood of an obstructive cardiac ischemic event (e.g., MI) or cerebral event (e.g., stroke) (Seaton et al., 1995, 045721).

Coagulation is regulated by intrinsic and extrinsic pathways. The intrinsic pathway occurs following activation of Factor XII and does not require the addition of an exogenous agent (Mackman, 2005, 156722). On the other hand, the extrinsic pathway is an inducible signaling cascade that can be activated by tissue factor (TF) produced in response to inflammation or endothelial injury (Karoly et al., 2007, 155890).

In general, platelets, red blood cells (RBCs) and endothelial cells are effector cells for inducing a pro-coagulant state in the vasculature. Circulating factors may enhance coagulation or promote activation of platelets. Cytokines formed during tissue damage and inflammation lead to TF induction. TF is the initiating stimulus for coagulation following vascular injury or plaque erosion. Complexes of TF:Factor VIIa form on endothelial cell surfaces and play a key role in thrombin generation by initiating the extrinsic blood coagulation pathway (Gilmour et al., 2005, 087410). Thrombin generates fibrin from fibrinogen and amplifies the intrinsic pathway (Karoly et al., 2007, 155890). TF and thrombin also have pro-inflammatory actions independent of coagulation functions (Chu, 2005, 155730); thus activation of coagulation may lead to or potentiate inflammation. Endothelial cell-derived von Willebrand factor also contributes to coagulation.

The fibrinolytic system opposes these processes by facilitating the removal of a clot. The fibrinolytic pathway is regulated by the ratio of tissue plasminogen activator (tPA) and plasminogen activator inhibitor (PAI). Furthermore, the endothelial cell surface has anti-thrombotic properties due to the expression of tissue factor pathway inhibitor (TFPI) and thrombomodulin (Mackman, 2005, 156722).

Inhibition of the fibrinolytic pathway, along with increased plasma viscosity and increased concentrations of plasma fibrinogen and Factor VII, contributes to a pro-thrombotic state (Gilmour et al., 2005, 087410). In acute lung injury, vascular cells have enhanced pro-coagulant activity and impaired fibrinolytic activity (Gilmour et al., 2005, 087410). In arterial atherosclerosis, TF expression is increased within plaques. As a result, spontaneous plaque rupture may trigger intravascular clotting (Karoly et al., 2007, 155890).

Acute phase responses also play a role in hemostasis by exerting pro-coagulant effects. Cytokines such as IL-6 stimulate the liver to produce acute phase proteins including C-reactive protein (CRP), fibrinogen and antiproteases (van Eeden et al., 2005, 157086). To date, there is limited evidence supporting a role for ambient PM in stimulating acute phase responses (Ruckerl et al., 2007, 156931 and reviewed therein) (also Section 6.2.7 and 6.2.8 in this ISA).

5.2.3. Atherosclerosis

Atherosclerosis is a chronic progressive disease which contributes greatly to cardiovascular morbidity (Libby, 2002, 192009). Mainly a disease of the large arteries, it is characterized by the accumulation of lipid and fibrous tissue in atheromas, or swellings of the vessel wall (Libby, 2002, 192009). Although a strong link is known to exist between hypercholesterolemia and atherogenesis, there is growing appreciation of the key role played by inflammation in the initiation and progression of atherosclerosis (Libby, 2002, 192009). Furthermore, inflammation has the potential to promote thrombosis which can complicate this disorder and lead to MI and stroke (Libby, 2002, 192009). As discussed above, PM exposure is associated with systemic inflammation, potentially contributing to the development of atherosclerosis.

Atheroma formation in experimental animals fed a high fat diet begins with the accumulation of modified lipoprotein particles in the arterial intima, as reviewed by Libby (2002, 192009). The modification of lipoprotein particles often involves oxidation. As discussed above, PM exposure is associated with oxidative stress, suggesting a potential role for PM in the modification of lipoprotein particles. Endothelial dysfunction may also be key to these early events (Halvorsen et al., 2008, 191149). Recent studies, which are discussed in later chapters, demonstrate PM-dependent endothelial dysfunction (Nurkiewicz et al., 2009, 191961). As described by Libby (2002, 192009), oxidative stress leads to lipid modification and uptake by endothelial cells and initiates an inflammatory response by activating NF-κB. As a result, cell adhesion molecules such as vascular cell adhesion molecule-1 (VCAM-1) are upregulated and expressed in endothelial cells. Pro-inflammatory cytokines associated with systemic inflammation may also contribute to adhesion molecule upregulation. Subsequently, monocytes and T cell lymphocytes adhere to the activated endothelium, then migrate into the tunica intima directed by chemokines such as monocyte chemoattractant protein-1 (MCP-1) and IL-8. Monocytes undergo transformation to tissue macrophages and later to foam cells. As a part of this transformation, monocyte/macrophages express scavenger receptors and bind to and internalize the modified lipoprotein particles. These cells secrete growth factors and cytokines, produce ROS, replicate within the lesion and contribute to further lesion progression. Macrophage colony-stimulating factor (M-CSF) and granulocyte-macrophage colony-stimulating factor (GM-CSF) are thought to be involved in these latter steps which eventually lead to the formation of a fatty streak. T cell lymphocytes also become activated in the atheroma and secrete pro- or anti-inflammatory cytokines. Degranulation of mast cells found in the atheroma may also contribute to the lesion.

Atheroma progression involves the proliferation of smooth muscle cells, which is stimulated by macrophage-derived growth factors (Libby, 2002, 192009). This results in smooth muscle accumulation in the lesion, the elaboration of extracellular matrix material and the formation of a more bulky lesion which can occlude the arterial lumen. Matrix proteins contribute to the evolution of the lesion from a fatty streak to a fibrous plaque. Mechanisms which trigger plaque disruption, including endothelial erosions and plaque rupture, can result in thrombosis as well as in further expansion of the lesion. Resident T cells, mast cells and circulating platelets may also play a role in destabilizing plaques (Halvorsen et al., 2008, 191149). It is thought that most atheromatous lesions progress in a discontinuous manner due to cycles of disruption, expansion and repair.

A major factor regulating plaque disruption is the thickness of the fibrous cap, with more stable plaques characterized by a thick fibrous cap (Libby, 2002, 192009). Collagen in the fibrous cap can be degraded by proteases, especially MMPs. Inflammation in the intima reduces collagen production by smooth muscle cells and promotes the expression and activation of MMPs. ROS may mediate MMP upregulation (Lund et al., 2009, 180257). Both macrophages and smooth muscle cells produce MMPs in the lesion areas (Halvorsen et al., 2008, 191149); fully differentiated macrophages selectively upregulate certain MMPs with more destructive potential (Newby, 2008, 191161). Rupture of the fibrous cap allows pro-thrombotic factors within the plaque (e.g., TF) to come into contact with coagulation factors in the blood possibly resulting in the formation of an occlusive blood clot. However in some cases, blood fibrinolytic mechanisms minimize clot formation and repair processes ensue. The result is a more fibrous plaque and/or an expanded lesion. The proposed role of PM in activating coagulation pathways, which was discussed above, may influence the outcome of plaque disruption.

In this manner oxidative stress, inflammation and pro-coagulant activity in the blood are involved in the initiation and progression of atheromatous lesions as well as plaque disruption and occlusive blood clot formation. PM exposure may contribute to these pathways and in fact, studies

described in later chapters demonstrate PM-dependent effects on atherosclerosis progression (Araujo et al., 2008, 156222; Chen and Nadziejko, 2005, 087219; Sun et al., 2005, 087952; Ying et al., 2009, 190111).

5.3. Activation of the Autonomic Nervous System by Pulmonary Reflexes

Chemosensitive receptors, including rapidly adapting receptors (RARs) and sensory C-fiber receptors, are found at all levels of the respiratory tract and are sensitive to irritant particles as well as to irritant gases (Alarie, 1973, 070967; Coleridge and Coleridge, 1994, 156362; Widdicombe, 2006, 155519). Activation of trigeminal afferents in the nose causes CNS reflexes resulting in decreases in respiratory rate through a lengthened expiratory phase, closure of the glottis, closure of the nares with increased nasal airflow resistance and effects on the cardiovascular system such as bradycardia, peripheral vasoconstriction and a rise in systolic arterial blood pressure (Alarie, 1973, 070967). Sneezing, rhinorrhea and vasodilation with subsequent nasal vascular congestion are also nasal reflex responses involving the trigeminal nerve (Sarin et al., 2006, 191166). Activation of vagal afferents in the tracheobronchial and alveolar regions of the respiratory tract causes CNS reflexes resulting in bronchoconstriction, mucus secretion, mucosal vasodilation, cough, apnea followed by rapid shallow breathing and effects on the cardiovascular system such as bradycardia and hypotension or hypertension (Coleridge and Coleridge, 1994, 156362; Widdicombe, 2003, 157145; 2006, 155519; Widdicombe and Lee, 2001, 019049). Some evidence suggests that cardiovascular responses may be mediated primarily by the C-fiber receptors (Coleridge and Coleridge, 1994, 156362) and that irritants in the lower respiratory tract cause more pronounced cardiovascular responses than irritants in the upper respiratory tract (Widdicombe and Lee, 2001, 019049).

Early experiments demonstrated that sectioning of the trigeminal nerve abrogated irritant effects on respiratory rate, heart rate and systolic arterial blood pressure (Alarie, 1973, 070967). These nasal reflexes were attributed to the ophthalmic branch of the trigeminal nerve since they were identical to reflex responses following diving or immersion of the face in water (Alarie, 1973, 070967). Early experiments also demonstrated that non-nasal reflexes were mediated by cholinergic parasympathetic pathways involving the vagus nerve and inhibited by atropine (Grunstein et al., 1977, 071445; Nadel et al., 1965, 014846). More recent experiments have shown that noncholinergic mechanisms may also be involved. For example, stimulation of C-fiber receptors can activate local axon reflexes. These local axon pathways are responsible for secretion of neuropeptides and the development of neurogenic inflammation (Widdicombe and Lee, 2001, 019049). It has been proposed that, in some cases, neurogenic pulmonary responses can switch from their normally protective function to one that perpetuates pulmonary inflammation (Wong et al., 2003, 097707). Differences in respiratory tract innervation between rodents and humans suggest that C-fiber mediated neurogenic inflammation may be more important in rodents than in humans (Groneberg et al., 2004, 138134; Widdicombe, 2003, 157145; Widdicombe and Lee, 2001, 019049) However, the role of neurogenic inflammation in mediating pulmonary responses in humans is an active area of investigation.

VR1 receptors represent a subset of neuropeptide and acid-sensitive irritant receptors which belong to the transient receptor potential (TRP) family. They are located on the sensory C-fibers which lie underneath and between lung epithelial cells and on immune and non-immune airway cells. Some investigators have focused on the role played by these receptors in mediating inflammation following exposure to PM (Veronesi and Oortgiesen, 2001, 015977). Exposure of bronchial epithelial cells and neurons to PM in vitro has been shown to result in an immediate increase in intracellular calcium followed by the release of neuropeptides and inflammatory cytokines (Veronesi et al., 1999, 048764; Veronesi et al., 2000, 017062). In one study, this response was found to be due to an intrinsic property of the particle core and was not metal-dependent (Oortgiesen et al., 2000, 013998), while in another study electrostatic charge was found to activate VR1 receptors (Veronesi et al., 2003, 094384). PM-mediated activation of VR1 receptors which results in increases in intracellular calcium and apoptosis in epithelial cells has also been demonstrated (Agopyan et al., 2003, 155649). New studies, discussed in later chapters, provide evidence for the involvement of TRPV1 irritant receptor involvement in PM-dependent responses (Ghelfi et al., 2008, 156468; Rhoden et al., 2005, 087878).

Recently it has been proposed that pulmonary reflex responses may be modulated by CNS plasticity (Bonham et al., 2006, 191140; Sekizawa et al., 2008, 191167). Plasticity is a property of neurons or synapses which allows change in response to previous events. In the case of the respiratory tract, visceral afferent inputs to the CNS are integrated primarily in the nucleus tractus soltarius (NTS) region of the brain (Bonham et al., 2006, 191140). Inputs from local networks, higher brain regions and circulating mediators contribute to the reflex output (Bonham et al., 2006, 191140). This integration allows for plasticity in that repeated or prolonged exposure to a particular stimuli may lead to altered reflex responses to the same or subsequent stimuli. An exaggerated reflex response was recently observed in guinea pigs exposed to ETS for an extended period of time (Sekizawa et al., 2008, 191167). It is not known whether CNS plasticity influences responses following acute and chronic exposure to ambient PM, but it is a mechanism that may possibly explain hyperresponsiveness and/or adaptation of reflex-related responses.

At this time, it is not clear how activation of the ANS by pulmonary reflexes contributes to the kinds of altered conduction and/or repolarization properties of the heart which may be linked to arrhythmias (Figure 5-5). Pulmonary reflexes, as they are currently understood, initially lead to increases in parasympathetic tone. However, decreased heart rate variability appears to be reflective of decreased parasympathetic tone and/or increased sympathetic tone. A PM-dependent sympathetic stress response mediated by cytokines has been postulated (Godleski et al., 2000, 000738), but there is little new information to support this mechanism. Thus, activation of the autonomic nervous system by mechanisms other than pulmonary reflexes seems likely in response to PM. Very little is known about putative alternative mechanisms leading to sympathoexcitatory responses although one study demonstrated a role for the olfactory bulb-NTS pathway in regulating cardiovascular functions following smoke exposure (Moffitt et al., 2002, 191160). In addition, sympathoexcitatory responses occur during myocardial ischemia, mediated by the release of adenosine or the production of ROS by the myocardium (Longhurst et al., 2001, 191158). Hence, PM-dependent effects leading to myocardial ischemia may stimulate sympathoexcitatory responses. Furthermore, the effects of pre-existing alterations in the ANS due to disease processes (e.g., increased sympathetic tone observed in cardiac diseases) on PM responses are not understood. Possibly, integration of neural signals resulting from pulmonary and cardiac reflexes at the level of the NTS may have an influence on ANS responses to PM. Further investigation will be required to clarify these mechanisms.

5.4. Translocation of UFPs or Soluble PM Components

UFPs can translocate across cell membranes by non-endocytotic mechanisms involving adhesive interactions and diffusion (Geiser et al., 2005, 087362), as described in Section 4.3.3.1. In this study, there was no measurable loss of PM from the lung over 24 h despite the rapid translocation of inhaled UFPs into alveolar epithelial cells and capillary endothelial cells. In another study, UFPs were localized in macrophage mitochondria as demonstrated by electron microscopy (Li et al., 2003, 042082). Other studies found extrapulmonary translocation of poorly soluble UFPs, but the process was slow and resulted in only a small amount leaving the lung. It is possible that in these studies PM gained access to the circulation after initial transport to the lymph nodes or the gastrointestinal system. Hence, there is limited evidence to date that UFPs or other PM size fractions access the circulation by traversing the epithelial barrier of the respiratory tract.

However, soluble components from all size fractions of PM have the potential to translocate across the airway epithelium into the bronchial circulation or across the alveolar epithelium into the systemic circulation as depicted in Figure 5-5. Absorption across nasal epithelium may also occur (Illum, 2006, 191205). Factors affecting this process include the rate of dissolution of the solute from the particle and the molecular weight of the solute (Section 4.4). More rapid dissolution of soluble components may occur in the case of UFPs due to the higher surface/volume ratios compared with larger particles.

Several interesting studies investigated the translocation of water-soluble metals from the lung. Gilmour et al. (2006, 156472) demonstrated the rapid appearance of Zn in the plasma of rats following IT instillation of zinc sulfate ($ZnSO_4$). Similarly, Wallenborn et al. (2007, 156144) demonstrated the rapid appearance of water-soluble metals in the blood, heart and liver following IT instillation of oil combustion PM in rats. Using a more sensitive technique, these same investigators demonstrated the accumulation of ^{70}Zn, a rare isotope of Zn, in blood, heart and liver following IT

instillation of $ZnSO_4$ (Wallenborn et al., 2009, 191172). In three other studies, soluble Zn and Cu were associated with cardiac effects following IT instillation of rats with different forms of Zn- and Cu-containing PM (Gilmour et al., 2006, 088489; Gottipolu et al., 2008, 191148; Kodavanti et al., 2008, 155907). These results suggest the possibility that PM-derived soluble Zn and Cu translocated across the alveolar-capillary barrier into the circulation and exerted effects on the heart. However, in the two studies in which barrier function was measured it was found to be compromised (Gilmour et al., 2006, 088489; Gottipolu et al., 2008, 191148) suggesting an acute lung injury response to IT instillation of high concentrations of metal. Acute lung injury is not likely to occur in healthy individuals exposed to PM at concentrations relevant to ambient levels. Cardiac effects were also observed following subchronic inhalation exposure to low concentrations of aerosolized $ZnSO_4$ (Wallenborn et al., 2008, 191171). Since it was not possible to measure extra-pulmonary Zn in this study, it remains unclear whether cardiac effects were a direct effect of translocated Zn or an indirect effect of exposure to Zn-containing PM. Nonetheless, translocation of soluble components derived from inhaled PM remains a viable hypothesis to explain some extra-pulmonary effects.

Epithelial permeability is a key determinant of translocation and is discussed in detail in Section 4.4.2. In brief, a number of studies have measured clearance of ^{99m}Tc-DTPA as an index of alveolar epithelial membrane integrity and permeability of alveolar-capillary barrier (Braude et al., 1986, 155701). Endothelial integrity also contributes to the alveolar-capillary barrier and is measured by transvascular protein flux but is not discussed here (Braude et al., 1986, 155701). In laboratory animals, increased alveolar permeability was shown in terminally senescent mice (Tankersley et al., 2003, 096363). In human volunteers, epithelial permeability was transiently increased following 3 h of moderate exercise but not following 24-h exposure to particle-rich urban air (Brauner et al., 2009, 190244). A previous study found that the exercise-induced increase in epithelial permeability was transient and suggested that it was due to increased ventilation and elevated vascular pressure which altered the properties of tight junctions (Hanel et al., 2003, 155826). Smokers (Jones et al., 1983, 155884) and individuals with acute respiratory distress syndrome (Braude et al., 1986, 155701) or interstitial lung disease (Rinderknecht et al., 1980, 191965) also exhibited increased alveolar epithelial permeability. The changes in smokers were reversible upon cessation of smoking. Increased airway epithelial permeability was found in asthmatics when ^{99m}Tc-DTPA clearance was used to measure the permeability of the bronchial mucosa (Ilowite et al., 1989, 156584). These studies demonstrate that epithelial permeability is increased following moderate exercise and in lung syndromes associated with inflammation and suggest that compromised epithelial barrier functions in the lung may contribute to PM-mediated effects.

Interaction of circulating PM or soluble PM components with vascular endothelial cells, platelets, and other leukocytes is a potential mechanism underlying the cardiovascular and systemic effects of inhaled PM. A role for PM-derived ROS and/or cellular-derived ROS has been proposed. Furthermore, soluble metals that do not redox-cycle may activate cell signaling pathways without the generation of ROS. In this way, PM may promote adverse cardiovascular effects such as endothelial dysfunction, atherosclerosis and thrombosis. Circulating PM or soluble PM components also have the potential to impact other organ systems. However, convincing evidence that this occurs to an appreciable extent in healthy individuals following inhalation of PM at concentrations relevant to ambient exposures is lacking.

5.5. Disease of the Cardiovascular and Other Organ Systems

As discussed above, deposition of PM in the lung may lead not only to pulmonary disease but also to diseases of other systems (Figure 5-5). In the cardiovascular system, myocardial ischemia and MI may occur as a result of the above proposed effects of PM on atherosclerosis, plaque instability, thrombosis, plaque rupture and/or altered vasoreactivity of coronary vessels. Myocardial ischemia and MI may alter the conduction and depolarization properties of the heart and lead to arrhythmic events. In addition, thrombosis may lead to stroke and/or thromboembolic disease. Many of these processes may be interlinked and responses to ambient PM exposures may involve multiple mechanisms simultaneously with some variability depending on PM composition. Furthermore, it is not clear at this time whether PM initiates cardiovascular disease or whether it perturbs existing disease.

In addition, recent studies which are discussed in later chapters have demonstrated PM-dependent effects on the CNS (Campbell et al., 2005, 087217; Kleinman et al., 2008, 190074; Sirivelu et al., 2006, 111151; Veronesi et al., 2005, 087481; Win-Shwe et al., 2008, 190146). At this time, it is not known whether this is a direct or indirect consequence of PM exposure. Translocation of soluble and poorly soluble particles from the olfactory mucosa via the axons to the olfactory bulb of the brain has been proposed as a possible mechanism by which PM or its components may directly access the CNS. Evidence for this pathway is discussed in Section 4.3.3.2. Alternative mechanisms proposed for PM-mediated CNS effects involve systemic inflammation and autonomic responses. These are new and intriguing possibilities which warrant further investigation.

PM-dependent effects on the reproductive system, reproductive outcomes and perinatal development have also been identified and are discussed in a later chapter. Mechanisms involved in these responses have not been determined. However, it seems possible that systemic inflammation and/or oxidative stress may play a role. Developmental windows of susceptibility may also be an important consideration. Furthermore, it has been hypothesized that oxygen gradients and redox status are key to cell differentiation and epigenetic processes occurring during development (Section 5.1.11) (Hitchler and Domann, 2007, 191151).

5.6. Acute and Chronic Responses

In general, repeated acute responses may lead to cumulative effects which manifest as chronic disease. Several examples relevant to the modes of action discussed in this chapter are that of allergic responses, atherosclerosis and lung development. Allergic responses require repeated exposures to antigen over time. Co-exposure to an adjuvant, possibly DEP or ultrafine concentrated ambient particles (CAPs), can enhance this response. Furthermore, the presence of oxidative stress, as may occur in response to PM, can contribute to allergic responses. Allergic sensitization often underlies allergic asthma, characterized by inflammation and AHR. In this way, repeated or chronic exposures involving multifactorial responses (immune system activation, oxidative stress, inflammation) can lead to irreversible outcomes. Similarly, the development of atherosclerosis involves inflammation and remodeling of the blood vessel wall. Factors contributing to this process include systemic inflammation, endothelial dysfunction, oxidative stress and high levels of circulating lipids. PM exposure is associated with three out of four of these processes. The role of PM in initiating, promoting or complicating this disease or its outcomes has yet to be determined. Critical windows of susceptibility during development also provide an opportunity for repeated exposures to injurious agents to lead to irreversible changes in organ structure and function. The extended period of postnatal lung development in humans and other species heightens this vulnerability. PM may serve as such an injurious agent as has been demonstrated previously for hyperoxia (Randell et al., 1990, 191956).

Furthermore, adverse outcomes may be precipitated by acute events superimposed on chronic disease states. In the case of allergic asthma, acute PM exposure may provoke asthmatic responses through oxidative stress and inflammatory pathways. Additionally, PM can act as a carrier of aeroallergens and other biological materials which can potentially trigger asthma attacks. Similarly, PM exposure may provoke inflammatory or thrombotic responses leading to rupture of an atherosclerotic plaque which subsequently results in acute MI. In this way, the outcome of an acute exposure to PM may be drastically worsened by the underlying chronic disease.

5.7. Results of New Inhalation Studies which Contribute to Modes of Action

Prior to this review, much of the evidence for the proposed modes of action was obtained from animal studies involving IT instillation or inhalation of high concentrations of PM and from cell culture experiments. In many cases, the types of PM used were of questionable relevance to ambient exposures (i.e., high concentrations of ROFA, metals and ambient PM collected on filters). Since then, many inhalation studies have been conducted using CAPs, combustion-derived PM, urban air

and carbon black, generally using concentrations of PM lower than 1 mg/m^3. Much of this research has been conducted in animal models of disease. These key new studies, described in detail in Chapters 6 and 7, add to the understanding of modes of action which are relevant to ambient PM exposure. A compilation of pertinent results is found below.

- Altered lung function including changes in respiratory frequency and AHR following short-term exposures to CAPs and combustion-derived PM (Section 6.3.2.3)
- Mild pulmonary inflammation in response to short-term exposures to CAPs, urban air, combustion-derived PM and carbon black (Section 6.3.3.3)
- Mild pulmonary injury in response to short-term exposure to CAPs and combustion-derived PM (Section 6.3.5.3)
- Inhibition of cell proliferation in the proximal alveolar region of neonatal animals following short-term exposure to iron-soot (Section 6.3.5.3)
- Pulmonary oxidative stress in response to short-term exposure to CAPs, urban air, combustion-derived PM, carbon black and iron-soot; pulmonary nitrosative stress in response to titanium dioxide (TiO_2) (Section 6.3.4.2)
- Antioxidant intervention which ameliorates PM effects on oxidative stress, allergic responses, and AHR (Sections 6.3.4.2)
- Allergic sensitization and exacerbation of allergic responses in response to CAPs and combustion-derived PM (Section 6.3.6.3)
- Altered methylation of promoter regions of IFN-γ and IL-4 genes suggestive of pro-allergic Th2 gene activation following short-term exposure to combustion-derived PM in an allergy model (Section 6.3.6.3)
- Increased susceptibility to respiratory infection following exposure to combustion-derived PM (Section 6.3.7.2)
- Effects on nasal epithelial mucosubstances, airway morphology and airway mucosubstances following chronic exposure to urban air-derived PM and woodsmoke (Section 7.3.5.1)
- Worsening of papain-induced emphysema following chronic exposure to urban air-derived PM (Section 7.3.5.1)
- Effects on lung development following chronic exposure to urban air-derived PM (Sections 7.3.2.2 and 7.3.5.1)
- Prolonged exposure to CAPs and combustion-derived PM leading sometimes to mild pulmonary inflammation, oxidative stress and injury and sometimes to loss of inflammatory, oxidative stress and AHR responses which were observed after short-term exposures (Sections 7.3.2.2, 7.3.3.2, 7.3.4.1, 7.3.5.1 and 7.3.6.2)
- Hypermethylation of lung DNA following chronic exposure to combustion-derived PM (Section 7.3.5.1)
- A role for TRPV1 irritant receptors in activating local axon and CNS reflexes following short-term exposure to CAPs and combustion-derived PM (Section 6.2.9.3)

- A role for TRPV1 irritant receptors in mediating lung and heart oxidative stress through increased parasympathetic and sympathetic activity in response to CAPs (Sections 6.2.9.3 and 6.3.4.2)

- Altered heart rate variability in response to CAPs, combustion-derived PM and carbon black (Section 6.2.1.3)

- Arrhymthmic events in response to CAPs and combustion-derived PM (Section 6.2.2.2)

- Altered cardiac contractility following short-term exposure to CAPs and carbon black (Section 6.2.6.1)

- Enhanced myocardial ischemia following short-term exposure to CAPs (Section 6.2.3.3)

- Endothelial dysfunction and altered vascular reactivity following short-term exposure to CAPs, combustion-derived PM and TiO_2 (Section 6.2.4.3)

- Increases in blood pressure following short-term exposure to CAPs and carbon black (Section 6.2.5.3)

- Changes in blood leukocyte counts following short-term exposure to CAPs and carbon black (Section 6.2.7.3)

- Increased levels of blood coagulation factors following short-term exposure to CAPs and on-road highway aerosols (Section 6.2.8.3)

- Systemic and cardiovascular oxidative stress in response to short-term exposure to CAPs, road dust and combustion-derived PM (Section 6.2.9.3)

- Progression of atherosclerosis, induction of TF in aortic plaques, vascular oxidative stress and altered vasomotor function following long-term exposure to CAPs in a susceptible animal model (Section 7.2.1.2)

- Vascular remodeling following chronic exposure to urban air-derived PM (Section 7.2.1.2).

- Enhanced angiotensin II-induced hypertension accompanied by vascular oxidative stress and altered vasoreactivity in response to chronic exposure to CAPs (Section 7.2.5.2)

- Exaggerated insulin resistance, visceral adiposity and systemic inflammation in response to chronic exposure to CAPs and a high-fat diet (Section 7.2.3.1)

- CNS responses following short- and long-term exposures to CAPs and combustion-derived PM (Section 6.4.3)

- Effects on the reproductive system, reproductive outcomes and developmental outcomes following chronic exposure to urban-air derived PM (Section 7.4.2)

- DNA adducts in nose, lung and liver following chronic exposure to urban air (Section 7.5.2.1)

- Germ line mutations, DNA strand breaks and global hypermethylation in sperm following chronic exposure to urban air-derived PM (Section 7.5.3)

5.8. Gaps in Knowledge

The new studies highlighted in Section 5.7 confirm and extend findings from older studies. However, this increasing body of evidence does not provide a complete picture of the biological pathways involved in mediating PM effects. For example, a lack of information regarding the time-dependence of many responses makes it difficult to understand the underlying biological mechanisms. Existing gaps in knowledge include:

- The spatial distribution of retained particles in the lung and its impact
- The deposition, uptake and clearance of UFPs in the lung
- Effects of ambient PM exposures on epithelial barrier function in the lung
- Time dependence of responses
- The putative modulation of neural reflexes by pre-existing disease or other factors
- The putative role of neural reflexes besides those involving pulmonary irritant receptors
- The putative role of ET in altering vasomotor tone following PM exposure
- The putative translocation of PM or soluble components across the epithelial barrier of the lung into the circulation
- The putative translocation of PM from olfactory epithelium to the olfactory bulb and other brain regions

Additional studies will be required to clarify the biological mechanisms underlying the health effects of PM.

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Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISA) and the Integrated Risk Information System (IRIS).

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Chapter 6. Integrated Health Effects of Short-Term PM Exposure

6.1. Introduction

This chapter reviews, summarizes, and integrates the evidence of relationships between short-term exposures to PM and a variety of health-related outcomes and endpoints. Cardiovascular and respiratory health effects of short-term exposure to various size fractions and sources of PM have been examined in numerous epidemiologic, controlled human exposure and toxicological studies. In addition, there is a large body of literature evaluating the relationship between mortality and short-term exposure to PM. The association between PM exposure and central nervous system function has also been assessed, although far fewer studies are available. The research approaches used to evaluate health effects of PM exposure are described in Section 1.5 along with advantages and limitations of the various study types. Chapter 5 provides an overview of the potential pathophysiological pathways and modes of action underlying the PM-induced health effects observed in animal and human studies. Evidence from the scientific literature of specific cardiovascular and systemic effects, respiratory effects, and central nervous system (CNS) effects associated with exposure to PM are presented in Sections 6.2, 6.3, and 6.4, respectively. Evidence of associations between short-term exposure to PM and mortality are described in Section 6.5. The chapter concludes with an evaluation of PM-induced health effects attributable to specific constituents or sources (Section 6.6). More detailed descriptions of each study evaluated for this assessment are presented in Annexes C, D, E, and F.

Findings for cardiovascular and respiratory effects are presented by specific endpoint or measure of effect, leading from more subtle health outcome measures (e.g., heart rate variability [HRV]) to the more severe, such as hospitalization and mortality for cardiovascular disease. Conclusions from the 2004 PM AQCD (U.S. EPA, 2004, 056905) are briefly summarized at the beginning of each section, and the evaluation of evidence from recent studies builds upon what was available during the previous review. For each health outcome, results are summarized for studies from the specific scientific discipline, i.e., epidemiologic, controlled human exposure, and toxicological studies. The sections conclude with summaries of the evidence on the various health outcomes and integration of the findings that leads to conclusions regarding causality based upon the framework described in Chapter 1. Determination of causality is made for the overall health effect category, such as cardiovascular effects, with coherence, consistency and biological plausibility being based upon the evidence from across disciplines and also across the suite of related health outcomes ranging from the more subtle health outcomes to cause-specific mortality. In the summary sections for cardiovascular and respiratory effects and all-cause mortality, the evidence is summarized and independent conclusions drawn for relationships with $PM_{2.5}$, $PM_{10-2.5}$, and ultrafine particles (UFPs) (Sections 6.2.12, 6.3.10, and 6.5.3, respectively). Evidence of central nervous system effects is also divided by scientific discipline; however, the lack of data does not allow for informative summaries of effect by PM metric in discussing CNS effects (Section 6.4.4).

▪ Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISA) and the Integrated Risk Information System (IRIS).

6.2. Cardiovascular and Systemic Effects

6.2.1. Heart Rate and Heart Rate Variability

Heart rate (HR), HRV, and BP are all regulated, in part, by the sympathetic and parasympathetic nervous systems. Changes in one or more may increase the risk of cardiovascular events (e.g., arrhythmias, MI, etc.). Decreases in HRV have been associated with cardiovascular mortality/morbidity in older adults and those with significant heart disease (TFESC, 1996, 003061). In addition, decreased HRV may precede some clinically important arrhythmias, such as atrial fibrillation, as well as sudden cardiac death, in high risk populations (Chen and Tan, 2007, 197461; Sandercock and Brodie, 2006, 197465; Thong and Raitt, 2007, 197462).

HRV is measured using electrocardiograms (ECG) and can be analyzed in the time domain (e.g., standard deviation of all NN intervals [SDNN], square root of the mean squared successive NN interval differences [rMSSD]), and/or the frequency domain measured by power spectral analysis (e.g., high frequency [HF], low frequency [LF], ratio of LF to HF [LF/HF]). SDNN generally reflects the overall modulation of HR by the autonomic nervous system (ANS), whereas rMSSD and frequency variations in HR generally reflect parasympathetic activity. Thus, rMSSD is generally well correlated with HF, which also reflects the parasympathetic modulation of HR. LF is predominately determined by both sympathetic parasympathetic tone and increased LF/HF indicates sympathoexcitation, which correlates with decreased overall HRV (SDNN, rMSSD). Thus LF/HF is thought to estimate the ratio of sympathetic influences on HR to parasympathetic influences.

While HRV is commonly described as being a reflection of vagal and adrenergic input to the heart, there is clearly a more complex phenomenon reflected in HRV parameters. Rowan et al. (2007, 191911) provide a review of HRV and its use and interpretation with respect to air pollution studies. To summarize, HRV indices are excellent measures of extrapulmonary effects from inhaled pollutants, but the characterization of the acute, reversible responses to air pollution as being either parasympathetic or sympathetic in origin, much less predictive of some adverse outcomes such as ventricular arrhythmia, is relatively unsupported by the clinical literature. This is consistent with the 2004 PM AQCD (U.S. EPA, 2004, 056905) which stated that there is inherent variability in the minute-to-minute spectral measurements, but long-term HRV measures demonstrate excellent day-to-day reproducibility.

The 2004 PM AQCD (U.S. EPA, 2004, 056905) presented limited evidence of PM-induced changes in HRV. However, findings from epidemiologic, controlled human exposure and toxicological studies demonstrated both decreases and increases in HRV following PM exposure. Recent epidemiologic studies have demonstrated a more consistent decrease in HRV (SDNN and rMSSD), which is supported by several controlled human exposure studies published since 2003. In these studies, decreases in HRV were observed among healthy adults following short-term exposures to $PM_{2.5}$ and $PM_{10-2.5}$ CAPs. It is interesting to note that these effects were not observed in adults with asthma or COPD. The effect of PM on HRV observed in animal toxicological studies continues to vary greatly, which may be due in part to strain differences in baseline HRV.

6.2.1.1. Epidemiologic Studies

The 2004 PM AQCD (U.S. EPA, 2004, 056905) reviewed several studies of PM exposure and HR or HRV and described mixed findings across studies. Several additional studies have investigated the association between acute changes in multiple HRV parameters and ambient air pollutant concentrations in the U.S., Canada, Europe, Mexico, and Asia. Features and results of these studies are presented in Table 6-1, and are summarized below.

In a multicity study, Liao and colleagues (2004, 056590) used data from the fourth cohort evaluation of the Atherosclerosis Risk in Communities (ARIC) Study (1996-1998). The 6,784 subjects were 45-64 yr of age and lived in Washington County, MD, Forsyth County, NC, or the suburbs of Minneapolis, MN. Linear regression models were used to examine the change in HRV associated with PM_{10}, O_3, SO_2, CO, and NO_2 concentrations in the 1-3 days prior to ECG measurement. Among all subjects, each 11.5 $\mu g/m^3$ increase in mean daily PM_{10} concentration 1 day before the ECG measurement was associated with a 0.06 ms^2 decrease in log-transformed HF (95%

CI: -0.10 to -0.02) and a 1.03 ms decrease in SDNN (95% CI: -1.64 to -0.42). A smaller non-significant decrease was also observed for log transformed LF. This reduction in cardiac autonomic control was larger among hypertensive subjects, suggesting that this group may be susceptible to the effects of PM.

In a study of randomly selected participants in the Women's Health Initiative (WHI), a multicity U.S. study, Whitsel et al. (2009, 191980) found decreases in rMMSD and SDNN in association with PM_{10} concentration. The associations were stronger among participants with diabetes. For example, in subjects with impaired fasting glucose, the reduction in rMSSD was 8.3% (-13.9, -2.4) among those with high levels of insulin and 0.6% (-2.1, 1.6) among those with low levels of insulin. Similar results were observed comparing high and low levels of insulin resistance.

Timonen et al. (2006, 088747) conducted a multicity panel study of elderly subjects with stable coronary heart disease who lived in 3 European cities (Amsterdam, the Netherlands; Erfurt, Germany; or Helsinki, Finland). They collected ECGs biweekly for six months in each subject. This analysis, done as part of the ULTRA Study, examined changes in HRV (resting, paced breathing, supine, and 5-min beat-to-beat NN intervals) associated with changes in fixed monitor particulate concentrations ($PM_{2.5}$, $PM_{10-2.5}$) with an emphasis on counts of UFPs (0.01-0.1 µm particles) and accumulation mode particles (ACP; 0.1-1.0 µm particles). Mixed models were first fit to estimate the change in HRV associated with PM (UFP, ACP, $PM_{2.5}$, and $PM_{10-2.5}$) concentrations on the same and previous 4 days in each city. In pooled analyses, the most consistent results identified were for LF/HF (Table 6-1). Estimates for $PM_{2.5}$, however, differed across cities. $PM_{2.5}$ was associated with decreased HF power and increased LF/HF in Helsinki, increased HF power and decreased LF/HF in Erfurt, and not associated with any HRV metric in Amsterdam. In a subsequent analysis, de Hartog et al. (2009, 191904) investigated whether exposure misclassification, effect modification by medication use, or particle composition differences across the three cities could explain the result observed. These authors found that $PM_{2.5}$ apportioned from traffic, long-range transported $PM_{2.5}$ and outdoor $PM_{2.5}$ were associated with reduced HRV most strongly among those not taking beta-blockers (Table 6-1). Indoor and personal $PM_{2.5}$ were not associated with decreased HRV in this study. Therefore, the authors concluded that effect modification by medication use and particle composition differences across the three cities may, in part, explain the heterogeneous $PM_{2.5}$ findings in the previous analysis.

The association between HRV and short-term increases in $PM_{2.5}$, $PM_{10-2.5}$, PM_{10}, other size fractions and components was also examined in single-city studies conducted in the U.S. or Canada (Table 6-1). Among U.S. and Canadian cities, increases in $PM_{2.5}$ were generally associated with decreased SDNN and/or decreased HF power but not in all studies. However, studies also reported increased SDNN associated with $PM_{2.5}$ concentrations (Riediker et al., 2004, 056992; Wheeler et al., 2006, 088453). In addition, Yeatts et al. (2007, 091266) reported increased rMSSD and HF power with increased $PM_{2.5}$ concentrations as well as SDANN5 (standard deviation of the average of normal to normal intervals in all 5-min intervals in a 24-h period), and SDNN24HR (standard deviation of the average of all normal to normal intervals in a 24-h period).

Other size fractions (e.g. coarse PM and UFPs) were also associated with decreases in HRV metrics in several single-city studies conducted in the U.S. or Canada. Lipsett et al. (2006, 088753) reported significantly decreased SDNN associated with increases in 2- and 6-h mean PM_{10} and $PM_{10-2.5}$ concentrations. Yeatts et al. (2007, 091266) reported decreased rMSSD, SDNN24HR, SDANN5, ASDNN5 (mean of the standard deviation in all 5-min segments of a 24-h recording), proportion of NN intervals <50 m apart (pNN50) (7 min and 24 h), and HF power associated with increased $PM_{10-2.5}$ concentration. Of those studies examining HRV associations with particle counts (Adar et al., 2007, 001458; Park et al., 2005, 057331), only Adar et al. (2007, 001458) found clear evidence of such effects (e.g., decreased SDNN, LF, HF). Decreased HRV was also associated with increases in ambient mean SO_4^{2-} concentration (Luttmann-Gibson et al., 2006, 089794), ambient mean BC concentration (Park et al., 2005, 057331; Schwartz et al., 2005, 074317), and traffic generated particles/pollution (Adar et al., 2007, 001458; Riediker et al., 2004, 056992) in these single-city studies.

Studies in Asia, Europe, and Mexico have also reported decreases in one or several HRV metrics (Table 6-1) associated with increases in $PM_{2.5}$ concentration or other size fractions. However, a study conducted in Scotland reported no PM-HRV associations (Barclay et al., 2009, 179935). Riojas-Rodriguez et al. (2006, 156913) reported significantly decreased LF and HF power associated with each 1 ppm increase in CO concentration, but only small non-significant decreases associated with $PM_{2.5}$.

Summary of Epidemiologic Studies of Heart Rate and HRV

HRV studies investigated lagged pollutant concentrations from 2 h-5 days before ECG measurement, reporting effects associated with mean pollutant concentrations lagged as short as 1-2 h, and more consistently with lags of 24-48 h. Taken together, these international and U.S./Canadian studies show decreases in HRV associated with $PM_{2.5}$ in most studies that use SDNN, rMSSD or HF power. The effects of $PM_{10-2.5}$, UFPs, and components were evaluated in fewer studies but associations with decreased HRV (e.g., both time and frequency measures) were observed. PM_{10} studies also found evidence for PM-induced alterations in HRV, however, it is difficult to determine which size fraction of PM_{10} (e.g., $PM_{10-2.5}$, $PM_{2.5}$ or UFPs) imparts the effects observed. As a result, PM_{10} studies provide supportive evidence for the overall effect of PM on HRV, but not for a specific size fraction. The proportion of studies reporting decreases in HRV may be inflated by publication bias (i.e., studies showing little or no effects are not submitted for publication).

HRV Studies Investigating Specific Mechanisms

Panel studies investigating PM-HRV associations have also been useful in investigating potential mechanistic pathways by which PM may elicit a cardiovascular response. A series of analyses using data from the Normative Aging Study, a cohort of older men living in the Boston metropolitan area, has also provided mechanistic insights into the PM-HRV association (Baccarelli et al., 2008, 191959; Chahine et al., 2007, 156327; Park et al., 2005, 057331; Park et al., 2006, 091245; Park et al., 2008, 156845; Schwartz et al., 2005, 086296).

Park et al. (2005, 057331) studied the association between short-term increases in ambient air pollution and changes in HRV using males enrolled in the Normative Aging Study. Using linear regression models, the association between HRV metrics and $PM_{2.5}$, O_3, NO_2, SO_2, CO, BC, and particle number count (PNC) moving averages (ma) in the previous 4, 24, and 48 h were examined. The modifying effects of hypertension, diabetes, ischemic heart disease (IHD), and use of hypertensive medications were also estimated. Of the pollutants examined, only $PM_{2.5}$ and O_3 were associated with reductions in HRV, and each pollutant's effect appeared independent of the other. Each 8 $\mu g/m^3$ increase in mean $PM_{2.5}$ concentration in the previous 48 h was associated with a 20.8% decrease in HF power (95% CI: -34.2 to -4.6), with larger effects among subjects with hypertension, IHD, and diabetes. The authors state that since BC concentrations were also associated with adverse changes in HRV, this suggests that traffic pollution may be partially responsible for the HRV changes.

Schwartz et al. (2005, 086296) examined the hypothesis that adverse changes in HRV due to $PM_{2.5}$ are mediated by an oxidative stress response among participants in the Normative Aging Study. They examined whether the change in HF power associated with each 10 $\mu g/m^3$ increase in 48-h mean $PM_{2.5}$ was modified by the presence or absence of the allele for glutathione S-transferase M1 (GSTM1), use of statins, obesity, high neutrophil counts, higher blood pressure (BP), and/or older age. In subjects without the GSTM1 allele and its protection against oxidative stress, each 10 $\mu g/m^3$ increase in 48-h mean $PM_{2.5}$ concentration was associated with a 34% decrease in HF power (95% CI: -52 to -9). There was no association among those with at least one copy of the allele. Obesity and high neutrophil counts also worsened the effect of PM on HRV regardless of allele.

Park et al. (2006, 091245) investigated whether transition metals may be responsible for cardiorespiratory effects that are observed in association with $PM_{2.5}$. Again using the Normative Aging Study cohort, they investigated whether subjects with two hemochromatosis (HFE) polymorphisms associated with increased iron uptake had a smaller decrease in HF power associated with PM than those subjects without either variant. Each 10 $\mu g/m^3$ increase in 48-h mean $PM_{2.5}$ was associated with a 31.7% decrease in HF (95% CI: -48.1 to -10.3) among subjects without either polymorphism, but not among those with the 2 protective HFE alleles.

Chahine et al. (2007, 156327) reported a 10.5% reduction in SDNN (95% CI: -18.2 to -2.2) associated with each 10 $\mu g/m^3$ increase in the mean 48-h $PM_{2.5}$ concentration among Normative Aging Study participants without the GSTM1 allele, but only a 2.0% SDNN decrease (95% CI: -11.3, 8.3) in those with the allele. This supports the PM-HF power findings of Schwartz et al. (2005, 086296). Further, subjects with the long repeat polymorphism in the HO-1 promoter had a greater decline in SDNN associated with each 10 $\mu g/m^3$ increase in the mean 48-h $PM_{2.5}$

concentration (-8.5% [95% CI: -14.8 to -1.8) than those with the short repeat polymorphism in HO-1 (7.4 % increase [95% CI: -8.7 to 26.2). Again, this suggests that PM-HRV changes are mediated, in part, by oxidative stress.

Baccarelli et al. (2008, 191959) investigated whether the $PM_{2.5}$-HRV association was modified by dietary intakes of methyl nutrients (folate, vitamins B6 and B12, and methionine) and related gene polymorphisms thought to either confer increased or decreased risk of CVD among men enrolled in the Normative Aging Study. Each 10 $\mu g/m^3$ increase in $PM_{2.5}$ in the previous 48 h was associated with -8.8% (95% CI: -16.7 to -0.2) and -11.8% (95% CI: -20.8 to -1.8) decreases in SDNN, among those with CC/TT genotypes of the C677T methylenetetrahydrofolate reductase (MTHFR) polymorphism, and the CC genotype of the C1420T cytoplasmic serine hydroxymethyltransferase (cSHMT) polymorphism, respectively. There were no changes among those with CC MTHFR and CC/TT cSHMT. Further, there were similar HRV reductions in those subjects with lower intakes of B6, B12, and/or methionine, but no decreases in those with high intakes. Thus these genetic and nutritional variations in the methionine cycle may modify the PM-HRV association.

Finally, among those Normative Aging Study subjects with high chronic lead exposure as measured using X-ray fluorescence of the tibia, each 7 $\mu g/m^3$ increase in mean $PM_{2.5}$ concentration in the previous 48 h was associated with a 22% decrease in HF power (95% CI: -37.4 to -1.7) (Park et al., 2008, 093027). Decreases in HF HRV were also associated with each 2.5 $\mu g/m^3$ increase in mean SO_4^{2-} concentration in the previous 48 h (22% decrease [95% CI: -40.4 to 1.6). The authors suggest that these findings are consistent with an oxidative stress response. Although this series of studies suggest a role of oxidative stress and perhaps methyl nutrients and related polymorphisms in these short-term associations of $PM_{2.5}$ with HRV, replication by other investigators in other cities and in other populations will aid interpretations of these findings.

Using data from a randomized controlled trial in Mexico City, Romieu et al. (2005, 086297) investigated whether omega-3 fatty acids in fish oil supplements would mitigate the adverse effects of acute PM exposure on HRV. Residents of a Mexico City nursing home were randomized to either 2 g/day of fish oil or 2 g/day of soy oil. They used random-effects regression models to estimate the change in HRV associated with mean $PM_{2.5}$ concentration in the pre-supplementation and supplementation phases. In the group receiving the fish oil supplement, each 8 $\mu g/m^3$ increase in 24-h mean total $PM_{2.5}$ exposure (weighted average of indoor and outdoor $PM_{2.5}$ based on time activity diaries) was associated with a 54% reduction (95% CI: -72 to -24) in log transformed HF power in the pre-supplementation phase. However, in the supplementation phase of the trial, each 8 $\mu g/m^3$ increase in 24-h mean total $PM_{2.5}$ concentration was associated with only a 7% reduction in log transformed HF power (95% CI: -20 to 7). Decreases in other HRV parameters associated with $PM_{2.5}$ were also muted in the supplementation phase. In the group receiving the soy oil supplement, the reduction in HF power was also smaller in magnitude during the supplementation phase. However, among those receiving the soy oil supplement, the differences between the pre-supplementation $PM_{2.5}$-HF change and the supplementation $PM_{2.5}$-HF change were smaller compared to those receiving the fish oil, and were not statistically significant. Romieu et al. (2008, 156922)also report that omega-3 polyunsaturated fatty acids appear to modulate the adverse effect of $PM_{2.5}$ based on measured biomarkers of oxidative response (Section 6.2.9.1).

Summary of HRV Studies Investigating Specific Mechanisms

In summary, several analyses of data from the Normative Aging Study have provided evidence that effect of $PM_{2.5}$ on HRV is modulated by genetic polymorphisms related to oxidative stress (Chahine et al., 2007, 156327; Park et al., 2006, 091245; Schwartz et al., 2005, 086296) or dietary methyl nutrients or related genetic polymorphisms (Baccarelli et al., 2008, 191959). In addition, preexisting conditions such as diabetes, IHD, and hypertension (Park et al., 2005, 057331; Whitsel et al., 2009, 191980), beta-blocker use (Folino et al., 2009, 191902; Park et al., 2005, 057331), chronic lead exposure (Park et al., 2008, 093027) and omega-3 fatty acid (Romieu et al., 2005, 086297) are reported to modulate the effect of $PM_{2.5}$ on HRV.

Table 6-1. Characteristics of epidemiologic studies investigating associations between PM and changes in HRV.

	PM Type, Exposure Lag	Study Subjects	Ambient Concentration ($\mu g/m^3$)*	Recording Length	SDNN	LF	HF, rMSSD	LF/HF
MULTICITY STUDIES								
Liao et al. (2004, 056590)	PM_{10}, 24-h, lag 1-day	N=6784 (mean age = 62 yrs), ARIC study: MD, NC, MN	24.3	5-min	↓	↓	↓	
Whitsel et al. (2009, 191980)	PM_{10}, 24-h, 3-d avg within 5 days preceding exam	N=4295 randomly selected participants in the WHI Trial	28 visit 1 27 visit 2 27 visit 3	10 second	↓		↓	
Timonen et al. (2006, 088747)	UFP, lags 0-2 days	Stable IHD patients (65+ yr) Amsterdam, Netherlands (N=37) Erfurt, Germany (N=47) Helsinki, Finland (N=47)	Amsterdam: 17,300 particles/cm^3 Erfurt: 21,100 particles/cm^3 Helsinki: 17,000 particles/cm^3	5-min (Pooled estimates during paced breathing presented to the right)	↓		↑	↓
	AC, lags 0-2 days		Amsterdam: 2100 particles/cm^3 Erfurt: 1800 particles/cm^3 Helsinki: 1400 particles/cm^3		↓		↑	↓
	$PM_{2.5}$, lags 0-2 days		Amsterdam: 20.0 Erfurt: 23.1 Helsinki: 12.7		↓		↑	↓
	$PM_{10-2.5}$, 2-day lag		Amsterdam: 15.3 Erfurt: 3.7 Helsinki: 6.7		→		→	↓
De Hartog et al. (2009, 191904)	24 h $PM_{2.5}$ outdoor, $PM_{2.5}$ traffic, long-range transported $PM_{2.5}$	Stable IHD patients (65+) Amsterdam, Netherlands (N=37) Erfurt, Germany (N=47) Helsinki, Finland (N=47) (Effects strongest among those NOT taking beta-blockers)	Median Outdoor: Amsterdam: 16.7 Erfurt: 16.3 Helsinki: 10.6	5 min	↓		↓	
U.S. AND CANADIAN STUDIES								
Park et al. (2005, 057331)	$PM_{2.5}$, 48-h avg	N=497 men (mean age = 73 yr), Normative Aging Study Boston, MA	24-h: 11.4 98th: 30.58	4-min	↓	↓	↓	↑
	PNC, 48-h avg		24-h: 28,942 (13,527) particles/cm^3		→	↓	↓	↓
	BC, 48-h avg		24-h: 0.92		↓	↓	↓	↑
Riediker et al. (2004, 056992)	In-vehicle $PM_{2.5}$ (mass) 9-h avg	N=9 healthy state police	9-h in-vehicle: 23	10-min	↑	→	↑	↓
Schwartz et al. (2005, 074317)	BC, 24-h	N=28 older adults (61-89 yr), 12 wk follow-up, Boston, MA	24-h Median: 1.0	23-min	↓		↓	↑
	$PM_{2.5}$, 24-h		24-h Median: 10		↓		↓	↑
	Secondary PM (estimated), 1-h		1-h Median: -1.7		↓		↓	↑
Yeatts et al. (2007, 091266)	$PM_{10-2.5}$, 24-h	N=12 adult asthmatics, Chapel Hill, NC	24-h: 5.3	5-min	↓	↓	↓	
	$PM_{2.5}$,24-h		24-h: 12.5		↑	↓	↑	

	PM Type, Exposure Lag	Study Subjects	Ambient Concentration ($\mu g/m^3$)*	Recording Length	SDNN	LF	HF, rMSSD	LF/HF
Wheeler et al. (2006, 088453)	$PM_{2.5}$, 4-h avg	N=18 COPD, Atlanta, GA	4-h: 17.8	20-min	↑	↑	↑	↑
	$PM_{2.5}$, 4-h avg	N=12 MI, Atlanta, GA			↓	↑	↓	↓
	EC, 4-h avg	N=18 COPD, Atlanta, GA	4-h: 2.3		↑			
	EC, 4-h avg	N=12 MI, Atlanta, GA			↓			
Dales 2004 (2004, 099036)	$PM_{2.5}$, 24-h avg (personal)	N=36 IHD patients, Toronto, Canada	24-h personal: 19.9	Not described	→	→	→	→
Luttmann-Gibson et al. (2006, 089794)	$PM_{2.5}$, lag 1-day	N=32 (65+ yr) Steubenville, OH	24-h: 19.7	~30-min	↓	↓	↓	
	Sulfate, lag 1-day		24-h: 6.9		↓	↓	↓	
	Nonsulfate PM, lag 1-day		24-h: 10.0		↓	↓	↓	
	EC, lag 1-day		24-h: 1.1		↑	↓	→	
Adar et al. (2007, 001458)	$PM_{2.5}$, 24-h avg	N=44 (60+ yr), diesel bus riders St. Louis, MO	24-h: 10.17 98th: 22.43	5-min	↓	↓	↓	↑
	BC, 24-h avg		330 ng/m^3		↓	↓	↓	↑
	PNC fine		42 particles/cm^3		↓	↓	↓	↑
	PNC course		0.02 particles/cm^3		↑	↑	↑	↓
Pope et al. (2004, 055238)	$PM_{2.5}$ (FRM), 24-h, lag 1-day	N=88 (65+ yr; 250 p-days), Utah Valley	23.7	24-h	↓		↓	
Sullivan et al. (2005, 109418)	$PM_{2.5}$, 1, 2, 24-h avg	N=21 (65+ yr) with CVD, Seattle WA	Median:10.7	20-min	→		→	
		N=13 (65+ yr) w/out CVD, Seattle WA			→		→	
Lipsett et al. (2006, 088753)	PM_{10},	N=19 IHD (65+ yr), 12 wk fu, Coachella Valley, CA	31.0 and 46.1	5-min Frequency domain; 2-h, 24-h Time domain	↓	↓	↓	
	$PM_{10-2.5}$		None given		↓	↓	→	
	$PM_{2.5}$		14 and 23.2		↓	↓	↑	
Ebelt et al. (2005, 056907)	PM_{10}, 24 h	N=16 COPD, Vancouver, Canada	17	24-h	↓		↓	
	$PM_{10-2.5}$		5.6		↑		→	
	$PM_{2.5}$, 24-h		11.4 98th: 23		↓		↓	
	$PM_{2.5}$ Sulfate, 24-h outdoor		2.0		↓		→	
Baccarelli et al. (2008, 191959)	$PM_{2.5}$, 48 h	N=549 Normative Aging Study and residents of Boston metropolitan area	Geometric mean (95% confidence interval) 10.5 (10.0, 10.9)	7 min	↓			
Fan et al. (2008, 191979)	$PM_{2.5}$ personal, 1 h	N=11 crossing guards in New Jersey	Only change in 1-h $PM_{2.5}$ reported Morning shift: 35.2 Afternoon shift: 24.1	24 h	↓			
INTERNATIONAL STUDIES								
Chan et al. (2004, 087398)	$NC_{0.02-1}$, 1-4 h	N=9 adults (19-29 yr) with lung function impairment, Taipei, Taiwan	23,407 (19,836) particles/cm^3	5 min	↓	↓	↓	↓
		N=10 adults (42-79 yr) with lung function impairment, Taipei, Taiwan	25,529 (20,783) particles/cm^3		↓	↓	↓	↓
Chuang et al. (2005, 087989)	$PM_{1.0-0.3}$, 1-4 h	N=16, Patients with IHD/ hypertension , Taipei, Taiwan	37.2	5-min	↓	↓	↓	↑
	$PM_{2.5-1.0}$, 1-4 h		12.6		↓	↓	↓	↑
	$PM_{10-2.5}$, 1-4 h		14.0		↓	↓	↓	↑

	PM Type, Exposure Lag	Study Subjects	Ambient Concentration ($\mu g/m^3$)*	Recording Length	SDNN	LF	HF, rMSSD	LF/HF
	$PM_{1.0-0.3}$, 1-4 h	N=10 IHD, Taipei, Taiwan	26.8		↓	↓	↓	→
	$PM_{2.5-1.0}$, 1-4 h		10.9		↓	↓	↓	↓
	$PM_{10-2.5}$, 1-4 h		16.4		↓	↓	↓	↑
Holguin et al. (2003, 057326)	$PM_{2.5}$, 24-h	N=21 without hypertension (60-96 yr), Mexico City	37.2	5-min		↓	↓	↑
		N=13 with hypertension (60-88 yr), Mexico City				↓	↓	↑
Romieu et al. (2005, 086297)	$PM_{2.5}$, 24-h (outdoor and indoor)	N=50 nursing home residents 65+ yr, Mexico City	Outdoor: 19.4 Indoor: 18.3	6-min (Indoor $PM_{2.5}$, pre-supplement phase presented)	↓	↓	↓	
Riojas-Rodriguez et al. (2006, 156913)	Personal $PM_{2.5}$	N=30 IHD patients, Mexico City	Geometric mean: 46.8	5-min		↓	↓	
Barclay et al. (2009, 179935)	PM_{10}, daily PNC, daily Estimated $PM_{2.5}$ and PNC	N=132, stable coronary heart failure Aberdeen, Scotland	Range of daily means: 7.4 to 68	24 h	→			
Cárdenas et al. (2008, 191900)	$PM_{2.5}$-outdoor $PM_{2.5}$-indoor	N=52 (31 women, 21 men; 20-40 yr), southeast of Mexico City	Median $PM_{2.5}$ outdoor: 28.3 $\mu g/m^3$ Median $PM_{2.5}$ indoor: 10.8	15 min		↓	↓	↓
Folino et al. (2009, 191902)	PM_{10}, 24 h $PM_{2.5}$, 24 h $PM_{0.25}$, 24 h	N=39 (36 male, 3 female; mean age = 60 yr) Padua, Italy	PM_{10} Summer: 46.4 Winter:73.0 Spring: 38.3 $PM_{2.5}$ Summer: 33.9 Winter: 62.1 Spring: 30.8 $PM_{0.25}$ Summer: 17.6 Winter: 30.5 Spring: 18.8	24 h	↓			
Min et al. (2008, 191901)	PM_{10}, 12 h	N=1349 (596 males; mean age = 44 yr), Korea	1-h avg: 33.2	5 min	↓	↓	↓	

Notes: Increases (↑), decreases (↓) and no effects (→) in HRV associated with PM concentration are indicated. Statistical significance was not necessary to categorize an effect as an increase or decrease. For time domain measures moving average lags up to 24-h were explored. For frequency domain measures lags of 2-h, 4-h and 24-h were explored.
** All concentrations are means measured in µ/m3, unless otherwise noted.

6.2.1.2. Controlled Human Exposure Studies

The 2004 PM AQCD (U.S. EPA, 2004, 056905) cited one study in which HRV indicators of parasympathetic activity increased relative to filtered air control following a 2-h exposure with intermittent exercise to $PM_{2.5}$ CAPs (avg concentration 174 $\mu g/m^3$) in both healthy and asthmatic volunteers (Gong et al., 2003, 042106). This effect was observed immediately following exposure and at 1 day post-exposure, but not at 4 h post-exposure. Although not statistically significant, HRV (total power) increased following exposure to filtered air and decreased following exposure to CAPs. More recent controlled human exposure studies are described below.

CAPs

Two new studies have evaluated the effect of $PM_{2.5}$ CAPs (2-h exposures to concentrations of 20-200 $\mu g/m^3$) on HRV in elderly subjects (Devlin et al., 2003, 087348; Gong et al., 2004, 087964). In both studies, subjects experienced significant decreases in HRV following exposure to CAPs relative to filtered air exposures. Interestingly, Gong et al. (2004, 087964) found that decreases in HRV were more pronounced in healthy older adults than in those with COPD. In another study,

healthy and asthmatic adults were exposed to $PM_{10-2.5}$ CAPs (avg concentration 157 μg/m^3) for 2 h with intermittent exercise (Gong et al., 2004, 055628). HRV was not affected immediately following the exposure, but decreased in both groups at 4 and 22 h after the end of the exposure, with greater responses observed in non-asthmatics. In a recent study among healthy adults exposed for 2 h with intermittent exercise to $PM_{10-2.5}$ CAPs (avg concentration 89 μg/m^3, MMAD 3.59 μm, Chapel Hill, NC), Graff et al. (2009, 191981) observed a significant decrease in overall HRV (SDNN) at 20 h post-exposure, although no other measures of HRV were affected. Using a similar study design, the same laboratory also evaluated the effect of ultrafine CAPs (avg concentration 49.8 μg/m^3, <0.16 μm in diameter) on various HRV parameters (Samet et al., 2009, 191913) Relative to filtered air, both HF and LF power increased 18 h following exposure to UF CAPs (36-42% increase per 10^5 particles/cm^3). Exposure to UF CAPs, expressed as mass concentration, was not associated with changes in HF power, and time domain parameters of HRV did not differ between CAPs and filtered air in the 24 h following exposure. Gong et al. (2008, 156483) also recently evaluated changes in HRV following controlled human exposures to UF CAPs and reported a small and transient decrease in LF power ($p < 0.05$) among healthy ($n = 17$) and asthmatic ($n = 14$) adults 4 h after the completion of a 2-h exposure with intermittent exercise in Los Angeles (avg concentration 100 μg/m^3, avg PNC 145,000/cm^3). No other measure of HRV was shown to be significantly affected by exposure to UF CAPs. In one of the largest studies of controlled human exposures to CAPs conducted to date, Fakhri et al. (2009, 191914) evaluated changes in HRV among 50 adult volunteers during 2-h exposures to $PM_{2.5}$ CAPs (127 μg/m^3) and O_3 (114 ppb), alone and in combination. Neither exposure to CAPs nor O_3 resulted in any significant changes in HRV relative to filtered air. However, trends were observed suggesting a negative concentration-response relationship between CAPs concentration and SDNN, rMSSD, HF power and LF power when subjects were concomitantly exposed to O_3.

Diesel Exhaust

In a double-blind, crossover, controlled-exposure study, Peretz et al. (2008, 156855) exposed three healthy adult volunteers and 13 adults with metabolic syndrome while at rest to filtered air and two levels of diluted DE ($PM_{2.5}$ concentrations of 100 and 200 μg/m^3) in 2-h sessions. HRV parameters were assessed prior to exposure, as well as at 1, 3, 6 and 22 h following the start of exposure, and included both time domain (SDNN and rMSSD) and frequency domain parameters (HF power, LF power, and the LF/HF ratio). In an analysis including all 16 subjects, the authors observed an increase in HF power and a decrease in LF/HF 3 h after the start of exposure to 200 μg/m^3 relative to filtered air. Although these changes were statistically significant ($p < 0.05$) the effects were not consistent among the study subjects. No other significant effect of DE on HRV was observed at either concentration or time point. The authors attributed the lack of consistent effects to the small and non-homogeneous population and the timing of measurement. There was no difference in either baseline or diesel-induced changes in HRV parameters between normal individuals and patients with metabolic syndrome, although the number of normal individuals was quite small. It is unclear if patients with metabolic syndrome were taking any medications.

Model Particles

Several additional recent controlled human exposure studies have evaluated the effect of laboratory generated particles on HRV in healthy and health-compromised individuals. In a random order crossover controlled human exposure study, Routledge et al. (2006, 088674) examined the effects of UF elemental carbon (EC) particles (50 μg/m^3) alone and in combination with 200 ppb SO_2 on HRV among 20 healthy older adults (age 56-75 yr), as well as 20 older adults with coronary artery disease (age 52-74 yr). Five minute recordings of HRV data were obtained prior to and immediately following the 1-h exposure, as well as 3 h post-exposure. In healthy subjects, exposure to EC particles resulted in small increases in RR-interval, SDNN, rMSSD, and LF power immediately following exposure compared to filtered air control. At 3 h post-exposure, there were no significant differences in HRV measures between EC particle and filtered air exposures. Conversely, SO_2-induced decreases in HRV were observed at 3 h, but not immediately following exposure. Concomitant exposure to EC particles and SO_2 followed a pattern similar to that observed with SO_2

alone, but did not reach statistical significance. Subjects with coronary artery disease did not experience any significant changes in HRV following exposure to either pollutant. The authors postulated that this lack of effect may be due to differences in medication between the two groups, as 70% of subjects with stable angina reported using β blockers, which are known to increase cardiac vagal control. The lack of any significant effects on HRV following exposure to EC particles is an important finding, as it provides evidence to suggest that the health effects observed following exposure to PM may be due to particle constituents other than carbon, or to reactive species found on the surface of the particle. These findings are in agreement with those of Zareba et al. (2009, 190101) who reported small and variable changes in HRV among a group of healthy adults following exposure to UF EC. While exposure both at rest and during exercise to 10 $\mu g/m^3$ UF EC resulted in an increase in time domain parameters (rMSSD and SNDD), no such effect was observed following exposure to a higher concentration of UF EC (25 $\mu g/m^3$) in the same subjects. A recent pilot study reported no effect of exposure to EC and ammonium nitrate particles (250-300 $\mu g/m^3$) on HRV parameters in five adults with allergic asthma (Power et al., 2008, 191982). However, when the exposure occurred concomitantly with O_3 (0.2 ppm), subjects were observed to experience significant changes in both time and frequency HRV parameters. These observations should be considered very preliminary as the study was limited by a small sample size (n = 5) and did not evaluate the effect of exposure to O_3 without particles. However, these findings are in agreement with the previously described study of CAPs and O_3 conducted by Fakhri et al. (2009, 191914). In addition to the studies of laboratory generated carbon described above, Beckett et al. (2005, 156261) used ZnO as a model particle and exposed twelve resting, healthy adults for 2 h to filtered air and 500 $\mu g/m^3$ in the ultrafine (40.4 ± 2.7 nm) and fine (291.2 ± 20.2 nm) modes. Neither ultrafine nor fine ZnO produced a significant change in any time or frequency domain parameter of HRV.

Summary of Controlled Human Exposure Study Findings for Heart Rate Variability

The results of several new controlled human exposure studies provide limited evidence to suggest that acute exposure to near ambient levels of PM may be associated with small changes in HRV. Changes in HRV parameters, however, are variable with some showing increased parasympathetic activity relative to sympathetic activity and others showing the opposite. Although a direct comparison between younger and older adults has not been made, PM exposure appears to result in a decrease in HRV more consistently in healthy older adults (Devlin et al., 2003, 087348; Gong et al., 2004, 087964).

6.2.1.3. Toxicological Studies

Toxicological studies that examined HR and HRV are presented in the 2004 PM AQCD (U.S. EPA, 2004, 056905) and overall demonstrated differing responses, which were collectively characterized as providing limited evidence for PM-related cardiovascular effects. The studies described that reported HR or HRV effects following PM exposure were conducted with a variety of particle types (CAPs, diesel, ROFA, metals), exposure methods (inhalation and IT instillation), and doses (100-3,000 $\mu g/m^3$ for inhalation; up to 8.3 mg/kg for IT instillation).

CAPs

Two groups of SH rats exposed to CAPs in Tuxedo, NY for 4 h (single-day mean $PM_{2.5}$ concentrations 80 and 66 $\mu g/m^3$; February 2001 and May 2001, respectively) demonstrated decreased HR when exposure groups were combined that returned to baseline values when exposure ceased (Nadziejko et al., 2002, 087460). Fine or UF H_2SO_4 exposure (mean concentration 225 and 468 $\mu g/m^3$) did not induce any HR effects. Another study demonstrated a trend toward increased HR in WKY rats following a 1- or 4-day $PM_{2.5}$ CAPs exposure in Yokohama City, Japan (4.5 h/day; May 2004, November 2004, and September 2005), but the correlation between change in HR and cumulative PM mass collected was not significant (Ito et al., 2008, 096823). Increased HR was observed in SH rats exposed to $PM_{2.5}$ CAPs for two 5-h periods during the spring (mean mass concentration 202 $\mu g/m^3$) in a suburb of Taipei, Taiwan (Chang et al., 2004, 055637). The response

was less prominent in the summer (mean mass concentration 141 μg/m^3), despite the number concentrations being similar for the two seasons (2.30×10^5 and 2.78×10^5 particles/cm^3, respectively).

For HRV, decreased SDNN was observed in SH rats exposed to $PM_{2.5}$ CAPs (mean mass concentration 202 μg/m^3; mean number concentration 2.30×10^5 particles/cm^3) for two 5-h periods separated by 24 h (Chang et al., 2005, 088662). Each of the four animals served as their own control and the estimated mean PM effects for the SDNN decreases during exposure were 85-60% of baseline. CAPs effects on rMSSD were less remarkable. In a study of Tuxedo, NY $PM_{2.5}$ CAPs, no acute changes in rMSSD or SDNN were observed in either ApoE$^{-/-}$ or C57 mice when the 48-h time period postexposure was evaluated (6 h/day×5 day/wk; mean mass concentration over 5-mo period 110 μg/m^3) (Chen and Hwang, 2005, 087218).

Diesel Exhaust

Anselme et al. (2007, 097084) used a MI model of congestive heart failure (CHF) where the left anterior descending coronary artery of WKY rats was occluded to induce ischemia. After 3 mo of recovery, rats were exposed to diesel emissions for 3 h (PM concentration 500 μg/m^3; mass mobility diameter 85 nm; NO_2 1.1 ppm; CO 4.3 ppm) and decreases in rMSSD were observed during the first 2 h of the exposure, which returned to baseline values for the last hour of exposure. Healthy rats also demonstrated decreased rMSSD when measured over the entire exposure period.

Model Particles

In WKY rats exposed to UF carbon particles (mass concentration 180 μg/m^3; mean number concentration 1.6×10^7 particles/cm^3) for 24 h, HR increased and SDNN decreased during particle inhalation (Harder et al., 2005, 087371). These measures returned to baseline values during the recovery period. This study provides evidence that ultrafine carbon exerts its effects through changes in ANS mediation, as the HR and HRV responses occurred quickly after exposure started and pulmonary inflammation was only observed at the 24-h time point (and not at 4 h). SH rats exposed to ultrafine carbon particles under the same conditions (mass concentration 172 μg/m^3; mean number concentration 9.0×10^6 particles/cm^3) demonstrated similar responses, albeit not until recovery days 2 and 3 (Upadhyay et al., 2008, 159345).

A model of premature senescence has been developed by Tankersley et al. (2003, 053919), using aged AKR mice whose body weight abruptly declines ~5 wk prior to death and is accompanied by deficiencies in other vital physiological function including HR and temperature regulation. When exposed to carbon black ([CB]; mean concentration 160 μg/m^3; 3 h/day×3 day), terminal senescent mice responded with robust cardiovascular effects, including bradycardia and increased rMSSD and SDNN (Tankersley et al., 2004, 094378). SDNN and LF/HF were also increased in healthy senescent mice exposed to CB. These studies indicate that HR regulatory mechanisms are altered in susceptible mice exposed to PM (sympathetic and parasympathetic changes in healthy senescent mice and increased parasympathetic influence in terminally senescent mice), which may translate into lowered homeostatic competence in these animals. Results from the near-terminal group should be interpreted with caution, as only three mice were in this group.

Subsequent research with a similar exposure protocol (mean CB concentration 159 μg/m^3) used C57BL/6J and C3H/HeJ mice to determine whether an acute PM challenge can modify HR regulation in two mice strains with differing baseline HR (Tankersley et al., 2007, 097910). There were no CB-specific effects on HR or HRV in C3H/HeJ compared to C57BL/6J mice (average HR ~80 bpm lower than C3H/HeJ at baseline). Administration of a sympathetic antagonist (propanolol) to C57BL/6J mice prior to CB exposure resulted in elevated HR and decreased rMSSD compared to air during the last 2 h of exposure, indicating withdrawal of parasympathetic tone. There may be differences in regional particle deposition based on strain-specific breathing patterns that may affect HR and HRV responses. However, this study revealed that inherent autonomic tone, which is genetically varied between these mouse strains, may affect cardiovascular responses following PM exposure. In extrapolating these results to humans, individual variation in genetic factors likely plays some role in PM-induced adjustments in HR control via the ANS.

A recent study in mice (C3H/HeJ, C57BL/6J, and C3H/HeOuJ) examined the effects of a 2-h O_3 (mean concentration 0.584 ppm) pretreatment followed by a 3-h exposure to CB (mean

concentration 536 μg/m^3) on HR and HRV measures (Hamade et al., 2008, 156515) HR decreased to the greatest extent during O_3 pre-exposure for all strains that were then exposed to CB. The percent change in SDNN and rMSSD were increased in C3H mice during O_3 pre-exposure and CB exposure compared to the filtered air group; however, these HRV parameters gradually decreased over the duration of the experiment and appeared to be O_3 dependent. Together, these findings indicate that increases in parasympathetic tone and/or decreases in sympathetic input may explain the observed bradycardia. In a subset of all mice pre-exposed to O_3, rMSSD remained significantly elevated during the CB exposure compared to filtered air. The results from this study confirm what was observed in Tankersley et al. (2007, 097910) in that genetic determinants affect HR regulation in mice with exposure to air pollutants.

Summary of Toxicological Study Findings for Heart Rate and Heart Rate Variability

Both increases and decreases in HR have been observed in rats or mice following PM exposure. Fine or UF H_2SO_4 did not result in HR changes in SH rats. Similarly, decreased SDNN was reported for UF CAPs exposure and lowered rMSSD was observed with diesel exposure. In near-terminal senescent mice, HRV responses were robust following CB exposure and represented increased parasympathetic influence. Strain differences in baseline HR and HRV likely contribute to PM responses. HRV changes with preexposure to O_3 and CB appeared to be O_3 dependent, although rMSSD remained elevated during PM exposure.

Source Apportionment and PM Components

An additional analysis of CAPs data (Chen and Hwang, 2005, 087218; Hwang et al., 2005, 087957) was conducted to link short-term HR and HRV effects to major PM source categories using source apportionment methodology (Lippmann et al., 2005, 087453).

The source categories were: (1) regional secondary SO_4^{2-} comprised of high S, Si, and OC (mean 63.41 μg/m^3); (2) resuspended soil characterized by high concentrations of Ca, Fe, Al, and Si (mean concentration 5.88 μg/m^3); (3) fly ash emissions from power plants burning residual oil in the eastern U.S. and containing high levels of V, Ni, and Se (mean concentration 1.53 μg/m^3); and (4) motor vehicle traffic and other unknown sources (34.92 μg/m^3) (Lippmann et al., 2005, 087453). Exposures occurred from 9:00 a.m. to 3:00 p.m., 5 days/wk for 5 mo. $PM_{2.5}$ mass was associated with a daily interquartile change of -4.1 beat/min HR during exposure in ApoE$^{-/-}$ mice[1] and a similar magnitude of effect was observed with resuspended soil (-4.5 beat/min). Resuspended soil was also associated with a HR increase in the afternoon post-exposure (2.6 beat/min); the secondary SO_4^{2-} factor was linked to lowered HR in the same period (-2.5 beat/min). A 6.2% increase in rMSSD collected in the afternoon post-exposure was associated with the residual oil factor, compared to a 5.6% and 2.4% decrease in rMSSD at night for secondary SO_4^{2-} and $PM_{2.5}$ mass, respectively. Resuspended soil was associated with a 4.3% increase in rMSSD the night following CAPs exposure. The residual oil and secondary SO_4^{2-} categories showed similar statistically significant parameter estimates for SDNN as rMSSD.

Recent studies of ECG alterations in mice have indicated a role for PM-associated Ni in driving the cardiovascular effects. Lippman et al. (2006, 091165) presented a posthoc analysis of daily variations in $PM_{2.5}$ CAPs (mean concentration: 85.6 μg/m^3; 7/21/ 2004–1/12/2005; Tuxedo, NY) and changes in cardiac dynamics in ApoE$^{-/-}$ mice. On the 14 days that the exposed mice had

[1] Atherosclerosis and related pathways have been studied primarily in the Apolipoprotein E (ApoE) knockout mouse. Developed by Nobuyo Maeda's group in 1992 (Piedrahita et al., 1992, 156868; Zhang et al., 1992, 157180), the ApoE-/- mouse and related models have become the workhorse of atherosclerosis research over the past 15 years. The ApoE molecule is involved in the clearance of fats and cholesterol. When ApoE (or the LDL receptor) is deleted from the genome, mice develop severely elevated lipid and cholesterol profiles; ApoE$^{-/-}$ mice on a high-fat ("Western") diet exhibit cholesterol levels exceeding 1000 mgdL (normal is ~150 mgdL) (Huber et al., 1999, 156575; Moore et al., 2005, 156780). As a result, the lipid uptake into the vasculature is increased and the atherosclerotic process is dramatically hastened. Furthermore, the LDLs in ApoE$^{-/-}$ mice are highly susceptible to oxidation (Hayek et al., 1994, 156527), which may be a crucial event in the air pollution-mediated vascular changes. However it should be noted that this model is primarily one of peripheral vascular disease rather than coronary artery disease.

unusually elevated HR, Ni, Cr, and Fe comprised 12.4% of the PM mass, compared to only 1.5% on the other 89 days. Back trajectory analyses indicated high-altitude winds from the northwest that did not traverse population centers and industrial areas except the Sudbury Ni smelter in Ontario, Canada. On the 14 days that high HR was observed, the HR elevation lasted for two days, but only the current day CAPs concentration was statistically significant. SDNN decreases were statistically significant for all three lags (0, 1, 2 days). The GAM regression analysis showed that only Ni produced a statistically significant effect for HR and SDNN.

6.2.2. Arrhythmia

Epidemiologic and toxicological studies presented in the 2004 PM AQCD (U.S. EPA, 2004, 056905) provided some evidence of arrhythmia following exposure to PM. However, a positive association between PM and ventricular arrhythmias among patients with implantable cardioverter defibrillators was only observed in one study conducted in Boston, MA, while toxicological studies reported arrhythmogenesis in rodents following exposure to ROFA, DE, or metals. Recent epidemiologic studies have confirmed the findings of PM-induced ventricular arrhythmias in Boston, MA, and have also reported increases in ectopic beats in studies conducted in the Midwest and Pacific Northwest regions of the U.S. In addition, two studies from Germany have demonstrated positive associations between traffic and combustion particles and changes in repolarization parameters among patients with IHD. Findings of recent toxicological studies are mixed, with both demonstrated decreases and increases in frequency of arrhythmia following exposure to CAPs.

6.2.2.1. Epidemiologic Studies

Studies of Arrhythmias Using Implantable Cardioverter Defibrillators

One study reviewed in the 2004 PM AQCD assessed the effect of short-term fluctuations in $PM_{2.5}$ on ventricular arrhythmias and several recent studies examining this relationship have been conducted. Ventricular ectopy and arrhythmia include ventricular premature beats (VPBs), ventricular tachycardia (VT), and ventricular fibrillation (VF). VPBs are spontaneous beats originating from either the right or left ventricles. VT refers to three or more VPBs in succession at a rate of 100 beats per minute or greater, while VF is characterized by rapid and disorganized ventricular electrical activation incapable of generating an organized mechanical contraction or cardiac output. AF is the most common type of arrhythmia. In this condition, ectopic electrical impulses arising in the atria or pulmonary veins, i.e., outside their normal anatomic origin (the sinoatrial node), can result in atrioventricular dilatation, dysfunction, and/or thromboembolism. Despite being common, clinical and subclinical forms of AF are associated with reduced functional status and quality of life. Moreover, the arrhythmia accounts for a large proportion of ischemic stroke (Laupacis et al., 1994, 190901; Prystowsky et al., 1996, 156031) and is a strong risk factor for CHF (Roy et al., 2009, 190902), contributing to both cardiovascular disease (CVD) and all-cause mortality (Kannel et al., 1983, 156623).

Ventricular arrhythmia is commonly associated with myocardial infarction, heart failure, cardiomyopathy, and other forms of structural (e.g., valvular) heart disease. Pathophysiologic mechanisms underlying this established cause of sudden cardiac death include activators and facilitators of arrhythmia, such as electrolyte abnormalities, modulation of the ANS, membrane channels, gap junctions, oxidant stress, myocardial stretch and ischemia.

Previously, Peters et al. (2000, 011347) conducted a pilot study in Boston, MA to examine the association between short-term changes in ambient air pollutant concentrations and increased risk of ventricular arrhythmias, among a cohort of patients with implantable cardioverter defibrillators (ICD). ICDs continuously monitor cardiac rhythm and upon detection of an abnormal rhythm (i.e., rapid HR), they can be programmed to deliver pacing and/or shock therapy to restore normal sinus rhythm. Those abnormal rhythms that are most severe or rapid are assumed to be due to VT or VF (i.e., life-threatening arrhythmias), and are thus treated with electric shock. These ICD devices also store information on each abnormal rhythm detected, including the date, time, and therapy given. Thus, using the date and time of those arrhythmias resulting in electric shock, Peters et al. (2000,

011347) reported an increased risk of ICD shock associated with mean NO_2 concentration in the previous two days. Among subjects with frequent events (10 or more during 3 yr of follow-up) an increased risk of ICD shock was also associated with interquartile range increases in CO, NO_2, $PM_{2.5}$, and BC in the previous 2 days. Several studies were conducted to confirm these findings. The study characteristics, as well as the reported effect estimates and 95% CI associated with each PM metric, are shown in Table 6-2.

Dockery et al. (2005, 078995; 2005, 090743) conducted a follow-up study of ICD patients living in eastern Massachusetts and followed subjects for a longer period of time (up to 7 yr). They were the first to review the ECG, classify each ICD-detected arrhythmia (e.g., ventricular arrhythmia, VF, atrial tachycardia, sinus tachycardia, etc.), and include only ventricular arrhythmias (VF or VT; excluding supraventricular arrhythmias). In single-pollutant models using generalized estimating equations, increased risks of confirmed ventricular arrhythmias were associated with IQR increases in every pollutant ($PM_{2.5}$, BC, SO_4^{2-}, NO_2, SO_2, O_3, and PNC). Among those with a prior ventricular arrhythmia in the past three days, interquartile range increases in 2-calendar-day mean $PM_{2.5}$, NO_2, SO_2, CO, O_3, SO_4^{2-}, and BC concentrations were all associated with significant and markedly higher risks of ventricular arrhythmia than among those without a prior arrhythmia. The pollutants associated with increased risk of ventricular arrhythmia implicate traffic pollution.

Rich et al. (2005, 079620) conducted a case-crossover analysis of these same data to investigate moving average pollutant concentrations lagged <48 h. They reported an increased risk of ventricular arrhythmia associated with mean $PM_{2.5}$ and O_3 concentrations in the 24 h before the arrhythmia. Each pollutant effect appeared independent in two pollutant models. In single-pollutant models, NO_2 and SO_2 were associated with increased risk, but when included in two pollutant models with $PM_{2.5}$, only $PM_{2.5}$ remained associated with increased risk. They did not, however, find evidence of a more acute arrhythmic response to pollution (i.e., larger risk estimates associated with moving averages <24 h before arrhythmia detection). In an ancillary case-crossover analysis of data from the Boston ICD study, Rich et al. (2006, 088427) identified 91 confirmed episodes of paroxysmal AF among 29 subjects. In single pollutant models, they reported a significantly increased risk of AF associated with mean O_3 and $PM_{2.5}$ concentrations in the hour before the arrhythmia and BC concentration in the 24 h before the arrhythmia.

Rich et al. (2006, 089814) conducted another case-crossover study in the St. Louis, MO metropolitan area. Using the same methods as in Boston, they reported increased risk of ventricular arrhythmia associated with mean SO_2 concentration in the 24 h before the arrhythmia, but not $PM_{2.5}$ (in single-pollutant models). Again, they found no evidence of an arrhythmic response with moving average pollutant concentrations <24 h before the arrhythmia.

In Vancouver, Canada, Vedal et al. (2004, 055630) did not find increased risk of ICD shocks associated with increases in any pollutant concentration (PM_{10}, O_3, SO_2, NO_2, and CO). Secondary analyses among those subjects with two or more discharges per year, and analyses stratified by season were also null for PM_{10}, although an association with SO_2 (lag 2 days) was observed. A case crossover analysis of these same data examining additional particle pollutant concentrations available for a shorter time frame (e.g., $PM_{2.5}$, SO_4^{2-}, EC, and OC) also found no increased risk of ICD shock associated with any pollutant (Rich et al., 2004, 055631).

The largest ICD study to date examined the risk of ventricular arrhythmias associated with increases in the daily concentration of numerous PM and gaseous pollutants in Atlanta, GA (Metzger et al., 2007, 092856) (see Table 6-2 for specific pollutants evaluated). Similar to Vedal et al. (2004, 055630), they did not find significant or consistently increased risk of a ventricular arrhythmia associated with any IQR increase in mean daily PM or gaseous pollutant concentration at any lag examined.

Ljungman et al. (2008, 180266) conducted a similar study, using case-crossover methods, on ICD patients in Gothenburg and Stockholm, Sweden. They investigated the triggering of confirmed ventricular arrhythmias by ambient PM_{10} and NO_2 concentrations, and reported increased relative odds of ventricular arrhythmia associated with each 10 $\mu g/m^3$ increase in the 2-h ma PM_{10} concentration (OR = 1.22 [95% CI: 1.00-1.51]), with a smaller non-significant risk associated with each 10.3 $\mu g/m^3$ increase in the 24-h ma PM_{10} concentration (OR = 1.23 [95% CI: 0.87-1.73]). The NO_2 and $PM_{2.5}$ effect estimates were much smaller and not statistically significant. Effect estimates were larger for events occurring near the air pollution monitors in Gothenburg (compared to Stockholm).

Albert et al. (2007, 156201), although not investigating associations with ambient pollution, conducted a case-crossover study of the association between ventricular arrhythmia and traffic

exposure in the hours before the arrhythmia. They reported an increased risk of ventricular arrhythmia associated with traffic exposure or driving in the previous hour. They hypothesized that this increased risk was due to either a stress response from being in a car in heavy traffic, or from traffic-generated air pollution, or a combination of both.

Table 6-2. Epidemiologic studies of ventricular arrhythmia and ambient PM concentration, in patients with implantable cardioverter defibrillators.

Reference	Outcome and Sample Size	Study Design and Analytic Method	Copollutants	PM Metric	Ambient Concentration	Lag and its Increment Units	OR	95% Confidence Interval
Dockery et al. (2005, 078995; 2005, 090743) Eastern MA	N=670 days with ≥ 1 confirmed ventricular arrhythmias among n=84 subjects	Generalized estimating equations Lags Evaluated: 2 calendar day means	NO_2, CO, SO_2, O_3	$PM_{2.5}$	Daily Median: 10.3 µg/m^3	2 day 6.9 µg/m^3	1.08	0.96, 1.22
				BC	Daily Median: 0.98 µg/m^3	2 day 0.74 µg/m^3	1.11	0.95, 1.28
				Sulfate	Daily Median: 2.55 µg/m^3	2 day 2.04 µg/m^3	1.05	0.92, 1.20
				PNC	Daily Median: 29,300 particles/cm^3	2 day 19,120 particles/cm^3	1.14	0.87, 1.50
Rich et al. (2005, 079620) Eastern MA	N=798 confirmed ventricular arrhythmias among n=84 subjects	Time-stratified case--crossover study. Conditional logistic regression. Lags evaluated: 3, 6, 24, 48-h ma	NO_2, CO, SO_2, O_3	$PM_{2.5}$	Daily Median: 9.8 µg/m^3	24-h ma 7.8 µg/m^3	1.19	1.02, 1.38
				BC	Daily Median: 0.94 µg/m^3	24-h ma 0.83 µg/m^3	0.93	0.74, 1.18
Rich et al. (2006, 089814) St. Louis metro area	N=139 confirmed ventricular arrhythmias among n=56 subjects	Time-stratified case-crossover study. Conditional logistic regression. Lags Evaluated: 6, 12, 24, 48-h ma	NO_2, CO, SO_2, O_3	$PM_{2.5}$	Daily Median: 16.2 µg/m^3	24-h ma 9.7 µg/m^3	0.95	0.72, 1.27
				EC	Daily Median: 0.6 µg/m^3	24-h ma 0.5 µg/m^3	1.18	0.93, 1.50
				Organic Carbon	Daily Median: 4.0 µg/m^3	24-h ma 2.3 µg/m^3	1.08	0.81, 1.43
Vedal et al. (2004, 055630) Vancouver, BC, Canada	N=257 days with ≥ 1 ICD shock among n=50 subjects	Generalized estimating equations Lags Evaluated: 0, 1, 2, 3 daily ma	NO_2, CO, SO_2, O_3	PM_{10}	Daily Median: 11.6 µg/m^3	Lag Day 0 5.6 µg/m^3	1.00*	0.82, 1.19*
Ljungman et al. (2008, 180266) Gothenburg and Stockholm, Sweden	N=114 ventricular arrhythmias among 73 subjects. 211 total subjects were followed.	Conditional logistic regression Lags evaluated: 2 h, 24 h	NO_2	PM_{10},	Median Gothenburg 2 h: 18.95 µg/m^3 24 h: 19.92 µg/m^3 Stockholm 2 h: 14.62 µg/m^3 24 h: 15.23 µg/m^3	2-h ma: 14.16 µg/m^3 24-h ma: 11:49 µg/m^3	2 h: 1.31 24 h: 1.24	1.00, 1.72 0.87, 1.76
				$PM_{2.5}$	Median Stockholm µg/m^3 2 h: 9.17 24 h: 9.49 µg/m^3	2-h ma: 6.69 µg/m^3 24-h ma: 5.27 µg/m^3	2 h: 1.23 24 h: 1.28	0.84, 1.80 0.90, 1.84
Rich et al. (2004, 055631) Vancouver, BC, Canada	N=77 to 98 days with ≥ 1 ICD shock among n=34 subjects	Ambi-directional case-crossover study. Conditional logistic regression Lags Evaluated: 0, 1, 2, and 3 day ma	NO_2, CO, SO_2, O_3	$PM_{2.5}$	Daily Mean: 8.2 µg/m^3	Lag Day 0 5.2 µg/m^3	1.0†	0.9, 1.1†
				PM_{10}	Daily Mean: 13.3 µg/m^3	Lag Day 0 7.4 µg/m^3	0.9†	0.5, 1.5†
				EC	Daily Mean: 0.8 µg/m^3	Lag Day 0 0.4 µg/m^3	1.1†	0.9, 1.3†
				Organic Carbon	Daily Mean: 4.5 µg/m^3	Lag Day 0 2.2 µg/m^3	1.1†	0.9, 1.3†
				Sulfate	Daily Mean: 1.3 µg/m^3	Lag Day 0 0.9 µg/m^3	0.9†	0.7, 1.2†

Reference	Outcome and Sample Size	Study Design and Analytic Method	Copollutants	PM Metric	Ambient Concentration	Lag and its Increment Units	OR	95% Confidence Interval
Metzger et al. (2007, 092856) Atlanta, GA	N=6287 confirmed ventricular arrhythmias among n=518 subjects	Generalized estimating equations Lags Evaluated: 0, 1, and 2 day ma	NO_2, CO, SO_2, O_3	$PM_{2.5}$	Daily Median: 16.2 μg/m^3	24-h ma 10 μg/m^3	1.00	0.95, 1.0
				PM_{10}	Daily Median: 26.4 μg/m^3	24-h ma 10 μg/m^3	1.00	0.97, 1.03
				$PM_{10-2.5}$	Daily Median: 8.7 μg/m^3	24-h ma 5 μg/m^3	1.03	1.00, 1.07
				$PM_{2.5}$ EC	Daily Median: 1.4 μg/m^3	24-h ma 1 μg/m^3	1.01	0.98, 105
				$PM_{2.5}$ OC	Daily Median: 3.9 μg/m^3	24-h ma 2 μg/m^3	1.01	0.98, 1.03
				$PM_{2.5}$ SO_4^{2-}	Daily Median: 4.1 μg/m^3	24-h ma 5 μg/m^3	0.99	0.93, 1.06
				$PM_{2.5}$ water soluble elements	Daily Median: 0.022 μg/m^3	24-h ma 0.03 μg/m^3	0.95	0.90, 1.00

Estimated from Figure 3 Vedal et al. (2004, 055630).† Estimated from Figure 3 Rich et al. (2004, 055631)

Summary of Epidemiologic Studies of Arrhythmias using ICDs

Since 2004, only two studies (in Boston and Sweden), reported adverse associations of $PM_{2.5}$, other size fractions and components with ICD-detected ventricular arrhythmias (Dockery et al., 2005, 078995; Dockery et al., 2005, 090743; Ljungman et al., 2008, 180266; Rich et al., 2005, 079620). Studies of ICD-detected ventricular arrhythmias conducted elsewhere did not report associations (Dusek et al., 2006, 155756; Metzger et al., 2007, 092856; Rich et al., 2004, 055631; Vedal et al., 2004, 055630) nor was an association observed in a study of PM_{10} and ICD shock in Vancouver, Canada (Vedal et al., 2004, 055630). A range in exposure lags was evaluated in the Boston study (3 h-3 days) (Dockery et al., 2005, 078995; Dockery et al., 2005, 090743; Rich et al., 2005, 079620) and Sweden study (2 h and 24 h) (Ljungman et al., 2008, 180266). Reasons for the inconsistent findings may include differing degrees of exposure misclassification within each study or city due to differences in PM composition and pollutant mixes (e.g., less transition metals and sulfates in the Pacific Northwest than the Northeast U.S.), and differences in the size of study areas (Boston: within 40 km of $PM_{2.5}$ monitoring site; Vancouver: Lower Mainland of British Columbia 90 km east of Vancouver). In addition, Rich et al. (2005, 079620) reported that use of the mean pollutant concentration from the specific 24 h before the arrhythmia rather than just the day of the arrhythmia, resulted in less exposure misclassification and less bias towards the null, possibly explaining the lack of association when using just the day of ICD discharge and daily PM concentrations.

Ectopy Studies Using ECG Measurements

A few panel studies have used ECG recordings to evaluate associations between ectopic beats (ventricular or supraventricular) and mean PM concentrations in the previous hours and/or days (Berger et al., 2006, 098702; Ebelt et al., 2005, 056907; Liao et al., 2009, 199519; Sarnat et al., 2006, 090489).

Ectopic beats are defined as heart beats that originate at a location in the heart outside of the sinus node. They are the most common disturbance in heart rhythm. Ectopic beats are usually benign, and may present with or without symptoms, such as palpitations or dizziness. Such beats can arise in the atria, AV node, conduction system or ventricles. When the origin is in the atria the beat is called an atrial or supraventricular ectopic beat. When such a beat occurs earlier than expected it is referred to as a premature supraventricular or atrial premature beat. Likewise, when the origin is in

the ventricle the beat is defined as a ventricular ectopic beat, or when early a premature ventricular beat. When three or more occur ectopic beats occur in succession, this is called a non-sustained run of either supraventricular (atrial) or ventricular origin. When the rate of the run is greater than 100 beats per minute it is defined as a tachycardia. Sustained VT are the arrhythmias investigated in the ICD studies described above.

Using data from the WHI done in 59 U.S. exam sites in 24 cities, Liao et al. (2009, 199519) estimated mean $PM_{2.5}$ and PM_{10} concentrations at the addresses of 57,422 study subjects undergoing ECG monitoring. They then estimated the risks of ventricular and supraventricular ectopy during that 10-s ECG recording associated with increases in mean PM_{10} and $PM_{2.5}$ concentrations on the same day and previous 2 days, as well as over the previous 30 days. Mean $PM_{2.5}$ and PM_{10} concentrations during the study period were 13.8 and 27.5 $\mu g/m^3$, respectively. Using a 2-stage random effects model, they reported that among smoking subjects, each 10 $\mu g/m^3$ increase in $PM_{2.5}$ concentration on lag day 1 was associated with a significantly increased risk of ventricular ectopy (OR = 2.0 [95% CI: 1.32-3.3]). Similarly, each 10 $\mu g/m^3$ increase in lag 1 PM_{10} concentration was associated with an increased risk of ventricular ectopy (OR = 1.32 [95% CI: 1.07-1.65]). The lag day 2 $PM_{2.5}$ risk estimate was similar in size, but not statistically significant. There were no associations between PM_{10}, $PM_{2.5}$ and supraventricular ectopy among smokers or non-smokers, and no association with any PM metric and ventricular ectopy among non-smokers.

Sarnat et al. (2006, 090489) conducted a panel study among 32 nonsmoking older adults residing in Steubenville, OH. In this study, the median daily $PM_{2.5}$, SO_4^{2-}, and EC concentrations were 17.7, 5.7, and 1.0 $\mu g/m^3$, respectively. They used logistic regression models to examine lagged effects of 1- to 10-day ma concentrations of $PM_{2.5}$, SO_4^{2-}, EC, O_3, NO_2, and SO_2. Supraventricular ectopy and ventricular ectopy were measured using Holter monitors during a 30-minute protocol of alternating rest in the supine position, standing, walking and paced breathing. In single-pollutant models, each 10.0 $\mu g/m^3$ increase in 5-day mean $PM_{2.5}$ concentration was associated with increased risk of supraventricular ectopy (OR = 1.42 [95% CI: 0.99-2.04]), but not ventricular ectopy (OR = 1.02 [95% CI: 0.63-1.65]). Similarly, increased risk of supraventricular ectopy, but not ventricular ectopy, was associated with each interquartile range increase in 5-day mean SO_4^{2-} and O_3 concentration.

Ebelt et al. (2005, 056907) conducted a repeated measures panel study of 16 patients with COPD in Vancouver, British Columbia. Their goal was to evaluate the relative impact of ambient and non-ambient exposures to $PM_{2.5}$, PM_{10}, and $PM_{10-2.5}$ on several health measures. Subjects wore an ambulatory ECG monitor for 24 h to record heart rhythm data and ascertain supraventricular ectopic beats. The mean $PM_{2.5}$ concentration during this study was 11.4 $\mu g/m^3$. Using mixed models with random subjects effects to investigate only same-day PM concentrations, an increase in supraventricular ectopic beats was associated with same day ambient exposures to each PM size fraction.

Berger and colleagues (2006, 098702) conducted a panel study of 57 men with coronary heart disease living in Erfurt, Germany. Using 24-h ECG measurements made once every 4 wk, they studied associations between runs of supraventricular and ventricular tachycardia and lagged concentrations of $PM_{2.5}$, UFP (0.01-0.1 µm), ACP (0.1-1.0 µm), SO_2, NO_2, CO, and NO. Using GAMs, as well as Poisson and linear regression models, they reported increases in supraventricular tachycardia and the number of runs of ventricular tachycardia associated with 5-day mean $PM_{2.5}$, UFP counts, and ACP counts. They found these associations at all lags evaluated (during ECG recording, 0-23 h before, 24-47 h before, 48-71 h before, 72-95 h before, and 5-day mean), but the largest effect estimates were generally associated with the 24- to 47-h mean and the 5-day mean.

Summary of Ectopy Studies Using ECG Measurements

Four studies of ectopic beats and runs of supraventricular and ventricular tachycardia, captured using ECG measurements, all report at least one positive association. Further, they report findings in regions other than Boston and Sweden (i.e., Midwest U.S., Pacific Northwest, 24 U.S. cities, and Erfurt, Germany). A range of lags and/or moving averages were investigated (0-30 days) with the strongest effects observed for either the 5-day mean, same day, or 1-day lagged PM concentrations. Taken together, these ICD studies and ectopy studies provide evidence of an arrhythmic response to PM, although further study is needed to understand the variable ICD study findings.

ECG Abnormalities Associated with the Modulation of Repolarization

No reported investigations of the relationship of PM concentration and ECG abnormalities indicating arrhythmia were conducted prior to 2002 and thus were not included in the 2004 PM AQCD (U.S. EPA, 2004, 056905). Abnormalities in the myocardial substrate, myocardial vulnerability, and resulting repolarization abnormalities are believed to be key factors contributing to the development of arrhythmogenic conditions such as those discussed above. These abnormalities include ECG measures of repolarization such as QT duration (time for depolarization and repolarization of the ventricles), T-wave complexity (a measure of repolarization morphology), and T-wave amplitude (height of the T-wave). Abnormalities in repolarization may also identify subjects potentially at risk of more serious events such as sudden cardiac death (Atiga et al., 1998, 156231; Berger et al., 1997, 155688; Chevalier et al., 2003, 156338; Okin et al., 2000, 156002; Zabel et al., 1998, 156176). Recent studies of changes in these measures following acute increases in air pollution are described below.

Two studies conducted in Erfurt, Germany, (Henneberger et al., 2005, 087960; Yue et al., 2007, 097968) examined the association between measures of repolarization (QT duration, T-wave complexity, T-wave amplitude, T-wave amplitude variability) and particulate air pollution. Henneberger et al. (2005, 087960) conducted a panel study of 56 males with IHD. Each subject was measured every 2 wk for 6 mo. During the study, the median daily $PM_{2.5}$, EC, and OC concentrations were 14.9, 1.8, and 1.4 $\mu g/m^3$,respectively. The median count of UFP was 11,444 particles/cm^3, while the median count of ACP (0.1-1.0 μm) was 1,238 particles/cm^3. They examined the change in these ECG parameters associated with the mean pollutant (UFP, ACP, $PM_{2.5}$, OC, and EC) concentrations 0-5, 6-11, 12-17, 18-23, and 0-23 h before, and 2-5 days before the ECG measurement. Significant decreases in T-wave amplitude were associated with $PM_{2.5}$ mass, UFP, and ACP. Each 16.4 $\mu g/m^3$ increase in the mean $PM_{2.5}$ concentration in the previous 5 h was associated with a 6.46 μV decrease in T-wave amplitude (95% CI: -10.88 to -2.04). Each 0.7 $\mu g/m^3$ increase in the mean OC concentration in the previous 5 h was associated with a 4.15 ms increase in QT interval (95% CI: 0.22-8.09). There was a similar sized effect for 24-h mean OC concentration. Significant increases in the variability of T-wave complexity were also associated with acute increases in EC and OC concentration.

Yue et al. (2007, 097968) then used positive matrix factorization to identify 5 sources of ambient PM (airborne soil, local traffic-related UFP, combustion-generated aerosols, diesel traffic-related particles, and secondary aerosols). Using similar statistical models, they examined the association between these same repolarization changes and incremental increases in the mean concentration of each particle source in the 24 h before the ECG measurement. They also examined associations with CRP and vWF concentrations in the blood. Both UFP from local traffic and diesel particles from traffic had the strongest associations with repolarization parameters.

Summary of Epidemiologic Studies of ECG Abnormalities Associated with the Modulation of Repolarization

These two analyses demonstrate associations between PM pollution and repolarization changes, at lags of 5 h to 2 days. Moreover, the findings from the Yue et al. (2007, 097968) study demonstrate a potential role of traffic particles/pollution.

6.2.2.2. Toxicological Studies

The ECG of animal research models frequently exhibit different characteristics than that of humans. Mice and rats are notable in this regard, as they do not have an isoelectric ST-segment typical of larger species, likely owing to their rapid heart rates (~600 and ~350 bpm, respectively) and repolarizing currents. However, the ultimate function of the pumping heart is conserved and reflected by the ECG in a remarkably consistent manner across species. Thus, atrial depolarization causes an electrical inflection represented by the P-wave, ventricular depolarization elicits the QRS complex, and the T-wave represents repolarization of the ventricles.

The earliest indication that there may be cardiovascular system effects of PM came from ECG studies in susceptible animal models (rats with pulmonary hypertension and dogs with coronary occlusion), which were summarized in the 2004 PM AQCD (U.S. EPA, 2004, 056905). However, a study of dogs exposed to ROFA did not demonstrate ECG changes, perhaps due to differences in disease state, as these were the oldest dogs in the colony with signs of preexisting, naturally occurring heart disease (Muggenburg et al., 2000, 010279). Much of the research conducted since the release of the last PM AQCD has been focused on exploring susceptibility or varying exposure methodologies, with little new evidence into the mechanisms for ECG changes of inhaled PM.

CAPs

Wellenius et al. (2004, 087874) used a susceptible model that was previously shown to produce significant results with exposures to ROFA (Wellenius et al., 2002, 025405) to examine ECG-related $PM_{2.5}$ effects. Using an anesthetized model of post-infarction myocardium sensitivity, Wellenius and colleagues tested the effects of Boston, MA CAPs on the induction of spontaneous arrhythmias in SD rats (1 h; mean mass concentration 523.11 $\mu g/m^3$; range of mass concentration 60.3-2202 $\mu g/m^3$). Decreased (67.1%) VPB frequency was observed during the post-exposure period in rats with a high number of pre-exposure VPB. No interaction was observed with coexposure to CO (35 ppm). CAPs number concentration or the mass concentration of any single element did not predict VPB frequency. In a follow-up publication, a decreased number of supraventricular ectopic beats (SVEB) was reported with CAPs (mean mass concentration 645.7 $\mu g/m^3$) (Wellenius et al., 2006, 156152). Furthermore, an increase in CAPs number concentration of 1,000 particles/cm^3 was associated with a 3.3% decrease in SVEB frequency. The findings of decreased ventricular arrhythmia differ from those observed following ROFA exposure in the same animal model in that an increased frequency of premature ventricular complexes was observed with ROFA, albeit the ROFA exposure concentration was >3,000 $\mu g/m^3$ (Wellenius et al., 2002, 025405). It is difficult to directly compare the results of these studies due to differences in exposure concentrations and particle type, but collectively they may suggest an important role for the soluble components of PM, including transition metals, as only ROFA induced increases in ventricular arrhythmia occurrence.

In older rats (Fisher 344; ~18 months) exposed to $PM_{2.5}$ CAPs in Tuxedo, NY (4 h; mean concentration 180 $\mu g/m^3$; August 2000), the frequency of delayed beats was greater than in rats exposed to air (Nadziejko et al., 2004, 055632). The majority of these beats were characterized as pauses (a delay of 2.5 times the adjacent interbeat intervals) rather than premature beats. When the same animals were exposed to generated UF carbon particles (single-day concentrations 500 and 1280 $\mu g/m^3$) or SO_2 (1.2 ppm), no significant differences were observed in arrhythmia frequency between air controls and exposed animals. The authors also report using the same protocol for young WKY rats (concentration 215 $\mu g/m^3$) and very few arrhythmias were observed, thus precluding statistical analysis. The results of this study indicate (1) involvement of the sino-atrial node, as the observed arrhythmias were mostly of a delayed nature; and (2) particle size and $PM_{2.5}$ constituents may play a role in these effects.

Diesel and Gasoline Exhaust

Anselme and colleagues (2007, 097084) exposed rats with and without induced CHF to DE for 3 h (PM concentration 500 $\mu g/m^3$; mass mobility diameter 85 nm; NO_2 1.1 ppm; CO 4.3 ppm). While no dramatic change was noted in HR, prominent increases in the incidence of VPB were observed in CHF rats, which lasted at least 4-5 h after exposure ceased. The duration of VPB attributable to diesel exposure in CHF rats lasted much longer than the rMSSD change (>5 h post-exposure), indicating that the HRV response was not driving the increased arrhythmia incidence. It is interesting to contrast the work of Anselme with the studies by Wellenius et al. (2002, 025405; 2004, 087874; 2006, 156152), as the arrhythmia incidence in the acute infarction model was greatest with ROFA, while the CHF model demonstrated sensitivity to DE exposure. However, several differences in the research designs preclude strong comparisons.

Using $ApoE^{-/-}$ mice on a high-fat diet as a model of pre-existing coronary insufficiency (Caligiuri et al., 1999, 157365), Campen and colleagues studied the impact of inhaled diesel and gasoline exhaust and road dust (6 h/day×3 day) on ECG morphology (Campen et al., 2005, 083977;

2006, 096879). Moreover, a high efficiency particle filter was used to compare the whole exhaust with an atmosphere containing only the gaseous components. For gasoline exhaust, the PM-containing atmosphere (PM mean concentration 61 μg/m^3; PNMD 15 nm; NO_X mean concentration 18.8 ppm; CO mean concentration 80 ppm) induced T-wave morphological alterations, while the PM-filtered atmosphere did not (Campen et al., 2006, 096879). Resuspended road dust ($PM_{2.5}$), at up to 3500 μg/m^3 had no impact on ECG. For DE (PM mean concentration 512, 770, or 3,634 μg/m^3; MMD 100 nm, CMD 80 nm; NO_X mean concentration 19, 105, 102 ppm for low whole exhaust, high PM filtered, and high whole exhaust, respectively), dramatic bradycardia, decreased T-wave area, and arrhythmia (atrioventricular-node block and VPB) were only observed in mice exposed to high filtered and high whole exhaust (Campen et al., 2005, 083977). These effects remained after filtration of PM, suggesting that the gaseous components of the whole DE drove the cardiovascular findings. The diesel- and gasoline-induced ECG changes contrast, in that the gasoline exhaust required particles to induce T-wave changes, whereas the DE did not require PM to cause an effect on ECG. However, the differing responses could be attributable to higher PM concentrations in the whole DE.

Summary of Toxicological Study Findings for ECG Abnormalities

The above toxicological studies demonstrate mixed results for arrhythmias, which may be somewhat attributable to the different disease models used. Wellenius et al. (2004, 087874; 2006, 156152) showed decreased frequency of VPB and SVEB following $PM_{2.5}$ CAPs exposure in rats with induced MI (>12 h prior to exposure). One study reported increased frequency of premature beats in older rats exposed to CAPs, which were not observed with UF carbon particles (Nadziejko et al., 2004, 055632). Rats with a MI model of CHF (3-mo recovery) had increased incidence of VPB with DE exposure (Anselme et al., 2007, 097084). As for ECG morphology changes, T-wave alterations were reported for gasoline exhaust that were absent when the PM was filtered (Campen et al., 2006, 096879). However, for DE, increased atrioventricular-node block, VPB, and decreased T-wave area were observed with whole exhaust and remained after filtration of PM, indicating that the gases were responsible for the effects (Campen et al., 2005, 083977).

6.2.3. Ischemia

Although no evidence from epidemiologic or controlled human exposure studies of PM-induced myocardial ischemia was included in the 2004 PM AQCD (U.S. EPA, 2004, 056905), one toxicological study was cited that observed ST-segment changes in dogs following a 3-day exposure to CAPs. In epidemiologic studies published since the 2004 PM AQCD (U.S. EPA, 2004, 056905), associations have been demonstrated between PM and ST-segment depression, and one new controlled human exposure study reported significant increases in exercise-induced ST-segment depression among men with prior MI following a controlled exposure to DE. Results from recent toxicological studies confirm the findings presented in the 2004 PM AQCD (U.S. EPA, 2004, 056905) and provide coherence and biological plausibility for the effects observed in epidemiologic and controlled human exposure studies.

6.2.3.1. Epidemiologic Studies

ECG Changes Suggestive of Increased Ischemia

The ST-segment duration is typically in the range of 0.08-0.12 s (80-120 ms). The direction of the ST change is influenced by the extent of the acute myocardial injury. If the ischemia or infarction is transmural, i.e., penetrates the entire thickness of the ventricular wall, it usually causes ST-segment elevation, while ischemia confined primarily to the ventricular endocardium often causes ST-segment depression. Clinical ischemia is typically defined to include a downsloping ST segment depression of ≥0.1 mV (ECG voltages are calibrated such that 1 mV equals 10 mm in the vertical direction). The studies described below evaluate a range of ECG changes suggestive of increased

ischemia including subclinical ST segment depressions (e.g. less than 0.1 mV or 1 mm) in relation to ambient PM concentration.

In a large study of the WHI Trial, Zhang et al. (2009, 191970) examined the change and risk of subclinical ST-segment abnormalities, T-wave abnormalities, and T-wave amplitude associated with ambient $PM_{2.5}$ concentrations on the same and previous 6 days. Using logistic regression, each 10 $\mu g/m^3$ increase in the mean $PM_{2.5}$, on lag days 0-2, was associated with a 4% (95% CI: -3 to 10) increase in the relative odds of a ST-segment abnormality, and a 5% (95% CI: 0-9) increase in the relative odds of a T-wave abnormality.

Gold et al. (2005, 087558) studied 24 elderly residents of Boston, MA (aged 61-88 yr) residing at or near an apartment complex that was ~ 0.5 km from an air pollution monitoring station. A protocol of continuous Holter monitoring including 5 min of rest, 5 min of standing, 5 min of outdoor exercise, 5 min of rest, and then 20 cycles of paced breathing was done up to 12 times for each subject (n = 269 ECG measurements for analysis). From these ECG measurements, they identified occurrences of ST-segment depression and examined whether mean BC, CO, and $PM_{2.5}$ concentrations in the previous 5 and 12 h were associated with ST-segment depression. The median 5-h and 12-h mean BC concentrations were 1.28 and 1.14 $\mu g/m^3$, respectively ($PM_{2.5}$ concentrations are in Table 6-3). The mean BC concentrations in the 5 and 12 h before testing predicted ST-segment depression in most portions of the protocol. However, these effects were strongest in the post-exercise periods. For example, during the post-exercise rest period, each 10th-90th percentile increase (1.59 $\mu g/m^3$) in the mean 5-h BC concentration was associated with a -0.11 mm ST-segment depression (95% CI: -0.18 to -0.05). In two pollutant models, CO did not appear to confound this association. $PM_{2.5}$ was not associated with ST-segment depression in this study. These findings suggest traffic-generated particulate pollution may be associated with ST-segment depression.

Previously, Pekkanen et al. (2002, 035050) conducted a panel study of 45 subjects with stable coronary heart disease living in Helsinki, Finland. Each subject had biweekly sub-maximal exercise testing for 6 mo (n = 342 exercise tests with 72 exercise-induced ST-segment depressions). The median daily count of ACP (ACP: 0.1-1.0 µm) was 1,200 particles/cm^3 ($PM_{2.5}$ concentrations are found in Table 6-3). They examined the risk of ST-segment depression associated with mean pollutant concentrations (UFP, ACP, PM_1, $PM_{2.5}$, $PM_{10-2.5}$, NO_2, CO) in the previous 24 h, and the 3 previous lagged 24-h periods. Each 7.9 $\mu g/m^3$ increase in mean $PM_{2.5}$ concentration, lagged 2 days, was associated with significantly increased risk of ST-segment depression >0.1 mV (OR: 2.84 [95% CI: 1.42-5.66]). Each 760 particles/cm^3 increase in the count of ACP, lagged 2 days, was also associated with significantly increased risk of ST-segment depression >0.1 mV (OR: 3.29 [95% CI: 1.57-6.92]). Similarly sized increased risks of ST-segment depression were also found for other particulate pollutants, including $PM_{10-2.5}$, PM_1, and UFP counts.

This same research group, then conducted a principal components analysis to identify five $PM_{2.5}$ sources (crustal, long range transport, oil combustion, salt, and local traffic) (Lanki et al., 2006, 088412). Using similar statistical models, each 1 $\mu g/m^3$ increase in "local traffic" particle concentration, lagged 2 days, was associated with increased risk of ST-segment depression (OR: 1.53 [95% CI: 1.19-1.97]). Similarly, each 1 $\mu g/m^3$ increase in "long-range transport" particle concentration was also associated with increased risk of ST-segment depression (OR: 1.11 [95% CI: 1.02-1.20]). No significant associations for other sources were reported for any lag time.

In Boston, Chuang et al. (2008, 155731) studied 48 patients with a prior percutaneous intervention following MI, acute coronary syndrome (ACS) without MI, or stable coronary artery disease without ACS,. Each patient had a 24-h ECG measurement up to four times during study follow-up. Using logistic regression, they estimated the risk of ST-segment depression of ≥0.1 mm, during 30-min segments, associated with increases in the mean $PM_{2.5}$, BC, CO, NO_2, O_3, and SO_2 concentration in the previous 24 h. Each 6.93 $\mu g/m^3$ increase in mean $PM_{2.5}$ concentration was associated with a significantly increased risk of ST-segment depression (OR = 1.50 [95% CI: 1.19-1.89]). Using linear additive models to estimate the change in ST level associated with the same $PM_{2.5}$ change, they observed a significant -0.031 mm change (95% CI: -0.042 to -0.019). In single pollutant models, risk estimates were of similar magnitude and statistically significant for BC, NO_2, and SO_2. In two pollutant models, however, $PM_{2.5}$ risk estimates were reduced to 1.0 in all models with BC, NO_2, and SO_2. In contrast, the risk estimates for BC, NO_2, and SO_2 remained elevated and statistically significant when modeled with $PM_{2.5}$.

In a panel study of 14 Helsinki resident, non-smoking, elderly subjects with coronary artery disease, Lanki et al. (2008, 191984) used logistic regression to report that each 10 $\mu g/m^3$ increase in personal $PM_{2.5}$ concentration in the previous hour was associated with a significantly increased risk

of ST-segment depression (OR = 3.26 [95% CI: 1.07-9.98]). In addition, each 10 μg/m^3 increase in outdoor mean $PM_{2.5}$ concentration in the previous 4 h was also associated with an increased risk (OR = 2.47 [95% CI: 1.05-5.85]). Last, the risk estimates for all time lags examined (1, 4, 8, 12, and 22 or 24 h) for all PM size fractions were increased, but none other than those described above were statistically significant.

Summary of Epidemiologic Study Findings for Ischemia

These studies demonstrate associations between $PM_{2.5}$ pollution and ST-segment depression at lags of 1 h-2 days. Moreover, these findings demonstrate a potential role for traffic (Chuang et al., 2008, 155731; Gold et al., 2005, 087558) and long-range transported $PM_{2.5}$ (Lanki et al., 2006, 089788). Mean and upper percentile concentrations reported in these studies are found in Table 6-3.

Table 6-3. PM Concentrations reported in epidemiologic studies ECG changes suggestive of ischemia.

Author	Location	Mean Concentration (μg/m^3)	Upper Percentile Concentrations (μg/m^3)
$PM_{2.5}$			
Zhang et al. (2009, 191970)	Mulitcity, US:WHI Clinical Trial	NR	NR
Pekkanen et al. (2002, 035050)	Helsinki, Finland	24-h avg: 10.6 (median)	75th: 16.0 Max: 39.8
Gold et al. (2005, 087558)	Boston, MA	5-h avg: 9.5 (median) 12-h avg: 9.8 (median)	5-h avg 90th: 25.6 Max: 41.0 12-h avg 90th: 25.9 Max: 35.6
Chuang et al. (2008, 155731)	Boston, MA	12-h avg: 9.91 (median) 24-h avg: 9.20 (median)	12-h avg 75th: 13.18 24-h avg max: 40.38
Lanki et al. (2008, 191984)	Helsinki, Finland	Personal 1-h avg: 11.5 (median) 4-h avg: 10.1 (median) 22-h avg: 9.3 (median) Outdoor 24-h avg: 12.5	Personal 1-h avg 75th: 17.2; Max: 746.3 4-h avg 75th: 15.7; Max 189.6 22-h avg 75th: 13.2; Max 52.9 Outdoor 24-h avg 75th: 17.7; Max: 30.5
$PM_{10-2.5}$			
Pekkanen et al. (2002, 035050)	Helsinki, Finland	24-h avg: 4.8 (median)	75th: 8.5 Max: 37.0

6.2.3.2. Controlled Human Exposure Studies

Diesel Exhaust

Among a group of 20 men with prior MI, Mills et al. (2007, 091206) found that DE (300 μg/m^3 particle concentration, median particle diameter 54 nm) significantly increased exercise-induced ischemic burden during exposure, calculated as the product of exercise duration and change in ST-segment amplitude. The mechanism by which DE induced the exacerbation of ischemic burden remains unclear, and appears to be unrelated to impaired vasodilation. However, the

authors suggest that this discrepancy may be due to the timing of the vascular assessment, as measures of blood-flow were taken 5 h after the observed increase in ischemic burden. Although it is reasonable to assume that the observed increase in ST-segment depression during exercise represents an increased magnitude of ischemia, it is important to note that there are other potential explanations for the ST change. For example, it is possible that the ST-segment depression could be secondary to heterogeneity of electrophysiological responses of particle exposure on the myocardium that is enhanced by the metabolic and ionic conditions associated with ischemia or increased HR. It is also important to note that the effects observed in this study cannot be conclusively attributed to the particles per se, as subjects were also exposed relatively high levels of NO (3.45 ppm), NO_2 (1.01 ppm), CO (2.9 ppm), and total hydrocarbons (2.8 ppm).

6.2.3.3. Toxicological Studies

CAPs

A study that examined ECG changes in dogs (female; retired mongrel breeder dogs) following $PM_{2.5}$ CAPs exposure in Boston, MA (mean mass concentration 345 μg/m^3; 9/2000-3/2001) and left anterior descending coronary artery occlusion as an indicator of myocardial ischemia reported changes in ST-segment (Wellenius et al., 2003, 055691). The experimental protocol was a 6-h exposure to CAPs via tracheostomy, followed by a preconditioning occlusion (5 min), rest interval (20 min), and the experimental occlusion (5 min). Increased ST-segment elevation was observed following $PM_{2.5}$ during the experimental occlusion period compared to filtered air. Furthermore, peak ST-segment elevation attributable to CAPs was reported with the experimental occlusion, which remained elevated 24 h post-exposure. Ventricular arrhythmias were rarely observed during occlusion and when observed, were unrelated to CAPs exposure. The results from this study support those previously observed (Godleski et al., 2000, 000738) and provides greater support that enhanced myocardial ischemia occurs relatively quickly (within hours) following PM exposure.

The Wellenius et al. (2003, 055691) study also attempted to link ST-segment changes with four CAPs elements (Si, Ni, S, and BC) as tracers of $PM_{2.5}$ sources in Boston. In the multivariate regression analyses, peak ST-segment elevation and integrated ST-segment change were significantly associated with only the mass concentration of Si (Si mean concentration 8.17 μg/m^3; Si concentration 2.31-13.93 μg/m^3). In the univariate regression analyses, Pb also demonstrated a significant association for both ST-segment measures, although the p-value was greater than that observed with Si.

A recent study in dogs (female mixed-breed canines) evaluated myocardial blood flow during myocardial ischemia following 5-h $PM_{2.5}$ Boston CAPs exposures (daily mean mass concentration 94.1-1556.8 μg/m^3; particle number concentration 3-69.3×10^3 particles/cm^3; BC concentration 1.3-32.0 μg/m^3) (Bartoli et al., 2009, 179904). Similar methods were used for the coronary occlusion and exposure method as Wellenius et al. (2003, 055691). Immediately following exposure, microspheres were injected (15 μm diameter) into the left atrium after 3 min of ischemia during the second occlusion. Post-mortem analysis of cardiac tissue and blood samples allowed for quantification of microspheres. CAPs-exposed dogs had decreased total myocardial blood flow and increased coronary vascular resistance during occlusion that was greatest in tissue within or near the ischemic zone. The rate-pressure product (product of HR and SBP) during occlusion was unchanged in animals exposed to CAPs, indicating that cardiac metabolic demand was not altered. The multilevel linear mixed models demonstrated that myocardial blood flow and coronary vascular resistance during occlusion were inversely and significantly associated with CAPs mass concentration, particle number concentration, and BC concentration, with the strongest effects observed with particle number concentration. The results of this study provide evidence that exacerbation of myocardial ischemia following PM exposure is due to reduced myocardial blood flow, perhaps via dysfunctional collateral vessels.

Intratracheal Instillation

Cozzi et al. (2006, 091380) exposed ICR mice to UF PM (100 µg IT instillation), followed by ischemia/reperfusion injury to the left anterior coronary artery 24 h later. The area-at-risk (the region of tissue perfused by the left anterior descending coronary artery) and the infarct size were measured 2 h following reperfusion, and while the area-at-risk was not affected by PM exposure, the infarct size was nearly doubled in mice who received UF PM. Increases in infarct size were associated with increased myocardial neutrophil density in the infarct zone and lipid peroxidation in the myocardium.

Summary of Toxicological Study Findings for Ischemia

The studies described above provide evidence that PM can induce greater myocardial responses following ischemic events, as demonstrated by, enhanced ischemia, decreased myocardial blood flow and increased coronary vascular resistance, and increased infarct size.

6.2.4. Vasomotor Function

The most noteworthy new cardiovascular-related revelation in the past six years with regards to PM exposure is that the systemic vasculature may be a target organ. The vasculature of all tissues is lined with endothelial cells that will naturally encounter any systemically absorbed toxin. The endothelium (1) maintains barrier integrity to ensure fluid compartmentalization; (2) communicates dilatory and constrictive stimuli to vascular smooth muscle cells; and (3) recruits inflammatory cells to injured regions. Smooth muscle cells lie within the layer of endothelium and are crucial to the regulation of blood flow and pressure. In states of injury and disease, both cell types can exhibit dysfunction and even pathological responses.

Endothelial dysfunction is a factor in many diseases and may contribute to the origin and/or exacerbation of perfusion-limited diseases, such as MI or IHD, as well as hypertension. Endothelial dysfunction is also a characteristic feature of early and advanced atherosclerosis. A primary outcome of endothelial dysfunction is impaired vasodilatation, frequently due to uncoupling of NOS. It is this uncoupling that appears central to impaired vasodilation and thus endothelial dysfunction.

One controlled human exposure study cited in the 2004 PM AQCD (U.S. EPA, 2004, 056905) reported a decrease in bronchial artery diameter (BAD) among healthy adults following exposure to CAPs in combination with O_3. Conclusions based on this finding were limited due to the concomitant exposure to O_3 as well as a lack of published results from epidemiologic and toxicological studies. Recent controlled human exposure studies have provided support to the findings described in the 2004 PM AQCD (U.S. EPA, 2004, 056905), with changes in vasomotor function observed following controlled exposures to DE and EC particles. In addition, epidemiologic studies have observed associations between PM and decreases in BAD and flow mediated dilatation (FMD) in healthy adults and diabetics. These findings are further supported by a large body of new toxicological evidence of impaired vasodilation following exposure to PM.

6.2.4.1. Epidemiologic Studies

O'Neill et al. (2005, 088423) examined the association between 2 measures of vascular reactivity, non-endothelium dependent nitroglycerin mediated reactivity and endothelium-dependent flow-mediated reactivity, and ambient mean particulate pollutant concentration ($PM_{2.5}$, SO_4^{2-}, BC, PNC) on the same and previous few days. They studied a panel of 270 subjects with diabetes or at risk for diabetes, who lived in the greater Boston metropolitan area. Using linear regression models, the change in vascular reactivity associated with moving average pollutant concentrations across the same and previous 5 days was estimated. Interquartile range (values not reported) increases in mean $PM_{2.5}$ concentration, BC concentration, and PNC over the previous 6 days were associated with decreased vascular reactivity among diabetics, but not among subjects at risk for diabetes. For SO_4^{2-}, the mean concentration on lag day 0, lag day 1, and the 3-day, 4-day, and 5-day ma all were associated with similarly sized reductions in both metrics of vascular reactivity. Among diabetics, each interquartile range increase in the mean SO_4^{2-} concentration over the previous 6 days was

associated with a 5.4% decrease in nitroglycerin-mediated reactivity (95% CI: -10.5 to -0.1) and flow-mediated reactivity (-10.7% [95% CI: -17.3 to -3.5]). Also among diabetics, each interquartile range increase in the mean $PM_{2.5}$ concentration over the previous 6 days was associated with a 7.6% decrease in nitroglycerin-mediated reactivity (95% CI: -12.8 to -2.1) and a non-significant 7.6% decrease in flow-mediated reactivity (95% CI: -14.9 to 0.4). Each interquartile range increase in the mean BC concentration over the previous 6 days was associated with a 12.6% decrease in flow mediated reactivity (95% CI: -21.7 to -2.4), but not nitroglycerin-mediated reactivity. PNC was associated with non-significant decreases in both measures. Effect estimates were larger for type 2 diabetics than type 1 diabetics.

Dales et al. (2007, 155743) conducted a panel study of 39 healthy volunteers who sat at 1 of 2 bus stops in Ottawa, Canada for 2 h. FMD of the brachial artery was measured immediately after the bus stop exposure, but not before. They examined the association between FMD and 2-h mean $PM_{2.5}$, PM_1, NO_2, and traffic density at the bus stop (vehicles/h). The authors report that each 30 $\mu g/m^3$ increase in 2-h mean $PM_{2.5}$ concentration was associated with a significant 0.48% reduction in FMD. This represented a 5% relative change in the maximum ability to dilate.

This same research group conducted a panel study of 25 type 1 or 2 diabetic subjects living in Windsor, Ontario (aged 18-65 yr) (Liu et al., 2007, 156705). For each subject, personal PM_{10} concentrations were measured for 24 h before measurements of BAD, FMD, and other biomarkers. Each 10 $\mu g/m^3$ increase in personal 24-h mean PM_{10} concentration was associated with a 0.20% increase in end-diastolic FMD (95% CI: 0.04-0.36) and a 0.38% increase in end-systolic FMD (95% CI: 0.03-0.73), but decreases in end-diastolic basal diameter (-2.52 µm [95% CI: -8.93 to 3.89]) and end-systolic basal diameter (-9.02 µm [95% CI: -16.04 to -2.00]).

Rundell et al. (2007, 156060) examined the change in FMD associated with high and low PM_1 (0.02-1.0 µm) pollution in a panel of 16 young intercollegiate athletes (mean age = 20.5±2.4 yr) in Scranton, PA, who were non-smokers, non-asthmatics, and free of cardiovascular disease (Rundell et al., 2007, 156060). Each subject had FMD of the brachial artery measured 10-20 min before and 20-30 min after each of two 30-min exercise tests (85-90% of maximal HR). The exercise tests were done outside either on an inner campus location free of automobile and truck traffic (low PM_1; mean = 5,309±1,942 particles/cm^3) or on a soccer field adjacent to a major highway (high PM_1; mean = 143,501±58,565 particles/cm^3). The order of the exercise test locations was chosen randomly. Using paired t-tests for analysis, they reported FMD was impaired after high PM_1 exposure (pre-exercise: 6.8±3.58%; post-exercise: 0.30±2.74%), but not low PM_1 exposure (pre-exercise: 6.6±4.04%; post-exercise: 4.89±4.42%). Further, they found basal brachial artery vasoconstriction (4%; pre-exercise BAD: 4.66±0.61 mm; post-exercise BAD: 4.47±0.63 mm) after the 'high PM_1' exposure, but not the 'low PM_1' exposure (-0.3% pre-exercise BAD: 4.66±0.63 mm; post-exercise BAD: 4.68±0.61 mm).

In a prospective panel study of 22 type 2 diabetics (aged 61 ± 8 yr), Schneider et al. (2008, 191985) examined the change in FMD, BAD, small artery elasticity index, larger artery elasticity index, and systemic vascular resistance associated with ambient $PM_{2.5}$ as measured in Chapel Hill, NC (November 2004-December 2005). Using additive mixed models with a random subject effect, each 10 $\mu g/m^3$ increase in $PM_{2.5}$ in the previous 24 h was associated with a decrease in FMD (-17.3% [95% CI: -34.6 to 0.0]). Similarly, each 10 $\mu g/m^3$ increases in $PM_{2.5}$ was associated with a decrease in small artery elasticity index lagged 1 day (-15.1% [95% CI: -29.3 to -0.9]), and lagged 3 days (-25.4% [95% CI: -45.4 to -5.3]). Significant decreases in larger artery elasticity index and increases in systemic vascular resistance lagged 2 and 4 days were also reported. Further, effects were greatest among those with high BMI, high glycosylated hemoglobin A1c, low adiponectin, or the null GSTM1 polymorphism. However, high myeloperoxidase (MPO) levels were associated with greater $PM_{2.5}$ effects on these measures.

In a similar study done in Paris, France, Briet (2007, 093049) similarly reported that each increase in $PM_{2.5}$ was associated with a -0.32% decrease in FMD (95% CI: -1.10 to 0.46). Significant FMD reductions were associated with increased SO_2, NO_2, and CO concentrations. Each 1 standard deviation increase (units not given) in $PM_{2.5}$ in the previous 2 wk was associated with a 15.68% (95% CI: 7.11-23.30) increase in small artery reactive hyperemia. Each 1 standard deviation increase (units not given) in PM_{10} in the previous 2 wk was associated with a 15.91% (95% CI: 7.74-24.0) increase in small artery reactive hyperemia.

Summary of Epidemiologic Study Findings for Vasomotor Function

Vasomotor function has been evaluated using several metrics in the studies described above, including FMD, small artery elasticity index, larger artery index, systemic vascular resistance, BAD, end diastolic basal diameter, and nitroglycerin-mediated reactivity. The most common measures evaluated were BAD, a measure of the relatively static, anatomic/physiological baseline vasomotor function, and FMD, the dynamic measure of post- minus pre-occlusion BAD. Each study demonstrated an acute association between these measures of vascular function and ambient $PM_{2.5}$ concentrations (Briet et al., 2007, 093049; Dales et al., 2007, 155743; Liu et al., 2007, 156705; O'Neill et al., 2005, 088423; Rundell et al., 2007, 156060; Schneider et al., 2008, 191985). An association with PM_{10} was observed in a study conducted in Windsor Ontario (Liu et al., 2007, 156705). Three studies evaluated effects on diabetics (Liu et al., 2007, 156705; O'Neill et al., 2005, 088423; Schneider et al., 2008, 191985), and three evaluated PM-related changes in vasomotor function on young healthy subjects (Briet et al., 2007, 093049; Dales et al., 2007, 155743; Rundell et al., 2007, 156060). Only two studies investigated multiple lags (lag days 0 to 6) (O'Neill et al., 2005, 088423; Schneider et al., 2008, 191985), with one reporting the strongest association with the 6-day mean PM concentration (O'Neill et al., 2005, 088423), and the other with lag day 0. In other studies, responses were observed in as short as 30 min after the exposure (Rundell et al., 2007, 156060). The Rundell et al. (2007, 156060) findings are consistent with other studies showing an adverse response to ambient particulate pollution emitted from vehicular traffic (Adar et al., 2007, 098635; Adar et al., 2007, 001458; Riediker et al., 2004, 056992; Riediker et al., 2004, 091261). Mean and upper percentile concentrations reported in these studies are found in Table 6-4.

Table 6-4. PM concentrations reported in epidemiologic studies of vasomotor function.

Author	Location	Mean Concentration (μg/m^3)	Upper Percentile Concentrations (μg/m^3)
$PM_{2.5}$			
Briet (2007, 093049)	Paris, France	NR	NR
Dales (2007, 155743)	Ottawa, Canada (bus stops)	Bus stop 1: 40 Bus stop 2: 10	NR
O'Neill (2005, 088423)	Boston, MA	11.5	Range: 1.1 - 20.0
Schneider (2008, 191985)	Chapel Hill, NC	13.6	NR
PM_{10}			
Briet (2007, 093049)	Paris, France	NR	NR
Liu (2007, 156705)	Windsor, Ontario	24h (personal): 25.5	5th to 95th: 9.8 – 133

6.2.4.2. Controlled Human Exposure Studies

Some evidence of a PM-induced increase in brachial artery vasoconstriction is presented in the 2004 PM AQCD (U.S. EPA, 2004, 056905). Brook et al. (2002, 024987) exposed 24 healthy adults to $PM_{2.5}$ CAPs (150 μg/m^3) along with 120 ppb O_3 for a period of 2 h. A significant decrease in BAD was observed immediately following exposure compared with filtered air control. No significant changes were observed in either endothelial-dependent or endothelial-independent vasomotor function, as determined by FMD and nitroglycerin-mediated dilatation, respectively. As described below, many more recent studies have evaluated the effects of various types of particles on vasomotor function following controlled exposures among healthy and health-compromised individuals.

CAPs

A subsequent analysis of the CAPs constituents from the Brook et al. (2002, 024987) study revealed a significant negative association between the post-exposure change in BAD and both the OC and EC concentrations of CAPs (Urch et al., 2004, 055629). However, the observed vasomotor effects cannot conclusively be attributed to $PM_{2.5}$, as subjects were exposed concurrently to $PM_{2.5}$ and O_3. Mills et al. (2008, 156766) evaluated the effect of fine and UF CAPs on vasomotor function in a group of 12 males with stable coronary heart disease (average age 59 yr), as well as in 12 healthy males (average age 54 yr). Relative to filtered air exposure, exposure to PM (average concentration 190 $\mu g/m^3$) did not significantly affect vascular function in either group. The authors attributed the lack of response in endothelial function to the composition of the CAPs used in the study, which were low in combustion-derived particles and consisted largely of sea salt.

Urban Traffic Particles

The effect of exposure to urban traffic particles on vasomotor function has recently been evaluated among a group of adult volunteers (Bräuner et al., 2008, 191966). In this study, healthy young adults (average age 27 yr) exposed for 24 h to urban traffic particles (average $PM_{2.5}$ concentration 10.5 $\mu g/m^3$) were not observed to experience any change in microvascular function after 6 or 24 h of exposure relative to filtered air.

Diesel Exhaust

Mills et al. (2005, 095757) exposed 30 healthy men (20-38 yr) to both diluted DE (300 $\mu g/m^3$) and filtered air control for 1 h with intermittent exercise. Half of the subjects underwent vascular assessments at 6-8 h following exposure to DE or filtered air, while in the other 15 subjects, vascular assessments were performed at 2-4 h post-exposure. DE attenuated forearm blood flow increase induced by bradykinin, acetylcholine (ACh), and sodium nitroprusside (SNP) infusion measured 2 and 6 h after exposure. The authors postulated that the effect of DE on vasomotor function may be the result of reduced NO bioavailability in the vasculature stemming from oxidative stress induced by the nanoparticulate fraction of DE. A DE-induced decrease in the release of tPA was also observed at 6 h post-exposure, which may provide additional mechanistic evidence supporting the observed association between air pollution and MI. As presented in Tornqvist et al. (2007, 091279), changes in vascular function were also evaluated 24 h following exposure in 15 of the 30 subjects. Compared with filtered air, exposure to DE significantly reduced endothelium-dependent (ACh) vasodilation at 24 h post exposure. Bradykinin-induced vasodilation was marginally attenuated by DE, while no effects of diesel on endothelium-independent vasodilation (SNP) were observed. Although the release of tPA was not affected by DE 24 h following exposure, the authors suggest that the persistent association between diesel exposure and vasomotor function observed in this study provides supporting mechanistic evidence of increases in cardiovascular events occurring 24 h after a peak in PM concentration.

To further investigate the effects of DE on vasomotor function, Mills et al. (2007, 091206) exposed 20 men (avg age 60 yr) with previous MI on two separate occasions to dilute DE (300 $\mu g/m^3$; mean particle size 54 nm) or filtered air for 1 h with intermittent exercise. Contrary to previous findings in younger, healthy adults (Mills et al., 2005, 095757), DE was found not to affect vasomotor function in peripheral resistance vessels at 6 h post-exposure as measured by endothelium-dependent (ACh) and endothelium-independent (SNP) vasodilation (forearm blood flow). However, vascular assessments were not performed at 2 h post-exposure in this study. The same laboratory evaluated the effect of exposure to DE with slightly higher particle concentrations (330 $\mu g/m^3$, particle number $1.26\times10^6/cm^3$) on arterial stiffness among healthy adults (Lundbäck et al., 2009, 191967). Using radial artery pulse wave analysis, significant increases in augmentation pressure and augmentation index, as well as a significant reduction in the time to wave reflection were observed 10 and 20 min following exposure to DE relative to filtered air. This finding of a DE-induced reduction in arterial compliance provides additional evidence to suggest that exposure to particles may adversely affect vasomotor function.

Peretz et al. (2008, 156854) exposed both healthy adults (n = 10) and adults with metabolic syndrome (n = 17) for 2 h to filtered air and two concentrations of diluted DE ($PM_{2.5}$ concentrations of 100 and 200 μg/m^3). Compared with filtered air, DE at 200 μg/m^3 elicited a statistically significant decrease in BAD (0.11 mm [95% CI: 0.02-0.18 mm]) immediately following exposure. A smaller DE-induced decrease in BAD (0.05 mm) was observed following exposure to 100 μg/m^3. Although this latter decrease was not statistically significant, the average decrease was approximately 50% of the decrease at the higher particle concentration, which provides suggestive evidence of a linear concentration response in this range of concentrations. Exposure to DE was not shown to significantly affect endothelium-dependent FMD. Plasma levels of endothelin-1 (ET-1) were observed to increase relative to filtered air exposure approximately 1 h after exposure to 200 μg/m^3 DE ($p = 0.01$). Samples collected following the 100 μg/m^3 exposure session were not assayed for ET-1. The results of this study provide evidence of an acute endothelial response and arterial vasoconstriction resulting from short-term exposure to DE. DE-induced changes in vasoconstriction and ET-1 release were more pronounced in the healthy subjects than in the subjects with metabolic syndrome. The authors postulated that subjects with metabolic syndrome may have stiffer vessels that are not as responsive to vasoconstrictor stimuli. In a study utilizing a similar exposure protocol, Lund et al. (2009, 180257) observed a significant increase in ET-1 in healthy adults following a 2-h exposure to DE with a particle concentration of 100 μg/m^3.

In the previously described studies by Mills et al. (2005, 095757; 2007, 091206), Peretz et al. (2008, 156854), Tornqvist et al. (2007, 091279) and Lund et al. (2009, 180257), subjects were exposed to DE, which, in addition to PM, includes DE gases such as NO_X, CO, and hydrocarbons. Therefore, it is possible that the observed effects may be due in part to exposure to non-particle components of DE. While the majority of these DE exposures have contained relatively high levels of gaseous emissions including NO_2 concentrations >2 ppm, the concentrations of these gases were much lower in the Peretz et al. (2008, 156854) study (NO_2 concentrations ≈ 20 ppb) which used a newer diesel engine (2002 Cummins B-series) operating under load at 75% of rated capacity. In this study, an apparent linear concentration response relationship was observed between increasing DE exposure and decreases in BAD at particle concentrations between 100 and 200 μg/m^3.

Gasoline Emissions

Rundell and Caviston (2008, 191986) exposed 15 college athletes to particles generated using a 2.5 hp gasoline engine, as well as a clean air control during 6-min periods of maximal exercise on a cycle ergometer. Subjects were exposed twice under each condition, with the two clean air exposures occurring first, separated by 3 days. The 2 exposures to gasoline emissions were also separated by 3 days, with the first exposure occurring 7 days after the second clean air exposure. During exposures to gasoline emissions, average PNC of PM <1.0 μm were reported as 336,730 and 396,200 particles/cm^3 during the first and second exposures, respectively, with an average CO concentration of 6.3 ppm. There were no differences observed in total work done (kJ) over the 6-min exercise periods between the two clean air exposures or between the clean air exposures and the first exposure to gasoline exhaust. However, the second gasoline exhaust exposure was demonstrated to significantly decrease work accumulated over the 6-min exercise period compared with either of the other exposure conditions. The results of this study provide limited evidence to suggest that a very short term exposure to gasoline emissions may affect exercise performance in healthy adults. The authors speculated that the observed effect of exposure on work accumulated during maximal exercise could be due to vasoconstriction and decrease in blood flow in the skeletal muscle microcirculation. However, the effect of exposure on vasoreactivity was not explicitly assessed.

Model Particles

The results of a recent study by Shah et al. (2008, 156970) provides evidence that exposure to UF EC particles (50 μg/m^3) without coexposure to organics, metals, or gaseous copollutants may alter vasomotor function in healthy adults. In this study, venous occlusion plethysmography was used to measure reactive hyperemia of the forearm prior to exposure, immediately following exposure, and 3.5 h, 21 h, and 45 h following a 2-h exposure with intermittent exercise. Peak

forearm blood flow was observed to increase after exposure to filtered air, but not following exposure to UF EC at 3.5 h post-exposure ($p = 0.03$).

Summary of Controlled Human Exposure Study Findings for Vasomotor Function

Taken together, the two studies by Mills et al. (2005, 095757; 2007, 091206) along with the studies by Peretz et al. (2008, 156854), Lund et al. (2009, 180257) and Tornqvist et al. (2007, 091279) suggest that, in healthy subjects, DE exposure inhibits endothelium-dependent and endothelium-independent vasodilation acutely (within 2-6 h), and that the suppression of endothelium-dependent vasodilation may remain up to 24 h following exposure. In patients with coronary artery disease, vasodilator function does not appear to be affected 6-8 h following exposure; however, vascular assessments were not performed at earlier time points. In addition, the use of medications in these patients may have blunted the response to PM. The findings of Shah et al. (2008, 156970) suggest that UFP carbon core may be sufficient to produce small changes in systemic vascular function, but the mechanisms remain obscure. The authors demonstrated a decrease in nitrate levels following exposure to UF EC; however, venous nitrite level, which more closely reflects NO production, was unchanged. Exposure to urban traffic particles was not demonstrated to alter vasomotor function among healthy adults.

6.2.4.3. Toxicological Studies

Vascular dysfunction is a function of altered production of vasoconstrictors and vasodilators. In the 2004 PM AQCD (U.S. EPA, 2004, 056905), studies examining ET as an activator of vasoconstriction were limited to those conducted by Bouthiller et al. (1998, 087110) and Vincent et al. (2001, 021184), in which increased plasma ET levels were observed in rats exposed to high concentrations (40 or 5 mg/m^3) of resuspended Ottawa (EHC-93) or diesel PM, respectively. The authors postulated that PM altered vasoconstriction via elevated ET. No studies were cited in the 2004 PM AQCD (U.S. EPA, 2004, 056905) that looked at direct measures of vasoreactivity.

As this area is newly emerging, some studies are included below that utilize IT exposure or high concentrations; the studies that exposed vessels directly to particles ex vivo are included in Annex D only, as their relevance is questionable. There is clearly a need for more toxicological research examining the relationship between vascular measurements and PM exposures using ambient particles at lower concentrations. Furthermore, no new studies have advanced the knowledge in regards to ET as a biomarker of PM-induced vasoconstriction since the last PM review.

CAPs

SD rats were exposed to $PM_{2.5}$ CAPs (5 h/day×3 days; daily mean mass concentration 73.5-733 $\mu g/m^3$; Boston, MA; 3/1997-6/1998) then the pulmonary arterial vasculature was evaluated (Batalha et al., 2002, 088109). Some animals were repeatedly exposed to SO_2 (5 h/day×5 days/wk×6 wk) to induce chronic bronchitis. Morphometric measurements indicated that the pulmonary artery lumen-to-wall (L/W) ratio (an indicator of arterial narrowing) was decreased for the both CAPs groups compared to the normal/air group. Furthermore, decreased L/W ratio in CAPs-exposed animals (regardless of pre-treatment) was significantly associated with particle mass and composition when the mean concentrations from the second and third exposure days were used in a univariate linear regression. These results indicate a change in vascular tone following acute exposure to PM. Univariate analyses were conducted that regressed log L/W on differential exposure concentrations of tracer elements determined using principal components analysis (Batalha et al., 2002, 088109). For CAPs exposure (regardless of pretreatment), CAPs mass, Si, Pb, SO_4^{2-}, EC, and OC were all negatively correlated with L/W ratio. Si and SO_4^{2-} were negatively correlated with L/W ratio in normal rats and Si and OC were negatively correlated with L/W ratio in bronchitic rats. When a multivariate analysis was conducted using normal and bronchitic animals, only the association with Si remained significant. V was not associated with L/W ratio in any analysis.

Diesel Exhaust

The venous circulation plays a prominent role in heart failure exacerbation (Gehlbach and Geppert, 2004, 155784). In heart failure, patients are often volume overloaded and are subsequently placed on diuretics to alleviate symptoms of pulmonary congestion and chest pain. Knuckles et al. (2008, 191987) hypothesized that if veins constrict in a manner similar to arteries, then patients with severe CHF may have temporary shunting of fluid to the pulmonary circulation, which may elicit signs and symptoms of CHF. Using mesenteric vessels from mice (C57BL/6) exposed to DE (350 μg/m^3×4 h; MMD 100 nm, CMD 80 nm), the authors reported a significant enhancement of ET-1-induced vasoconstriction in veins with much weaker responses in arteries. In an ex vivo experiment, venous constriction was blocked by the arginine analog, L-NAME, which eliminates the feedback NOS activation via endothelial ET_B receptors; this is indicative of impaired or uncoupled eNOS. The authors hypothesized that volatile organic compounds might be responsible these effects, but no significant effects were observed for acetaldehyde, formaldehyde, acetone, hexadecane, or pristane.

Model Particles

A study by Nurkiewicz et al. (2008, 156816) compared the arteriole dilation responses in the spinotrapezius muscle with inhalation exposure to fine or UF TiO_2 (1 μm and 21 nm, respectively; mean mass concentration 3-16 and 1.5-12 mg/m^3, respectively) for durations of 4-12 h in SD rats. Both size fractions of TiO_2 induced impaired dilation with a NO-dependent Ca^{2+} ionophore in a dose-dependent manner. When fine and UF TiO_2 were compared at similar mass doses, the systemic microvascular dysfunction was greater with the UFPs. Furthermore, three exposures of differing durations and concentrations that produced equal calculated pulmonary deposition of UF TiO_2 (30 μg) demonstrated similar dilation responses, indicating that impairment is dependent upon the time×concentration product. No effects on dilation were observed with a dose of 4 μg UF TiO_2 (1.5 mg/m^3 for 4 h) or 8 μg fine TiO_2 (3 mg/m^3 for 4 h).

In a follow-up study, Nurkiewicz et al. (2009, 191961) examined the effect of pulmonary fine and UF TiO_2 exposure on endogenous microvasculature NO production in SD rats. The exposure concentrations and durations were selected to produce ~50% impairment of microvascular reactivity (67 and 10 μg for fine[1] and UF[2] TiO_2, respectively). Similar to the study above (Nurkiewicz et al., 2008, 156816), impaired endothelium-dependent arteriolar dilation was observed 24 h post-exposure with infusion of a Ca^{2+} ionophore. Earlier studies that used residual oil fly ash (ROFA) or TiO_2 via IT instillation reported similar findings, regardless of particle type (Nurkiewicz et al., 2004, 087968; Nurkiewicz et al., 2006, 088611). There was no difference in arteriolar dilation between sham and TiO_2 exposed groups with direct administration of the NO donor SNP to the exterior arteriolar wall and this response was consistent with that observed following ROFA administered intratracheally (Nurkiewicz et al., 2004, 087968). The lack of response to SNP indicates that vascular smooth muscle sensitivity to NO is not altered after particle exposure. The amount of ROS in the microvascular wall was increased following exposure to either TiO_2 size. Local ROS may consume endothelial-derived NO and generate peroxynitrite radicals, as microvascular nitrotyrosine (NT) formation (the end product of peroxynitrite reactions) was demonstrated after TiO_2 exposure. NO production was compromised in a dose-dependent manner following particle exposure (8-90 μg for fine and 4-38 μg for UF TiO_2), and was partially restored with agents for radical scavenging or enzyme inhibition for NADPH oxidase and MPO.

Intratracheal Instillation

Nurkiewicz et al. (2004, 087968; 2006, 088611) have shown impairment of endothelium-dependent dilation in the systemic microvasculature of SD rats following ROFA or TiO_2 exposure (0.1 or 0.25 mg/rat). NO-independent arteriolar dilation was also impaired by ROFA,

[1] Produced by a 300-min exposure to 16 mg/m^3 of fine TiO_2

[2] Produced by a 240-min exposure to 6 mg/m^3 of ultrafine TiO_2

but arteriole adrenergic sensitivity to phenylephrine (PHE) was not affected by 0.25 mg ROFA, indicating that contractile activity was unchanged. In addition, increased venular leukocyte rolling and adhesion in the spinotrapezius muscle was also observed following ROFA exposure (Nurkiewicz et al., 2004, 087968).

Further characterization of the leukocyte adherence and "rolling" effects for both ROFA and TiO_2 were indicative of an activated endothelium (Nurkiewicz et al., 2006, 088611). Vascular deposition of MPO was observed in the spinotrapezius muscle 24 h post-exposure and the authors suggested that the adherent leukocytes may have deposited the MPO to be taken up by endothelial cells (Nurkiewicz et al., 2006, 088611). However, this is in contrast to another study (Cozzi et al., 2006, 091380) that did not find changes in blood neutrophil MPO release in ICR mice exposed to UF PM (100 μg from Chapel Hill, NC; assessed 24 h post-exposure), although this finding may be a reflection of differing protocols. Increased oxidative stress in the arteriolar wall was also reported with exposure to 0.25 mg ROFA. TiO_2 and ROFA induced varying degrees of pulmonary inflammation in these animals, but elicited very similar vascular effects, indicating that the vascular responses may be due to PM presence in the lung rather than its physiochemical properties or intrinsic pulmonary toxicity.

PM_{10}

Tamagawa et al. (2008, 191988) reported reduced ACh-stimulated relaxation in carotid arteries from rabbits (New Zealand White) exposed to PM_{10} (EHC-93) via intrapharyngeal instillation for 5 days or 4 wk (total doses 8 and 16 mg/kg, respectively). Endothelium-dependent NO-mediated vasorelaxation correlated with increased serum IL-6 levels in the acute study and during wk 1 and 2 of the 4-wk exposure, which may indicate a role for systemic inflammation in the response. Maximal SNP-induced dilation was not affected by PM exposure, indicating that the dilatory response was not acting via endothelium-independent NO-mediated mechanisms. This finding is consistent with that by Nurkiewicz et al. (2004, 087968) and suggests that the arteriolar smooth muscle is not involved in the PM-impaired dilatation response.

Vasoreactivity of aortic rings was measured in SH rats following exposure to 10 mg/kg PM_{10} (EHC-93), with an increase in ACh-induced vasorelaxation observed (Bagate et al., 2004, 087945). This endothelium-dependent response was greatest at 4 h and was still present at 24 h. Similarly, vasorelaxation induced by SNP 4-h post-PM exposure was enhanced. The vasorelaxation response was attenuated after denudation of the aortic rings, suggesting that the effect was endothelium dependent. The findings of enhanced dilation with PM exposure contrast with those reported by Nurkiewicz et al. (2004, 087968; 2006, 088611), Tamagawa et al. (2008, 191988), and Cozzi et al. (2006, 091380) and may be attributable to differences in PM type, animal species, or disease models. The authors attribute their findings to the SH rat as a well-documented model of sympathetic hyperactivity (increased affinity of aortic smooth muscle α-adrenergic receptors) that demonstrates upregulation of NO formation and/or release (Safar et al., 2001, 156068). No change in vasoconstriction was observed with PM with PHE or potassium chloride.

Consistent with the impaired vasodilatory responses observed in the microvasculature and aortic rings following PM exposure, Courtois et al. (2008, 156369) demonstrated less relaxation to ACh in intrapulmonary arteries of Wistar rats exposed to a high dose (5 mg) of ambient PM (SRM1648). This response was only observed 12 h after PM exposure and not at shorter (6 h) or longer (24 or 72 h) time points. Fine TiO_2 did not alter ACh-induced relaxation.

Ultrafine PM

Cozzi et al. (2006, 091380) used ICR mice to examine the effects of UF PM exposure (100 μg collected from Chapel Hill, NC) on vascular reactivity following PM exposure and ischemia/reperfusion injury. Aortic rings were evaluated for their contractile and dilatory responses 24 h post-exposure and following the ischemia/reperfusion protocol. Maximum ACh-induced relaxation was impaired in UF PM-exposed vessels, as well as a rightward shift in sensitivity to ACh. There was no difference in constriction to PHE between aortic rings from control and PM-exposed mice. The reduced ACh-induced relaxation may be important for reperfusion of critical vascular beds following occlusion, potentially leading to a greater area of infarction (as in this study). A new study in dogs supports the results observed in the above study and provides evidence of reduced myocardial blood flow following PM exposure (Bartoli et al., 2009, 179904), and is discussed in more detail in Section 6.2.3.3.

Summary of Toxicological Study Findings for Vasoreactivity

The toxicological findings with respect to vascular reactivity are generally in agreement and demonstrate impaired dilation following PM exposure that is likely endothelium dependent. These effects have been demonstrated in varying vessels (right spinotrapezius muscle, carotid arteries, and aortic rings) and in response to different PM types (ROFA, TiO_2, EHC-93, UF ambient PM). The work by Nurkiewicz et al. (2004, 087968; 2006, 088611; 2008, 156816; 2009, 191961) supports a role for increased ROS and RNS production in the microvascular wall that leads to altered NO bioavailability and dysfunction following particle exposure. Only one study showed enhanced dilation with PM exposure, but the authors attributed the conflicting results to the SH rat. No constriction changes in response to PHE were observed following PM exposure. The responses observed in the pulmonary circulation after PM exposure include pulmonary vasoconstriction, decreased L/W ratio, and impaired vasodilation in intrapulmonary arteries. These results are consistent and indicate altered vascular tone. Enhancement of vasoconstriction in mesenteric veins following DE is the first study of its kind to report on venous circulatory effects.

Endothelin

In addition to studies that look at vascular reactivity, three recent studies have examined plasma ET levels following exposure to vehicle emissions and a few studies examined the mRNA expression of ET-1 and ET receptors in the hearts of rodents following PM exposure.

CAPs

The upregulation of mRNA expressions of ET-1 and the ET_A receptor in WKY rats exposed to CAPs (1 or 4 days; 4.5 h/day; mean mass concentration range 1,000-1,900 $\mu g/m^3$; Yokohoma City, Japan) was correlated with increasing PM cumulative mass collected on chamber filters (Ito et al., 2008, 096823). Furthermore, relative cardiac mRNA expressions of ET-1 and ET_A receptor were significantly correlated with CYP1B1 and HO-1 expression, indicating a possible relationship between ET-1 metabolism and oxidative stress.

Another plasma mediator of vasomotor tone is asymmetric dimethylarginine (ADMA), which is an endogenous inhibitor of NOS that is associated with impaired vascular function and increased cardiovascular events. Dvonch et al. (2004, 055741) assessed levels of ADMA in Brown Norway rats 24 h following a 3-day $PM_{2.5}$ CAPs exposure in southwest Detroit (8 h/day; July 2002). CAPs (mean mass concentration 354 $\mu g/m^3$) resulted in increased plasma ADMA compared to air controls, although the levels reported were well below the 2 μM range associated with increased CVD risk in humans in chronic studies. Therefore, the preliminary results identified a new potential biomarker of vascular tone that had not previously been used in air pollution toxicological studies.

Traffic-Related Particles

A study of old rats (21 mo; F344) exposed to on-road highway aerosols (number concentration range $0.95\text{-}3.13\times10^5$ particles/cm^3; Interstate 90 between Rochester and Buffalo, NY) for 6 h demonstrated decreased plasma ET-2 (18 h post-exposure) and unchanged levels of ET-1 and ET-3 (Elder et al., 2004, 087354).

Gasoline Exhaust

In contrast to the study above, circulating levels of ET-1 (measured 18 h post-exposure) were elevated in animals exposed to gasoline exhaust and filtration of particles did not reduce this effect (study details in Section 6.2.2.2) (Campen et al., 2006, 096879). The results of Campen et al. (2006, 096879) are consistent with those observed by Bouthillier et al. (1998, 087110) following a very high exposure to EHC-93, but it is difficult to attribute the effects to PM alone, as Campen et al. (2006, 096879) showed that the gaseous components of the gasoline mixture were required for the ET-1 increase.

Aorta ET-1 mRNA expression was increased with a 7-day gasoline exhaust exposure (60 $\mu g/m^3$) in $ApoE^{-/-}$ mice, but was not changed following a single-day exposure (Lund et al., 2009, 180257). The expression and activity of MMP-2 and -9 and oxidative stress in aortas of exposed

mice were also elevated. The ET-1 and MMP-9 mRNA expressions were attenuated with the addition of an ET_A receptor antagonist (but not a radical scavenger), indicating that ET-1 may mediate the expression of MMP-9 through the ET_A receptor.

Model Particles

Another study examined the effects of UF carbon particles (mass concentration 172 $\mu g/m^3$; mean number concentration 9.0×10^6 particles/cm^3) and there was no difference in ET-1, ET_A or ET_B receptor mRNA expression between air- and particle-exposed SH rats 1 or 3 days post-exposure (Upadhyay et al., 2008, 159345). In lung homogenates, ET-1, ET_A and ET_B receptor mRNA expressions were elevated 3 days after exposure to UF carbon particles (Upadhyay et al., 2008, 159345).

Summary of Toxicological Study Findings for Endothelin

The ET responses were mixed, with one study demonstrating ET-1 increases after exposure to gasoline emissions that were particle independent and another reported decreased ET-2, but no change in ET-1 or ET-3 with on-road highway exposure. Elevated levels of ET-1 and ET_A receptor mRNA expression were noted in hearts of rats exposed to CAPs, but not in rats exposed to UF carbon particles. However, ET-1, ET_A and ET_B receptor mRNA expressions were increased in lung homogenates of rats following UF carbon exposure. The ET_A receptor was found to be involved in the ET-1 and MMP-9 responses in the aortas of mice exposed to gasoline exhaust. A relatively novel marker, ADMA, was used to evaluate vasomotor tone in rats and was found to be elevated following exposure to CAPs, although the results are preliminary and have not been confirmed.

6.2.5. Blood Pressure

One of the potential outcomes of air pollution-mediated alterations in vascular tone is its impact on variable BP or hypertension. BP is tightly regulated by autonomic (central and local), cardiac, renal, and regional vascular homeostatic mechanisms with changes in arterial tone being countered by changes in cardiac contractility, HR, or fluid volume. The evidence of PM-induced changes in BP presented in the 2004 PM AQCD (U.S. EPA, 2004, 056905) is limited and inconsistent. Recent epidemiologic, controlled human exposure, and toxicological studies have similarly reported conflicting results regarding the effect of PM on BP. However, the majority of these studies have evaluated changes in BP at some point following exposure to PM. Significant increases in DBP have been observed in controlled human exposure studies that evaluated BP during exposure (concomitant exposure to CAPs and O_3). In addition, evidence from toxicological studies suggests that the effect of PM on BP may be modified by health status, as PM-induced increases in BP have been more consistently observed in SH rats.

6.2.5.1. Epidemiologic Studies

Increased BP was associated with PM concentration in two of three studies reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905). Increases in left ventricular BP (systolic and diastolic) are well established risk factors for cardiovascular mortality/morbidity (Welin et al., 1993, 156151). Changes in HR and BP both reflect changes in autonomic tone, and have been examined following short-term increases in PM pollution in several recent studies.

Ibald-Mulli et al. (2004, 087415) examined associations between BP and ambient $PM_{2.5}$ concentrations, UFP counts, and ACP counts in a multicity panel study (Amsterdam, the Netherlands; Helsinki, Finland; Erfurt, Germany) of 131 adults with coronary heart disease. Although based on the same ULTRA Study (Timonen et al., 2006, 088747) with study methods as described previously in Section 6.2.1.1, the study period was different. They investigated changes in BP (SBP and DBP) associated with mean $PM_{2.5}$, UFP, and ACP concentration/counts (lag days 0, 1, and 2, as well as the 5-day mean) in each city and then generated a pooled estimate across the cities. The median $PM_{2.5}$ concentration for each city is provided in Table 6-5. Pooled analyses across all 3 cities showed small, but statistically significant decreases in SBP and DBP associated with various single day lagged concentrations/counts of each particulate pollutant. Each 10 $\mu g/m^3$ increase in the

mean $PM_{2.5}$ concentration over the previous 5 days was associated with a 0.36 mmHg decrease in SBP (95% CI: -0.99 to 0.27) and a 0.39 mmHg decrease in DBP (95% CI: -0.75 to -0.03). Each 10,000 particles/cm^3 increase in UFP was associated with a 0.72 mmHg decrease in SBP (95% CI: -1.92 to 0.49), and a 0.70 mmHg decrease in DBP (95% CI: -1.38 to -0.02). Each 1,000 particles/cm^3 increase in 5-day avg ACP was associated with a 1.11 mmHg decrease in SBP (95% CI: -2.12 to -0.09) and a 0.95 mmHg decrease in DBP (95% CI: -1.53 to -0.37). The authors concluded that these findings do not support previous findings of an increase in BP associated with increases in particulate pollutant concentrations.

Single-city studies examining the association between BP and particulate air pollution have been done in several U.S. and Canadian cities. Dales et al. (2007, 155743) conducted a panel study of 39 healthy volunteers who sat outside at two different bus stops for 2-h in Ottawa, Canada. The median $PM_{2.5}$ concentrations measured at the bus stops during each 2-h exposure session were 40 and 10 $\mu g/m^3$. Post-exposure SBP and DBP were not associated with the mean $PM_{2.5}$ concentration measured at the bus stops during the 2-h exposure session. The change in BP from pre- to post-exposure was not evaluated, as health measurements were only made after the 2-h exposure sessions.

Jansen et al. (2005, 082236) studied changes in BP among 16 older subjects (aged 60-86 yr) with asthma or COPD in Seattle, Washington, associated with indoor, outdoor, and personal PM_{10}, $PM_{2.5}$, and BC concentrations on 12 consecutive days. The study authors reported that no associations were observed between BP and daily mean PM_{10}, $PM_{2.5}$, or BC concentrations.

Zanobetti et al. (2004, 087489) examined the association between BP (SBP, DBP, and mean arterial BP) and mean $PM_{2.5}$ concentrations in the previous 24, 48, 72, 96, and 120 h in 62 elderly, cardiac rehabilitation patients in Boston, MA (Zanobetti et al., 2004, 087489). Each 10.4 $\mu g/m^3$ increase in mean $PM_{2.5}$ concentration in the previous 120 h was associated with significant increases in resting DBP (2.82 mmHg [95% CI: 1.26-4.41]), SBP (2.68 mmHg [95% CI: 0.04-5.38]), and mean arterial BP (2.76 mmHg [95% CI: 1.07-4.48]).

Mar et al. (2005, 087566) studied this same $PM_{2.5}$-BP association in 88 subjects aged >57 yr in Seattle, WA. Among healthy subjects taking medications (bronchodilators, inhaled corticosteroids, anti-hypertensives, β-blockers, calcium channel blockers, and/or cardiac glycosides), each 10 $\mu g/m^3$ increase in mean outdoor $PM_{2.5}$ concentration on the same day as the BP measurement was made was associated with small increases in SBP and DBP. However, among all subjects, each 10 $\mu g/m^3$ increase in same day mean $PM_{2.5}$ concentration was associated with non-significant decreases in SBP (-0.81 mmHg [95% CI: -2.34 to 0.73]) and DBP (-0.46 mmHg [95% CI: -1.49 to 0.57]).

As described earlier, Ebelt et al. (2005, 056907) conducted a repeated measures panel study of 16 patients with COPD in the summer of 1998 in Vancouver, British Columbia to evaluate the relative impact of ambient and non-ambient exposures to $PM_{2.5}$, PM_{10}, and $PM_{10-2.5}$ on multiple health outcomes including ectopy and BP. Using the same analytic methods, pollutant concentrations, and lags, they reported decreased SBP associated with same day ambient exposures to each PM size fraction.

Two similar studies were done in Incheon, South Korea (Choi et al., 2007, 093196) and Taipei, Taiwan (Chuang et al., 2005, 156356). Choi et al. (2007, 093196) reported significantly increased SBP and DBP associated with the mean PM_{10} concentration over the same and previous 2 days in the warm season only (July to September). Chuang et al. (2005, 156356) reported significant increases in SBP and DBP associated with the mean UFP count (0.01-0.1 μm particles) 1-3 h before the BP measurement.

Summary of Epidemiologic Studies of Blood Pressure

These studies (Choi et al., 2007, 093196; Chuang et al., 2005, 156356; Dales et al., 2007, 155743; Ibald-Mulli et al., 2004, 087415; Mar et al., 2005, 087566; Zanobetti et al., 2004, 087489) are not entirely consistent with regard to their BP-PM associations. Most have reported increases in SBP and DBP associated with increases in either $PM_{2.5}$, PM_{10}, or UFP (Choi et al., 2007, 093196; Chuang et al., 2005, 156356; Mar et al., 2005, 087566; Zanobetti et al., 2004, 087489). However, two studies reported small decreases in BP associated with multiple particulate pollutants (Ibald-Mulli et al., 2004, 087415; Mar et al., 2005, 087566), Dales et al. (2007, 155743) reported no change in BP associated with a 2-h exposure to bus stop $PM_{2.5}$ and Jansen at al. (2005, 082236) reported null findings among older adults in Seattle, WA. Exposure lags ranging from 1-3 h (Chuang et al., 2005,

156356), to the same day(Ebelt et al., 2005, 056907; Mar et al., 2005, 087566), to the mean across the previous 5 days (Zanobetti et al., 2004, 087489) were reported as having the strongest associations with BP. Mean and upper percentile concentrations for PM from these studies are presented in Table 6-5.

Table 6-5. Mean PM concentrations reported in epidemiologic studies of blood pressure.

Author	Location	Mean Concentration ($\mu g/m^3$)	Upper Percentile Concentrations ($\mu g/m^3$)
$PM_{2.5}$			
Dales (2007, 155743)	Ottawa, Canada (bus stops)	Bus stop 1: 40 Bus stop 2: 10	NR
Ebelt (2005, 056907)	Vancouver, Canada	Ambient (measured): 11.4 Personal (estimated): 7.9 Personal (measured): 18.5	Ambient (measured) range: 4.2-28.7 Personal (estimated) range: 0.9-21.3 Personal (measured) range: 2.2-90.9
Ibald-Mulli (2004, 087415)	Amsterdam, Netherlands	20	50th: 16.9 75th: 23.9 Max: 82.2
	Erfurt, Germany	23.1	50th: 16.3 75th: 27.4 Max: 118.1
	Helsinki, Finland	12.7	50th: 10.6 75th: 16 Max: 39.8
Jansen (2005, 082236)	Seattle, WA	10.47	NR
Mar (2005, 087566)	Seattle, WA	Healthy: Personal- 9.3 Indoor- 7.4 Outdoor- 9 CVD: Personal- 10.8 Indoor- 9.5 Outdoor- 12.6 COPD: Personal- 10.5 Indoor- 8.5 Outdoor- 9.2	NR
Zanobetti (2004, 087489)	Boston, MA	Median: 8.8	90th: 17.6
$PM_{10-2.5}$			
Ebelt (2005, 056907)	Vancouver, Canada	Ambient (calculated): 5.6 Personal (estimated): 2.4	Ambient (calculated) range: -1.2 to 11.9 Personal (estimated) range: -0.4 to 7.2
PM_{10}			
Choi (2007, 093196)	Incheon, South Korea	July-Sept: 42.1 Oct.-Dec: 53.5	July-Sept.: 75%: 52.2 Max: 136.7 Oct.-Dec.: 75%: 64.5 Max: 209.6

Author	Location	Mean Concentration (μg/m^3)	Upper Percentile Concentrations (μg/m^3)
Chuang (2005, 156356)	Taipei, Taiwan	54.1	Range: 10.3-139.8
Ebelt (2005, 056907)	Vancouver, Canada	Ambient (calculated): 17 Personal (estimated): 10.3	Ambient (calculated) range: 7-36 Personal (estimated) range: 1.5-23.8
Jansen (2005, 082236)	Seattle, WA	13.47	NR
Mar (2005, 087566)	Seattle, Washington	Healthy: 14.5 CVD: 18 COPD: 14.3	NR

Right Ventricular Pressure

Several recent studies, summarized in the section on hospital admissions and emergency department (ED) visits for CVD causes, have reported increased risk of hospital admissions for CHF associated with increased PM concentration on the same day (Wellenius et al., 2005, 087483; 2006, 088748). As a possible mechanism for these reported associations, Rich et al. (2008, 156910) hypothesized that these hospital admissions for decompensation of heart failure would be preceded by more subtle increases in pulmonary arterial (PA) and right ventricular (RV) diastolic pressures. They used passively monitored PA and RV pressures on 5,807 person-days, among 11 subjects implanted with the Chronicle Implantable Hemodynamic Monitor [Medtronic, Inc. Medtronic, MN]). Using a two-stage modeling process, they examined the change in daily mean right heart pressures associated with mean $PM_{2.5}$ concentration on the same and previous 6 days. Each 11.62 μg/m^3 increase in same day mean $PM_{2.5}$ concentration was associated with small, but statistically significant increases in estimated PA diastolic pressure (0.19 mmHg [95% CI: 0.05-0.33]) and RV diastolic pressure (0.23 mmHg [95% CI: 0.11-0.34]). These effects were not attenuated when controlling for all lags simultaneously. Thus, PM induced right heart pressure increases may mark another potential pathway between PM exposure and incidence of cardiovascular events, but further studies on this same hypothesis are needed for confirmation.

Wellenius et al. (2007, 092830) conducted a panel study of 28 subjects living in the greater Boston metropolitan area, each with chronic stable heart failure and impaired systolic function. They hypothesized that circulating levels of B-type natriuretic peptide (BNP), measured in whole blood at 0, 6, and 12 wk, were associated with acute changes in ambient air pollution, as a possible mechanistic explanation for the observed association between hospital admissions for CHF and ambient PM concentration (Wellenius et al., 2005, 087483; 2006, 088748). During the study, the mean $PM_{2.5}$ concentration was 10.9 μg/m^3, while the mean BC concentration was 0.73 μg/m^3. Using linear mixed models, they reported no association between any pollutant ($PM_{2.5}$, CO, SO_2, NO_2, O_3, and BC) and BNP at any lag (e.g., each 10 μg/m^3 increase in mean daily $PM_{2.5}$ concentration [0.8% increase in BNP (95% CI: -16.4 to 21.5)]) (Wellenius et al., 2007, 092830). However, BNP the active peptide has a very short half-life and might not be the best biomarker for such a study. Thus the absence of a correlation between PM and BNP may not suggest that PM does not have an impact on RV or LV function in individuals with impaired cardiac mechanics.

6.2.5.2. Controlled Human Exposure Studies

Only one controlled human exposure study cited in the 2004 PM AQCD (U.S. EPA, 2004, 056905) reported any PM-induced changes in BP. Gong et al. (2003, 042106) found that exposure to $PM_{2.5}$ (174 μg/m^3) decreased SBP in asthmatics, but increased SBP in healthy subjects. Among healthy adults, BP was not affected following 2-h exposures to 200 μg/m^3 diesel PM (Nightingale et al., 2000, 011659), 150 μg/m^3 $PM_{2.5}$ CAPs with 120 ppb O_3 (Brook et al., 2002, 024987), or 10 μg/m^3 UF carbon particles (Frampton, 2001, 019051). The effect of PM on BP has been further investigated in several recent controlled human exposure studies, which are described below.

CAPs

One recent study demonstrated a significant increase (9.3%) in DBP among healthy adults immediately prior to the end of a 2-h exposure to 150 μg/m^3 $PM_{2.5}$ CAPs in combination with 120 ppb O_3 (Urch et al., 2005, 081080). The authors also found that the magnitude of change in BP was significantly associated with $PM_{2.5}$ carbon content, but not total $PM_{2.5}$ mass. It was postulated that the disparity between these findings and those of a similar study by the same group (Brook et al., 2002, 024987) could be due to differences in experimental methods. The Brook et al. (2002, 024987) study measured post-exposure BP approximately 10 min following exposure, while the study by Urch et al. (2005, 081080) measured BP during exposure. In a follow up study that evaluated changes in BP during a 2-h exposure to $PM_{2.5}$ CAPs, Fakhri et al. (2009, 191914) reported a significant increase in DBP with exposure to CAPs with, but not without, coexposure to O_3.

Diesel Exhaust

Several recent studies have assessed BP changes following a 1-h exposure to DE with a particle concentration of 300 μg/m^3. Mills et al. (2005, 095757) evaluated changes in BP 2 h following exposure to DE and found a 6 mmHg increase in DBP of marginal statistical significance ($p = 0.08$) compared to filtered air control. In this same group of subjects, Tornqvist et al. (2007, 091279) did not observe any such changes in BP 24 h following DE exposure. At lower particle concentrations in diluted DE (100-200 μg/m^3 $PM_{2.5}$), Peretz et al. (2008, 156854) did not observe any changes in systolic or DBP in either healthy adults or adults with metabolic syndrome immediately following a 2-h exposure. Further, although Lundback et al. (2009, 191967) reported an increase in arterial stiffness following exposure to DE with a particle concentration of 330 μg/m^3 among healthy young adults, no changes in systolic or diastolic BP were observed during or following exposure relative to filtered air.

Model Particles

Routledge et al. (2006, 088674) did not observe any changes in BP among healthy older adults and older adults with stable angina following a 1-h exposure to UF EC (50 μg/m^3), with or without coexposure to 200 ppb SO_2. Similarly, neither Shah et al. (2008, 156970), nor Beckett et al. (2005, 156261) reported any changes in BP among healthy adults following exposure to UF EC (50 μg/m^3) or ZnO (500 μg/m^3 fine and ultrafine), respectively.

Summary of Controlled Human Exposure Study Findings for BP

The findings of these new studies do not provide convincing evidence of an association between PM exposure and an increase in BP; however, they do suggest that there is a need for additional investigations of PM-induced changes in BP at various time points following exposure.

6.2.5.3. Toxicological Studies

In healthy animal models, little evidence exists for significant BP changes following inhalation exposure to environmentally-relevant concentrations of PM. Only one animal toxicological study is mentioned in the 2004 PM AQCD (U.S. EPA, 2004, 056905) that examined BP with PM exposure and no effect was observed (Vincent et al., 2001, 021184).

CAPs

In a recent study of dogs, exposure to $PM_{2.5}$ CAPs from Boston (mean mass concentration 358.1 μg/m^3; mass concentration 94.1-1557 μg/m^3) for 5 h resulted in increased SBP (2.7 mmHg), DBP (4.1 mmHg), mean arterial pressure (3.7 mmHg), and lowered pulse pressure (1.7 mmHg) when measured upstream of the femoral artery (Bartoli et al., 2009, 156256). Administration of an

α-adrenergic antagonist (prazosin) prior to CAPs attenuated the BP responses. These findings indicate that CAPs exposure may have activated α-adrenergic receptors and increased peripheral vascular resistance. Baroreflex sensitivity was measured immediately before and after exposure during a transient elevation of arterial pressure that was induced by PHE; increased baroreflex sensitivity was observed in subgroup of dogs exposed to CAPs, which is consistent with an upregulation of vagal reflexes.

Chang et al. (2004, 055637) noted slight increases in SH rat BP (5-10 mmHg) when exposed to $PM_{2.5}$ CAPs (mean mass concentration 202 $\mu g/m^3$) during spring months. However, during summer months, when the CAPs exposure level was less (140 $\mu g/m^3$), this effect was not observed. It was unclear, therefore, whether the effects were seasonal or dose-related. In a preliminary study of SH rats exposed to CAPs during a dust storm event, mean BP was elevated the third and fourth hour of a 6-h exposure, although interpretation of this finding is difficult due to few animals in the exposure group (n = 2) (Chang et al., 2007, 155719). In another study, the increased change in mean BP measured using the tail cuff method following CAPs exposure weakly correlated with PM mass accumulated on chamber filters over the entire exposure duration (Section 6.2.4.3 for details) (Ito et al., 2008, 096823). Furthermore, ET_A receptor mRNA expression in cardiac tissue was positively correlated with the change in mean BP.

Model Particles

In WKY rats, 24-h exposure to UF carbon particles (mass concentration 180 $\mu g/m^3$; mean number concentration 1.6×10^7 particles/cm^3) did not alter mean BP during exposure or the recovery periods (Harder et al., 2005, 087371). SH rats exposed to UF carbon particles for 24 h (mass concentration 172 $\mu g/m^3$; mean number concentration (9.0×10^6 particles/cm^3) resulted in elevated mean BP (by 6 mmHg) on the first and second days of recovery following exposure that was attributable to increases in both SBP and DBP (Upadhyay et al., 2008, 159345). Increased plasma renin concentrations were observed in CB-exposed rats on the first and second days of recovery, although renin activity and angiotensin (Ang) I and II concentrations were not affected by particle exposure.

Summary of Toxicological Study Findings for Blood Pressure

Limited toxicological evidence provides support for elevated BP in dogs or compromised rats with CAPs, UF CAPs, CAPs during a dust storm event, or UF carbon particle exposure. However, most of the CAPs studies were conducted outside of the U.S.

6.2.6. Cardiac Contractility

The 2004 PM AQCD (U.S. EPA, 2004, 056905) did not include any toxicological studies that evaluated cardiac contractility either directly or indirectly following exposure to PM. Two recent animal toxicological studies have demonstrated reductions in cardiac fractional shortening, diminished ejection shortening, or changes in the QA interval following PM exposure. The results of these studies provide some evidence of PM-induced changes in cardiac contractility in animal models.

6.2.6.1. Toxicological Studies

The strength of the contracting heart is reflected by its contractility. In heart failure, contractility wanes significantly and the heart cannot compensate during periods of increased physical activity. Measuring true contractility in a whole animal is difficult, requiring extensive surgical instrumentation and monitoring.

CAPs

Using radiotelemetry to indirectly measure cardiac contractility through the QA interval, SH rats were repeatedly and alternately exposed to UF CAPs in Taiwan on separate days in spring or summer (details provided in Section 6.2.5.3) (Chang et al., 2004, 055637). The QA interval was calculated as the time duration between the Q wave in the ECG and point A (upstroke in aortic pressure) in the pressure trace and is not as reliable as other measures, such as echocardiography. During the spring exposure, QA interval decreased by 1.6 ms (as demonstrated by fixed effects in linear mixed-effects modeling), which indicates an increase in cardiac contractility. There were no changes in QA interval observed for the summer months, which may be attributable to lower UF PM concentrations (mean mass concentration 140 $\mu g/m^3$) or differing PM compositions.

Model Particles

A recent study using old (18-28-mo) mice (C57BL/6, C3H/HeJ, and B6C3F1) demonstrated significant reductions in cardiac fractional shortening (due to increased left ventricular end-diastolic and end-systolic diameters) following a 4-day (3 h/day) exposure to CB ($PM_{2.5}$ mean concentration 401 $\mu g/m^3$; PM_{10} mean concentration 553 $\mu g/m^3$) using echocardiography (Tankersley et al., 2008, 157043). Hemodynamic measurements of diminished ejection fraction and maximum change in pressure over time further supported lowered myocardial contractility. Furthermore, increased right ventricular pressure associated with elevated right atrial and pulmonary vascular pressures and resistance, was indicative of pulmonary vasoconstriction in CB-exposed mice. Heart tissue and isolated cardiomyocytes from exposed animals demonstrated enhanced ROS that was partially attributable to NOS3-uncoupling and elevated MMP-2 and MMP-9 levels, which may implicate myocardial remodeling. The combined results from this study suggest that cellular mechanisms involving NOS-uncoupled ROS generation likely mediate PM-induced cardiac effects. Furthermore, mRNA expression for atrial and brain natriuretic peptides was increased in hearts from exposed mice compared to control, which is consistent with pulmonary congestion. There were no reported strain-related differences in any response.

Intratracheal Instillation

Similar to the responses observed by Tankersley et al. (2008, 157043), decreases in fractional shortening and increases in left ventricular end diastolic diameter measured by echocardiography were also reported for SD rats at 24 h post-IT exposure to DE particles (250 μg) (Yan et al., 2008, 098625). A subset of rats received isoproterenol to induce myocardial injury prior to IT instillation of DE particles and these animals demonstrated lowered fractional shortening at baseline, which was decreased to an even greater extent with DE particle exposure; left ventricular end diastolic diameter was not affected by DE particles in these rats.

Summary of Toxicological Study Findings for Cardiac Contractility

The studies above provide some evidence that cardiac contractility may be altered immediately following PM exposure in animal models. Results from the Tanksersley (2008, 157043) and Yan (2008, 098625) studies provide the strongest support for PM-induced contractility changes with inhalation exposure, as echocardiography and hemodynamic measurements are well-established for examining cardiac function.

6.2.7. Systemic Inflammation

The evidence presented in the 2004 PM AQCD (U.S. EPA, 2004, 056905) of increases in markers of systemic inflammation associated with PM was limited and not sufficient to formulate a definitive conclusion. Recent controlled human exposure and toxicological studies continue to provide mixed results for an effect of PM on markers of systemic inflammation including cytokine

levels, C-reactive protein (CRP), and white blood cell (WBC) count. While results from recent epidemiologic studies have also been inconsistent across studies, there is some evidence to suggest that PM levels may have a greater effect on inflammatory markers among populations with preexisting diseases.

6.2.7.1. Epidemiologic Studies

Several studies reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905) investigated the association of short-term fluctuations in PM concentration with markers of inflammation. These studies were found to offer limited support for mechanistic explanations of the associations between PM concentration and heart disease outcomes. Recent studies, published since 2002, are reviewed below. CRP was measured in multiple studies, allowing the consistency of findings across epidemiologic studies to be evaluated. Several other markers were examined in only a few studies, in relation to a wide range PM size fractions and components. These markers included IL-6, TNF-α, vascular cell adhesion molecule-1 (VCAM-1), intercellular adhesion molecule-1 (ICAM-1), soluble CD40 ligand (sCD40L), WBCs, and soluble adhesion molecules (sP-selectin and e-selectin).

Diez-Roux et al. (2006, 156400) examined whether CRP increased in response to changes in the mean ambient $PM_{2.5}$ concentrations in the prior day, prior 2 days, prior week, prior 30 days, and prior 60 days among participants in the Multi-Ethnic Study of Atherosclerosis (MESA) cohort. Subjects (n = 5,634) lived in either Baltimore City or County, MD, Chicago, IL, Forsyth County, NC, Los Angeles County, CA, Northern Manhattan and the Bronx, NY, or St. Paul, MN. The authors report finding no evidence of a short-term effect of $PM_{2.5}$ on CRP in their population-based sample. Of the five exposure measures examined, only the 30-day and 60-day mean exposures showed positive associations with $PM_{2.5}$ (3% [95% CI: -2 to 10] and 4% [95% CI: -3 to 11] per 10 $\mu g/m^3$, respectively).

Ruckerl et al. (2007, 156931) conducted a multicity longitudinal study to examine whether changes in markers of inflammation were associated with short-term increases in particulate concentrations (PM_{10}, $PM_{2.5}$, PNC) and gaseous pollutant (NO_2, SO_2, CO, O_3). Study subjects were MI survivors (n= 1,003) living in either Athens, Greece; Augsburg, Germany; Barcelona, Spain; Helsinki, Finland; Rome, Italy; or Stockholm, Sweden. Repeated measurements of IL-6 and CRP were made during the study. Fibrinogen was also measured in this study and results are discussed in Section 6.2.8.1. The mean city-specific pollutant concentrations during the study are shown below in Table 6-6. In pooled analyses, each interquartile range (not provided) increase in PNC in the 12-17 h before the health measurement was associated with a 2.7% increase in the geometric mean IL-6 levels (95% CI: 1.0-4.6). None of the pollutants, at any lag, were associated with CRP levels in these subjects. There did not appear to be effect modification of these results by smoking, diabetes, or heart failure. Ljungman et al. (2009, 191983) studied the modification of the IL-6 association with several PM size fractions (PM_{10}, $PM_{2.5}$, PNC) by three IL-6 SNPs, one fibrinogen α chain (FGA) single-nucleotide polymorphism (SNP) and one fibrinogen β chain (FGB) SNP. The associations of $PM_{2.5}$ and PM_{10} with plasma level of IL-6 were stronger among those with the homozygous minor allele genotype of FGB rs1800790 and among those homozygous for the major allele genotype of IL-6 rs2069832. Gene-environment interactions were most pronounced for CO. Modification the PNC-IL-6 association by genotype was not apparent in these data, nor was modification of the PM-IL-6 associations by FBA.

Single-city studies of systemic inflammation have also been conducted in the U.S. and Canada. Delfino et al. (2008, 156390) measured CRP, IL-6, TNF-α, sP-selectin, sVCAM-1 and sICAM-1 in blood during a period of 12 wk. Associations of these markers with average PM concentration ($PM_{0.25}$, $PM_{0.25\text{-}2.5}$, $PM_{10\text{-}2.5}$, PNC, EC, OC, BC, primary OC, secondary OC) 24 h to 9 days prior to the blood draw were examined. Subjects included residents of two downtown Los Angeles nursing homes who were >65 yr old with a history of coronary artery disease. Both 24-h avg and multiday average concentrations of $PM_{0.25}$, EC, primary OC, BC, PNC and gaseous pollutants were associated with CRP, IL-6 and sP-selectin.

Pope et al. (2004, 055238) conducted a panel study of 88 non-smoking, elderly subjects residing in the Salt Lake City, Ogden, and Provo metropolitan area of Utah. Each 100 $\mu g/m^3$ increase in same day mean $PM_{2.5}$ concentration was associated with a 0.81 mg/dL increase in CRP (95% CI: 0.48-1.14), but not WBCs. However, when excluding 1 influential subject, each 100 $\mu g/m^3$ increase in same day mean $PM_{2.5}$ concentration was associated with only a 0.19 mg/dL increase in

CRP (95% CI: -0.01 to 0.39). Several markers of coagulation were examined in this study and are discussed in Section 6.2.8.1.

Zeka et al. (2006, 157177) studied 710 elderly members of the VA Normative Aging Study to examine changes in CRP, sediment rate and WBCs with acute changes in PM concentrations in the previous 48 h, 1 wk, and 4 wk. Results for fibrinogen are discussed in Section 6.2.8.1. They did not find consistent or significant associations with any pollutant and CRP or WBC count. Sediment rate was significantly increased with PNC, BC and $PM_{2.5}$ concentration averaged over the previous 4 wk period. Modification of these PM effects by obesity, GSTM1 genotype and statin use was suggested in this study.

O'Neill et al. (2007, 091362) conducted a cross-sectional study of 92 Boston residents with type 2 diabetes, to examine the association between plasma levels of ICAM-1, VCAM-1 and PM concentrations. Results for markers of coagulation measured in this study are discussed in Section 6.2.8.1. $PM_{2.5}$, BC, and SO_4^{2-} concentrations were measured 0.5 km from the patient exam site. For all moving averages examined (1-6 days), increases in mean $PM_{2.5}$ and BC concentration were associated with increased ICAM-1 and VCAM-1 concentrations. Each 7.6 $\mu g/m^3$ increase in the mean $PM_{2.5}$ concentration over the previous 6 days was associated with a 11.76 ng/mL increase in VCAM-1 (95% CI: 3.48-20.70), and each 0.6 $\mu g/m^3$ increase in the mean BC concentration over the previous 6 days was associated with a 27.51 ng/mL increase in VCAM-1 (95% CI: 11.96-45.21). There were no consistent associations between mean SO_4^{2-} concentration and any marker at any lag.

Sullivan et al. (2007, 100083) conducted a panel study of 47 subjects (aged >55 yr) either with COPD (n = 23) or without COPD (n = 24) in Seattle, WA. They examined the association between levels of CRP and mean daily $PM_{2.5}$ concentration. Most values for IL-6 and TNF-α were below the limit of detection, so these cytokines were not included in the analyses. Results for fibrinogen and D-dimer are discussed in Section 6.2.8.1. They did not find any associations between 24-h mean $PM_{2.5}$ concentrations and levels of CRP in individuals with or without COPD.

In the study by Liu et al. (2006, 192002; 2007, 156705), conducted in Toronto, Ontario, neither CRP (0.11 μg/mL [95% CI: -0.03 to 0.25]) nor TNF-α (0.03 pg/mL [95% CI: -0.07 to 0.13]) was associated with personal exposure to PM_{10} (24-h averaging time).

Similarly, there was no association with IL-6. However, significant positive associations with markers of oxidative stress, FMD and BP were found and are discussed in Sections 6.2.9.1, 6.2.4.1, and 6.2.5.1, respectively.

In the St. Louis Bus Study, each 5.4 $\mu g/m^3$ increase in the mean $PM_{2.5}$ concentration over the previous week was associated with 5.5% increase in WBCs (95% CI: 0.10-11) (Dubowsky et al., 2006, 088750). Each 6.1 $\mu g/m^3$ increase in the mean $PM_{2.5}$ concentration over the previous 5 days was associated with a 14% increase in CRP among all subjects (95% CI: -5.4 to 37), but an 81% increase in CRP (95% CI: 21-172) among subjects with diabetes, obesity, and/or hypertension. Associations between $PM_{2.5}$ and IL-6 were only observed among those with diabetes, obesity, and/or or hypertension. In another study of in-vehicle $PM_{2.5}$, each 10 $\mu g/m^3$ increase during a work-shift was associated with decreased lymphocytes, increased mean corpuscular volume, neutrophils, and CRP over the next 10-14 h among 9 healthy North Carolina state troopers (Riediker et al., 2004, 056992). Associations of roadside and ambient $PM_{2.5}$ with systemic inflammatory markers were weaker and non-significant in this population.

International studies of the effect of air pollution on markers of inflammation have been conducted with mixed results. Two studies conducted among 57 male patients with coronary heart disease in Erfurt, Germany, found associations of UFP, ACP and PM_{10} with CRP (Ruckerl et al., 2006, 088754) and UFP and ACP with sCD40L, a marker for platelet activation (Ruckerl et al., 2007, 156931). In a large cross-sectional study of healthy subjects in Tel Aviv, Steinvil et al. (2008, 188893) examined biological markers of inflammation (CRP and WBCs) collected as part of routine health examinations for 3,659 individuals. Associations with air pollutants (including PM_{10}) measured at local monitoring sites for the day of the examination and up to 7 days prior were examined. No significant associations were found between pollutant levels and indications of enhanced inflammation. By contrast, PM_{10}, $PM_{2.5}$, SO_4^{2-} and nitrate (3-day avg concentrations) were associated with increases in hs-CRP in healthy students in Taiwan (Chuang et al., 2007, 091063). PM_{10}, $PM_{2.5}$ and $PM_{0.25}$ were not associated with CRP in a study of MI patients in Italy, although associations with autonomic dysregulation and more severe arrhythmias were observed (Folino et al., 2009, 191902). Kelishadi et al. (2009, 191960) reports that CRP, as well as markers of insulin resistance and oxidative stress (discussed in Section 6.2.9.1), were associated with PM_{10} in a cross-

sectional study of a population-based sample of children 10-18 yr old in Iran (mean PM_{10} concentration 122.08 µg/m^3).

Summary of Epidemiologic Study Findings for Systemic Inflammation

The most commonly measured marker of inflammation in the studies reviewed was CRP. CRP was not consistently associated with short-term PM concentrations ($PM_{2.5}$, PM_{10}, SO_4^{2-}, EC, OC, PNC). A multicity study of MI survivors in Europe (Ruckerl et al., 2007, 156931) failed to provide evidence of an effect of PM (e.g., PM_{10}, $PM_{2.5}$, PNC) on CRP and no effect was observed by Diez-Roux et al. (2006, 156400) in a population-based study when concentrations were averaged over periods less than 30 days. Several other markers of inflammation have been examined in relation to several PM size fractions and components, but the number of studies examining the same marker/PM metric combination is too few to allow results to be compared across epidemiologic studies. Mean and upper percentile concentrations for those epidemiologic studies that evaluated systemic inflammation are included in Table 6-6.

Table 6-6. PM concentrations reported in epidemiologic studies of inflammation, hemostasis, thrombosis, coagulation factors and oxidative stress.

Author	Location	Mean Concentration (µg/m^3)	Upper Percentile Concentrations (µg/m^3)
$PM_{2.5}$			
Chuang (2007, 091063)	Taipei, Taiwan	1-day avg: 31.8 2-day avg: 36.4 3-day avg: 36.5	1-day avg (range): 16.2-50.1 2-day avg (range): 15-53.4 3-day avg (range): 12.7-59.5
Diez-Roux (2006, 156400)	Chicago, IL Baltimore, MD Forsyth County, NC Los Angeles, CA New York City, NY St. Paul, MN	Prior day (median): 14.3 Prior 2 days (median): 14.4 Prior 7 days (median): 15.24 Prior 30 days (median): 15.69 Prior 60 days (median): 15.9	Prior day (75th): 20.9 Prior 2 days (75th): 20.35 Prior 7 days (75th): 19.7 Prior 30 days (75th): 19.22 Prior 60 days (75th): 19.08
Dubowsky (2006, 088750)	St. Louis (bus stops)	16	75th: 22 100th: 28
Folino (2009, 191902)	Padua, Italy	Summer: 33.9 Winter: 62.1 Spring: 30.8	NR
O'Neill (2007, 091362)	Boston, MA	11.4	Range: 0.07-33.7
Park (2008, 156845)	Boston, MA	12	Range: 2-62
Peters (2009, 191992)	Helsinki, Finland Stockholm, Sweden Augsburg, Germany Rome, Italy Barcelona, Spain	Helsinki: 8.2 Stockholm: 8.8 Augsburg: 17.4 Rome: 24.5 Barcelona: 24.2 Total: 16.4	Helsinki (range): 1-28 Stockholm (range): 0-27 Augsburg (range): 6-39 Rome (range): 4-95 Barcelona (range): 3-95 Total (range): 0-95

Author	Location	Mean Concentration (μg/m^3)	Upper Percentile Concentrations (μg/m^3)
Pope (2004, 055238)	Salt Lake City, Ogden, Provo Utah	FRM-Filled: 23.7 Not filled: 25.8 TEOM: 18.9 RAMS/PC-BOSS: 26.5	FRM-Filled (range): 1.7-74 Not filled (range): 1.7-74 TEOM (range): 2.2-61.5 RAMS/PC-BOSS (range): 5.6-72.4
Riediker (2004, 056992)	North Carolina State Troopers	Light Scatter: 24.1 Mass: 23 Ambient: 32.3 Roadside: 32.1	Light Scatter (range): 4.5-54.4 Mass (range): 7.1-38.7 Ambient (range): 9.9-68.9 Roadside (range): 8.9-62.2
Ruckerl (2007, 156931)	Helsinki, Finland Stockholm, Sweden Augsburg, Germany Rome, Italy Barcelona, Spain Athens, Greece	8.2 (19.4) 8.8 (19.1) 17.4 (29.3) 24.5 (54.1) 24.2 (64.7) 23 (46)	NR NR NR NR NR NR
Sørensen (2003, 157000)	Copenhagen, Denmark	Personal (median): 16.1 Urban background (median): 9.2	Personal (Q25-Q75): 10-24.5 Urban background (Q25-Q75): 5.3-14.8
Sullivan (2007, 100083)	Seattle, WA	Outdoor (median): 7.7 Indoor (median): 7.7	Outdoor: 75th- 11.5 90th- 19.9 Max- 33.9 Indoor: 75th- 12.1 90th- 16 Max- 81.4
Zeka (2006, 157177)	Boston, MA	48h (median): 9.39	75th: 14.57 90th: 21.48
$PM_{10-2.5}$			
Delfino (2008, 156390)	Los Angeles, CA	Outdoor: 10.04 (4.07) Indoor: 4.12 (4.76)	Outdoor (range): 1.76-22.38 Indoor (range): 0.12-37.63
Peters (2009, 191992)	Helsinki, Finland Stockholm, Sweden Augsburg, Germany Rome, Italy Barcelona, Spain	Helsinki: 8.9 Stockholm: 9 Augsburg: 15.8 Rome: 16.8 Barcelona: 16.5 Total: 13.3	Helsinki (range): 1-38 Stockholm (range): 0-40 Augsburg (range): -1 to 35 Rome (range): -33 to 65 Barcelona (range): 1-102 Total (range): -33 to 102
PM_{10}			
Baccarelli (2007, 090733)	Lombardia Region, Italy	Sep-Nov (median): 51.2 Dec-Feb (median): 68.5 Mar-May (median): 64.1 Jun-Aug (median): 44.3	Sep-Nov (max): 148.9 Dec-Feb (max): 238.3 Mar-May (max): 158.5 Jun-Aug (max): 94.7
Baccarelli (2007, 091310)	Lombardia Region, Italy	Median: 34.1	Maximum: 390
Chuang (2007, 091063)	Taipei, Taiwan	1-day avg: 49.2 2-day avg: 55.3 3-day avg: 54.9	1-day avg (range): 29.5-83.4 2-day avg (range): 25.5-85.1 3-day avg (range): 22.2-87.2

Author	Location	Mean Concentration (μg/m^3)	Upper Percentile Concentrations (μg/m^3)
Folino (2009, 191902)	Padua, Italy	Summer: 46.4 Winter: 73 Spring: 38.3	NR
Kelishadi (2009, 191960)	Isfahan, Iran	122.08	75th: 153 100th: 191
Liao (2005, 088677)	Washington County, MD Forsyth County, NC Minneapolis, MN (suburbs)	29.9	Q4: 47.3
Liu (2007, 156705)	Windsor, Ontario, Canada	Personal (median): 0-24 h before clinical visit: 25.5 0-6 h before clinical visit: 15.3 7-12 h before clinical visit: 17 13-18 h before clinical visit: 28.5 19-24 h before clinical visit: 30.5	Personal (5th to 95th): 0-24 h before clinical visit: 9.8-133 0-6 h before clinical visit: 5.3-83.2 7-12 h before clinical visit: 7.1-186.3 13-18 h before clinical visit: 11.4-167 19-24 h before clinical visit: 10.1-148.2
Peters (2009, 191992)	Helsinki, Finland Stockholm, Sweden Augsburg, Germany Rome, Italy Barcelona, Spain	Helsinki: 17.1 Stockholm: 17.8 Augsburg: 33.1 Rome: 42.1 Barcelona: 40.7 Total: 30.3	Helsinki (range): 4-53 Stockholm (range): 0-57 Augsburg (range): 7-71 Rome (range): 15-91 Barcelona (range): 6-194 Total (range): 0-194
Ruckerl (2007, 156931)	Helsinki, Finland Stockholm, Sweden Augsburg, Germany Rome, Italy Barcelona, Spain Athens, Greece	17.1 17.8 33.1 42.1 40.7 38.5	NR NR NR NR NR NR
Steinvil (2008, 188893)	Tel Aviv, Israel	64.5	75th: 60.7

6.2.7.2. Controlled Human Exposure Studies

Several controlled human exposure studies were included in the 2004 PM AQCD (U.S. EPA, 2004, 056905) which evaluated markers of systemic inflammation following exposure to PM. Salvi et al. (1999, 058637) exposed 15 healthy volunteers (21-28 yr) for 1 h to DE (300 μg/m^3 particle concentration) and observed a significant increase in neutrophils in peripheral blood 6 h post-exposure compared with filtered air control. However, Ghio et al. (2003, 087363) reported no changes in plasma cytokine levels (e.g., IL-6 and TNF-α), WBC count, or CRP 0 or 24 h following a 2-h exposure to $PM_{2.5}$ CAPs (120 μg/m^3). Gong et al. (2003, 042106) did not observe any effect of $PM_{2.5}$ CAPs (174 μg/m^3) on serum amyloid A, while Frampton (2001, 019051) reported no change in leukocyte activation following exposure to a low concentration (10 μg/m^3) of UF carbon. The results of studies published since the completion of the 2004 PM AQCD (U.S. EPA, 2004, 056905) are discussed below.

CAPs

Several controlled human exposure studies have reported no change in plasma CRP levels 0-24 h after exposure to UF (avg concentration 50-100 μg/m^3), $PM_{2.5}$ (avg concentration 190 μg/m^3), or $PM_{10-2.5}$ (avg concentration 89 μg/m^3) CAPs (Gong et al., 2008, 156483; Graff et al., 2009, 191981; Mills et al., 2008, 156766; Samet et al., 2009, 191913). In a study of exposures to $PM_{2.5}$ CAPs (200 μg/m^3), Gong et al. (2004, 087964) observed increased peripheral basophils 4 h following a 2-h exposure in a group of healthy older adults, which provides limited evidence of a CAPs-induced systemic inflammatory response.

Urban Traffic Particles

In a recent investigation of controlled exposures (24 h) to urban traffic particles, Bräuner et al. (2008, 191966) observed no effect of PM concentration (avg $PM_{2.5}$ concentration 10.5 μg/m^3) on markers of inflammation including CRP, IL-6 and TNF- α in peripheral venous blood.

Diesel Exhaust

Recent controlled human exposure studies have observed no effect of DE on plasma CRP concentrations or peripheral blood cell counts (Blomberg et al., 2005, 191991; Carlsten et al., 2007, 155714; Mills et al., 2005, 095757; Mills et al., 2007, 091206; Tornqvist et al., 2007, 091279). Mills et al. (2005, 095757) found no effect of DE (300 μg/m^3) on serum IL-6 or TNF-α among healthy adult volunteers 6 h after exposure. However, as reported by Tornqvist et al. (2007, 091279), a significant increase in these cytokines was observed 24 h after exposure. Although the physiological significance of this finding is unclear, this study does provide evidence of a mild systemic inflammatory response induced by exposure to DE. In an effort to better understand the inflammatory response of exposure to PM, Peretz et al. (2007, 156853) conducted a pilot study in which gene expression in peripheral blood mononuclear cells (PBMCs) of healthy human volunteers was evaluated following a 2-h controlled exposure to DE (200 μg/m^3 $PM_{2.5}$). Adequate RNA samples for microarray analysis from both pre- and 4 h post-exposure to filtered air and DE were available in 4 of the 11 subjects enrolled. The authors found differential expression of 10 genes involved in the inflammatory response when comparing DE exposure (8 upregulated, 2 downregulated) to filtered air. Two participants had paired samples from 20 h post-exposure which were adequate for analysis. At this time point, DE was associated with 4 differentially expressed genes (1 upregulated, 3 downregulated). However, this study is limited by a small sample size with limited statistical power.

Wood Smoke

Barregard et al. (2006, 091381) recently reported an increase in serum amyloid A at 0, 3, and 20 h following a 4-h exposure to wood smoke ($PM_{2.5}$ concentrations of 240-280 μg/m^3) among a group of 13 healthy adults (20-56 yr).

Model Particles

Frampton et al. (2006, 088665) evaluated the effect of varying concentrations (10-50 μg/m^3) of UF EC on blood leukocyte expression of adhesion molecules in healthy and asthmatic adults. Healthy subjects (n = 40) were exposed for 2 h to filtered air and UF EC under three separate protocols: 10 μg/m^3 at rest (n = 12), 10 and 25 μg/m^3 with intermittent exercise (n = 12), and 50 μg/m^3 with intermittent exercise (n = 16). Asthmatics (n = 16) were exposed at a single concentration (10 μg/m^3) for 2 h with intermittent exercise. Leukocyte expression of surface markers were quantified using flow cytometry on peripheral venous blood samples collected prior to and immediately following exposure, as well as at 3.5 and 21 h post-exposure. Among healthy resting adults, UF EC exposure at a concentration of 10 μg/m^3 had no effect on blood leukocytes. The expression of adhesion molecules CD54 and CD18 on monocytes, and CD18 on PMNs was shown

to decrease with UF EC exposure in healthy exercising adults. In exercising asthmatics, expression of CD11b on monocytes and eosinophils, as well as CD54 on PMNs were reduced following exposure to UF EC. In both asthmatics and healthy adults, a UF EC-induced decrease in eosinophils and basophils was observed 0-21 h following exposure. Although the clinical significance of these findings is unclear, the authors concluded that their findings of UF EC-induced changes in leukocyte distribution and expression were consistent with increased retention of leukocytes in the pulmonary vasculature, which may be due to an increase in pulmonary vasoconstriction. Other studies have reported no changes in plasma cytokine levels, peripheral blood counts, or CRP following exposure to ZnO or UF EC (Beckett et al., 2005, 156261; Routledge et al., 2006, 088674).

Summary of Controlled Human Exposure Study Findings for Systemic Inflammation

New studies involving controlled exposures to various particle types have provided limited and inconsistent evidence of a PM-induced increase in markers of systemic inflammation.

6.2.7.3. Toxicological Studies

There has been limited evidence that enhanced hematopoiesis may occur in animals exposed to PM. Two studies in the 2004 PM AQCD (U.S. EPA, 2004, 056905) provided support for this effect, with one study measured stimulated release of PMNs from bone marrow and another examined peripheral blood PMN and blood cell counts; however, one study did not find associations between CAPs and peripheral blood counts. Thus, it was concluded that consistent evidence of PM-induced hematopoiesis remained to be demonstrated. However, in a study of humans exposed to biomass burning during the 1997 Southeast Asian smoke-haze episodes, PM_{10} demonstrated the best relationship with blood PMN band cell counts expressed as a percentage of total PMN at lag 0 and 1, indicating a relatively quick response (Tan et al., 2000, 002304).

CAPs

A 2-day CAPs study employing SH rats did not report increased WBCs 18-20 h post-exposure (Kodavanti et al., 2005, 087946). A study utilizing fine and/or UF CAPs demonstrated decreased WBCs in SH rats 18 h after a 2-day (6 h/day) exposure (Kooter et al., 2006, 097547). The decrease was largely attributable to lowered neutrophils in the fine CAPs-exposed rats and reduced lymphocytes in the fine+UF CAPs-exposed animals.

Model Particles

In a study of fine and UF CB particles (WKY rats; 7 h; mean mass concentration 1,400 and 1,660 $\mu g/m^3$ for fine and UF CB, respectively; mean number concentration 3.8×10^3 and 5.2×10^4 particles/cm^3, respectively), only UF CB induced elevated blood leukocytes at 0 and 48 h post-exposure compared to the control rats and no effect was observed at 16 h (Gilmour et al., 2004, 054175). In another study of SH rats exposed to UF carbon particles for 24 h (mass concentration 172 $\mu g/m^3$; mean number concentration 9.0×10^6 particles/cm^3), the percent neutrophils and lymphocytes were increased on the first recovery day, but not the third day (Upadhyay et al., 2008, 159345); CRP was unchanged. In another study, blood neutrophils were decreased in SH rats exposed to UF CB for 6 h and no effects were observed in old F344 rats (Elder et al., 2004, 055642). Plasma IL-6 levels were unchanged (Elder et al., 2004, 055642).

Coal Fly Ash

Smith et al. (2006, 110864) examined the hematology parameters in SD rats following a 3-day inhalation exposure (4 h/day) to coal fly ash (mean mass concentration 1,400 $\mu g/m^3$) and reported increased blood neutrophils and reduced blood lymphocytes at 36 h but not 18 h post-exposure.

Intratracheal Instillation

Elevated systemic IL-6 and TNF-α levels were observed following PM_{10} instillation in mice (details provided in Section 6.2.8.3) (Mutlu et al., 2007, 121441). IL-6 was decreased with PM exposure in macrophage-depleted mice, indicating that some of the IL-6 release originated from macrophages. For mice (male C57Bl/6J) exposed to $PM_{10-2.5}$ derived from coal fly ash (200 μg), increased plasma IL-6 levels were only observed in animals that also received 100 μg of LPS (Finnerty et al., 2007, 156434) and this response was not observed with LPS alone, indicating a role for $PM_{10-2.5}$.

Summary of Toxicological Study Findings for Systemic Inflammation

Overall, these studies provide evidence of time-dependent responses of systemic inflammation induced by PM exposure. Alterations in WBCs have been reported generally as elevations immediately (0 h) or <36 h post-exposure and no change or reductions are noted from 18-24 h.

6.2.8. Hemostasis, Thrombosis and Coagulation Factors

The 2004 PM AQCD (U.S. EPA, 2004, 056905) presented limited and inconsistent evidence from epidemiologic, controlled human exposure, and toxicological studies of PM-induced changes in blood coagulation markers. The body of scientific literature investigating hemostatic effects of PM has grown significantly since the publication of the 2004 PM AQCD (U.S. EPA, 2004, 056905), with a limited number of epidemiologic studies demonstrating consistent increases in von Willebrand factor (vWf) associated with PM and less consistent associations with fibrinogen. Recent controlled human exposure and toxicological studies have also observed changes in blood coagulation markers (e.g., fibrinogen, vWf, factor VII, t-PA) following exposure to PM. However, the findings of these studies are somewhat inconsistent, which may be due in part to differences in the post-exposure timing of the assessment.

6.2.8.1. Epidemiologic Studies

Several studies investigating the association of short-term fluctuations in PM concentration with markers of coagulation (e.g., blood viscosity and fibrinogen) were included in the 2004 PM AQCD (U.S. EPA, 2004, 056905). These preliminary studies offered limited support for mechanistic explanations of the associations of PM concentration with heart disease outcomes. New studies, published since 2002, are reviewed in this section. Only vWF and fibrinogen were measured in enough comparable studies to allow the consistency of findings to be evaluated across epidemiologic studies. Other markers of coagulation studied included D-dimer, prothombin time, Factor VII/VIII and tPA.

Liao et al. (2005, 088677) used a cross-sectional study to examine the association between short-term increases in air pollutant concentrations (mean PM_{10}, NO_2, CO, SO_2, and O_3 over the previous 3 days) and several plasma hemostatic markers (fibrinogen, factor VIII-C, vWF, albumin). Study subjects were middle aged participants in the ARIC (Atherosclerosis Risk in Communities) study (n = 10,208), and were residents of Washington County, MD, Forsyth County, NC, selected suburbs of Minneapolis, MN, or Jackson, MS. Each 12.8 $\mu g/m^3$ increase in the mean PM_{10} concentration 1 day before the health measurements were made was associated with a 3.93% increase in vWF (95% CI: 0.40-7.46) among diabetics, but not among non-diabetics (-0.54% [95% CI: -1.68 to 0.60]). Each 12.8 $\mu g/m^3$ increase in the mean PM_{10} concentration 1 day before the health measurements were made was also associated with a 0.006 g/dL decrease in serum albumin (95% CI: -0.012 to 0.000) among those with cardiovascular disease (CVD), but not among those without CVD (0.029 g/dL increase [95% CI: -0.004 to 0.062]). The mean CO concentration on the previous day was also associated with a significant decrease in serum albumin. The authors reported significant curvilinear associations between PM_{10} and factor VIII-C, which may indicate a threshold effect. Similar curvilinear associations were observed between O_3 with fibrinogen, and vWF, and SO_2 with factor VIII-C, WBC, and serum albumin (Liao et al., 2005, 088677). No significant associations with fibrinogen and PM10 or gaseous pollutants were observed.

In the European multicity study described in Section 6.2.7.1, Ruckerl et al. (2007, 156931) found that each 13.5 μg/m^3 increase in the mean PM_{10} concentration over the previous 5 days was associated with a 0.6% increase in the arithmetic mean fibrinogen level (95% CI: 0.1-1.1). Further these investigators found that promoter polymorphisms within FGA and FGB modified the association of 5-day avg PM_{10} concentration with plasma fibrinogen levels (Peters et al., 2009, 191992). This association was 8-fold higher among those homozygous for the minor allele genotype of FGB rs1800790 compared with those homozygous for the major allele.

Several smaller studies have been conducted in the U.S. and Canada. Delfino et al. (2008, 156390) measured fibrinogen and D-dimer in blood of subjects who resided at two downtown Los Angeles nursing homes. As described in Section 6.2.7.1, measurements were made over a period of 12 wk and subjects were >65 yr old with a history of coronary artery disease. These markers were not associated with the broad array PM metrics studied (e.g., $PM_{0.25}$, $PM_{0.25-2.5}$, $PM_{10-2.5}$, EC, OC, primary OC, BC). In the study of 92 Boston residents with type 2 diabetes described previously, O'Neill et al. (2007, 091362) found that increases in mean $PM_{2.5}$ and BC concentration were associated with vWF concentrations for all moving averages examined (1-6 days). Reidiker et al. (2004, 056992) reported that in-vehicle $PM_{2.5}$ was associated with increased vWF over the next 10-14 h among nine police troopers. Sullivan et al. (2007, 100083) did not observe associations with fibrinogen, or D-dimer in individuals with or without COPD. Red blood cells (RBCs), platelets, nor blood viscosity were associated with $PM_{2.5}$ concentration in a panel study of 88 non-smoking elderly subjects residing in the Salt Lake City, Ogden and Provo metropolitan area of Utah (Pope et al., 2004, 055238). Although Zeka et al. (2006, 157177) did not observe an association with CRP in the analysis of the Normative Aging Study population in Boston (Section 6.3.7.1), increased fibrinogen level was associated with increases in the number of particles/cm^3 over the previous 48 h and 1 wk, and an incremental increase in BC concentration over the previous 4 wk. There were no consistent findings for lagged $PM_{2.5}$ or sulfates (Zeka et al., 2006, 157177).

Several studies of coagulation markers were conducted outside the U.S. and Canada. In a study of healthy individuals in Taiwan, associations were observed for $PM_{2.5}$, PM_{10}, nitrate, and SO_4^{2-} concentrations with fibrinogen and plasminogen activator fibrinogen inhibitor-1 (PAI-1) (Chuang et al., 2007, 091063). In a large cross-sectional study of healthy subjects in Tel-Aviv, Steinvil et al. (2008, 188893) examined fibrinogen collected as part of routine health examinations for 3,659 individuals. No significant associations were found between pollutant levels (lagged 1-7 days) and fibrinogen. Finally, Baccarelli and colleagues reported associations between PM_{10} and prothrombin time among normal subjects (Baccarelli et al., 2007, 090733).

Summary of Epidemiologic Study Findings for Hemostasis, Thrombosis and Coagulation

The most commonly measured markers of coagulation in the studies reviewed were fibrinogen and vWF. Associations of PM_{10} (Liao et al., 2005, 088677) and $PM_{2.5}$ (O'Neill et al., 2007, 091362; Riediker et al., 2004, 056992) with increased vWF were observed across the limited number of studies examining this association among both diabetics and healthy state troopers state troopers (Liao et al., 2005, 088677; Riediker et al., 2004, 056992). Results for fibrinogen were not consistent across epidemiologic studies. Positive associations with fibrinogen were reported in older adults residing in Boston (Zeka et al., 2006, 157177) and in the multicity European study of MI survivors. Liao et al. (2005, 088677) in a population based multicity study and Sullivan et al. (2007, 100083) did not observe associations of PM_{10} or $PM_{2.5}$ with fibrinogen. Several other markers have been examined (e.g., D-dimer, prothrombin time), but not in adequate numbers of studies to allow comparisons across epidemiologic studies. Mean and upper percentile concentrations of the studies discussed in this section are listed in Table 6-6.

6.2.8.2. Controlled Human Exposure Studies

In two separate studies conducted by Ghio and colleagues, controlled exposures (2 h) to fine CAPs (Chapel Hill, NC) at concentrations between 15 and 350 μg/m^3 were shown to increase blood fibrinogen 18-24 h following exposure among healthy adults (Ghio et al., 2000, 012140; Ghio et al., 2003, 087363). Increases in blood fibrinogen or factor VII would suggest an increase in blood coagulability, which could result in an increased risk of coronary thrombosis. However, a similar

study conducted in Los Angeles observed a $PM_{2.5}$ CAPs-induced decrease in factor VII blood levels in healthy subjects and found no association between $PM_{2.5}$ CAPs and blood fibrinogen among healthy and asthmatic volunteers (Gong et al., 2003, 042106). Since the publication of the 2004 PM AQCD (U.S. EPA, 2004, 056905), several new controlled human exposure studies have evaluated the effects of PM on blood coagulation markers.

CAPs

Two studies of controlled human exposures to Los Angeles CAPs among older adults with COPD ($PM_{2.5}$ CAPs) and adults with and without asthma (UF CAPs) reported no significant association between exposure and blood coagulation markers at 0, 4, or 22 h post-exposure (Gong et al., 2004, 087964; 2008, 156483). Graff et al. (2009, 191981) observed a decrease in the concentration of D-dimer of marginal statistical significance in healthy adults (11.3% decrease per 10 $\mu g/m^3$, $p = 0.07$) following exposure to $PM_{10-2.5}$ CAPs (89 $\mu g/m^3$). At 20 h post-exposure, levels of tPA in plasma were shown to decrease by 32.9% from baseline per 10 $\mu g/m^3$ increase in CAPs concentration. No other markers of hemostasis or thrombosis were affected by exposure to $PM_{10-2.5}$ CAPs. However, in a similar study from the same laboratory, Samet et al. (2009, 191913) reported a statistically significant increase in D-dimer immediately following, as well as 18 h, after a 2-h exposure to UF CAPs (49.8 $\mu g/m^3$; 120,662 particles/cm^3) in a group of healthy adults (18-35 yr). Plasma concentrations of PAI-1 were also reported to increase 18 h after exposure to UF CAPs, although this increase was not statistically significant ($p = 0.1$). No changes in fibrinogen, tPA, vWF, plasminogen, or factor VII were observed. The finding of an increase in D-dimer following exposure to UF CAPs provides potentially important information in elucidating the relationship between elevated concentrations of PM and cardiovascular morbidity and mortality observed in epidemiologic studies. Whereas many coagulation markers provide evidence of an increased potential to form clots (e.g., an increase in fibrinogen or a decrease in tPA), D-dimer is a degradation product of a clot that has formed.

Urban Traffic Particles

In a study of controlled 24-h exposures to urban traffic particles (avg $PM_{2.5}$ concentration 10.5 $\mu g/m^3$) among 29 healthy adults, Bräuner et al. (2008, 191966) did not observe any particle-induced change in plasma fibrinogen, factor VII, or platelet count after 6 or 24 h of exposure. Similarly, Larsson et al. (2007, 091375) observed no change in PAI-1 or fibrinogen in peripheral blood of healthy adult volunteers 14 h after a 2-h exposure to road tunnel traffic with a $PM_{2.5}$ concentration of 46-81 $\mu g/m^3$.

Diesel Exhaust

Mills and colleagues have recently demonstrated a significant effect of DE (particle concentration 300 $\mu g/m^3$) on fibrinolytic function both in healthy men ($n = 30$) and in men with coronary heart disease ($n = 20$) (Mills et al., 2005, 095757; 2007, 091206). In both groups of volunteers, bradykinin-induced release of tPA was observed to decrease 6 h following exposure to DE compared to filtered air exposure. The same laboratory did not observe an attenuation of tPA release 24 h after a 1-h exposure to DE (300 $\mu g/m^3$) in a group of health adults (Tornqvist et al., 2007, 091279), or observe any change in markers of hemostasis or thrombosis 6 or 24 h following DE exposure at the same particle concentration among a group of older adults with COPD (Blomberg et al., 2005, 191991). Carlsten et al. (2007, 155714) conducted a similar study involving exposure of healthy adults to DE with a $PM_{2.5}$ concentration of 200 $\mu g/m^3$. Although the authors observed an increase in D-dimer, vWF, and platelet count 6 h following exposure to DE, these increases did not reach statistical significance. In a subsequent study with a similar study design, the same laboratory found no effect of a 2-h exposure to DE (100 and 200 $\mu g/m^3$ $PM_{2.5}$) on prothrombotic markers in a group ($n = 16$) of adults with metabolic syndrome (Carlsten et al., 2008, 156323). The authors postulated that the lack of significant findings could be due to a relatively small sample size. In addition, Carlsten et al. (2007, 155714; 2008, 156323) exposed subjects at rest

while Mills et al. (2005, 095757) exposed subjects to a higher concentration (300 μg/m^3) with intermittent exercise. A more recent study of DE which exposed healthy adults to a slightly higher particle concentration (330 μg/m^3) evaluated the effect of DE on thrombus formation using an ex vivo perfusion chamber (Lucking et al., 2008, 191993). Thrombus formation, as well as in vivo platelet activation, was observed to significantly increase 2 h following exposure to DE relative to filtered air, thus providing some evidence of a potential physiological mechanism which may explain in part the associations between PM and cardiovascular events observed in epidemiologic studies.

Wood Smoke

Barregard et al. (2006, 091381) recently evaluated the effect of wood smoke on markers of coagulation, inflammation, and lipid peroxidation. Subjects (n = 13) were healthy males and females (20-56 yr) and were exposed for 4 h to $PM_{2.5}$ concentrations of 240-280 μg/m^3. The authors reported an increase in the ratio of factor VIII/vWF, which is an indicator of an increased risk of venous thromboembolism, at 0, 3, and 20 h following exposure to wood smoke.

Model Particles

Routledge et al. (2006, 088674) did not observe any changes in fibrinogen or D-dimer following a 1-h exposure to UF carbon among a group of resting healthy older adults and older adults with stable angina. Similarly, Beckett et al. (2005, 156261) found no changes in hemostatic markers (e.g., factor VII, fibrinogen, and vWF) following exposure to UF and fine ZnO (500 μg/m^3).

Summary of Controlled Human Exposure Study Findings for Hemostasis, Thrombosis and Coagulation

Taken together, these new studies have provided some additional evidence that short-term exposure to PM at near ambient levels may have small, yet statistically significant effects on hemostatic markers in healthy subjects or patients with coronary artery disease.

6.2.8.3. Toxicological Studies

In general, the limited toxicological studies reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905) reported positive and negative findings for plasma fibrinogen levels or other factors involved in the coagulation cascade. Rats exposed to New York City CAPs did not have any exposure-related effects on any measured coagulation markers (Nadziejko et al., 2002, 050587), whereas rats exposed to a high concentration of ROFA demonstrated increased plasma fibrinogen (Kodavanti et al., 2002, 025236).

CAPs

A $PM_{2.5}$ CAPs exposure conducted for 2 days (4 h/day; mean mass concentration 144-2,758 μg/m^3; 8-10/2001; RTP, NC) in SH rats induced plasma fibrinogen increases (measured 18-20 h post-exposure) in 5 of 7 separate studies (Kodavanti et al., 2005, 087946). Fibrinogen was not different from the air control group on the two days with the highest CAPs concentrations (1,129 and 2,758 μg/m^3), indicating that the response was likely not attributable to mass alone.

In SH rats exposed to $PM_{2.5}$ CAPs for 6 h in one of three locations in the Netherlands (mean mass concentration range 270-2,400; 335-3,720; and 655-3,660 μg/m^3), plasma fibrinogen was increased 48 h post-exposure when all CAP-exposed animals were combined in the analysis (Cassee et al., 2005, 087962). In WKY rats pre-exposed to O_3 (8 h; 1,600 μg/m^3) and CAPs for 6 h, increases in RBCs, hemoglobin, and hematocrit were observed 2 days after CAPs exposure. For SH rats exposed to CAPs only, decreased mean corpuscular hemoglobin concentration were reported.

A similar study conducted by the same group (Kooter et al., 2006, 097547) reported no changes in plasma fibrinogen measured 18 h after a 2-day exposure (6 h/day) to $PM_{2.5}$ or $PM_{2.5}$+UF CAPs (mean mass concentration range 399.0-1,067.5 and 269.0-555.8 μg/m^3, respectively; 1/2003-4/2004). However, elevated vWF was observed in SH rats exposed to the highest concentration of $PM_{2.5}$ CAPs. Decreases in mean corpuscular volume (MCV), and elevations in mean platelet volume (MPV) and mean platelet component (MPC) were reported in SH rats 18 h following a 2-day exposure to $PM_{2.5}$+UF CAPs in a freeway tunnel.

Traffic-Related Particles

Plasma fibrinogen levels were elevated 18 h following a single 6-h exposure to on-road highway aerosols when groups of rats pretreated with saline or influenza virus were combined (i.e., there was a significant effect of particles) (Elder et al., 2004, 087354).

Model Particles

The coagulation effects of inhaled UF CB at a concentration of 150 μg/m^3 (number count not provided) for 6 h were evaluated 24 h post-exposure in two aged rat models (11-14 mo SH and 23 mo F344), some of which received LPS via intraperitoneal injection prior to particle exposure (Elder et al., 2004, 055642). LPS has been shown to induce the expression of molecules involved in coagulation, inflammation, oxidative stress, and the acute-phase response. In those animals only exposed to CB, SH rats demonstrated increased thrombin-anti-thrombin complexes (TAT) and decreased fibrinogen. For F344 rats, TAT complexes and fibrinogen were elevated only in those that received LPS and CB. Whole-blood viscosity was not altered in either rat strain with particle exposure.

In another study of SH rats exposed to UF carbon particles for 24 h (mass concentration 172 μg/m^3; mean number concentration 9.0×10^6 particles/cm^3), the number of RBCs and platelets and hematocrit percent, were unchanged 1 and 3 days following exposure (Upadhyay et al., 2008, 159345). Fibrinogen levels were similar in both air and UF carbon-exposed groups. However, mRNA expression of PAI-1 and TF in lung homogenates (but not in heart) was increased on recovery day 3 after exposure. A study of similar design that employed SH rats did not report any effect on plasma fibrinogen 4 or 24 h following UF carbon exposure (mass concentration 180 μg/m^3; mean number concentration 1.6×10^7 particles/cm^3) (Harder et al., 2005, 087371). Similarly, clotting factor VIIa and thrombomodulin, PAI-1, and tPA mRNA expression were not affected by UF carbon exposure at 24 h post-exposure.

Coal Fly Ash

One study that employed coal fly ash (mean mass concentration 1,400 μg/m^3; 4 h/day×3 days) demonstrated increases in hematocrit and MCV in SD rats at 36 h but not 16 h post-exposure (Smith et al., 2006, 110864).

Intratracheal Instillation

Mutlu et al. (2007, 121441) used a PM_{10} sample collected from Dusseldorf, Germany, in mice (C57BL/6) with and without the gene coding for IL-6. The authors report using a moderate IT instillation dose (10 μg/mouse; roughly equivalent to 400-500 μg/kg); the PM sample had previously been characterized as having significant Fe, Ni, and V content (Upadhyay et al., 2003, 097370). In C57BL/6 mice, the Dusseldorf PM shortened bleeding (32%), prothrombin (13%), and activated partial thromboplastin (16%) times and increased platelet count, fibrinogen, and Factors II, VIII, and X activities 24 h following exposure. The authors further demonstrated accelerated coagulation by a reduction in the left carotid artery occlusion time (experimentally-derived by direct application of $FeCl_3$). Additional experiments demonstrated that IL-6$^{-/-}$ or macrophage-depleted mice showed dramatically attenuated effects of PM_{10} on hemostatic indices, thrombin generation, and occlusion

time. In IL-$6^{-/-}$ mice, there was no change in total cell counts or differentials in BALF compared to the wild-type mice, despite the lack of IL-6. In contrast, the model of macrophage depletion had reduced levels of macrophages and IL-6 in BALF, following PM exposure. These studies suggest that instillation of Dusseldorf PM_{10} activates clotting through an alveolar macrophage-dependent release of IL-6; however, other factors may also be involved in the prothrombotic response (i.e., activation of neutrophils, other inflammatory cells, or alterations in the levels of other cytokines).

In a study employing $PM_{10-2.5}$ collected from six European locations with contrasting traffic profiles, fibrinogen increases were observed in SH rats exposed to 10 mg/kg via IT instillation at 24 h post-exposure and similar responses were observed with $PM_{2.5}$ (Gerlofs-Nijland et al., 2007, 097840). $PM_{10-2.5}$ and $PM_{2.5}$ samples from Prague or Barcelona administered intratracheally to SH rats (7 mg/kg) resulted in elevated plasma fibrinogen levels 24 h post-exposure compared to rats instilled with water (Gerlofs-Nijland et al., 2009, 190353). No changes were observed in vWF for whole particle suspensions, but Barcelona $PM_{10-2.5}$ organic extract induced greater levels of vWF than Barcelona $PM_{10-2.5}$.

Summary of Toxicological Study Findings for Hemostasis, Thrombosis and Coagulation

Increases in coagulation and thrombotic markers were observed in some studies of rats or mice exposed to PM. Plasma TAT complexes were increased in CB-exposed SH rats and shortened bleeding, prothrombin, and activated partial thromboplastin times were observed in mice exposed via IT instillation to PM_{10}. Furthermore, the latter study also reported increased levels of Factors II, VIII, and X activities in mice. Another study demonstrated increased vWF in response to $PM_{2.5}$ CAPs. As for plasma fibrinogen, these studies provide some evidence that increased levels are observed 18-48 h post-exposure to PM, although one study reported no change and another reported a decrease in this biomarker. Alterations in platelet measurements have also been observed with PM exposure, including increased platelet number, mean platelet volume, and mean platelet component. The toxicological results of RBC-related measurements are limited and inconsistent following PM exposure, which may be attributable to different exposure protocols, time of analysis, or rat strain.

6.2.9. Systemic and Cardiovascular Oxidative Stress

Very little information on systemic oxidative stress associated with PM was available for inclusion in the 2004 PM AQCD (U.S. EPA, 2004, 056905). However, recent epidemiologic studies have provided consistent evidence of PM-induced increases in markers of systemic oxidative stress including plasma thiobarbituric acid reactive substances (TBARS), CuZn-super oxide dismutase (SOD), 8-oxo-7-hydrodeoxyguanosine (8-oxodG), and total homocysteine. This is supported by a limited number of controlled human exposure studies that observed PM-induced increases in free-radical mediated lipid peroxidation, as well as upregulation of the DNA repair gene hOGG1. In addition, recent toxicological studies have demonstrated an increase in cardiovascular oxidative stress following PM exposure in rats.

6.2.9.1. Epidemiologic Studies

No studies of markers of oxidative stress were reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905). Since 2002, numerous studies have examined whether short-term increases in mean PM concentrations are associated with changes in systemic markers of oxidative stress.

In an analysis of the randomized trial of omega-3 fatty acid supplementation in Mexico City nursing home residents described previously (Section 6.2.1.1), Romieu et al. (2008, 156922) investigated the effect of this intervention on markers of systemic oxidative stress (Cu/Zn SOD activity, LPO in plasma and GSH in plasma). A significant decrease of Cu/Zn SOD was associated with a 10 $\mu g/m^3$ increase of $PM_{2.5}$ in both groups (Fish oil: $\beta = -0.17$ [SE = 0.05], $p = 0.002$; Soy oil: $\beta = -0.06$ [SE = 0.02], $p < 0.001$). A decrease in GSH was associated with a 10 $\mu g/m^3$ increase in $PM_{2.5}$ in the fish oil group ($\beta = -0.09$ [SE = 0.04], $p = 0.017$).

Two studies evaluated plasma homocysteine levels in relation to PM. Baccarelli et al. (2007, 091310) investigated fasting and post-methionine load total homocysteine (tHcy) among 1,213 normal subjects in Lombardia, Italy. Plasma homocysteine is a risk factor for CVD and a marker for oxidative stress. Among smokers, average PM_{10} level during the 24 h preceding the measurement was associated with 6.3% (95% CI: 1.3-11.6) and 4.9% (95% CI: 0.5-9.6) increases in fasting and post-methionine load tHcy, respectively. No associations were observed among non-smokers. Park et al. (2008, 156845) investigated the association of BC, OC, SO_4^{2-} and $PM_{2.5}$ with tHcy among 960 male participants of the Normative Aging Study. Effect modification by folate and vitamins B6 and B12 was also examined. BC and OC were associated with increases in tHcy and associations were more pronounced in those with lower plasma folate and vitamin B12.

In smaller studies with 25-50 healthy or diseased participants, several markers of oxidative stress have been associated with PM size fractions or components. These associations include TBARS with 24-h PM_{10} (Liu et al., 2006, 192002); Cu/Zn-SOD with several PM metrics (e.g., UF, $PM_{10-2.5}$, EC, OC, BC and PNC) (Delfino et al., 2008, 156390); $PM_{2.5}$, BC, V and Cr with plasma proteins (Sørensen et al., 2003, 157000); DNA damage assessed by 8-oxodG in lymphocytes (Sørensen et al., 2003, 157000), and 8-OHdG with sulfates (Chuang et al., 2007, 091063). In addition, a cross-sectional study of children (10-18 yr) in Iran showed an association of PM_{10} with oxidized LDL (oxLDL), malondialdehyde (MDA) and conjugated diene (CDE) (Kelishadi et al., 2009, 191960).

Summary of Epidemiologic Study Findings for Systemic and Cardiovascular Oxidative Stress

Oxidative stress responses measured by one or more markers (plasma tHcy, CuZn-SOD, TBARS, 8-oxodG, oxLDL and MDA) have been consistently observed (Baccarelli et al., 2007, 091310; Chuang et al., 2007, 091063; Delfino et al., 2008, 156390; Kelishadi et al., 2009, 191960; Liu et al., 2007, 156705; Romieu et al., 2008, 156922; Sørensen et al., 2003, 157000). In addition, a series of analyses examining the modification the PM-HRV association by genetic polymorphisms related to oxidative stress has provided insight into the possible mechanisms of CVD observed in association with PM concentrations (Section 6.2.1.1). Mean and upper percentile concentrations of the epidemiologic studies of systemic oxidative stress are included in Table 6-6.

6.2.9.2. Controlled Human Exposure Studies

Urban Traffic Particles

Bräuner et al. (2007, 091152) recently investigated the effect of urban traffic particles on oxidative stress-induced damage to DNA. Healthy adults (20-40 yr) were exposed to low concentrations of urban traffic particles as well as filtered air for periods of 24 h, with and without two 90-min periods of exercise. Exposures took place in an exposure chamber above a busy road with high traffic density in Copenhagen. Non-filtered air was pumped into the chamber from above the street, with avg $PM_{2.5}$ and $PM_{10-2.5}$ mass concentrations of 9.7 $\mu g/m^3$ and 12.6 $\mu g/m^3$, respectively. The UF/$PM_{2.5}$ (6-700 nm) particle number concentration was continuously monitored throughout the exposure (avg PNC 10,067 particles/cm^3). The $PM_{2.5}$ fraction was rich in sulfur, V, Cr, Fe, and Cu. PBMCs were isolated from blood samples collected at 6 and 24 h. DNA damage, as measured by strand breaks (SB) and formamidopyrimidine-DNA glycosylase (FPG) sites, was evaluated using the Comet assay. The activity and mRNA levels of the DNA repair enzyme 7,8-dihydro-8-oxoguanine-DNA glycosylase (OGG1) were also measured. The authors observed increased levels of DNA strand breaks and FPG sites following 6 and 24 h of exposure to PM. Using a mixed-effects regression model, the particle concentration at the 57 nm mode was found to be the major contributor of these measures of DNA damage. The results of this study suggest that short-term (6-24 h) exposure to ambient levels of UFPs cause systemic oxidative stress resulting in damage to DNA.

Diesel Exhaust

Tornqvist et al. (2007, 091279) reported an increase in plasma antioxidant capacity in a group of healthy volunteers 24 h after a 1-h exposure to DE with a particle concentration of 300 μg/m^3. The investigators suggested that systemic oxidative stress occurring following exposure may have caused this up-regulation in antioxidant defense. Peretz et al. (2007, 156853) observed some significant differences in expression of genes involved in oxidative stress pathways between exposure to DE (200 μg/m^3 $PM_{2.5}$) and filtered air. However, the conclusions of this investigation are limited by a small number of subjects (n = 4).

Wood Smoke

In a controlled human exposure study of controlled exposure to wood smoke, Barregard et al. (2006, 091381) found an increase in urinary excretion of free 8-iso-prostaglandin2α among healthy adults (n = 9) approximately 20 h following a 4-h exposure to $PM_{2.5}$ (mass concentration of 240-280 μg/m^3). This finding provides evidence of a PM-induced increase in free-radical mediated lipid peroxidation. From the same study, Danielsen et al. (2008, 156382) reported an increase in the mRNA levels of the DNA repair gene hOGG1 in peripheral mononuclear cells 20 h after exposure to wood smoke relative to filtered air.

Summary of Controlled Human Exposure Study Findings for Systemic and Cardiovascular Oxidative Stress

Based on the results of these studies, it appears that exposure to PM at or near ambient levels may increase systemic oxidative stress in human subjects.

6.2.9.3. Toxicological Studies

Very little information was available for inclusion in the 2004 PM AQCD (U.S. EPA, 2004, 056905) on oxidative stress in the cardiovascular system. A few new studies have evaluated ROS in blood or the heart following PM exposure. Some studies have used chemiluminescence (CL), which is measured using the decay of excited states of molecular oxygen, and may also be prone to artifact.

CAPs

Gurgueira et al. (2002, 036535) measured oxidative stress in SD rats immediately following a 5-h CAPs exposure ($PM_{2.5}$ mean mass concentration 99.6-957.5 μg/m^3; Boston, MA; 7/2000-2/2001) and reported increased in situ CL in hearts of CAPs-exposed animals. CL evaluated after 1- and 3-h CAPs exposure did not demonstrate changes from the filtered air group, although a 5-h exposure resulted in increased CL in hearts. When animals were allowed to recover for 24 h, oxidative stress returned to control values. To compare potential particle-induced differences in CL, rats were exposed to ROFA (1.7 mg/m^3 for 30 min) or CB (170 μg/m^3 for 5 h) and only the ROFA-treated animals exhibited increased CL in cardiac tissue. Additionally, levels of antioxidant enzymes in the heart (Cu/Zn-SOD and MnSOD) were increased in CAPs-exposed rats. Individual PM component concentrations were linked to CL levels in rat heart tissue using separate univariate linear regression models, with total PM mass, Al, Si, Ti, and Fe having p-values ≤ 0.007 (Gurgueira et al., 2002, 036535). The highest R^2 value in the regression analyses was for Al (0.67) and its concentration ranged from 0.000 to 8.938 μg/m^3.

Recently, Rhoden et al. (2005, 087878) tested the role of the ANS in driving CAPs-induced cardiac oxidative stress in heart tissues of SD rats. At $PM_{2.5}$ mass concentrations of 700 μg/m^3 (Boston, MA), pretreatment with an antioxidant, a β_1-receptor antagonist, or a muscarinic receptor antagonist attenuated the CL and TBARS effects observed in the heart following a 5-h $PM_{2.5}$ exposure. The wet/dry ratio (edema) of cardiac tissue also returned to control values in animals treated with the antioxidant prior to CAPs. These combined results indicate involvement of both the

sympathetic and parasympathetic pathways in the cardiac oxidative stress response observed following PM exposure.

More recently, a type of irritant receptor, the transient receptor potential vanilloid receptor 1 (TRPV1), was identified as central to the inhaled CAPS-mediated induction of cardiac tissue CL and TBARS in SD rats (Ghelfi et al., 2008, 156468). In these studies ($PM_{2.5}$ mean mass concentration 218 $\mu g/m^3$; Boston, MA), capsazapine (a TRPV1 inhibitor) abrogated cardiac CL, TBARS, edema, and QT-interval shortening when measured at the end of the 5-h exposure. These studies provide some evidence that the ANS may be involved in producing cardiac oxidative stress following exposure to CAPs. Furthermore, this response could be acting, at least in part, via TRPV receptors.

In WKY rats exposed to $PM_{2.5}$ CAPs in Japan, relative mRNA expression of HO-1 was increased in cardiac tissue and was also significantly correlated with the cumulative mass of PM collected on chamber filters throughout the exposure (Ito et al., 2008, 096823).

Road Dust

A composite of $PM_{2.5}$ road dust samples obtained from New York City, Los Angeles, and Atlanta induced cardiac ROS as measured by CL in the low exposure group (306 $\mu g/m^3$) and TBARS in the high exposure group (954 $\mu g/m^3$); thus, the CL and TBARS methods provided different results for the various source types (Seagrave et al., 2008, 191990).

Gasoline and Diesel Exhaust

Gasoline exhaust exposure also resulted in increased ROS (measured by TBARS) in aortas of $ApoE^{-/-}$ mice, as discussed in Section 6.2.4.3 (Lund et al., 2009, 180257). Similarly, a 6-h exposure to gasoline exhaust (PM mass concentration 60 $\mu g/m^3$, CMD 15-20 nm; MMD 150 nm; CO concentration 104 ppm, NO concentration 16.7 ppm, NO_2 concentration 1.1 ppm, SO_2 concentration 1.0 ppm) in SD rats demonstrated increased CL in the heart, but no change in TBARS and the CL response was not duplicated when the particles were filtered (Seagrave et al., 2008, 191990). Increased lipid peroxides in the serum of male SH rats exposed to gasoline exhaust (PM mass concentration 59.1 $\mu g/m^3$; NO concentration 18.4 ppm; NO_2 concentration 0.9 ppm; CO concentration 107.3 ppm; SO_2 concentration 0.62 ppm) was observed following a 1-wk exposure to gasoline exhaust and this effect was attenuated with particle filtration (Reed et al., 2008, 156903). An IT instillation study of diesel particles in mice demonstrated increased myocardial MPO activity 12 and 24 h post-exposure to the residual particle component that remained after extraction with dichloromethane (Yokota et al., 2008, 190109).

Model Particles

Other studies previously presented also demonstrated ROS (via CL) and NT expression (via ELISA) in the left ventricle with CB exposure (Tankersley et al., 2008, 157043) and oxidative stress in the systemic microvasculature following TiO_2 inhalation (Nurkiewicz et al., 2009, 191961) or ROFA IT instillation exposure (Nurkiewicz et al., 2006, 088611). Decreased HO-1 mRNA expression in hearts of SH rats exposed to UF carbon particles was observed 3 days following exposure (Upadhyay et al., 2008, 159345) and there was a trend toward increased HO-1 mRNA expression 1 day post-exposure.

Summary of Toxicological Study Findings for Systemic and Cardiovascular Oxidative Stress

When considered together, the above studies provide evidence that PM exposure results in oxidative stress as measured in cardiac tissue by CL, TBARS, HO-1 mRNA expression, and NT expression. However, the PM concentration/dose and method of ROS measurement could also affect the response. Cardiac oxidative stress may have resulted from PM stimulation of the ANS, although these studies have only been conducted in one laboratory. Multiple studies from two different

laboratories provide support for vascular oxidative stress as demonstrated in aortas following gasoline exhaust exposure and in the microvasculature after TiO_2 inhalation or ROFA IT exposure.

6.2.10. Hospital Admissions and Emergency Department Visits

The 1996 PM AQCD (U.S. EPA, 1996, 079380) considered just two time-series studies regarding the association between daily variations in PM levels and the risk of CVD morbidity as measured by the number of daily hospitalizations with primary discharge diagnoses related to CVD (Burnett et al., 1995, 077226; Schwartz and Morris, 1995, 046186). In contrast, the 2004 PM AQCD (U.S. EPA, 2004, 056905) reviewed more than 25 publications relating PM and risk of CVD hospitalizations. Results from a handful of larger multicity studies were emphasized, with the greatest emphasis placed on findings from the U.S. National Morbidity, Mortality, and Air Pollution Study (NMMAPS) (Samet et al., 2000, 010269) and a subsequent reanalysis (Zanobetti and Schwartz, 2003, 157174). The NMMAPS study evaluated the effect of daily changes in ambient PM levels on total CVD hospitalizations among elderly Medicare beneficiaries in 14 U.S. cities and found a ~1% excess risk per 10 $\mu g/m^3$ increase in PM_{10}. The 2004 PM AQCD concluded that these results, along with those of the other single- and multicity studies reviewed "generally appear to confirm likely excess risk of CVD-related hospital admissions for U.S. cities in the range of [0.6-1.7% per 10 $\mu g/m^3$] PM_{10}, especially among the elderly" (U.S. EPA, 2004, 056905). The 2004 PM AQCD (U.S. EPA, 2004, 056905) also concluded that there was some evidence from single-city studies suggesting an excess risk specifically for hospitalizations related to IHD and heart failure. Furthermore, the 2004 PM AQCD (U.S. EPA, 2004, 056905) found that "insufficient data exist from the time-series CVD admissions studies […] to provide clear guidance as to which ambient PM components, defined on the basis of size or composition, determine ambient PM CVD effect potency" (U.S. EPA, 2004, 056905). The key studies reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905) on this topic included those by Burnett and colleagues (1997, 084194; 1999, 017269), Lippman and colleagues (2000, 011938), Ito (2003, 042856), and Peters et al. (2001, 016546).

Recent large studies conducted in the U.S., Europe, and Australia and New Zealand have confirmed these findings for PM_{10}, and have also observed consistent associations between $PM_{2.5}$ and cardiovascular hospitalizations. However, findings from single-city studies have demonstrated regional heterogeneity in effect estimates. It is apparent from these recent studies that the observed increases in cardiovascular hospitalizations are largely due to admissions for IHD and CHF rather than CBVDs (such as stroke). The new literature on hospitalizations and ED visits for cardiovascular causes published since 2002 is reviewed in the following sections. First, the specific CVD outcomes captured using ICD codes from hospital admissions databases are discussed. Second, the methods used in the large and multicity studies are described. For each outcome considered, evidence from large/multicity studies is emphasized and results from U.S. and Canadian single-city studies are also discussed. Although the single-city studies may lack statistical power needed to evaluate interactions and detect some of the subtle effects of air pollution, they inform the interpretation of the heterogeneous effect estimates that have been observed across North America.

Cardiovascular Disease ICD Codes

When the 2004 PM AQCD (U.S. EPA, 2004, 056905) was written, few studies had evaluated the link between ambient PM and specific CVD outcomes such as CHF, IHD or ischemic stroke. In contrast, the majority of recent studies have focused on specific CVD outcomes. This trend is justified by the fact that the short-term exposure effects of PM may be very different for different cardiovascular outcomes. For example, given the current putative biological pathways involved in the acute response to PM exposure, there is no *a priori* reason why short-term fluctuations in PM levels would have similar effects on the risk of acute MI, chronic atherosclerosis of the coronary arteries, and hemorrhagic stroke.

Almost all of the published time-series studies of cardiovascular hospitalizations and ED visits identified cases based on administrative discharge diagnosis codes as defined by the International Classification of Disease 9th revision (ICD-9) or 10th revision (ICD-10) (NCHS, 2007, 157194). A complicating factor in interpreting the results of these studies is the lack of consistency in both defining specific health outcomes and in the nomenclature used.

Table 6-7. Description of ICD-9 and ICD-10 codes for diseases of the circulatory system.

Description	ICD-9 Codes	ICD-10 Codes
All Cardiovascular Disease	390-459	I00-I99
IHD	410-414	I20-I25
Acute MI	410	I21
Diseases Of Pulmonary Circulation	415-417	I26-I28
CHF	428	I50
Arrhythmia	427	I47, I48, I49
CBVD	430-438	I60-I69
Ischemic Stroke And Transient Ischemic Attack (TIA)	430-432	I63
Hemorrhagic Stroke	433-435	I60-I62
Peripheral Vascular Disease (PVD)	440-448	I70-I79

Table 6-7 shows major groups of diagnostic codes used in air pollution studies for diseases of the circulatory system. The codes ICD-9: 390-459 are frequently used to identify all CVD morbidity. Note that this definition of CVD includes diseases of the heart and coronary circulation, CBVD, and peripheral vascular disease. In contrast, the term cardiac disease specifically excludes diseases not involving the heart or coronary circulation. While this distinction is conceptually straightforward, the implementation of the definition of cardiac disease in terms of ICD-9 or ICD-10 codes varies among authors. Even greater heterogeneity can be found among studies in the implementation of definitions related to CBVD.

Design and Methods of Large and Multicity Hospital Admission and ED Visit Studies

Recently, multiple research groups in the U.S., Europe, and Australia have created large datasets to evaluate specific CVD and respiratory endpoints using more detailed and relevant measures of PM concentration. In the U.S., the MCAPS analyses of Dominici et al. (2006, 088398), Bell et al. (2008, 156266) and Peng et al. (2008, 156850) are large, comprehensive and informative studies based on Medicare hospitalization data. Likewise, the Atlanta-based SOPHIA study (Metzger et al., 2004, 044222; Peel et al., 2005, 056305; Tolbert et al., 2007, 090316) is the largest and most comprehensive study of U.S. cardiovascular and respiratory ED visits. In Europe, the APHEA initiative (Le Tertre et al., 2002, 023746; Le Tertre et al., 2003, 042820) the more recent HEAPSS study (Von Klot et al., 2005, 088070), and the French PSAS program (Host et al., 2008, 155852; Larrieu et al., 2007, 093031) are similarly noteworthy for their large sample size, geographic diversity, and consideration of specific CVD and/or respiratory endpoints. These studies contain adequate data to examine interactions by season and region; the effects of different size fractions, components and sources of PM; or the effect of PM on susceptible populations. The following section provides a detailed review of the study design and methods used by each of the large studies. A discussion of the results of each study can be found later in Section 6.2.10.

MCAPS: Medicare Air Pollution Study

Dominici et al. (2006, 088398) created a database of daily time-series of hospital admission rates (1999-2002) for a range of cardiovascular and respiratory outcomes among Medicare beneficiaries aged ≥65 yr, ambient $PM_{2.5}$ levels, and meteorological variables for 204 U.S. urban counties. The specific CVD outcomes considered were: CBVD (ICD-9: 430-438), peripheral vascular disease (440-448), IHD (410-414, 429), heart rhythm disturbances (426, 427), and CHF

(428). Injuries (800-849) were evaluated as a control outcome. Gaseous and other particulate pollutant size fractions were not considered.

Data on $PM_{2.5}$ were obtained from the AQS database of the U.S. EPA. Within each county, associations between cause-specific hospitalization rates and same-day $PM_{2.5}$ levels were evaluated using Poisson regression models controlling for long-term temporal trends and meteorologic conditions with natural cubic splines. County-specific results were subsequently averaged using Bayesian hierarchical models. In addition to evaluating single-day lags, 3-day distributed lag models (lags 0, 1, and 2 days) were also considered in a subset of 90 U.S. counties with daily $PM_{2.5}$ data available during the study time period.

Subsequently, Peng et al. (2008, 156850) and Bell et al. (2008, 156266) extended the database of daily time-series of hospital admissions, $PM_{2.5}$, and other covariates for 202 U.S. counties through 2005. Importantly, Peng et al. (2008, 156850) added data on $PM_{10-2.5}$ to this database for 108 U.S. counties with one or more co-located $PM_{2.5}$ and PM_{10} monitors. Analyses with $PM_{10-2.5}$ were carried out using similar methods to those of Dominici et al. (2006, 088398). Peng et al. (2008, 156850) evaluated the robustness of $PM_{2.5}$ associations to adjustment for $PM_{10-2.5}$ (Peng et al., 2008, 156850). Gaseous pollutants were not considered in these analyses.

SOPHIA: Study of Particulates and Health in Atlanta

SOPHIA investigators (Metzger et al., 2004, 044222; Peel et al., 2005, 056305; Tolbert et al., 2000, 010320) compiled data on 4,407,535 ED visits between 1993 and 2000 to 31 hospitals in the Atlanta metropolitan statistical area (20 counties). Specific cardiovascular outcomes considered were: IHD (ICD-9: 410-414), acute MI (410), cardiac dysrhythmias (427), cardiac arrest (427.5), CHF (428), peripheral vascular and CBVD (433-437, 440, 443-444, 451-453), atherosclerosis (440), and stroke (436). Finger wounds (883.0) were evaluated as a control outcome.

The air quality data included measurements of criteria pollutants (PM and gaseous pollutants) for the entire study period, as well as detailed measurements of mass concentrations for $PM_{2.5}$ and $PM_{10-2.5}$ and several physical and chemical characteristics of $PM_{2.5}$ for the final 25 mo of the study using data from the ARIES monitoring station. Rates of ED visits for specific causes were assessed in relation to the 3-day ma (lags 0-2 days) of daily measures of air pollutants using Poisson generalized linear models (GLMs) controlling for long-term temporal trends and meteorologic conditions with cubic splines. Tolbert et al. (2007, 090316) published interim results of this study in relation to both cardiovascular and respiratory disease visits, Metzger et al. (2004, 044222) published the main results for CVD visits, and Peel et al. (2005, 056305) published the main results for respiratory conditions. An analysis of co-morbid conditions that may make individuals more susceptible to PM-related cardiovascular risk was carried out by Peel et al. (2007, 090442). Tolbert et al. (2007, 090316) extended the available data through 2002 and compared results from single and multipollutant models, while Sarnat et al. (2008, 097972) evaluated the risk of ED visits for cardiovascular and respiratory diseases in relation to specific sources of ambient PM using the extended dataset.

APHEA and APHEA-2: Air Pollution and Health: a European Approach

APHEA-2 investigators compiled daily data on cardiovascular (Le Tertre et al., 2002, 023746; 2003, 042820) and respiratory (Atkinson et al., 2001, 021959; 2003, 042797) disease hospital admissions in the following 8 European locations: Barcelona, Birmingham, London, Milan, the Netherlands (considered a "city" for this study, due to its small size and dense population), Paris, Rome, and Stockholm. (The publications on respiratory diseases were reviewed in the 2004 PM AQCD). The specific CVD outcomes considered in each city were: cardiac diseases (ICD-9: 390-429), IHD (410-413) and CBVDs (430-438). Routine registers in all cities provided daily data on hospitalizations. Only emergency hospitalizations were considered, except in Milan, Paris, and Rome where only general admissions data were available.

Ambient PM_{10} levels were available in all cities except Paris (PM_{13} used), and Milan and Rome (TSP used). Data on gaseous pollutants (NO_2, SO_2, CO, and O_3) were also available in most cities. Five of the eight cities provided data on black smoke (BS). The length of the available time-series varied by city but generally spanned from the early to mid-1990s.

Within each city, associations between cause-specific hospitalization rates and same-day $PM_{2.5}$ levels were evaluated using Poisson GAMs controlling for long-term temporal trends and meteorologic conditions. City-specific results were subsequently averaged using standard

meta-analytic methods. The original analyses (Atkinson et al., 2001, 021959; Le Tertre et al., 2002, 023746) were carried out using general additive models (GAM) and LOESS smoothers. Following reports of problems associated with using the default convergence criteria in the standard S-plus GAM procedure (Dominici et al., 2002, 030458), study authors reanalyzed the data on cardiac admissions using GAMs and stricter convergence criteria, and GLMs with natural splines and penalized splines (Atkinson et al., 2003, 042797; Le Tertre et al., 2003, 042820). The authors found that the results of the original analyses were insensitive to the choice of convergence criteria and that the use of GLMs with penalized splines yielded very similar results.

HEAPSS: Health Effects of Air Pollution among Susceptible Subpopulations

HEAPSS investigators collected data on patients hospitalized for a first MI in five European cities between 1992 and 2000. Patients were identified from MI registers in Augsburg and Barcelona, and from hospital discharge registers in Helsinki, Rome and Stockholm. Data on daily levels of PM_{10}, were measured at central monitoring sites in each city. Particle number concentration was measured for a year in each city and then modeled retrospectively for the whole study period. Associations of outcomes with gaseous criteria pollutants were also evaluated.

Von Klot et al. (2005, 088070) identified 22,006 survivors of a first MI in the five participating European cities and collected data on subsequent first cardiac re-hospitalizations between 1992 and 2001. Readmissions of interest were those with primary diagnoses of acute MI, angina pectoris, or cardiac disease (which additionally includes dysrhythmias and CHF). Within each city, associations between cause-specific hospitalization rates and same-day levels of PM_{10} were evaluated using Poisson GAMs controlling for long-term temporal trends and meteorologic conditions using penalized splines. City-specific results were combined using standard meta-analytic methods. Subsequently, Lanki et al. (2006, 089788) used HEAPSS data from 26,854 patients to evaluate the association between daily PM_{10} and particle number concentrations and the risk of hospitalization for first MI.

PSAS: The French National Program on Air Pollution Health Effects

Larrieu et al. (2007, 093031) evaluated the association between PM_{10} and the risk of hospitalization in eight French cities between 1998 and 2003. The cities examined were: Bordeaux, Le Havre, Lille, Lyon, Marseille, Paris, Rouen and Toulouse. The specific CVD outcomes considered in each city included: total CVD (ICD-10: I00-I99), cardiac disease (I00-I52), IHD (I20-I25) and stroke (I60-I64, G45-G46). The available data did not differentiate between emergency and non-emergency hospitalizations. Daily mean PM_{10} and NO_2 levels as well as 8-h max O_3 levels were obtained from a network of monitors in each city.

Within each city, associations between cause-specific hospitalization rates and 2-day ma (lag 0-1 days) levels of PM_{10} were evaluated using Poisson GAMs controlling for long-term temporal trends and meteorologic conditions using penalized splines. City-specific results were combined using standard meta-analytic methods. Host et al. (2008, 155852) used a subset of these data (6 cities, 2000-2003) to compare the effects of $PM_{2.5}$ and $PM_{10-2.5}$ on the risk of cardiovascular and respiratory admissions. CVD outcomes assessed in this analysis were all CVD (ICD-10 I00-I99), cardiac disease (I00-I52) and IHD (I20-I25). $PM_{2.5}$ levels were obtained from the same network of background monitors described above. $PM_{10-2.5}$ was calculated by subtracting $PM_{2.5}$ levels from PM_{10} levels. Gaseous pollutants and hospital admissions for stroke were not considered in this analysis.

Multicity Studies in Australia and New Zealand

Barnett et al. (2006, 089770) collected data on daily CVD emergency hospital admissions among older adults and pollution data between 1998 and 2001 in five Australian cities (Brisbane, Canberra, Melbourne, Perth, Sydney) and two cities in New Zealand (Auckland, Christchurch). In 2001, these cities covered 53% of the Australian population and 44% of the New Zealand population. The specific outcomes considered in each city were: all circulatory diseases (ICD-9 390-429, ICD-10 I00-I99 with exclusions); CHF (ICD-9 428, ICD-10 I50); arrhythmia (ICD-9 427 ICD-10 I46-49); cardiac disease (ICD-9 390-429, ICD-10 I00-I52, I97.0, I97.1, I98.1); IHD (ICD-9 410-413, ICD-10 I20-24, I25.2); acute MI (ICD-9 410, ICD-10 I21-22); and stroke (ICD-9 430-438, ICD-10 I60-66, I67, I68, I69, G45-46 with exclusions).

Air pollutants considered were 24-h avg PM_{10}, 24-h avg $PM_{2.5}$, BSP and gaseous pollutants. Within each city, associations between cause-specific hospitalization rates and 2-day ma (lags 0-1 days) of PM_{10} were evaluated using the time-stratified case-crossover approach which controls for long-term and seasonal time trends by design rather than analytically. City-specific results were combined using random effects meta-analytic methods.

EMECAS: Spanish Multicentric Study on the Relation between Air Pollution and Health

Ballester et al. (2006, 088746) collected data on daily cardiovascular emergency hospital admission and air pollution data between approximately 1995 and 1999 in 14 cities in Spain. The specific outcomes considered in each city were: total CVD (ICD-9: 390-459) and heart diseases (410-414, 427, 428). Air pollutants considered were PM_{10}, TSP, BS, SO_2, NO_2 (24-h avg), CO and O_3 (8-h max).

Within each city, associations between cause-specific hospitalization rates and daily levels of each pollutant metric were evaluated using Poisson GAMs with strict convergence criteria. In all models, pollutants were entered as linear continuous variables and included control for confounding by meteorological variables, influenza rates, long-term time trends, and unusual events. The authors considered both distributed lag models (lags 0-3 days) and the 2-day ma of pollution (lags 0-1 days). City-specific results were combined using standard meta-analytic methods.

6.2.10.1. All Cardiovascular Disease

The 2004 PM AQCD (U.S. EPA, 2004, 056905) incorporated the results of a large number of time-series studies in the U.S. and elsewhere relating ambient PM levels and risk of hospitalization for CVD. The 2004 PM AQCD (U.S. EPA, 2004, 056905) noted that the strongest evidence for this association came from the NMMAPS study (Samet et al., 2000, 010269) and the subsequent reanalysis by Zanobetti and Schwartz (2003, 157174).

Since then, the U.S. MCAPS study evaluated the association between $PM_{2.5}$ and risk of CVD hospitalization in 202 U.S. counties between 1999 and 2005 and found a 0.8% (95% posterior interval (PI): 0.6-1.0) increase in risk per 10 $\mu g/m^3$ increase in $PM_{2.5}$ on the same day (Bell et al., 2008, 156266; Peng et al., 2008, 156850). In 108 U.S. counties with co-located PM_{10} and $PM_{10-2.5}$ monitors, Peng et al. found a 0.4% (95% PI, 0.1- 0.7, lag 0) increase in risk per 10 $\mu g/m^3$ $PM_{10-2.5}$ and no associations at lags of 1 and 2 days (Peng et al., 2008, 156850). In a two-pollutant model adjusted for $PM_{2.5}$, the association between $PM_{10-2.5}$ and CVD hospitalization lost precision (0.3% [95% PI: −0.1 to 0.6, lag 0]). Bell et al. (2008, 156266) found evidence of substantial and statistically significant variability in the effects of $PM_{2.5}$ on cardiovascular hospitalizations by season and region, with the highest national average estimates occurring in the winter and the highest regional estimates in the northeastern U.S. (1.08% [95% PI: 0.79-1.37, lag 0, per 10 $\mu g/m^3$ increase in $PM_{2.5}$]). Estimates for the nation (1.49% [95% PI: 1.09-1.89, lag 0]) and northeast (2.01% [95% PI: 1.39-2.63, lag 0]) were highest in the winter.

Bell et al. (2009, 191997) and Peng et al. (2009, 191998) used data from the MCAPS study and the EPA's Speciation Trends Network (STN) to identify the components of $PM_{2.5}$ that are most strongly associated with hospitalizations for CVD. Peng et al. (2009, 191998) focused on the components that make up the majority of $PM_{2.5}$ mass (SO_4^{2-}, NO_3^-, Si, EC, OC, Na^+ and NH_4^+) and found that in multipollutant models, only EC and OC were significantly associated with risk of hospitalization for CVD. Bell et al. (2009, 191997) used data from 20 $PM_{2.5}$ components and found that EC, Ni, and V were most positively and significantly associated with the risk of cardiovascular hospitalizations. These results suggest that the observed associations between $PM_{2.5}$ and CVD hospitalizations may be primarily due to particles from oil combustion and traffic.

Additional evidence is provided by several large multicity studies conducted outside of the U.S. The European APHEA2 study (Le Tertre et al., 2002, 023746) looked at admissions for CVD among those aged ≥65 and found a 0.7% (95% CI: 0.4-1.0, lag 0-1 day avg) increase in risk per 10 $\mu g/m^3$ PM_{10}. The Spanish EMECAS study (Ballester et al., 2006, 088746) looked at admissions for CVD and found a 0.9% (95% CI: 0.4-1.5, lag 0-1 day avg) increase in risk per 10 $\mu g/m^3$ PM_{10}. The French PSAS program looked at CVD hospitalizations among the elderly and found a 1.9% (95% CI: 0.9-3.0, lag 0-1 day avg) increase in risk with a 10 $\mu g/m^3$ increase in $PM_{2.5}$ and a 1.1% (95% CI: 0.5-1.7) increase in risk with PM_{10} (Host et al., 2008, 155852; Larrieu et al., 2007, 093031). Non-significant increases in CVD hospital admissions association with $PM_{10-2.5}$ were

reported (1.0% [95% CI: -1.0 to 3.0]) (Host et al., 2008, 155852). In multiple cities across New Zealand and Australia, Barnett et al. (2006, 089770) found a 1.3% (95% CI: 0.6-2.0, lag 0-1 day avg) increase in risk per 10 $\mu g/m^3$ increase in $PM_{2.5}$.

The Atlanta-based SOPHIA study found a 3.3% (95% CI: 1.0-5.6, lag 0-2 day avg) and a 0.9% (95% CI: -0.2 to 1.9, lag 0-2 day avg) increase in risk with a 10 $\mu g/m^3$ increase in $PM_{2.5}$ and PM_{10}, respectively (Metzger et al., 2004, 044222). In a more recent analysis from this study with an additional four years of data, ED visits for CVD were not significantly associated with PM_{10} or $PM_{2.5}$, but were significantly associated with total carbon (1.6% [95% CI: 0.5-2.6, per IQR increase]), EC (1.5% [95% CI: 0.5-2.5, per IQR increase]) and OC (1.5% [95% CI: 0.5-2.6, per IQR increase]) components of $PM_{2.5}$ (2007, 090316). A weak non-significant association $PM_{10-2.5}$ was observed in these data (Tolbert et al., 2007, 090316) More recently, Sarnat et al. (2008, 097972) used multiple source-apportionment methods to evaluate the association between all CVD ED visits and specific $PM_{2.5}$ sources and found consistent positive associations with sources related to motor vehicles and biomass combustion. These results were insensitive to the source-apportionment technique used. It is noteworthy that other traffic-related gaseous pollutants were associated with CVD ED visits in the SOPHIA study (Metzger et al., 2004, 044222).

Using meta-regression techniques and the reported association between PM_{10} and CVD hospitalizations from the 14 cities included in the NMMAPS analysis, Janssen et al. (2002, 016743) examined whether the between-city variability in relative risk estimates were related to the local contribution of a number of PM sources. The authors found that in multivariate analyses PM_{10} coefficients increased significantly with increasing percentage of PM_{10} emissions from highway vehicles/diesels and oil combustion.

A small number of additional single-city studies have been published showing positive associations between hospital admissions and ambient PM in Copenhagen, Denmark (Andersen et al., 2007, 093201), weak nonsignificant associations in Spokane, WA (Schreuder et al., 2006, 097959; Slaughter et al., 2005, 073854), and no associations in two small counties in Idaho (Ulirsch et al., 2007, 091332). Schreuder et al. (2006, 097959) performed a source apportionment analysis using seven years of daily speciation data from the same residential monitor in Spokane, WA used by Slaughter et al. (2005, 073854). These authors related daily levels of four sources (wood smoke, an As-rich source, motor vehicle emissions, and airborne soil) to the excess risk of cardiovascular ED visits. During the heating season, the only notable association for CVD-related ED visits was with wood smoke, while in the non-heating season the only notable association was with airborne soil. While neither of these associations reached statistical significance, the study likely lacked the statistical power to find effects of the expected magnitude. In fact, it is doubtful that studies conducted outside of large metropolitan areas have sufficient statistical power to detect associations of the expected magnitude. Delfino et al. (2009, 191994) evaluated the effects of the 2003 California wildfires and observed a slightly larger excess risk of total CVD admissions during the wildfire period compared to the period prior to the wildfire, although excess risk estimates were generally weak and non-significant.

Studies in several cities in Australia have investigated the association of CVD admissions with PM concentration and sources. A study from Sydney, Australia found a 1.8% (95% CI: 0.4-3.2) and 0.3% (95% CI: -0.8 to 1.4) excess risk per 10 $\mu g/m^3$ increase in the 2-day ma (lags 0-1 days) in $PM_{2.5}$ and PM_{10}, respectively (Jalaludin et al., 2006, 189416). Johnston et al. (2007, 155882) and Hanigan et al. (2008, 156518) studied the association between PM_{10} and cardiovascular and respiratory hospitalizations in Darwin, Australia, where the predominant source of PM is from biomass combustion. The authors found little or no evidence of an association between PM_{10} and CVD hospital admissions in the general population.

Crustal material has also been investigated in an effort to explain associations of PM concentration with CVD admissions. Studies of a dust storm in the Gobi desert that transported PM across the Pacific Ocean reaching the western U.S. in the spring of 1998 have been conducted. An analysis of the health impacts of this event on the population of British Columbia's (Canada) Lower Fraser Valley found no excess risk of cardiac or respiratory hospital admissions despite hourly PM_{10} levels >100 $\mu g/m^3$ (Bennett et al., 2006, 088061). On the other hand, a number of studies in Asia and eastern Europe have reported associations between CVD hospital admissions and dust storm events. Middleton et al. (2008, 156760) found that dust storms in Cyprus were associated with a 4.7% (95% CI: 0.7-9.0) and 10.4% (95% CI: -4.7 to 27.9) increase in risk of hospitalization for all causes and CVD, respectively. Chan et al. (2008, 093297) studied the effects of Asian dust storms on cardiovascular hospital admissions in Taipei, Taiwan and also found significant adverse effects

during 39 Asian dust events with high PM_{10} levels (daily PM_{10} >90 µg/m^3). Bell et al. (2008, 091268) analyzed these data independently and concluded that Asian dust storms were positively associated with risk of hospitalization for IHD.

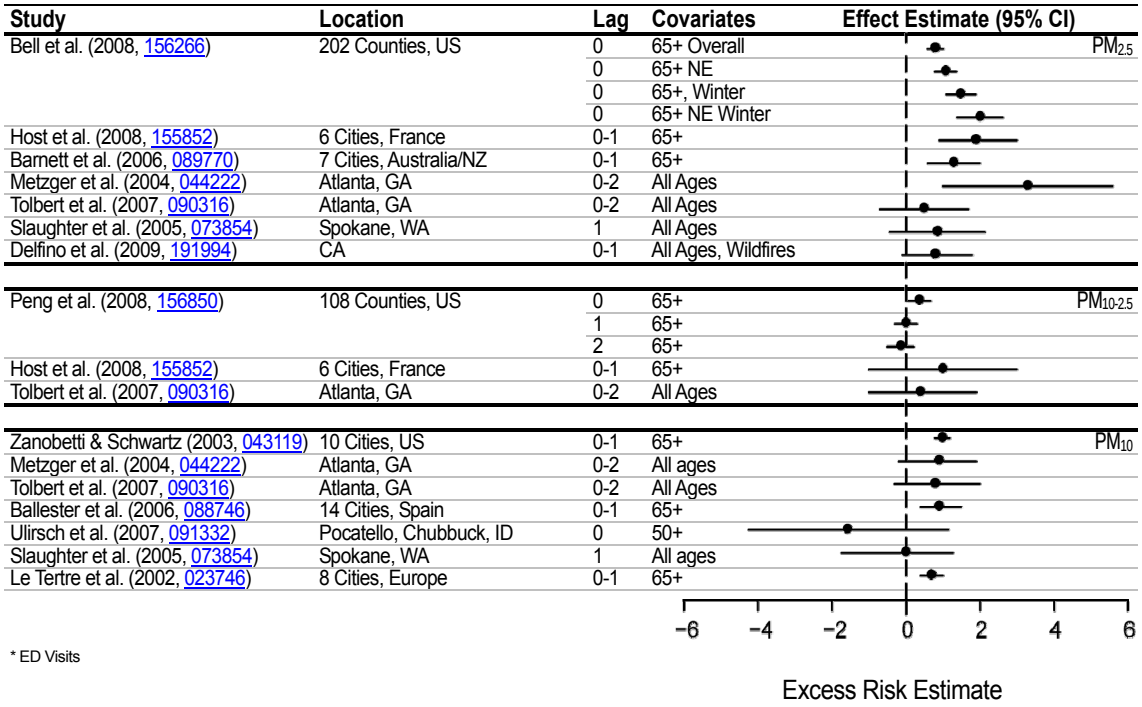


Figure 6-1. Excess risk estimates per 10 µg/m^3 increase in 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10} concentration for CVD ED visits and HAs. Studies represented in the figure include all multicity studies, as well as single-city studies conducted in the U.S. or Canada.

The effect estimates from multicity studies and single-city studies conducted in the U.S. and Canada are included in Figure 6-1. Information on PM concentrations during the relevant study period is presented in Table 6-8. In summary, large studies from the U.S., Europe, and Australia/New Zealand published since the 2004 PM AQCD (U.S. EPA, 2004, 056905) provide support for an association between short-term increases in ambient levels of $PM_{2.5}$ and PM_{10} and increased risk of hospitalization for total CVD. The evidence for an association of CVD hospitalization with $PM_{10-2.5}$ is relatively limited. Peng et al. (2008, 156850) reported that their $PM_{10-2.5}$ estimate was not robust to adjustment for $PM_{2.5}$ and estimates from the other studies are imprecise. The average excess risk among the U.S. elderly is likely in the range of 0.5-1.0% per 10 µg/m^3 increase in $PM_{2.5}$, although substantial variability by region of the country and season has been demonstrated. An excess risk of ED visits for CVD of a similar magnitude appears likely. The excess risk of CVD hospitalization may be somewhat greater in Europe and Australia/New Zealand than in the U.S. Sources including wood burning, oil burning, traffic and crustal material have been associated with increases in cardiovascular hospitalization or ED visits, but the best evidence suggests that in the U.S., oil combustion, wood burning, and traffic are likely the sources of $PM_{2.5}$ most strongly associated with cardiovascular hospitalizations or ED visits.

Table 6-8. Characterization of ambient PM concentrations in epidemiologic studies of hospital admission and ED visits for cardiovascular diseases.

Pollutant	Study	Location	Mean Concentration ($\mu g/m^3$)	Upper Percentile Concentration ($\mu g/m^3$)
$PM_{2.5}$				
	Barnett et al. (2006, 089770)	7 cities in Australia	8.1-11.0	NR
	Bell et al. (2008, 156266)	202 counties in the U.S.	12.92	34.16
	Burnett et al. (1999, 017269)	Toronto Canada	18	95th: 34.0, Max: 90
	Dominici et al. (2006, 088398)	204 counties in the U.S.	13.4	NR
	Delfino et al. (2009, 191994)	6 counties CA	18.4-32.7	45.3-76.1 (wildfire period)
	Host et al. (2008, 155852)	6 cities in France	13.8-18.8	95th: 25-33
	Ito et al. (2003, 042856); Lippman (2000, 011938)	Detroit, MI	18	98th: 55.2
	Lisabeth et al. (2008, 155939)		7	75th: 10
	Metzger et al. (2004, 044222)	Atlanta, GA	17.8	90th: 32.3 98th: 39.8
	Pope et al. (2006, 091246)	Wasatch Front, Utah	10.1-11.3	Max: 82-144
	Slaughter et al. (2005, 073854)	Spokane, WA	NR	90th: 20.2
	Sullivan et al. (2005, 050854)	King County, WA	12.8	90th 27.3, Max: 147
	Symons et al. (2006, 091258)	Baltimore, MD	16	Max: 69.2
	Tolbert et al. (2007, 090316)	Atlanta, GA	17.1	98th: 38.7
	Villenueve et al. (2006, 090191)	Edmonton, Canada	8.5	75th: 11
	Zanobetti and Schwartz (2005, 088069)	Boston, MA	11.1 (median)	95th: 26.31 98th: 55.2
$PM_{10-2.5}$				
	Burnett et al. (1999, 017269)	Toronto, Canada	12.2	Max: 68
	Host et al. (2008, 155852)	6 cities in France	7-11	95th: 12.5-21.0
	Ito et al. (2003, 042856); Lippman (2000, 011938)	Detroit, MI	13	Max: 50
	Le Tertre et al. (2002, 023746)	8 cities in Europe	NR	NR
	Metzger et al. (2004, 044222)	Atlanta, GA	9.1	90th: 16.2
	Peng et al. (2008, 156850)	204 cities in the U.S.	9.8 (Median)	75th: 15.0
	Peters et al. (2001, 016546)	Boston, MA	7.4	95th: 15.2
	Slaughter et al. (2005, 073854)	Spokane, WA	NR	NR
	Tolbert et al. (2007, 090316)	Atlanta, GA	9	Max: 50.3
PM_{10}				
	Ballester et al. (2006, 088746)	14 cities in Spain	32.8-43.2	90th: 50.3-62.6
	Barnett et al. (2006, 089770)	7 cities in Australia and New Zealand	16.5-20.6	NR
	Burnett et al. (1999, 017269)	Toronto, Canada	30.2	95th: 56.0
	Ito et al. (2003, 042856); Lippman (2000, 011938)	Detroit, MI	31	NR
	Jalaludin et al. (2006, 189416)	Sydney, Australia	16.8	75th: 19.9 Max: 103.9
	Larrieu et al. (2007, 093031)	8 cities in France	21.0-28.9	NR
	Le Tertre et al. (2002, 023746)	8 cities in Europe	Range: 15.5-55.7	Range 75th: 19.9-66

Pollutant	Study	Location	Mean Concentration ($\mu g/m^3$)	Upper Percentile Concentration ($\mu g/m^3$)
	Linn et al. (2000, 002839)	Los Angeles, California	45	78 (summer) -132 (fall)
	Metzger et al. (2004, 044222)	Atlanta, GA	26.3	90th: 44.7
	Morris et al. (1998, 024924)	Chicago, Illinois	41	75th: 51 Max: 117
	Peters et al. (2001, 016546)	Boston, MA	19.4	95th: 37.0
	Schwartz et al. (1995, 046186)	Detroit, MI	48	90th: 82
	Slaughter et al. (2005, 073854)	Spokane, WA	NR	90th: 41.9
	Tolbert et al. (2007, 090316)	Atlanta, GA	26.6	Max: 98.4
	Ulirsch et al. (2007, 091332)*	2 cities in southeast Idaho	24.2/23.2	90th: 40.7/37.4
	Wellenius et al. (2005, 087483)	Pittsburgh, PA	31.1	95th: 70.5
	Wellenius et al. (2005, 088685)	9 cities in the U.S.	28.4 (median)	90th: 57.9
	Wellenius et al. (2006, 088748)	7 cities in the U.S.	28.3 (median)	90th: 57
	Zanobetti and Schwartz (2005, 088069)	Boston, MA	28.4 (median)	90th: 53.6

*Results presented separately for 2 separate time series

6.2.10.2. Cardiac Diseases

Cardiac disease represents a subset of CVD which specifically excludes hospitalizations for CBVD, peripheral vascular disease, and other circulatory diseases not involving the heart or coronary circulation. Only a small number of studies published since the 2004 PM AQCD (U.S. EPA, 2004, 056905) have evaluated the association between ambient PM and hospitalizations for cardiac diseases, as most investigators have focused instead on more narrowly defined outcomes.

The French PSAS program found a 2.4% (95% CI: 1.2-3.7, lag 0-1) and 1.5% (95% CI: 0.5-2.2, lag 0-1) excess risk among the elderly per 10 $\mu g/m^3$ increase in $PM_{2.5}$ and PM_{10}, respectively (Host et al., 2007, 155851; Larrieu et al., 2007, 093031). Host et al. (2008, 155852) also found a positive less precise association with $PM_{10-2.5}$, (excess relative risk per 10 $\mu g/m^3$: 1.6% [95% CI: -0.8 to 4.1]). The European HEAPSS study looked at cardiac readmissions among survivors of a first MI and found a 2.1% (95% CI: 0.4-3.9, lag 0) excess risk per 10 $\mu g/m^3$ increase in PM_{10} (Von Klot et al., 2005, 088070). A 1.9% (95% CI: 1.0-2.7, lag 0-1) excess risk per 10 $\mu g/m^3$ increase in $PM_{2.5}$ was observed in several cities in Australia and New Zealand (Barnett et al., 2006, 089770). Single-city studies of hospital admissions from Kaohsiung and Taipei, Taiwan, and an ED visit study from Sydney, Australia also reported statistically significant positive associations(Chang et al., 2005, 080086; Jalaludin et al., 2006, 189416; Yang et al., 2004, 094376). On the other hand, Slaughter et al. (2005, 073854) found no association between either $PM_{2.5}$ or PM_{10} and risk of cardiac hospitalization in Spokane, Washington.

In summary, although relatively few studies have focused on all cardiac diseases, large studies from Europe and Australia/New Zealand published since the 2004 PM AQCD (U.S. EPA, 2004, 056905) report positive associations between short-term increases in ambient levels of $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10} and increased risk of hospitalization for cardiac disease. The results from small single-city studies are less consistent. The excess risk for cardiac hospitalizations may be somewhat larger than for total CVD hospitalizations.

6.2.10.3. Ischemic Heart Disease

IHD represents a subset of all cardiac disease hospitalizations and typically includes acute MI (ICD 9: 410), other acute and subacute forms of IHD (411), old MI (412), angina pectoris (413), and other forms of chronic IHD (414). Some authors term this category coronary heart disease. Published studies evaluating IHD as a single outcome are considered first, followed by consideration of studies looking at acute MI, a specific form of IHD.

In one of the first studies to evaluate IHD, Schwartz and Morris (1995, 046186) reported a 0.6% (95% CI: 0.2-1.0) excess risk of hospitalization for IHD per 10 $\mu g/m^3$ increase in mean PM_{10}

levels over the previous two days among elderly Medicare beneficiaries living in Detroit between 1986 and 1989. As reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905), similar associations were subsequently observed in many single-city studies including: London, England (Atkinson et al., 1999, 007882), Toronto, Canada (Burnett et al., 1999, 017269), and Seoul, Korea (Lee et al., 2003, 095552). Studies in Hong Kong (Wong et al., 1999, 009172; Wong et al., 2002, 023232), Birmingham, England (Anderson et al., 2001, 017033), and London, England (Wong et al., 2002, 023232) yielded positive point estimates of a similar magnitude, but did not reach statistical significance.

The positive associations between short-term changes in PM and IHD hospitalizations observed in the early single-city studies have been confirmed in several large multicity studies. The U.S. MCAPS study (Dominici et al., 2006, 088398) found a 0.4% (95% CI: 0.0-0.8) excess risk of hospitalization for IHD per 10 $\mu g/m^3$ increase in $PM_{2.5}$ two days earlier. The European APHEA-2 study (Le Tertre et al., 2002, 023746) considered PM_{10} and found a 0.8% (95% CI: 0.3-1.2, lag 0-1) excess risk among those aged ≥65 yr. Among the elderly in 5 cities in Australia and New Zealand (Barnett et al., 2006, 089770) there was a 4.3% (95% CI: 1.9-6.4, lag 0-1) excess risk per 10 $\mu g/m^3$ increase in $PM_{2.5}$. Among the elderly in several French cities there was a 4.5% (95% CI: 2.3-6.8, lag 0-1), 6.4% (95% CI: 1.6-11.4, lag 0-1) and 2.9% (95% CI: 1.5-4.3, lag 0-1) excess risk per 10 $\mu g/m^3$ increase in $PM_{2.5}$, $PM_{10-2.5}$ (Host et al., 2008, 155852), and PM_{10}, respectively (Larrieu et al., 2007, 093031).

With regard to ED visits, the Atlanta-based SOPHIA study (Metzger et al., 2004, 044222) found positive associations with $PM_{2.5}$ and PM_{10} (ranging from 1.1 to 2.3%), but the effect estimates did not reach statistical significance. Similarly, associations of EC and OC with IHD were increased but not significant. In 6 cities across Canada, Szyszkowicz (2009, 191996) observed a 2.4% (95% CI: 1.2-3.6) and 1.4% (95% CI: 0.7-2.0) excess risk of ED visits for angina per 10 $\mu g/m^3$ increase in same-day $PM_{2.5}$ and PM_{10}, respectively. Although excess risks were generally weak and non-significant, Delfino et al. (2009, 191994) observed a slightly larger excess risk of IHD during wildfires compared to the pre-wildfire period. In Sydney, Australia, Jalaludin et al. (2006, 189416) found a 2.6% (95% CI: 0.1-5.2) and 0.8% (95% CI: -1.2 to 2.8) excess risk of ED visits for IHD per 10 $\mu g/m^3$ increase in 2-day ma of $PM_{2.5}$ and PM_{10}, respectively. A recent study in Helsinki, Finland, found no evidence of an association of IHD hospital admissions with UFP, ACP, $PM_{2.5}$, $PM_{10-2.5}$, or source-specific $PM_{2.5}$ (Halonen et al., 2009, 180379).

To explore this link further, Pope et al. (2006, 091246) used data from an ongoing registry of patients undergoing coronary angiography at a single referral center in Salt Lake City, UT, between 1994-2004. The authors found a 4.8% (95% CI: 1.0-8.8, lag 0) excess risk of acute MI or unstable angina per 10 $\mu g/m^3$ increase in $PM_{2.5}$ among 4,818 patients. These results were robust to changes in the definition of the outcome. The results of this study are particularly noteworthy given the high specificity of the outcome definition.

In summary, large studies from the U.S., Europe, and Australia/New Zealand published since the 2004 PM AQCD (U.S. EPA, 2004, 056905) provide support for an association between short-term increases in ambient levels of PM_{10} and $PM_{2.5}$ and increased risk of hospitalization or ED visits for ischemic heart diseases. Although estimates are less precise for $PM_{10-2.5}$, most results from single pollutant models provide evidence of a positive association between $PM_{10-2.5}$ and IHD. Moreover, Host et al. (2008, 155852) found that the effect estimates for the association of $PM_{2.5}$ and $PM_{10-2.5}$ with IHD were very similar when scaled to the IQR of each metric. Estimates of the excess risk vary considerably between studies, but as was the case for total CVD hospitalizations, the excess risk appears to somewhat greater in Europe and Australia/New Zealand. Results from multicity studies and U.S. and Canadian single-city studies are presented in Figure 6-2.

Study	Location	Lag	Age	Effect Estimate (95% CI)
ISCHEMIC HEART DISEASE				
Ito (2003, 042856)	Detroit, MI	1	65+	$PM_{2.5}$
Pope et al. (2006, 091246)	Utah Valley, UT	0	All	
Host et al. (2007, 155851)	6 Cities, France	0-1	All	
Metzger et al. (2004, 044222)*	Atlanta, GA	0-3	All	
Barnett et al. (2006, 089770)	Australia/NZ	0-1	15-64	
Dominici et al. (2006, 088398)	204 Counties, US	0	65+	
		1	65+	
		2	65+	
		0-2 DL	65+	
Barnett et al. (2006, 089770)	Australia/NZ	0-1	65+	
Host et al. (2007, 155851)	6 Cities, France	0-1	65+	
Burnett et al. (1999, 017269)	Toronto, Can	0,1	All	
Delfino et al. (2009, 191994)	6 Counties, CA (Wildfires)	0,1	All	
Ito (2003, 042856)	Detroit, MI	1	65+	$PM_{10-2.5}$
Metzger et al. (2004, 044222)*	Atlanta, GA	0-3	All	
Host et al. (2007, 155851)	6 Cities, France	0-1	All	
		0-1	65+	
Burnett et al. (1999, 017269)	Toronto, Can	0	All	
Ito (2003, 042856)	Detroit, MI	1	65+	PM_{10}
Le Tertre et al. (2002, 023746)	8 Cities, Europe	0-1	<65	
Metzger et al. (2004, 044222)*	Atlanta, GA	0-2	All	
Larrieu et al. (2007, 093031)	8 Cities, France	0-1	All	
Burnett et al. (1999, 017269)	Toronto, Can	0-1	All	
Le Tertre et al. (2002, 023746)	8 Cities, Europe	0-1	65+	
Jalaludin et al. (2006, 189416)*	Sydney, Australia	0-1	65+	
Larrieu et al. (2007, 093031)	8 Cities, France	0-1	65+	
MYOCARDIAL INFARCTION				$PM_{2.5}$
Peters et al. (2001, 016546)	Boston, MA	2 h	61.6 Mean	
		24 h	61.6 Mean	
Sullivan et al. (2005, 050854)	King County, WA	1 h	21-98	
		2 h	21-98	
		4 h	21-98	
		24 h	21-98	
Zanobetti & Schwartz (2006, 090195)	Boston, MA	0	65+	
				$PM_{10-2.5}$
Peters et al. (2001, 016546)	Boston, MA	2 h	61.6 Mean	
		24 h	61.6 Mean	
Linn et al. (2000, 002839)	Los Angeles, CA	0	>30	PM_{10}
Peters et al. (2001, 016546)	Boston, MA	2 h	61.6 Mean	
		24 h	61.6 Mean	
Zanobetti & Schwartz (2005, 088069)	21 Cities, US	0	65+	

* ED Visits
DL Distributed Lag

Excess Risk (%)

Figure 6-2. Excess risk estimates per 10 µg/m^3 increase in 24-h avg (unless otherwise noted) $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10} concentration for MI and IHD ED visits and HAs. Studies represented in the figure include all multi-city studies as well as single-city studies conducted in U.S. or Canada.

6.2.10.4. Acute Myocardial Infarction

Because even IHD refers to a heterogeneous collection of diseases and syndromes, several authors have evaluated the association between short-term fluctuations in ambient PM and acute MI, a specific form of IHD.

In 2001, Peters et al. (2001, 016546) published their study evaluating the effects of PM on the risk of MI among 772 Boston-area participants in the Determinants of MI Onset Study. The authors found that a 10 μg/m^3 increase in the 2-h or 24-h avg levels of $PM_{2.5}$ was associated with a 17% (95% CI: 4-32) and 27% (95% CI: 6-53) excess risk of MI, respectively. An imprecise, non-significant association between $PM_{10-2.5}$ and onset of MI was observed in Boston. In contrast, a study among 5793 patients in King County, WA that used similar methods, found no association with $PM_{2.5}$ with lag times of 1, 2, 4, or 24 h (Sullivan et al., 2005, 050854). Among 852 hospitalized patients in Augsburg, Germany, Peters et al. (2005, 087759) also found no association between $PM_{2.5}$ and MI risk within this time frame, although they did find a positive and statistically significant association with time spent in traffic (Peters et al., 2004, 087464).

These three studies are particularly important because in each one: (1) cases were prospectively identified based on clinical criteria rather than retrospectively based on discharge diagnoses; and (2) time of MI symptom onset was used for exposure assessment rather than date of hospital admission. Whether the discrepant results among these studies are due to regional differences in population characteristics and/or air pollution sources remains unclear. The King County study suggests that differences in statistical approaches are unlikely to account for the discrepant results (Sullivan et al., 2005, 050854). Analyses from the U.S. MCAPS study suggest that substantial heterogeneity of effects are to be expected across regions of the country (Bell et al., 2008, 156266)

Several studies have assessed the association between acute exposure to ambient PM and MI using administrative databases. In the U.S., MI was not one of the specific endpoints evaluated in the MCAPS study (Dominici et al., 2006, 088398) or in the Atlanta-based SOPHIA study of ED visits (Metzger et al., 2004, 044222). However, Zanobetti and Schwartz (2005, 088069) found a 0.7% (95% CI: 0.3-1.0) excess risk of MI per 10 μg/m^3 increase in same-day PM_{10} among elderly Medicare beneficiaries in 21 cities. Subsequently, the same authors found that among elderly Medicare beneficiaries living in the Boston metropolitan region, a 10 μg/m^3 increase in $PM_{2.5}$ was associated with a 4.9% (95% CI: 1.1-8.2) excess risk on the same day (Zanobetti and Schwartz, 2006, 090195).

This body of evidence may implicate traffic-related pollution generally as a risk factor for MI. In the study described above, Peters et al. (2001, 016546) found positive associations between risk of hospitalization for MI and potential markers of traffic-related pollution measured at a central monitor including BC, CO and NO_2. However, none of these associations were statistically significant in models adjusting for season, meteorological variables, and day of week. Zanobetti and Schwartz (2006, 090195) examined the association between traffic-related pollution and risk of hospitalization for MI among Medicare beneficiaries in the Boston area and found that MI risk was positively and significantly associated with measures of $PM_{2.5}$, BC, NO_2, and CO, but not with levels of non-traffic-related $PM_{2.5}$. Peters et al. (2004, 087464) interviewed 691 subjects with MI who survived at least 24-h after the event and found a strong positive association between self-reported exposure to traffic and the onset of MI within 1 h (OR: 2.9 [95% CI: 2.2-3.8]). The association was somewhat stronger among subjects traveling by bicycle or public transportation in the hour prior to the event. Of note, however, this study did not directly measure traffic-related pollution.

Similar studies with administrative databases have been conducted in Europe, Australia, and New Zealand. Barnett et al. (2006, 089770) observed that in five cities in Australia and New Zealand, a 10 μg/m^3 increase in $PM_{2.5}$ was associated with a 7.3% (95% CI: 3.5-11.4, lag 0-1 day) excess risk. In Rome, D'Ippoliti et al. (2003, 074311) carried out a case-crossover study and found a statistically significant positive association between TSP and the risk of hospitalization for MI. In contrast, the HEAPSS study found no evidence of an association between PM_{10} and risk of hospitalization for a first MI in five European cities (Lanki et al., 2006, 089788), although there is some indication that among survivors of a first MI, risk of re-hospitalization for MI may be related to transient elevations in PM_{10} (Von Klot et al., 2005, 088070).

In summary, large studies from the U.S., Europe, and Australia/New Zealand published since the 2004 PM AQCD (U.S. EPA, 2004, 056905) provide support for an association between short-term increases in ambient levels of $PM_{2.5}$ and $PM_{10}$and increased risk of hospitalization for MI. Some of the heterogeneity of results is likely explained by regional differences in pollution sources,

components, and measurement error. One study of the effect of 2- and 24-h avg $PM_{10-2.5}$ concentration on admissions for MI produced effect estimates that were positive, but imprecise (Peters et al., 2001, 016546). These results need to be interpreted together with those studies evaluating hospitalization for IHD since MIs make up the majority of hospitalizations for IHD. U.S. studies of MI are included in Figure 6-2.

6.2.10.5. Congestive Heart Failure

Perhaps the first suggestion of an association between ambient PM and hospitalization for CHF was provided by the study of Schwartz and Morris (1995, 046186). These authors reported that among elderly Medicare beneficiaries living in Detroit between 1986-1989, a 10 $\mu g/m^3$ increase in mean PM_{10} levels over the previous two days was associated with a 1.0% (95% CI: 0.4-1.6) increase in risk of hospitalization for CHF. As reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905), using similar approaches, statistically significant positive associations with $PM_{2.5}$ or PM_{10} were subsequently reported in single-city studies looking at hospitalizations for CHF in Toronto (Burnett et al., 1999, 017269), Hong Kong (Wong et al., 1999, 009172), and Detroit (Ito, 2003, 042856), but not Los Angeles (Linn et al., 2000, 002839) or Denver (Koken et al., 2003, 049466). Burnett et al. (1999, 017269) reports a significantly increased risk of CHF hospitalization with $PM_{10-2.5}$ while Metzger et al. (2004, 044222) and Ito et al. found (2003, 042856) less precise associations.

Subsequent multicity studies support the presence of a positive association between PM concentration and CHF hospitalization. In the U.S., the MCAPS study found a 1.3% (95%: 0.8-1.8) excess risk per 10 $\mu g/m^3$ increase in same-day $PM_{2.5}$ (Dominici et al., 2006, 088398). In addition, Wellenius et al. (2006, 088748) reported a 0.7% (95% CI: 0.4-1.1) excess risk of hospitalization for CHF per 10 $\mu g/m^3$ increase in same-day PM_{10} among elderly Medicare beneficiaries in seven cities. In Australia and New Zealand, Barnett et al. (2006, 089770) found a 9.8% (95% CI: 4.8-14.8, lag 0-1 day) and 4.6% (95% CI: 2.8-6.3, lag 0-1 days) excess risk of hospitalization for CHF associated with a 10 $\mu g/m^3$ increase in $PM_{2.5}$ and PM_{10}, respectively. Results from more recent single-city studies in Pittsburgh (Wellenius et al., 2005, 087483), Utah's Wasatch Front (Pope et al., 2008, 191969), Kaohsiung, Taiwan (Lee et al., 2007, 196613) and Taipei, Taiwan (Yang, 2008, 157160) have also reported positive associations between PM and CHF hospital admissions. In addition, Yang et al. (2009, 190341) found that hospitalizations for CHF were elevated during or immediately following 54 Asian dust storm events (while single day lags 0-3 were evaluated, maximum excess risk occurred at lag 1: 11.4% [95% CI: -0.7 to 25.0]). Delfino et al. (2009, 191994) observed a slightly larger excess risk of total CHF during wildfires occurring in California compared to the period before the wildfires.

While most studies suggest an association at very short lags (0-1 days), the study by Pope et al. (2008, 191969) failed to find such short term associations and instead suggested that $PM_{2.5}$ levels averaged over the past 2-3 wk may be more important. Pope et al. (2008, 191969) observed a 13.1% (95% CI: 1.3-26.2) increase in CHF hospitalization per 10 $\mu g/m^3$ increase in $PM_{2.5}$ (imputed values used in analysis). Whether findings at longer lags in this population represent true cumulative effects of PM or are due to misclassification of symptom onset times remains to be determined.

Findings from the Atlanta-based SOPHIA study (Metzger et al., 2004, 044222) also support the presence of a positive association between PM and CHF ED visits. Specifically, the SOPHIA study found a 5.5% (95% CI: 0.6-10.5, lag 0-2 days) excess risk of ED visits for CHF per 10 $\mu g/m^3$ increase in the 3-day ma of $PM_{2.5}$. Positive associations were also observed for CHF and EC and OC components of $PM_{2.5}$. No associations were observed with PM_{10} and a weak, imprecise increase was observed in association with $PM_{10-2.5}$.

Only one published study has attempted to evaluate the effects of ambient particles on CHF symptom exacerbation using data which was not derived from administrative databases. Symons et al. (2006, 091258) interviewed 135 patients with prevalent CHF hospitalized for symptom exacerbation in Baltimore, MD. The authors found a 7.4% (95% CI: -7.5 to 24.2) excess risk of hospitalization per 10 $\mu g/m^3$ increase in $PM_{2.5}$ two days prior to symptom onset. This finding did not reach statistical significance and may be attributable to the lack of statistical power needed to find an effect of the expected magnitude.

In summary, large studies from the U.S., Europe, and Australia/New Zealand published since the 2004 PM AQCD (U.S. EPA, 2004, 056905) provide support for an association between short-term increases in ambient levels of $PM_{2.5}$ and PM_{10} and increased risk of hospitalization and ED visits for CHF. Although the number of studies is fewer (and only Metzger et al., 2004, 044222

is new since the 2005 AQCD), elevated risks of hospitalization or ED visits for CHF in association with $PM_{10-2.5}$ have been observed. The excess risks associated with CHF hospitalizations and ED visits are consistently greater than those observed for other CVD endpoints. The results of multicity studies and U.S. and Canadian single-city studies are summarized in Figure 6-3.

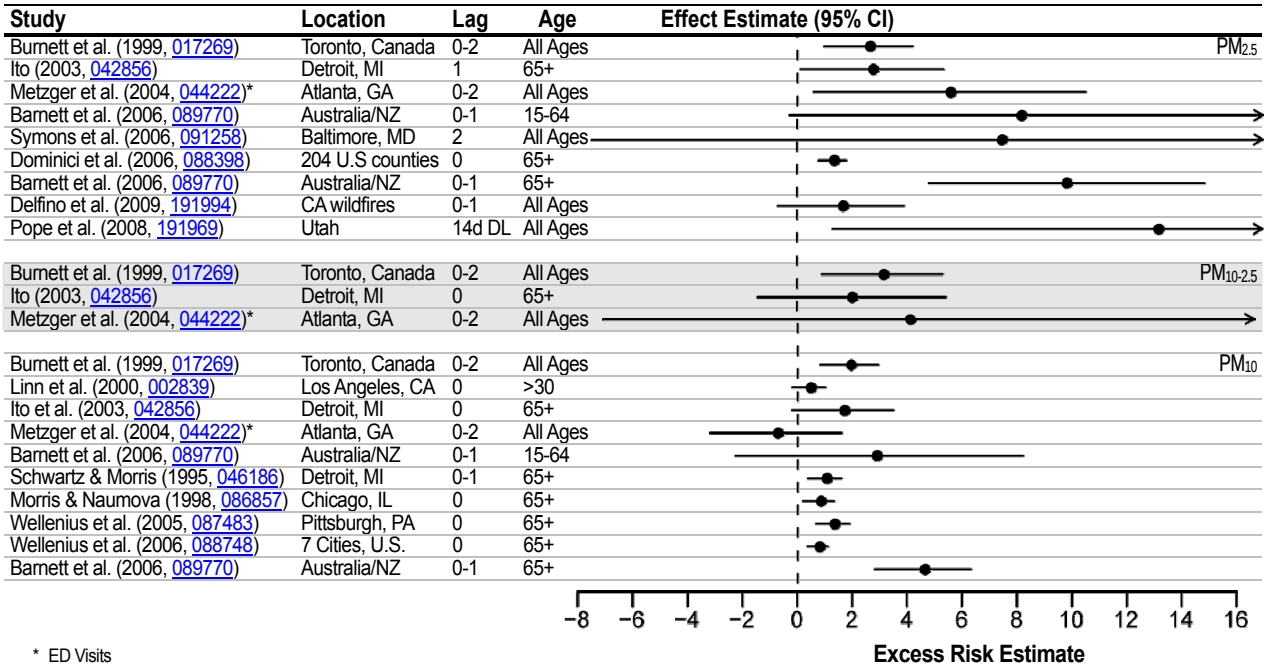


Figure 6-3. Excess risk estimates per 10 µg/m^3 increase in 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10} concentration for CHF ED visits and HAs. Studies represented in the figure include all multicity studies as well as single-city studies conducted in the U.S. and Canada.

6.2.10.6. Cardiac Arrhythmias

A number of studies based on administrative databases have sought to evaluate the association between short-term fluctuations in ambient PM levels and the risk of hospitalization for cardiac arrhythmias (also known as dysrhythmias). Typically in these studies a primary discharge diagnosis of ICD-9 427 has been used to identify hospitalized patients. However, ICD-9 427 includes a heterogeneous group of arrhythmias including paroxysmal ventricular or supraventricular tachycardia, atrial fibrillation and flutter, ventricular fibrillation and flutter, cardiac arrest, premature beats, and sinoarterial node dysfunction. One study in the Netherlands found that the positive predictive value of ICD-9 codes related to ventricular arrhythmias and sudden cardiac death was 82% (De Bruin et al., 2005, 155746). The positive predictive value of other codes related to cardiac arrhythmias is unknown, but likely to be lower.

The results from early studies of arrhythmia-related hospitalizations have been inconsistent, with positive findings in Toronto (Burnett et al., 1999, 017269) and null findings in Detroit (Schwartz and Morris, 1995, 046186), Los Angeles (Linn et al., 2000, 002839), and Denver (Koken et al., 2003, 049466). The U.S. MCAPS study found a statistically significant 0.6% (95% CI: 0.0-1.2) excess risk of hospitalization for the combined outcome of cardiac arrhythmias and conduction disorders (ICD-9: 426, 427) per 10 µg/m^3 increase in same-day $PM_{2.5}$ (Dominici et al., 2006, 088398). A multicity study in Australia and New Zealand found no evidence of an association between arrhythmia hospitalizations and either $PM_{2.5}$ or PM_{10} (Barnett et al., 2006, 089770). A study in Helsinki, Finland, found no evidence of an association between either $PM_{2.5}$ or $PM_{10-2.5}$ and risk of hospitalization for arrhythmias (Halonen et al., 2009, 180379), although there was an association with smaller particles (0.03-0.1 µm).

With regard to ED visits, the Atlanta-based SOPHIA study found no evidence of an association between any measure of ambient PM and the rate of ED visits for cardiac arrhythmias (Metzger et al., 2004, 044222). However, in São Paulo, Brazil, Santos et al. (2008, 192004) found a 3.0% (95% CI: 0.5-5.4) excess risk of ED visits for arrhythmias per 10 $\mu g/m^3$ increase in PM_{10} on the same day.

In summary, the current evidence does not support the presence of a consistent association between short-term increases in ambient levels of $PM_{2.5}$, $PM_{10-2.5}$, or PM_{10} and increased risk of hospitalization for cardiac arrhythmias. However, it should be noted that studies of hospital admissions or ED visits are ill-suited to the study of cardiac arrhythmias since most arrhythmias do not lead to hospitalization. Studies in patients with implanted defibrillators, human panel studies with ambulatory ECG recordings, and animal toxicological studies provide a more appropriate setting for evaluating this endpoint. Results of these studies are described in Section 6.2.2.

6.2.10.7. Cerebrovascular Disease

Time-series studies evaluating the hypothesis that short-term increases in ambient $PM_{2.5}$ or PM_{10} levels are associated with increased risk of hospitalization for CBVD have been inconsistent, with few studies reporting positive associations (Chan et al., 2006, 090193; Dominici et al., 2006, 088398; Metzger et al., 2004, 044222; Wordley et al., 1997, 082745), and several studies reporting null or negative associations (Anderson et al., 2001, 017033; Barnett et al., 2006, 089770; Burnett et al., 1999, 017269; Halonen et al., 2009, 180379; Jalaludin et al., 2006, 189416; Larrieu et al., 2007, 093031; Le Tertre et al., 2002, 023746; Peel et al., 2007, 090442; Villeneuve et al., 2006, 090191; Wong et al., 1999, 009172).

The U.S. MCAPS study found a 0.8% (95% CI: 0.3-1.4) excess risk of hospitalization for CBVD per 10 $\mu g/m^3$ increase in same-day $PM_{2.5}$ (Dominici et al., 2006, 088398). The association showed regional variability with the strongest associations observed in the eastern U.S. The Atlanta-based SOPHIA study found a 5.0% (95% CI: 0.8-9.3, lag 0-2 days) excess risk of ED visits for cerebrovascular and peripheral vascular disease combined (excluding hemorrhagic strokes) per 10 $\mu g/m^3$ increase in $PM_{2.5}$ and a 2.0% (95% CI: -0.1 to 4.3, lag 0-2 days) excess risk for PM_{10} (Metzger et al., 2004, 044222). Delfino et al. (2009, 191994) observed a weak association between excess risk of CBVD admissions before and during a wildfire occurring in California and slightly higher risks after the wildfire period.

Large multicity studies conducted outside of North America have failed to observe an association between PM and CBVD hospitalizations. The APHEA study found no excess risk (0.0% [95% CI: -0.3 to 0.3]) of hospitalization for CBVD per 10 $\mu g/m^3$ increase in the 2-day ma of PM_{10} in 8 European cities (Le Tertre et al., 2002, 023746). Investigators from the French PSAS program reported a 0.8% (95% CI: -0.9 to 2.5, lag 0-1 days) excess risk per 10 $\mu g/m^3$ increase in PM_{10} among patients aged ≥65 yr and a 0.2% (95% CI: -1.6 to 1.9, lag 0-1 days) excess risk among all patients (Larrieu et al., 2007, 093031). Although neither estimate was statistically significant, the estimated excess risk among the elderly is very similar to that observed in the U.S. MCAPS study. Barnett et al. (2006, 089770) examined this hypothesis in New Zealand and Australia and reported no association.

All of the above studies have identified cases of CBVD based on ICD-9 or ICD-10 codes (most commonly ICD-9 430-438). However, the range of ICD codes commonly used in these studies includes ischemic strokes, hemorrhagic strokes, transient ischemic attacks (TIAs) and several poorly defined forms of acute neurological events (e.g., seizures from a vascular cause) (Table 6-7). It is plausible that ambient PM has different effects on each of these disparate outcomes.

Ischemic Strokes and Transient Ischemic Attacks

An increasing number of studies have specifically evaluated the association between PM_{10} and $PM_{2.5}$ and the risk of ischemic stroke (Chan et al., 2006, 090193; Henrotin et al., 2007, 093270; Linn et al., 2000, 002839; Lisabeth et al., 2008, 155939; Low et al., 2006, 090441; Szyszkowicz, 2008, 192128; Tsai et al., 2003, 080133; Villeneuve et al., 2006, 090191; Wellenius et al., 2005, 087483). Linn et al. (2000, 002839) found a 1.3% (95% CI: 1.0-1.6 per 10 $\mu g/m^3$, PM_{10} lag 0) excess risk of hospitalization for ischemic stroke in the Los Angeles metropolitan area. Wellenius et al. (2005, 087483) reported a statistically significant 0.4% (95% CI: 0.0-0.9) excess risk per 10 $\mu g/m^3$ increase

in same-day PM_{10} among elderly Medicare beneficiaries in nine U.S. cities. Low et al. (2006, 090441) reported an absolute increase of 0.08 (95% CI; 0.002-0.16) ischemic stroke hospitalizations per 10 $\mu g/m^3$ increase in PM_{10} in New York City. In Kaohsiung, Taiwan, Tsai et al. (2003, 080133) found a 5.9% (95% CI: 4.3-7.4, lag 0-2 days) excess risk of hospitalization for ischemic stroke per 10 $\mu g/m^3$ increase in PM_{10} after excluding days with mean daily temperature <20°C. Meanwhile, in Taipei, Taiwan, Chan et al. (2006, 090193) found a 3.0% (95% CI: -0.8 to 6.6, lag 3) and 1.6% (95% CI: -0.8 to 3.9, lag 3) excess risk per 10 $\mu g/m^3$ increase in $PM_{2.5}$ and PM_{10}, respectively. Villeneuve et al. (2006, 090191) and Szyszkowicz et al. (2008, 192128) found no association between either $PM_{2.5}$ or PM_{10} and ED visits for acute ischemic stroke in Edmonton, Canada.

Two recent studies are particularly noteworthy given the high specificity of the outcome definition. Henrotin et al. (2007, 093270) used data on 1432 confirmed cases of ischemic stroke from the French Dijon Stroke Register and found 0.9% (95% CI: -7.0 to 9.4) excess risk of ischemic stroke per 10 $\mu g/m^3$ increase in PM_{10} on the same day and a 1.1% (95% CI: -0.2 to 9.4) excess risk on the previous day (lag 1 day). Lisabeth et al. (2008, 155939) used data on 2,350 confirmed cases of ischemic stroke and 1,158 cases of TIA from the Brain Attack Surveillance in Corpus Christi Project (BASIC), a population-based stroke surveillance project designed to capture all strokes in Nueces County, Texas. The authors found a 6.0% (95% CI: -0.8 to 13.2) and 6.0% (95% CI: -1.8 to 14.4) excess risk of ischemic stroke/TIA per 10 $\mu g/m^3$ increase in $PM_{2.5}$ on the previous day and the same day, respectively.

Only the study by Villeneuve et al. (2006, 090191) specifically evaluated the association between ambient PM and the risk of TIAs. This study failed to find any evidence of an association with either $PM_{2.5}$ or PM_{10}.

A limitation of all of these studies is that they have assessed exposure based on the date of hospital admission or ED presentation rather than the date and time of stroke symptom onset. It has been shown that this can bias health effect estimates towards the null by up to 60% (Lokken et al., 2009, 186774). Therefore, if there is a causal link between PM and the risk of stroke, it is likely that the existing studies underestimate the true effects. Moreover, most of these studies have evaluated only very short-term effects (lags of 0-2 days) and none have considered lags longer than 5 days. It is possible that the lag structure of the association between PM and stroke differs from that of other CVDs and it might even differ by stroke type.

Hemorrhagic Strokes

Most of the studies in the preceding section also evaluated the association between ambient PM and the risk of hemorrhagic stroke (Chan et al., 2006, 090193; Henrotin et al., 2007, 093270; Tsai et al., 2003, 080133; Villeneuve et al., 2006, 090191; Wellenius et al., 2005, 087483). In Kaohsiung, Taiwan, Tsai et al. (2003, 080133) noted a 6.7% (95% CI: 4.2-9.4, lag 0-2 days) excess risk of hospitalization for hemorrhagic stroke per 10 $\mu g/m^3$ increase in PM_{10}, after excluding days where the mean temperature was <20°C. However, in the U.S., Wellenius et al. (2005, 088685) failed to find any association between ambient PM_{10} levels and risk of hemorrhagic stroke among Medicare beneficiaries in nine U.S. cities. Similarly, Villeneuve et al. (2006, 090191) found no evidence of an association between ED visits for hemorrhagic stroke and either $PM_{2.5}$ or PM_{10} levels in Edmonton, Canada. Henrotin et al. (2007, 093270) found no evidence of an association between risk of hospitalization and PM_{10} levels in Dijon, France, and Chan et al. (2006, 090193) found no evidence of an association between risk of hospitalization and either $PM_{2.5}$ or PM_{10}levels in Taipei, Taiwan.

In summary, large studies from the U.S., Europe, and Australia/New Zealand published since the 2004 PM AQCD (U.S. EPA, 2004, 056905) provide inconsistent support for an association between short-term increases in ambient levels of $PM_{2.5}$ and PM_{10} and risk of hospitalization and ED visits for CBVD (Figure 6-4). Studies of $PM_{10-2.5}$ and CBVD or stroke have not been conducted. The heterogeneity in results is likely partly attributed to: (1) differences in the sensitivity and specificity of the various outcome definitions used in the studies; (2) lag structures between PM exposure and stroke onset which may vary by stroke type and patient characteristics; and (3) exposure misclassification due to the use of hospital admission date rather than stroke onset time, which may vary by region, population characteristics, and stroke type. Effect estimates from multicity studies and single-city U.S. and Canadian studies are included in Figure 6-4.

6.2.10.8. Peripheral Vascular Disease

In the U.S., the large MCAPS study Dominici et al. (2006, 088398) evaluated the association between mean daily $PM_{2.5}$ levels and the risk of hospitalization among elderly Medicare beneficiaries in 204 urban counties and found that a 10 μg/m^3 increase in $PM_{2.5}$ was not significantly associated with risk of hospitalization for peripheral vascular disease 0-2 days later. An earlier study in Toronto (Burnett et al., 1999, 017269) found a negative association with $PM_{2.5}$ (point estimate and confidence intervals not reported), a positive statistically significant association with $PM_{10-2.5}$ (2.2% [95% CI: 0.1-4.3]), and a positive non-significant association with PM_{10} (0.5% [95% CI: -0.5 to 1.6]). The Atlanta-based SOPHIA study (Metzger et al., 2004, 044222) of ED visits grouped visits for PVD with those for CBVD, making interpretation of these results challenging.

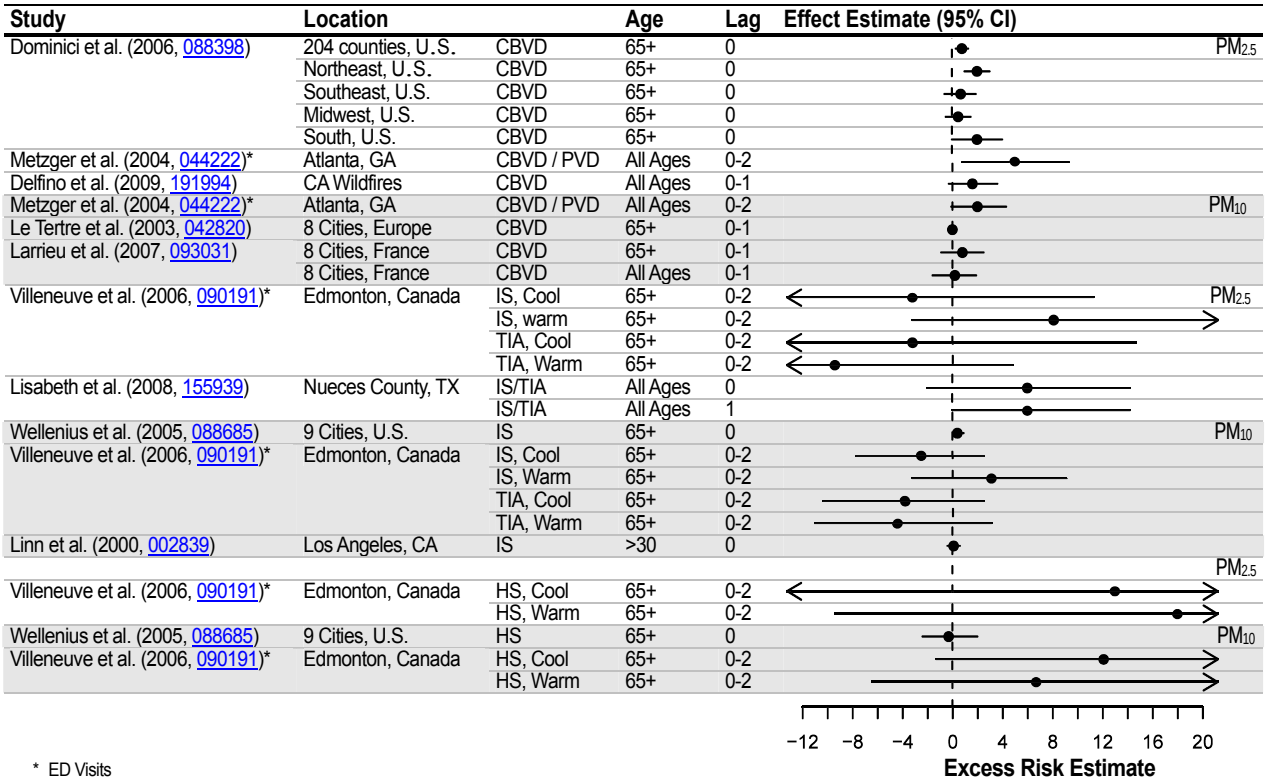


Figure 6-4. Excess risk estimates per 10 μg/m^3 increase in 24-h avg $PM_{2.5}$ and PM_{10} concentration for CBVD ED visits and HAs. Studies represented in the figure include all multicity studies as well as single-city studies conducted in the U.S. and Canada.

In summary, there is insufficient published data to determine whether or not there may be an association between short-term increases in ambient levels of, $PM_{2.5}$, $PM_{10-2.5}$, or PM_{10} and increased risk of hospitalization and ED visits for PVD.

6.2.10.9. Copollutant Models

Relatively few studies have evaluated the effects of $PM_{2.5}$ and $PM_{10-2.5}$ on the risk of hospital admissions and ED visits in the context of two-pollutant models. Generally, results for health effects of both size fractions are similar even after controlling for SO_2 or O_3 levels (Figure 6-5). However, controlling for NO_2 or CO has yielded mixed results. Among the large multicity studies, the Atlanta-based SOPHIA study found that the association between $PM_{2.5}$ (total carbon) and risk of cardiovascular ED visits was somewhat attenuated in two-pollutant models additionally controlling for either CO or NO_2 (Tolbert et al., 2007, 090316). Barnett et al. (2006, 089770) found that the

associations they observed between $PM_{2.5}$ and cardiac hospitalizations in Australia and New Zealand were attenuated after control for 24-h NO_2, but not after control for CO.

Only a few studies have attempted to evaluate the effects of one PM size fraction while controlling for another PM size fraction. The large U.S. MCAPS study evaluating the effects of $PM_{10-2.5}$ on cardiovascular hospital admissions lost precision after controlling for $PM_{2.5}$, but did not consider gaseous pollutants (Peng et al., 2008, 156850). Andersen et al. (2008, 189651) found that associations between both PM_{10} and $PM_{2.5}$ and cardiovascular hospitalizations in Copenhagen were not attenuated by control for particle number concentration.

A number of studies have also evaluated PM_{10} effects in the context of two-pollutant models with inconsistent results. The multicity Spanish EMECAS study (Ballester et al., 2006, 088746) found that the statistically significant positive associations observed between PM_{10} and cardiac hospitalizations were robust to control for other pollutants in two-pollutant models. Jalaludin et al. (2006, 189416) found that the effects of PM_{10} as well as $PM_{2.5}$ on cardiovascular ED visits in Sydney Australia were attenuated by additional control for either NO_2 or CO. Wellenius et al. (2005, 087483) found that the PM_{10}-related risk of hospitalization for CHF in Allegheny County, PA, was attenuated in two-pollutant models controlling for either CO or NO_2. In contrast, Chang et al. (2005, 080086) examined CVD hospitalizations in Taipei and found attenuation of PM_{10} effects by control for NO_2 or CO, but only during warm days. In Kaohsiung, Taiwan, Tsai et al. (2003, 080133) found that the association between PM_{10} and ischemic stroke hospitalizations was not materially attenuated in two-pollutant models controlling for either NO_2 or CO.

The inconsistent findings after controlling for gaseous pollutants or other size fractions are likely due to differences in the correlation structure among pollutants, as well as differing degrees of exposure measurement error.

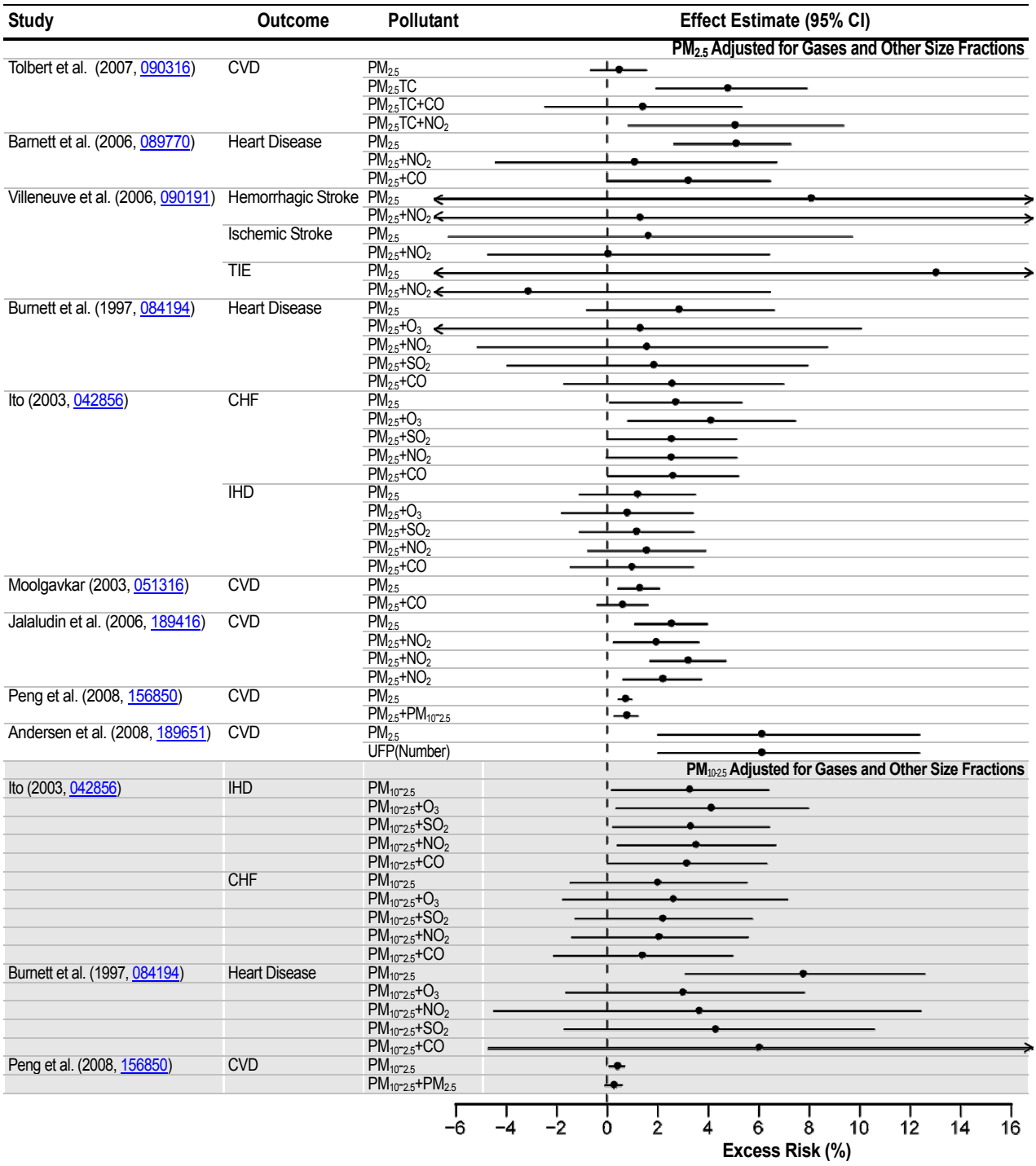


Figure 6-5. Excess risk estimates per 10 µg/m^3 increase in 24-h avg $PM_{2.5}$, and $PM_{10-2.5}$ for cardiovascular disease ED visits or HAs, adjusted for co-pollutants.

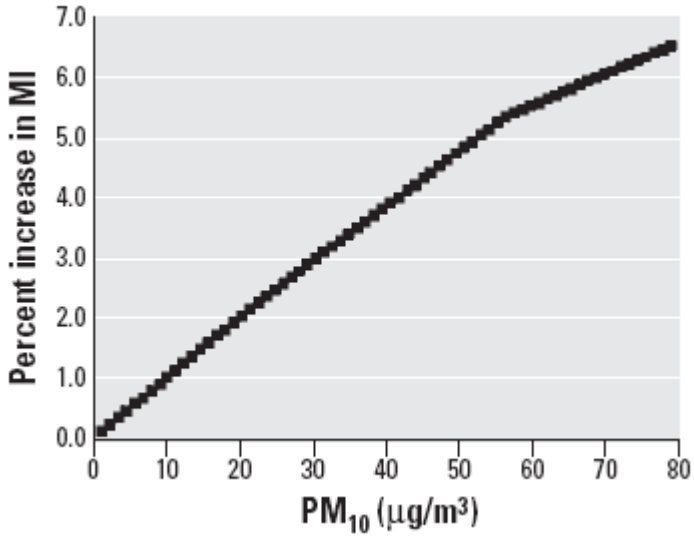
6.2.10.10. Concentration Response

The concentration-response relationship has been extensively analyzed primarily through studies that examined the relationship between PM and mortality. These studies, which have focused on short- and long-term exposures to PM have consistently found no evidence for deviations from linearity or a safe threshold (Daniels et al., 2004, 087343; Samoli et al., 2005, 087436; Schwartz, 2004, 078998; Schwartz et al., 2008, 156963) (Sections 6.5.2.7 and 7.1.4). Although on a more limited basis, studies that have examined PM effects on cardiovascular hospital admissions and ED visits have also analyzed the PM concentration-response relationship, and contributed to the overall body of evidence which suggests a log-linear, no-threshold PM concentration-response relationship.

The evaluation of cardiovascular hospital admission and ED visit studies in 2004 PM AQCD (U.S. EPA, 2004, 056905) found no evidence for a threshold in the dose-response relationship between short-term exposure to PM_{10} and IHD hospital admissions (Schwartz and Morris, 1995, 046186). An evaluation of recent single- and multicity studies of hospital admission and ED visits for CVD further supports this finding.

Ballester et al. (2006, 088746) examined the linearity of the relationship between air pollutants (including PM_{10}) and cardiovascular hospital admissions in 14 Spanish cities within the EMECAM project. In this exploratory analysis, the authors examined the models used when pollutants were added in either a linear or non-linear way (i.e., with a spline smoothing function) to the model. Although the study does not present the results for each of the pollutants evaluated individually, overall Ballester et al. (2006, 088746) found that the shape of the pollutant-cardiovascular hospital admission relationship was most compatible with a linear curve. Wellenius et al. (2005, 087483) conducted a similar analysis when examining the relationship between PM_{10} and CHF hospital admissions among Medicare beneficiaries. The authors examined the assumption of linearity using fractional polynomials and linear splines. The results of both approaches contributed to Wellenius et al. (2005, 087483) concluding that the assumption of linearity between the log relative risk of cardiovascular hospital admissions and PM concentration was reasonable.

Unlike the aforementioned studies that examined the linearity in the concentration-response curve as part of the model selection process (i.e., to determine the most appropriate model to use to examine the relationship between PM and cardiovascular hospital admissions and ED visits), Zanobetti and Schwartz (2005, 088069) conducted an extensive analysis of the shape of the concentration-response curve and the potential presence of a threshold when examining the association between PM_{10} and MI hospital admissions among older adults in 21 U.S. cities. The authors examined the concentration-response curve by fitting a piecewise linear spline with slope changes at 20 and 50 $\mu g/m^3$. This approach resulted in an almost linear concentration-response relationship between PM_{10} and MI hospital admissions with a steeper slope occurring below 50 $\mu g/m^3$ (Figure 6-6). Additionally, Zanobetti and Schwartz (2005, 088069) found no evidence for a threshold.



Source: Zanobetti and Schwartz (2005, 088069).

Figure 6-6. Combined random-effect estimate of the concentration-response relationship between MI emergency hospital admissions and PM_{10}, computed by fitting a piecewise linear spline, with slope changes at 20 µg/m^3 and 50 µg/m^3.

Overall, the limited evidence from the studies that examined the concentration-response relationship between PM and cardiovascular hospital admissions and ED visits supports a no-threshold, log-linear model, which is consistent with the observations made in studies that examined the PM-mortality relationship (Section 6.5.2.7).

6.2.10.11. Out of Hospital Cardiac Arrest

One study of out of hospital cardiac death conducted in Seattle, WA (Checkoway et al., 2000, 015527), which reported no association with PM was included in the 2004 PM AQCD (U.S. EPA, 2004, 056905). In the U.S., the survival rate of sudden cardiac arrest is less than 5%. In addition, as discussed in Section 6.5, Zeka et al. (2006, 088749) found that the estimated mortality risk due to short-term exposure to PM_{10} was much higher for out-of-hospital cardiovascular deaths than for in-hospital cardiovascular deaths. The analysis of studies that examine the association between PM and cardiac arrest could provide evidence for an important link between the morbidity and mortality effects attributed to PM.

Sullivan et al. (2003, 043156) examined the association between the incidence of primary cardiac arrest and daily measures of $PM_{2.5}$ (measured by nephelometry) using a case-crossover analysis of 1,206 Washington State out-of-hospital cardiac arrests (1985-1994) among persons with (n = 774) and without (n = 432) clinically recognized heart disease. The authors examined PM associations at 0- through 2-day lags using the time-stratified referent sampling scheme (i.e., the same day of the week and month of the same year). The estimated relative risk for a 13.8-µg/m^3 increase in 1-day lag $PM_{2.5}$ (nephelometry: IQR = 0.54 10^{-1} km^{-1} bsp) was 0.94 (95% CI: 0.88-1.02), or 0.96 (95% CI: 0.91-1.0) per 10 µg/m^3 increase. Similar estimates were reported for 0- or 2-day lags. The presence or absence of clinically recognized heart disease did not alter the result. This finding is consistent with the previous study of cardiac arrest in Seattle (Levy et al., 2001, 017171) that reported no PM association. It is also consistent with the Sullivan et al. (2005, 050854) analysis of PM and onset of MI, and the Sullivan et al. (2007, 100083) analysis of PM and blood markers of inflammation in the elderly population, both of which were conducted in Seattle. Note also that the analysis of the NMMAPS data for the years 1987-1994 also found no PM_{10} association for all-cause mortality in Seattle. Overall, the results of studies conducted in Seattle consistently found no association between PM and cardiovascular outcomes or all-cause mortality.

Rosenthal et al. (2008, 156925) examined associations between $PM_{2.5}$ and out-of-hospital cardiac arrests in Indianapolis, Indiana for the years 2002-2006 using a case-crossover design with time-stratified referent sampling. Using all the cases (n = 1,374), they found no associations between $PM_{2.5}$ and cardiac arrest in any of the 0- through 3-day lags or multiday averages thereof (e.g., for 0-day lag, OR = 1.02 [CI: 0.94-1.11] per 10 $\mu g/m^3$ increase in $PM_{2.5}$). However, for cardiac arrests witnessed by bystanders (n = 511), they found a significant association with $PM_{2.5}$ exposure (by TEOM, corrected with FRM measurements) during the hour of the arrest (OR = 1.12 [CI: 1.01-1.25] per 10 $\mu g/m^3$ increase in $PM_{2.5}$), and even larger risk estimates for older adults (age 60-75) or those that presented with asystole. There have been very few PM studies that used hourly PM measurements, and further studies are needed to confirm associations at such time scales.

In Rome, Forastiere et al. (2005, 086323) examined associations between air pollution (PNC, PM_{10}, CO, NO_2, and O_3) and out-of-hospital coronary deaths (n = 5,144) for the study period of 1998-2000. A case-crossover design with the time-stratified referent sampling was used to examine the pollution indices at lag 0- through 3 days and the average of 0-1 lags. They found associations between deaths and PNC (lag 0 and 0-1), PM_{10} (lag 0, 1, and 0-1), and CO (lag 0 and 0-1) but not with NO_2 or O_3. The risk estimate for 0-day lag PM_{10} was 1.59% (CI: 0.03-3.18) per 10 $\mu g/m^3$ increase. The older adults (65-74 and ≥75 age groups) showed higher risk estimates than the younger (35-64) age group. Because PNC is considered to be associated with UFPs, and CO was also associated with out-of-hospital cardiac arrests, combustion sources were implicated.

In summary, only a few studies have examined out-of-hospital cardiac arrest or deaths. The two studies from Seattle, WA consistently found no association (also consistent with other cardiac effects and mortality studies conducted in that locale); a study in Indianapolis, IN found an association with hourly $PM_{2.5}$ but not daily $PM_{2.5}$; and a study in Rome found an association with PM_{10}, but also with PNC and CO. Because multicity mortality studies examining this association found heterogeneity in PM risk estimates across regions, future studies of out-of-hospital cardiac arrest will need to consider location and the air pollution mixture during their design. Mean and upper percentile concentrations are found in Table 6-9.

Table 6-9. PM concentrations reported in studies of out-of-hospital cardiac arrest.

Author	Location	Mean Concentration ($\mu g/m^3$)	Upper Percentile Concentrations ($\mu g/m^3$)
$PM_{2.5}$			
Sullivan et al. (2003, 043156)	Washington State	Nephelometry: 0.71 x 10^{-1} km^{-1} bsp	Maximum: 5.99 x 10^{-1} km^{-1} bsp
Rosenthal et al. (2008, 156925)	Indianapolis, Indiana	NR	NR
PM_{10}			
Sullivan et al. (2003, 043156)	Washington State	28.05	89.83
Zeka et al. (2006, 088749)		Range in Means: 15.9 (Honolulu) - 37.5 (Cleveland)	NR
Forastiere et al. (2005, 086323)	Rome, Italy	52.1	75th: 65.7

6.2.11. Cardiovascular Mortality

An evaluation of studies that examined the association between short-term exposure to $PM_{2.5}$ and $PM_{10-2.5}$ and mortality provides additional evidence for PM-related cardiovascular health effects. Although the primary analysis in the majority of mortality studies evaluated consists of an examination of the relationship between $PM_{2.5}$ or $PM_{10-2.5}$ and all-cause (nonaccidental) mortality, some studies have examined associations with cause-specific mortality including cardiovascular-related mortality.

Multicity mortality studies that examined the $PM_{2.5}$-cardiovascular mortality relationship on a national scale (Franklin et al. (2007, 091257) – 27 U.S. cities; Franklin et al. (2008, 097426) – 25 U.S. cities; and Zanobetti and Schwartz (2009, 188462) – 112 U.S. cities) have found consistent positive associations between short-term exposure to $PM_{2.5}$ and cardiovascular mortality ranging from 0.47 to 0.85% per 10μg/m^3 at lag 0-1 (Section 6.5). The associations observed on a national scale are consistent with those presented by Ostro et al. (2006, 087991) in a study that examined the $PM_{2.5}$-mortality relationship in nine California counties (0.6% [95% CI: 0-1.1] per 10 μg/m^3). Of the multicity studies evaluated, one examined single day lags and found evidence for slightly larger effects at lag 1 compared to the average of lag days 0 and 1 for cardiovascular mortality (94% [95% CI: -0.14 to 2.02] per 10 μg/m^3) (Franklin et al., 2007, 091257). Although the overall effect estimates reported in the multicity studies evaluated are consistently positive, it should be noted that a large degree of variability exists between cities when examining city-specific effect estimates potentially due to differences between cities and regional differences in $PM_{2.5}$ composition (Figure 6-24). Only a limited number of studies that examined the $PM_{2.5}$-mortality relationship have conducted analyses of potential confounders, such as gaseous copollutants, and none examined the effect of copollutants on $PM_{2.5}$ cardiovascular mortality risk estimates. Although the recently evaluated multicity studies did not extensively examine whether $PM_{2.5}$ mortality risk estimates are confounded by gaseous copollutants, evidence from the limited number of single-city studies evaluated in the 2004 PM AQCD (U.S. EPA, 2004, 056905) suggests that gaseous copollutants do not confound the $PM_{2.5}$-cardiovascular mortality association. This is further supported by studies that examined the PM_{10}-mortality relationship in both the 2004 PM AQCD (U.S. EPA, 2004, 056905) and this review. The evidence from epidemiologic, controlled human exposure, and toxicological studies that examined the association between short-term exposure to $PM_{2.5}$ and cardiovascular morbidity provide coherence and biological plausibility for the cardiovascular mortality effects observed. Overall, the cardiovascular mortality $PM_{2.5}$ effects were similar to those reported for all-cause (nonaccidental) mortality (Section 6.5), and are consistent with the effect estimates observed in the single- and multicity studies evaluated in the 2004 PM AQCD (U.S. EPA, 2004, 056905).

Zanobetti and Schwartz (2009, 188462) also examined $PM_{10-2.5}$ mortality associations in 47 U.S. cities and found evidence for cardiovascular mortality effects (0.32% [95% CI: 0.00-0.64] per 10 μg/m at lag 0-1) similar to those reported for all-cause (nonaccidental) mortality (0.46% [95% CI: 0.21-0.67] per 10 μg/m). In addition, Zanobetti and Schwartz (2009, 188462) reported seasonal (i.e., larger in spring and summer) and regional differences in $PM_{10-2.5}$ cardiovascular mortality risk estimates. A few single-city studies evaluated also reported associations, albeit somewhat larger than the multicity study, between $PM_{10-2.5}$ and cardiovascular mortality in Phoenix, AZ (Wilson et al., 2007, 157149) (3.4-6.6% at lag 1) and Vancouver, Canada (Villeneuve et al., 2003, 055051) (5.4% at lag 0). The difference in the $PM_{10-2.5}$ risk estimates observed between the multi- and single-city studies could be due to a variety of factors including differences between cities and compositional differences in $PM_{10-2.5}$ across regions (Figure 6-29). Only a small number of studies have examined potential confounding by gaseous copollutants or the influence of model specification on $PM_{10-2.5}$ mortality risk estimates, but the effects are relatively consistent with those studies evaluated in the 2004 PM AQCD (U.S. EPA, 2004, 056905).

6.2.12. Summary and Causal Determinations

6.2.12.1. $PM_{2.5}$

Several studies cited in the 2004 AQCD reported positive associations between short-term $PM_{2.5}$ concentrations and hospital admissions or ED visits for CVD, although few were statistically significant. In addition, U.S. and Canadian-based studies (both multi- and single-city) that examined the $PM_{2.5}$-mortality relationship reported associations for cardiovascular mortality consistent with those observed for all-cause (nonaccidental) mortality and relatively stronger than those for respiratory mortality. Significant associations were also observed between MI and short-term $PM_{2.5}$ concentrations (averaged over 2 or 24 h), as well as decreased HRV in association with $PM_{2.5}$. Several controlled human exposure and animal toxicological studies demonstrated HRV effects from exposure to $PM_{2.5}$ CAPs, as well as changes in blood coagulation markers. However, the effects in these studies were variable. Arrhythmogenesis was reported for toxicological studies and generally

these results were observed in animal models of disease (SH rat, MI, pulmonary hypertension) exposed to combustion-derived $PM_{2.5}$ (i.e., ROFA, DE, metals). One study demonstrated significant vasoconstriction in healthy adults following controlled exposures to CAPs, although this response could not be conclusively attributed to the particles as subjects were concomitantly exposed to relatively high levels of O_3. The results reported for systemic inflammation in toxicological studies were mixed.

A large body of evidence from studies of the effect of $PM_{2.5}$ on hospital admissions and ED visits for CVD has been published since the 2004 PM AQCD. Associations with $PM_{2.5}$ are consistently positive with the majority of studies reporting increases in hospital admissions or ED visits ranging from 0.5 to 3.4% per 10 $\mu g/m^3$ increase in $PM_{2.5}$ (Section 6.2.10). The largest U.S.-based multicity study, MCAPs, reported excess risks in the range of approximately 0.7% with the largest excess risks in the Northeast (1.08%) and in the winter (1.49%), providing evidence of regional and seasonal heterogeneity (Bell et al., 2008, 156266; Dominici et al., 2006, 088398). Weak or null findings for $PM_{2.5}$ have been observed in two single-city studies both conducted in Washington state (Slaughter et al., 2005, 073854; Sullivan et al., 2007, 100083) and may be explained by this heterogeneity. Weak associations were also reported in Atlanta for $PM_{2.5}$ and CVD ED visits, with $PM_{2.5}$ traffic components being more strongly associated with CVD ED visits than other components (Tolbert et al., 2007, 090316). Multicity studies conducted outside the U.S. and Canada have shown positive associations with $PM_{2.5}$. Studies of specific CVD outcomes indicate that IHD and CHF may be driving the observed associations (Sections 6.2.10.3 and 6.2.10.5, respectively). Although estimates from studies of cerebrovascular diseases are less precise and consistent, ischemic diseases appear to be more strongly associated with $PM_{2.5}$ compared to hemorrhagic stroke (Section 6.2.10.7). The available evidence suggests that these effects occur at very short lags (0-1 days), although effects at longer lags have rarely been evaluated. Overall, the results of these studies provide support for associations between short-term $PM_{2.5}$ exposure and increased risk of cardiovascular hospital admissions in areas with mean concentrations ranging from 7 to 18 $\mu g/m^3$.

Epidemiologic studies that examined the association between $PM_{2.5}$ and mortality provide additional evidence for $PM_{2.5}$-related cardiovascular effects (Section 6.2.11). The multicity studies evaluated found consistent, precise positive associations between short-term exposure to $PM_{2.5}$ and cardiovascular mortality ranging from 0.47 to 0.85% at mean 24-h avg $PM_{2.5}$ concentrations above 13 $\mu g/m^3$. These associations were reported at short lags (0-1 days), which is consistent with the associations observed in the hospital admission and ED visit studies discussed above. Although only a limited number of studies examined potential confounders of the $PM_{2.5}$-cardiovascular mortality relationship, the studies evaluated in both this review and the 2004 PM AQCD (U.S. EPA, 2004, 056905) support an association between short-term exposure to $PM_{2.5}$ and cardiovascular mortality.

Recent studies that apportion ambient $PM_{2.5}$ into sources and components suggest that cardiovascular hospital admissions associated with $PM_{2.5}$ may be attributable to traffic-related pollution and, in some cases, biomass burning (Section 6.2.10). Further supporting evidence is provided by studies that have used PM_{10} collection filters (median diameter generally <2.5 μm) to identify combustion- or traffic-related sources associated with cardiovascular hospital admissions. Metals have also been implicated in these effects (Bell et al., 2009, 191997). A limited number of older publications have reported that particle acidity of $PM_{2.5}$ is not more strongly associated with CVD hospitalizations or ED visits than other PM metrics.

Changes in various measures of cardiovascular function have been demonstrated by multiple independent laboratories following controlled human exposures to different types of $PM_{2.5}$. The most consistent effect is changes in vasomotor function, which has been demonstrated following exposure to CAPs and DE. The majority of the new evidence of particle-induced changes in vasomotor function comes from studies of exposures to DE (Section 6.2.4.2). None of these studies have evaluated the effects of DE with and without a particle trap. Therefore, the changes in vasomotor function cannot be conclusively attributed to the particles in DE as subjects are also concomitantly exposed to relatively high levels of NO_2, NO, CO, and hydrocarbons. However, it is important to note that a study by Peretz et al. (2008, 156854) used a newer diesel engine with lower gaseous emissions and reported significant DE-induced decreases in BAD. In addition, increasing the particle exposure concentration from 100 to 200 $\mu g/m^3$, without proportional increases in NO, NO_2, or CO, resulted in an approximate 100% increase in response. An additional consideration is that, while fresh DE used in these studies contains relatively high concentrations of $PM_{2.5}$, the MMAD is typically ≤ 100 nm, which makes it difficult to determine whether the observed effects are due to

$PM_{2.5}$ or, more specifically, due to the UF fraction. Further evidence of a particle effect on vasomotor function is provided by significant changes in BAD demonstrated in healthy adults following controlled exposure to CAPs with O_3 (Brook et al., 2002, 024987). These findings are consistent with epidemiologic studies of various measures of vasomotor function (e.g., FMD and BAD were the most common), which have demonstrated an association with short-term $PM_{2.5}$ concentration in healthy and diabetic populations (Section 6.2.4.1). A limited number of epidemiologic studies examined multiple lags and the strongest associations were with either the 6-day mean concentration (O'Neill et al., 2005, 088423) or the concurrent day (Schneider et al., 2008, 191985).

The toxicological findings with respect to vascular reactivity are generally in agreement and demonstrate impaired dilation following $PM_{2.5}$ exposure that is likely endothelium dependent (Section 6.2.4.3). These effects have been demonstrated in varying vessels and in response to different $PM_{2.5}$ types, albeit using IT instillation exposure in most studies. Further support is provided by IT instillation studies of ambient PM_{10} that also demonstrate impaired vasodilation and a $PM_{2.5}$ CAPs study that reported decreased L/W ratio of the pulmonary artery. An inhalation study of Boston $PM_{2.5}$ CAPs reported increases in coronary vascular resistance during ischemia, which indicated a possible role for PM-induced coronary vasoconstriction. The mechanism behind impaired dilation following PM exposure may include increased ROS and RNS production in the microvascular wall that leads to altered NO bioavailability and endothelial dysfunction. Despite the limited number of inhalation studies conducted with concentrations near ambient levels, the toxicological studies collectively provide coherence and biological plausibility for the myocardial ischemia observed in controlled human exposure and epidemiologic studies.

Consistent with the observed effects on vasomotor function, one recent controlled human exposure study reported an increase in exercise-induced ST-segment depression (a potential indicator of ischemia) during exposure to DE in a group of subjects with prior MI (Mills et al., 2007, 091206). In addition, toxicological studies from Boston that employed CAPs provide further evidence for $PM_{2.5}$ effects on ischemia, with changes in ST-segment and decreases in total myocardial blood flow reported (Section 6.2.3.3). These findings from toxicological and controlled human exposure studies provide coherence and biological plausibility for the associations observed in epidemiologic studies, particularly those of increases in hospital admissions and ED visits for IHD. Several epidemiology studies have reported associations between short-term $PM_{2.5}$ concentration (including traffic sources or components such as BC) and ST-segment depression or abnormality (Section 6.2.3.1).

Toxicological studies provide biological plausibility for the $PM_{2.5}$ associations with CHF hospital admissions by demonstrating increased right ventricular pressure and diminished cardiac contractility in rodents exposed to CB and DE (Section 6.2.6.1). Similarly, increased coronary vascular resistance was observed following $PM_{2.5}$ CAPs exposure in dogs with experimentally-induced ischemia. Further, a recent epidemiology study reported small but statistically significant decreases in passively monitored diastolic pressure and right ventricular diastolic pressure (Rich et al., 2008, 156910).

In addition to the effects of PM on vasomotor response, there is a growing body of evidence that demonstrates changes in markers of systemic oxidative stress following controlled human exposures to DE, wood smoke, and urban traffic particles. However, these effects may be driven in part by the UF fraction of $PM_{2.5}$. Toxicological studies provide evidence of increased cardiovascular ROS following $PM_{2.5}$ exposure to CAPs, road dust, CB, and TiO_2, as well as increased systemic ROS in rats exposed to gasoline exhaust (Section 6.2.9.3). Epidemiologic studies of markers of oxidative stress (e.g., tHcy, CuZn-SOD, TBARS, 8-oxodG, oxLDL and MDA) are consistent with these toxicological findings (Section 6.2.9.1).

A few epidemiologic studies of ventricular arrhythmias recorded on ICDs that were conducted in Boston and Sweden (Table 6-2) found associations with short-term $PM_{2.5}$ concentration (also BC and sulfate). While Canadian and U.S. studies conducted outside of Boston did not find positive associations between $PM_{2.5}$ and ICD recorded ventricular arrhythmias, several such studies observed associations with ectopic beats and runs of supraventricular or ventricular tachycardias (Section 6.2.2.1). Toxicological studies also provide limited evidence of arrhythmia, mainly in susceptible animal models (i.e., older rats, rats with CHF) (Section 6.2.2.2).

Most epidemiologic studies of HRV have reported decreases in SDNN, LF, HF, and rMSSD (Section 6.2.1.1). While there are also a significant number of controlled human exposure studies reporting PM-induced changes in HRV, these changes are often variable and difficult to interpret (Section 6.2.1.2). Similarly, HRV increases and decreases have been observed in animal toxicological studies that employed CAPs or CB (Section 6.2.1.3). In a study in mice, resuspended

soil, secondary sulfate, residual oil, and motor vehicle/other sources, as well as Ni were implicated in HRV effects (Lippmann et al., 2006, 091165). Further, cardiac oxidative stress has been implicated as a consequence of ANS stimulation in response to CAPs. Modification of the PM-HRV association by genetic polymorphisms related to oxidative stress has been observed in a series of analyses of the population enrolled in the Normative Aging Study. Changes in HRV measures (whether increased or decreased) are likely to be more useful as indicators of PM exposure rather than predictive of some adverse outcome. Furthermore, the HRV result may be reflecting a fundamental response of an individual that is determined in part by a number of factors including age and pre-existing conditions.

Although not consistently observed across studies, some investigators have reported $PM_{2.5}$-induced changes in BP, blood coagulation markers, and markers of systemic inflammation in controlled human exposure studies (Sections 6.2.5.2, 6.2.8.2, and 6.2.9.2, respectively). Findings from epidemiologic studies, which are largely cross-sectional and measure a wide array markers of inflammation and coagulation, are not consistent; however, a limited number of recent studies of gene-environment interactions offer insight into potential individual susceptibility to these effects (Ljungman et al., 2009, 191983; Peters et al., 2009, 191992). Similarly, toxicological studies demonstrate mixed results for systemic inflammatory markers and generally indicate relatively little change at 16-20 h post-exposure (Section 6.2.7.3). Increases in BP have been observed in toxicological studies (Section 6.2.5.3), with the strongest evidence coming from dogs exposed to $PM_{2.5}$ CAPs. For blood coagulation parameters, the most commonly reported change in animal toxicological studies is elevated plasma fibrinogen levels following $PM_{2.5}$ exposure, but this response is not consistently observed (Section 6.2.8.3).

In summary, associations of hospital admissions or ED visits with $PM_{2.5}$ for CVD (predominantly IHD and CHF) are consistently positive with the majority of studies reporting increases ranging from 0.5 to 3.4% per 10 $\mu g/m^3$ increase in $PM_{2.5}$. Seasonal and regional variation observed in the large multicity study of Medicare recipients is consistent with null findings reported in several single city studies conducted in the Western U.S. The results from the hospital admission and ED visit studies are supported by the associations observed between $PM_{2.5}$ and cardiovascular mortality, which also provide additional evidence for regional and seasonal variability in $PM_{2.5}$ risk estimates. Changes in various measures of cardiovascular function that may explain these epidemiologic findings have been demonstrated by multiple independent laboratories following controlled human exposures to different types of $PM_{2.5}$. The most consistent $PM_{2.5}$ effect is for vasomotor function, which has been demonstrated following exposure to CAPs and DE. Toxicological studies finding reduced myocardial blood flow during ischemia and altered vascular reactivity provide coherence and biological plausibility for the myocardial ischemia that has been observed in both controlled human exposure and epidemiologic studies. Further, $PM_{2.5}$ effects on ST-segment depression have been observed across disciplines. In addition to ischemia, $PM_{2.5}$ may act through several other pathways. Plausible biological mechanisms (e.g., increased right ventricular pressure and diminished cardiac contractility) for the associations of $PM_{2.5}$ with CHF have also been proposed based on toxicological findings. There is a growing body of evidence from controlled human exposure, toxicological and epidemiologic studies demonstrating changes in markers of systemic oxidative stress with $PM_{2.5}$ exposure. Inconsistent effects of PM on BP, blood coagulation markers and markers of systemic inflammation have been reported across the disciplines. Together, the collective **evidence is sufficient to conclude that a causal relationship exists between short-term $PM_{2.5}$ exposures and cardiovascular effects**.

6.2.12.2. $PM_{10-2.5}$

There was little evidence in the 2004 AQCD regarding $PM_{10-2.5}$ cardiovascular health effects. Two single-city epidemiologic studies found positive associations of $PM_{10-2.5}$ with cardiovascular hospital admissions in Toronto (Burnett et al., 1999, 017269) and Detroit, MI (Ito, 2003, 042856; Lippmann, 2000, 024579) and the effect estimates were of the same general magnitude as for PM_{10} and $PM_{2.5}$. Both studies reported positive associations and estimates appeared robust to adjustment for gaseous copollutants in two-pollutant models. An imprecise, non-significant association between $PM_{10-2.5}$ and onset of MI was observed in Boston (Peters et al., 2001, 016546). No controlled human exposure or toxicological studies of $PM_{10-2.5}$ were presented in the 2004 AQCD.

Several recent epidemiologic studies of the effect of ambient $PM_{10-2.5}$ concentration on hospital admissions or ED visits for CVD were conducted (Section 6.2.10). In a study of Medicare patients in

108 U.S. counties, Peng et al. (2008, 156850) reported a significant association between $PM_{10-2.5}$ and CVD hospitalizations in their single pollutant model. In a study of six French cities, Host et al. (2008, 155852) reported a significant increase in IHD hospital admissions in association with $PM_{10-2.5}$. In contrast, associations of cardiovascular outcomes with $PM_{10-2.5}$ were weak for CHF and null for IHD in the Atlanta-based SOPHIA study (Metzger et al., 2004, 044222). Results from single-city studies are generally positive, but effect sizes are heterogeneous and estimates are imprecise (Section 6.2.10). Crustal material from a dust storm in the Gobi desert that was largely coarse PM (generally indicated using PM_{10}) was associated with hospitalizations for CVD, including IHD and CHF in most studies (Section 6.2.10). Mean $PM_{10-2.5}$ concentrations in the hospital admission and ED visit studies ranged from 7.4-13 $\mu g/m^3$. A few epidemiologic studies that examined the association between short-term exposure to $PM_{10-2.5}$ and cardiovascular mortality (Section 6.2.11) provide supporting evidence for the hospital admission and ED visit studies at similar 24-h avg $PM_{10-2.5}$ concentrations (i.e., 6.1-16.4 $\mu g/m^3$). A multicity study reported risk estimates for cardiovascular mortality of similar magnitude to those for all-cause (nonaccidental) mortality (Zanobetti and Schwartz, 2009, 188462). However, the single-city studies evaluated (Villeneuve et al., 2003, 055051; Wilson et al., 2007, 157149) reported substantially larger effect estimates, but this could be due to differences between cities and compositional differences in $PM_{10-2.5}$ across regions. Of note is the lack of analyses within the studies evaluated that examined potential confounders of the $PM_{10-2.5}$-cardiovascular mortality relationship.

The U.S. study of Medicare patients (Peng et al., 2008, 156850) and the multicity study that examined the association between $PM_{10-2.5}$ and mortality (Zanobetti and Schwartz, 2009, 188462) were the only studies to adjust $PM_{10-2.5}$ for $PM_{2.5}$. Peng, et al. (2008, 156850) found that the $PM_{10-2.5}$ association with CVD hospitalizations remained, but diminished slightly after adjustment for $PM_{2.5}$. These results are consistent with those reported by Zanobetti and Schwartz (2009, 188462), which found $PM_{10-2.5}$-cardiovascular mortality risk estimates remained relatively robust to the inclusion of $PM_{2.5}$ in the model. Because of the greater spatial heterogeneity of $PM_{10-2.5}$, exposure measurement error is more likely to bias health effect estimates towards the null for epidemiologic studies of $PM_{10-2.5}$ versus PM_{10} or $PM_{2.5}$, making it more difficult to detect an effect of the coarse size fraction. In addition, models that include both $PM_{10-2.5}$ and $PM_{2.5}$ may suffer from instability due to collinearity. Further, the lag structure of $PM_{10-2.5}$ effects on risk of cardiovascular hospital admissions and ED visits, as well as mortality, has not been examined in detail.

Several epidemiologic studies of cardiovascular endpoints including HRV, BP, ventricular arrhythmia, and ECG changes indicating ectopy or ischemia were conducted since publication of the 2004 PM AQCD. Supraventricular ectopy and ST-segment depression were associated with $PM_{10-2.5}$ (Section 6.2.3.1), and the only study to examine the effect of $PM_{10-2.5}$ on BP reported a decrease in SBP (Ebelt et al., 2005, 056907) (Section 6.2.5.1). HRV findings were mixed across the epidemiologic studies (Section 6.2.1.1). A limited number of studies have evaluated the effect of controlled exposures to $PM_{10-2.5}$ CAPs on cardiovascular endpoints in human subjects. These studies have provided some evidence of decreases in HRV (SDNN) and tPA concentration among healthy adults approximately 20 hours following exposure (Section 6.2.1.2). However, it is important to note that no other measures of HRV (e.g., LF, HF, or LF/HF), nor other hemostatic or thrombotic markers (e.g., fibrinogen) were significantly affected by particle exposure in these studies.

There are very few toxicological studies that examined the effect of exposure to $PM_{10-2.5}$ on cardiovascular endpoints or biomarkers in animals. The few studies that evaluated cardiovascular responses were comparative studies of various size fractions, and only blood or plasma parameters were measured (Sections 6.2.7.3 and 6.2.8.3). These studies used IT instillation methodologies, as there are challenges to exposing rodents via inhalation to $PM_{10-2,5}$, due to near 100% deposition in the ET region for particles >5 μm (Raabe et al., 1988, 001439) and only 44% nasal inhalability of a 10 μm particle in the rat (Ménache et al., 1995, 006533). These studies also employed relatively high doses of $PM_{10-2.5}$. Despite these shortcomings, increased plasma fibrinogen was observed and the response was similar to that observed with $PM_{2.5}$. At this time, evidence of biological plausibility for cardiovascular morbidity effects following $PM_{10-2.5}$ exposure is sparse, due to the small number of studies, few endpoints examined, and the limitations related to the interpretation of IT instillation exposures.

In summary, several epidemiologic studies report associations with cardiovascular endpoints including IHD hospitalizations, supraventricular ectopy, and changes in HRV. Further, dust storm events resulting in high concentrations of crustal material are linked to increases in cardiovascular disease hospital admissions or ED visits for cardiovascular diseases. A large proportion of inhaled

coarse particles in the 3-6 μm (d_{ae}) range can reach and deposit in the lower respiratory tract, particularly the TB airways (Figures 4-3 and 4-4). The few toxicological and controlled human exposure studies examining the effects of $PM_{10-2.5}$ provide limited evidence of cardiovascular effects and biological plausibility to support the epidemiologic findings. Therefore the available evidence is **suggestive of a causal relationship between $PM_{10-2.5}$ exposures and cardiovascular effects**.

6.2.12.3. UFPs

There was very little evidence available in the 2004 PM AQCD (U.S. EPA, 2004, 056905) on the cardiovascular effects of UFPs. Findings from one study presented in the 2004 PM AQCD (U.S. EPA, 2004, 056905) of controlled exposures to UF EC suggested no particle-related effects on various cardiovascular endpoints including blood coagulation, HRV, and systemic inflammation. No epidemiologic studies of short-term UFP concentration and cardiovascular endpoints were included in the 2004 AQCD and there were no relevant toxicological studies reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905) that exposed animals to UFPs. A small number of new epidemiologic studies, as well as several controlled human exposure and toxicological studies have been conducted in recent years, but substantial uncertainties remain as to the cardiovascular effects of UFPs. For a given mass, the enormous number and large surface area of UFPs highlight the importance of considering the size of the particle in assessing response. For example, UFPs with a diameter of 20 nm, when inhaled at the same mass concentration, have a number concentration that is approximately six orders of magnitude higher than for a 2.5-μm diameter particle. Particle surface area is also greatly increased with UFPs. Many studies suggest that the surface of particles or substances released from the surface (e.g., transition metals, organics) interact with biological substrates, and that surface-associated free radicals or free radical-generating systems may be responsible for toxicity, resulting in greater toxicity of UFPs per particle surface area than larger particles. Additionally, smaller particles may have greater potential to cross cell membranes and epithelial barriers.

Controlled human exposure studies are increasingly being utilized to evaluate the effect of UFPs on cardiovascular function. While the number of studies of exposure to UFPs is still limited, there is a relatively large body of evidence from exposure to fresh DE, which is typically dominated by UFPs. As described under the summary for $PM_{2.5}$, studies of controlled exposures to DE (100-300 $\mu g/m^3$) have consistently demonstrated effects on vasomotor function among adult volunteers (Section 6.2.4.2). In addition, exposure to UF EC (50 $\mu g/m^3$, 10.8×10^6 particles/cm^3) was recently shown to attenuate FMD (Shah et al., 2008, 156970). Changes in vasomotor function have been observed in animal toxicological studies of UFPs, although very few studies have been conducted (Section 6.2.4.3). Inhaled UF TiO_2 impaired arteriolar dilation when compared to fine TiO_2 at similar mass doses (Nurkiewicz et al., 2008, 156816). This response may have been due to ROS in the microvascular wall, which may have led to consumption of endothelial-derived NO and generation of peroxynitrite radicals. Support for an UFP effect on altered vascular reactivity is also provided by studies of DE and IT instillation exposure to ambient PM. The response to DE did not appear to be due to VOCs. One epidemiologic study showed that PNC was associated with a nonsignificant decrease in flow- and nitroglycerine-mediated reactivity as measures of vasomotor function in diabetics living in Boston (O'Neill et al., 2005, 088423).

New studies have reported increases in markers of systemic oxidative stress in humans following controlled exposures to different types of PM consisting of relatively high concentrations of UFPs from sources including wood smoke, urban traffic particles, and DE (Section 6.2.9.2). Increased cardiac oxidative stress has been observed in mice and rats following gasoline exhaust exposure and it appeared the effect was particle-dependent (Section 6.2.9.3).

The associations between UFPs and HRV measures in epidemiologic studies include increases and decreases (Section 6.2.1.1), providing some evidence for an effect. Exposure to UF CAPs has been observed to alter parameters of HRV in controlled human exposure studies, although this effect has been variable between studies (Section 6.2.1.2). Alterations in HR, HRV, and BP were reported in rats exposed to <200 $\mu g/m^3$ UF CB (<1.6×10^7 particles/cm^3) (Sections 6.2.1.3 and 6.2.5.3). The effects of UFPs on BP have been mixed in epidemiologic studies (Section 6.2.5.1).

There is some evidence of changes in markers of blood coagulation in humans following controlled exposure to UF CAPs, as well as wood smoke and DE; however, these effects have not

been consistently observed across studies (Section 6.2.8.2). Toxicological studies demonstrate mixed results for systemic inflammation and blood coagulation as well (Sections 6.2.7.3 and 6.2.8.3).

Few time-series studies of CVD hospital admissions have evaluated UFPs. The SOPHIA study found no association between any outcome studied (all CVD, dysrhythmia, CHF, IHD, peripheral vascular and cerebrovascular disease) and 24-h mean levels of UFP (Metzger et al. 2004). The median UF particle count in Atlanta during the study period was 25,900 particles/cm^3. UFP were not associated with CVD hospitalizations in the elderly in Copenhagen, Denmark, but were associated with cardiac readmission or fatal MI in the European HEAPSS study (Section 6.2.10). In the Copenhagen study, the mean count of particles with a 100 nm mean diameter was 0.68×10^4 particles/cm^3, whereas the PNC range was approximately $1.2\text{-}7.6\times10^4$ particles/cm^3 in HEAPSS study. Spatial variation in UFP concentration, which diminishes within a short distance from the roadway, may introduce exposure measurement error, making it more difficult to observe an association if one exists.

A limited number of epidemiologic studies have evaluated subclinical cardiovascular measures and a number of these were conducted in Boston. UFPs have been linked to ICD-recorded arrhythmias in Boston and supraventricular ectopic beats in Erfurt, Germany (Section 6.2.2.1). One study reported no UFP association with ectopy (Barclay et al., 2009, 179935). ST-segment depression in subjects with stable coronary heart disease was associated with UFPs in Helsinki (Section 6.2.3.1). The limited number of studies that examine this size fraction makes it difficult to draw conclusions about these cardiovascular measures.

In summary, there is a relatively large body of evidence from controlled human exposure studies of fresh DE, which is typically dominated by UFPs, demonstrating effects of UFP on the cardiovascular system. In addition, cardiovascular effects have been demonstrated by a limited number of laboratories in response to UF CB, urban traffic particles and CAPs. Responses include altered vasomotor function, increased systemic oxidative stress and altered HRV parameters. Studies using UF CAPs, as well as wood smoke and DE, provide some evidence of changes in markers of blood coagulation, but findings are not consistent. Toxicological studies conducted with UF TiO_2, CB, and DE demonstrate changes in vasomotor function as well as in HRV. Effects on systemic inflammation and blood coagulation are less consistent. PM-dependent cardiac oxidative stress was noted following exposure to gasoline exhaust. The few epidemiologic studies of UFPs conducted do not provide strong support for an association of UFPs with effects on the cardiovascular system. Based on the above findings, the evidence is **suggestive of a causal relationship between ultrafine PM exposure and cardiovascular effects.**

6.3. Respiratory Effects

6.3.1. Respiratory Symptoms and Medication Use

The 2004 PM AQCD (U.S. EPA, 2004, 056905) presented evidence from epidemiologic studies of increases in respiratory symptoms associated with PM, although this was not supported by the findings of a limited number of controlled human exposure studies. Recent epidemiologic studies have provided evidence of an increase in respiratory symptoms and medication use associated with PM among asthmatic children, with less evidence of an effect in asthmatic adults. The lack of an observed effect of PM exposure on respiratory symptoms in controlled human exposure studies does not necessarily contradict these findings, as very few studies of controlled exposures to PM have been conducted among groups of asthmatic or healthy children.

6.3.1.1. Epidemiologic Studies

The 2004 PM AQCD (U.S. EPA, 2004, 056905) concluded that the effects of PM_{10} on respiratory symptoms in asthmatics tended to be positive, although they were somewhat less consistent than PM_{10} effects on lung function. Most studies showed increases in cough, phlegm, difficulty breathing, and bronchodilator use, although these increases were generally not statistically significant for PM_{10}. The results from one study of respiratory symptoms and $PM_{10\text{-}2.5}$ (Schwartz and

Neas, 2000, 007625) found a statistically significant association with cough with $PM_{10-2.5}$. The results of two studies examining respiratory symptoms and $PM_{2.5}$ revealed slightly larger effects for $PM_{2.5}$ than for PM_{10}.

Asthmatic Children

Two large, longitudinal studies in urban areas of the U.S. investigated the effects of ambient PM on respiratory symptoms and/or asthma medication use with similar analytic techniques (i.e., multistaged modeling and generalized estimating equations [GEE]): the Childhood Asthma Management Program (CAMP) (Schildcrout et al., 2006, 089812) and the National Cooperative Inner-City Asthma Study (NCICAS) (Mortimer et al., 2002, 030281). A number of smaller panel studies conducted in the U.S. evaluated the effects of ambient PM concentrations on respiratory symptoms and medication use among asthmatic children (Delfino et al., 2002, 093740; 2003, 090941; 2003, 050460; Gent et al., 2003, 052885; 2009, 180399; 2006, 088031; Slaughter et al., 2003, 086294).

In the CAMP study, the association between ambient air pollution and asthma exacerbations in children (n = 990) from eight North American cities was investigated (Schildcrout et al., 2006, 089812). In contrast to several past studies (Delfino et al., 1996, 080788; 1998, 051406), no associations were observed between PM_{10} and asthma exacerbations or medication use. PM_{10} concentrations were measured on less than 50% of study days in all cities except Seattle and Albuquerque. While PM_{10} effects were not observed for the entire panel of children, they were observed in recent reports on the children participating at the Seattle center (Slaughter et al., 2003, 086294; Yu et al., 2000, 013254). In a smaller panel study of asthmatic children (n = 133) enrolled in the CAMP study, daily particle concentrations averaged over three central sites in Seattle was used as the exposure metric (Slaughter et al., 2003, 086294). Children were followed for 2 months, on average. Daily health outcomes included both a 3-category measure of asthma severity based on symptom duration and frequency, and inhaled albuterol use. In single-pollutant models, an increased risk of asthma severity was associated with a 10 $\mu g/m^3$ increase in lag 1 $PM_{2.5}$ (OR 1.20 [95% CI: 1.05-1.37]) and with a 10 $\mu g/m^3$ increase in lag 0 PM_{10} (OR 1.12 [95% CI: 1.05-1.22]). In copollutant models with CO, the associations remained (OR for $PM_{2.5}$ 1.16 [95% CI: 1.03-1.30]; OR for PM_{10} 1.11 [95% CI: 1.03-1.19]). Associations between inhaler use and PM were positive in single-pollutant models (RR lag 1 $PM_{2.5}$ 1.08 [95% CI: 1.01-1.15]; RR lag 0 PM_{10} 1.05 [95% CI: 1.00-1.09]), but attenuated and no longer statistically significant in copollutant models.

The eight cities included in the NCICAS (Mortimer et al., 2002, 030281) were all in the East or Midwest: New York City (Bronx, E. Harlem), Baltimore, Washington DC, Cleveland, Detroit, St. Louis, and Chicago. In this study, 864 asthmatic children, aged 4-9 yr, were followed daily for four 2-wk periods over the course of nine months. Morning and evening asthma symptoms (analyzed as none vs. any) and peak flow were recorded. For the three urban areas with air quality data, each 10 $\mu g/m^3$ increase in the mean of the previous 2 days (lag 1-2) PM_{10}, increased the risk for morning asthma symptoms (OR 1.12 [95% CI: 1.00-1.26]). This effect was robust to the inclusion of O_3 (OR 1.12 [95% CI: 0.98-1.27]). In a related study, O'Connor et al. (2008, 156818) examined the relationship between short-term fluctuations in outdoor air pollutant concentrations and changes in pulmonary function and respiratory symptoms among children with asthma in seven U.S. inner-city communities. $PM_{2.5}$ concentration was not statistically associated with respiratory symptoms in this study.

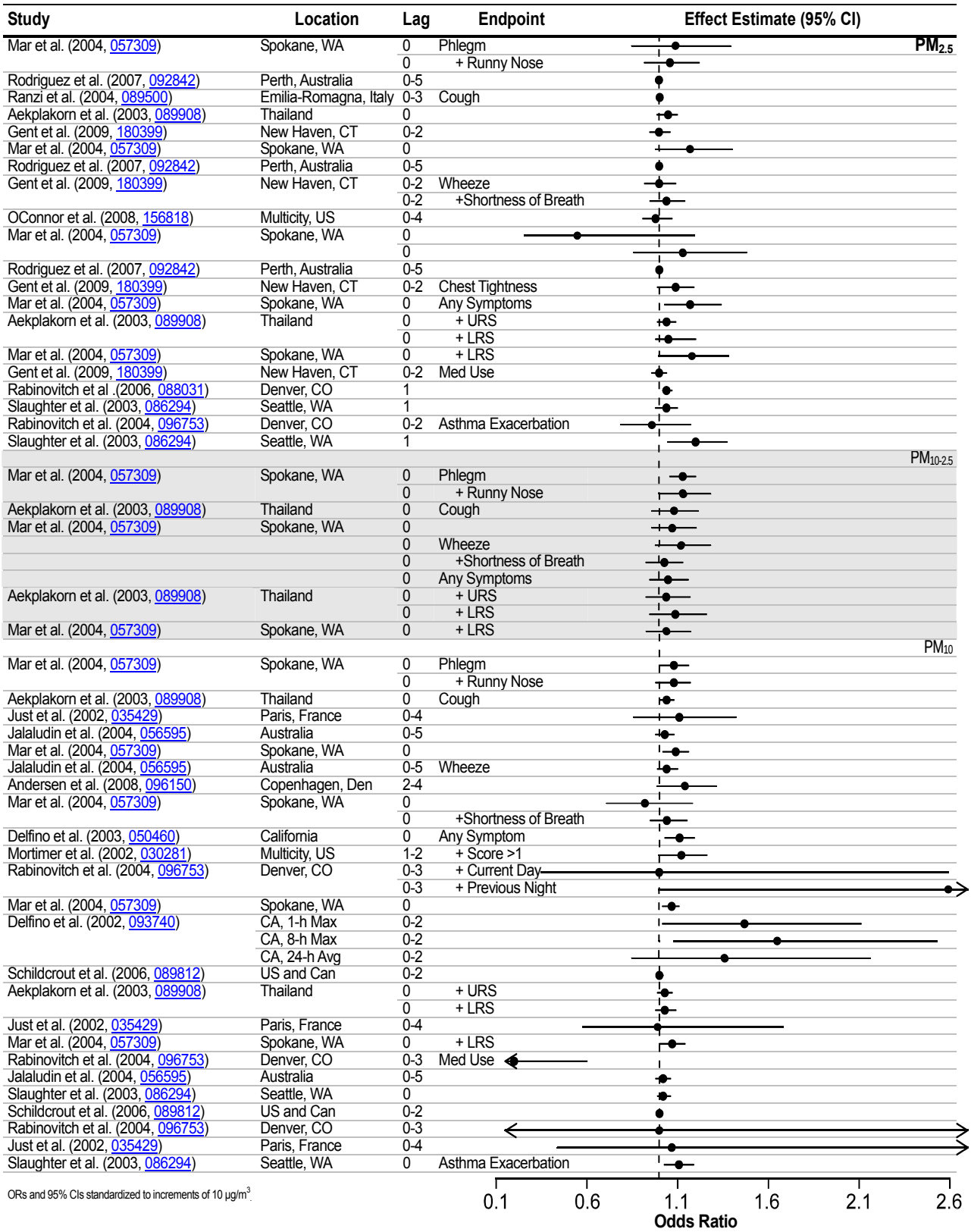


Figure 6-7. Respiratory symptoms and/or medication use among asthmatic children following acute exposure to PM.

Table 6-10. Characterization of ambient PM concentrations from epidemiologic studies of respiratory morbidity and short-term exposures in asthmatic children and adults. All concentrations are for the 24-h avg unless otherwise noted.

Study	Location	Mean Concentration ($\mu g/m^3$)	Upper Percentile Concentrations ($\mu g/m^3$)
$PM_{2.5}$			
Adamkiewicz et al. (2004, 087925)	Steubenville, OH	20.43	75th: 23 98th: 51.79 Max: 51.79
Adar et al. (2007, 001458)	St. Louis, MO	10.13	98th: 22.43 Max: 23.24
Aekplakorn et al. (2003, 089908)	North Thailand		Max: 24.8-26.3
Allen et al. (2008, 156208)	Seattle, WA	11.2	Max: 40.38
Barraza-Villarreal et al. (2008, 156254)	Mexico City	8-h max: 28.9	Max: 102.8
Bourotte et al. (2007, 150040)	Sao Paulo, Brazil	11.9	Max: 26.6
de Hartog et al. (2003, 001061)	Multicity, Europe	12.8-23.4	Max: 39.8-118.1
Delfino et al. (2006, 090745)	Southern CA	3.9-6.9	Max: 8.8-11.6
DeMeo et al. (2004, 087346)	Boston, MA	10.8	NR
Ebelt et al. (2005, 056907)	Vancouver, Canada	11.4	98th: 23 Max: 28.7
Ferdinands et al. (2008, 156433)	Atlanta, GA	27.2	Max: 34.7
Fischer et al. (2007, 156435)	The Netherlands	56	75th: 187
Gent et al. (2003, 052885)	CT & MA	13.1	60th: 12.1 80th: 19.0
Gent et al. (2009, 180399)	New Haven, CT	17.0	NR
Girardot et al. (2006, 088271)	Smoky Mountains	13.9	Max: 38.4
Hogervorst et al. (2006, 156559)	The Netherlands	19.0	NR
Hong et al. (2007, 091347)	Incheon City, Korea	20.27	Max: 36.28
Jansen et al. (2005, 082236)	Seattle, WA	14.0	Max: 44
Johnston et al. (2006, 091386)	Darwin, Australia	11.1	Max: 36.5
Koenig et al. (2003, 156653)	Seattle, WA	13.3	Max: 40.4
Lagorio et al. (2006, 089800)	Rome, Italy	27.2	Max: 100
Lee et al. (2007, 093042)	Seoul, South Korea	51.15	75th: 87.54 Max: 92.71
Lewis et al. (2004, 097498)	Detroit, MI	15.7-17.5	Max: 56.1
Liu et al. (2009, 192003)	Windsor, Ontario	7.1	95th: 19.0 98th: 19.0.
Mar et al. (2004, 057309)	Spokane, WA	8.1-11.0	NR
Mar et al. (2005, 088759)	Seattle, WA	5-26	NR
McCreanor et al. (2007, 092841)	London, England	1-h avg: 11.9-28.3	1-h max: 55.9-76.1
Moshammer et al. (2006, 090771)	Linz, Austria	8-h avg: 15.70	Max 24-h avg: 76.39
Murata et al. (2007, 189159)	Tokyo, Japan	39.0	Max 1-h avg: 120
O'Connor et al. (2008, 156818)	Multicity, U.S.	14	Max: 35

Study	Location	Mean Concentration ($\mu g/m^3$)	Upper Percentile Concentrations ($\mu g/m^3$)
Peled et al. (2005, 156015)	Multicity, Israel	23.9-29.2	NR
Penttinen et al. (2006, 087988)	Helsinki, Finland	8.37	75th: 11.15 Max: 33.53
Rabinovitch et al. (2004, 096753)	Denver, CO	10.8	98th: 29.3 Max: 53.5
Rabinovitch et al. (2006, 088031)	Denver, CO	10.8	98th: 23.4
Ranzi et al. (2004, 089500)	Emilia-Romagna, Italy	Urban: 53.07 Rural: 29.11	NR
Rodriguez et al. (2007, 092842)	Perth, Australia	1-h avg: 20.8 24-h avg: 8.5	Max 1-h avg: 93.4 Max 24-h avg: 39.4
Slaughter et al. (2003, 086294)	Seattle, WA	7.3[a]	75th: 11.3
Strand et al. (2006, 089203)	Denver, CO	12.7	Max: 32.3
Timonen et al. (2004, 087915)	Multicity, Europe	12.7-23.1	Max: 39.8-118.1
Trenga et al. (2006, 155209)	Seattle, WA	8.6-9.6[a]	75th: 13.1-14.8 Max: 40.4-41.5
von Klot et al. (2002, 034706)	Erfurt, Germany	30.3[b]	75th: 41.3[b] Max: 133.8[b]
Ward et al. (2002, 025839)	Birmingham and Sandwell, U.K.	12.3-12.7	Max: 28-37
$PM_{10-2.5}$			
Aekplakorn et al. (2003, 089908)	North Thailand	NR	NR
Bourotte et al. (2007, 150040)	Sao Paulo, Brazil	21.7	Max: 62.0
Ebelt et al. (2005, 056907)	Vancouver, Canada	5.6	Max: 11.9
Lagorio et al. (2006, 089800)	Rome, Italy	15.6	Max: 39.6
Mar et al. (2004, 057309)	Spokane, WA	8.7-13.5	NR
von Klot et al. (2002, 034706)	Erfurt, Germany	10.3	75th: 14.6 Max: 64.3
PM_{10}			
Aekplakorn et al. (2003, 089908)	North Thailand	31.9-37.5	Max: 113.3-153.3
Andersen et al. (2008, 096150)	Copenhagen, Denmark	25.1	75th: 30.2
Boezen et al. (2005, 087396)	The Netherlands	26.6-44.1	Max: 89.9-242.2
de Hartog et al. (2003, 001061)	Multicity, Europe	19.6-36.5	Max: 67.4-112.0
Delfino et al. (2002, 093740)	Alpine, CA	20	90th: 32 Max: 42
Delfino et al. (2003, 050460)	Los Angeles, CA	59.9	90th: 86/0/Max: 126
Delfino et al. (2004, 056897)	Alpine, CA	29.7	90th: 40.9 Max: 50.7
Delfino et al. (2006, 090745)	Southern CA	35.7-70.8	Max: 105.5-154.1
Desqueyroux et al. (2002, 026052)	Paris, France	23-28	Max: 63-84
Ebelt et al. (2005, 056907)	Vancouver, Canada	17	Max: 36
Hong et al. (2007, 091347)	Incheon City, Korea	35.3	Max: 124.87
Jalaludin et al. (2004, 056595)	Sydney, Australia	22.8	75th: 122.8
Jansen et al. (2005, 082236)	Seattle, WA	18.0	Max: 51

Study	Location	Mean Concentration ($\mu g/m^3$)	Upper Percentile Concentrations ($\mu g/m^3$)
Johnston et al. (2006, 091386)	Darwin, Australia	20	Max: 43.3
Just et al. (2002, 035429)	Paris, France	23.5	Max: 44.0
Lagorio et al. (2006, 089800)	Rome, Italy	42.8	Max: 123
Laurent et al. (2008, 156672)	Strasbourg, France	20.8	Max: 106.3
Lee et al. (2007, 093042)	Seoul, South Korea	71.40	75th: 87.54 Max: 148.34
Mar et al. (2004, 057309)	Spokane, WA	16.8-24.5	NR
Mortimer et al. (2002, 030281)	Multicity, U.S.	53	NR
Moshammer et al. (2006, 090771)	Linz, Austria	8-h avg: 24.85	Max 24-h: 76.39
Odajima et al. (2008, 192005)	Fukuoka, Japan	3-h avg: 32.6-41.5	Max 3-h avg: 126.0-191.3
Peacock et al. (2003, 042026)	Southern England	21.2	Max: 87.9
Peled et al. (2005, 156015)	Multicity, Israel	31.0-67.1	NR
Preutthipan et al. (2004, 055598)	Bangkok, Thailand	111.0	Max: 201
Rabinovitch et al. (2004, 096753)	Denver, CO	28.1	Max: 102.0
Ségala et al. (2004, 090449)	Paris, France	24.2	Max: 97.4
Schildcrout et al. (2006, 089812)	Multicity, U.S.	17.7-32.4[a]	75th: 26.2-42.7 90th: 32.5-53.9
Slaughter et al.(2003, 086294)	Seattle, WA	21.0[a]	75th: 29.3
Steinvil et al. (2008, 188893)	Tel Aviv, Israel	64.5	75th: 60.7
von Klot et al. (2002, 034706)	Erfurt, Germany	45.4	75th: 59.7 Max: 172.4

[a]Median
[b]Includes UFP, for complete information on number concentration from this study, please see corresponding table in Annex E.

Mar et al. (2004, 057309) studied asthmatic children (n = 9) in Spokane, WA. Increases in 0-, 1- or 2-day lags of each of the PM size classes studied were associated with cough. When all lower respiratory tract symptoms (wheeze, cough, shortness of breath, sputum production) were grouped together, positive associations were reported for each 10 $\mu g/m^3$ increase in same-day PM_{10} (OR 1.07 [95% CI: 1.00-1.14]), or lag 0 or lag 1 $PM_{2.5}$ (OR 1.18 [95% CI: 1.00-1.38]; OR 1.21 [95% CI: 1.00-1.46], respectively), and 10 $\mu g/m^3$ increase in lag 0 and lag 1 $PM_{1.0}$ (OR 1.21 [95% CI: 1.01-1.44]; OR 1.25 [95% CI: 1.01-1.55], respectively). No associations were reported for $PM_{10-2.5}$ and grouped lower respiratory tract symptoms (Mar et al., 2004, 057309).

Gent et al. (2003, 052885) reported on daily symptom and medication use during one summer for 271 asthmatic children living in southern New England. In single-pollutant models for users of maintenance medication (n = 130), $PM_{2.5}$ $\geq$19 $\mu g/m^3$ lagged by 1 day was associated with a 10-25% increase in risk of symptoms compared to $PM_{2.5}$ <6.9 $\mu g/m^3$: OR for persistent cough 1.12 (95% CI: 1.02-1.24); OR for chest tightness 1.21 (95% CI: 1.00-1.46); OR for shortness of breath 1.26 (95% CI: 1.02-1.54). Effects were attenuated in models including O_3 (OR for persistent cough 1.00 [95% CI: 0.88-1.15]; OR for chest tightness 0.91 [95% CI: 0.71-1.17]; OR for shortness of breath 1.20 [95% CI: 0.94-1.52]). No statistical associations between ambient particle exposure and respiratory health were found for asthmatic children not on maintenance medication.

Annual $PM_{2.5}$ levels at monitoring sites in New Haven, CT exceed the annual standard of 15 $\mu g/m^3$. Gent et al. (2009, 180399) conducted a study here to examine the associations between daily exposure to $PM_{2.5}$ components and sources identified through source apportionment, and daily symptoms and medication use in asthmatic children. Asthmatic children (n = 149) aged 4-12 yr were enrolled in the study between 2000 and 2003. Factor analysis was used to identify six sources of $PM_{2.5}$ (motor vehicle, road dust, sulfur, biomass burning, oil, and sea salt). Total $PM_{2.5}$ was not associated with any symptoms or medication use; however trace elements originating from motor vehicle, road dust, biomass burning and oil sources were associated with symptoms and/or

medication use. For example, an increased risk of wheeze, shortness of breath, chest tightness or short-acting inhaler use was associated with increasing EC mass concentration. Risks remain in models that include all six $PM_{2.5}$ sources as well as NO_2, which may be considered a marker for traffic. NO_2 was found to be an independent risk factor for increased wheeze.

Two panel studies were conducted over the course of three winters at a school in Denver (Rabinovitch et al., 2004, 096753; 2006, 088031). In the first report, approximately 86 different children contributed data on asthma symptoms and medication use over three consecutive winters (Rabinovitch et al., 2004, 096753). The exposure metric was the 3-day average concentration of $PM_{2.5}$ measured at a site located next to the school for the first two winters and from a central site located 4.8 km (3 miles) away for the third. A strong correlation was observed during the first two winters between $PM_{2.5}$ values measured locally and at a downtown monitoring station (Pearson product-moment correlation = 0.93) and between PM_{10} values measured locally and at a downtown monitoring station (correlation = 0.84). Therefore, in year 3, all ambient data were collected from nearby community monitoring stations. No statistical associations were found between asthma symptoms or medication use and PM. Rabinovitch et al. (2006, 088031) enrolled a panel of 73 children and evaluated associations with morning maximum $PM_{2.5}$ measured at the central site. PM measurements were available hourly from two co-located monitors, an FRM and a TEOM monitor. Each 10 $\mu g/m^3$ increase in morning maximum 1-h $PM_{2.5}$ concentration was associated with an increased likelihood of rescue medication use (OR for FRM 1.02 [95% CI: 1.01-1.03]; OR for TEOM 1.03 [95% CI: 1.00-1.6]). Interestingly, the association between inhaler use and particle exposure was not evident when the 24-h avg $PM_{2.5}$ was used in the model.

Two smaller panel studies enrolling asthmatic children conducted by Delfino et al. (2002, 093740; 2003, 050460) in southern California examined the health effects of different averaging times for PM_{10} (1-h, 8-h, 24-h) (Delfino et al., 2002, 093740), and 24-h avg of two PM_{10} components (EC and OC) (Delfino et al., 2003, 050460). In the first study, 22 children living in a "lower" pollution area were followed daily for two months in spring. In contrast with Gent et al. (2003, 052885), positive statistical associations with asthma symptoms (measured on a 6-point severity scale) were found only for the children not taking anti-inflammatory medication. For these 12 children, in single-pollutant models each 10 $\mu g/m^3$ increase in lag 0 1-h max PM_{10} nearly doubled the risk of clinically meaningful symptoms (i.e., an asthma symptom score $\geq$3) (OR 1.14 [95% CI: 1.04-1.24]) and each 10 $\mu g/m^3$ increase in 3-day avg 24-h PM_{10} increased the risk by 1.25 (95% CI: 1.06-1.48). No statistical associations were found between exposure to ambient particles and symptoms in the ten children who were taking anti-inflammatory medication. No multipollutant models were reported. The second study enrolled 22 asthmatic children living in an area of higher pollution. For children living in this community, each 10 $\mu g/m^3$ increase in lag 0, 24-h PM_{10} was associated with an increased risk of asthma symptom score >1: OR 1.10, (95% CI: 1.03-1.19) (Delfino et al., 2003, 050460). The correlation among PM_{10}, EC and OC was substantial: 0.80 between PM_{10} and either EC or OC, and 0.94 between EC and OC. Associations between EC or OC and asthma symptoms were very similar to those for PM_{10}: each 3 $\mu g/m^3$ increase in lag 0, 24-h EC or 5 $\mu g/m^3$ increase in lag 0, 24-h OC was associated with an increased risk of asthma symptoms (OR 1.85 [95% CI: 1.11-3.08] or OR 1.88 [95% CI: 1.12-3.17], respectively) (Delfino et al., 2003, 050460).

The association between incident wheezing symptoms and air pollution was assessed in the Copenhagen Prospective Study of Asthma in Children among a birth cohort of 205 children in Copenhagen, Denmark. In addition to PM_{10} and other gaseous air pollutants, the study examined UFP concentrations collected from a central background monitoring station. This is the only study identified that examined the association between UFPs and respiratory symptoms in children. There were strong adverse effects for PM_{10} and UFPs, as well as for NO_2, NO_X, and CO for wheezing symptoms in infants which attenuated after the age of 1 yr (lag 2-4 PM_{10} OR 1.21 (95% CI 0.99-1.48); lag 2-4 UFP OR 1.92 (95% CI: 0.98-3.76)). These associations remained in copollutant models including NO_2, NO_X and CO.

Studies from Australia (Rodriguez et al., 2007, 092842), Europe (Andersen et al., 2008, 096150; Laurent et al., 2008, 156672; Laurent et al., 2009, 192129; Ranzi et al., 2004, 089500), and Asia (Aekplakorn et al., 2003, 089908) provide additional evidence of an association between ambient PM and respiratory symptoms and/or medication use among asthmatic children. Two studies (Jalaludin et al., 2004, 056595; Just et al., 2002, 035429) found no association between ambient PM levels and these health endpoints.

Asthmatic Adults

Since the 2004 PM AQCD (U.S. EPA, 2004, 056905), one U.S. and several European studies have investigated the effects of ambient PM levels on respiratory symptoms and medication use among asthmatic adults. The respiratory symptom and medication use results from these studies are summarized by particle size and displayed in Table 6-10 and Figure 6-8. Relatively few studies examined these effects in healthy adults, and they did not identify a relationship between ambient PM levels and respiratory symptoms or medication use. These studies of healthy adults are summarized in Annex E, but will not be described in detail in this section.

Mar et al. (2004, 057309) studied asthmatic adults (n = 16) in Spokane, WA over a 3-yr time period. No associations were found between PM and respiratory symptoms among the adults.

Several panel studies conducted in Europe have examined effects of daily exposures to air pollution on adults with asthma, including studies in the Pollution Effects on Asthmatic Children in Europe (PEACE) study (Boezen et al., 2005, 087396), Exposure and Risk Assessment for Fine and UFPs in Ambient Air (ULTRA) study (De Hartog et al., 2003, 001061), in Germany (Von et al., 2002, 034706), and in Paris (Desqueyroux et al., 2002, 026052; 2004, 090449). Boezen et al. (2005, 087396) enrolled 327 elderly adults in the Netherlands to examine the role of airway hyperresponsiveness (AHR) and IgE levels in susceptibility to air pollution. For subjects with both AHR (defined as $\geq$ 20% FEV_1 decline at $\leq$ 2 mg cumulative methacholine [Mch]) and high total IgE (>20 kU/L), each 10 $\mu g/m^3$ increase in lag 2 PM_{10} concentration was associated with an increased risk of upper respiratory symptoms (URS) among males (OR 1.06 [95% CI: 1.02-1.10]), and at lag 0 with increased cough among females (OR 1.04 [95% CI: 1.00-1.08]). Each 10 $\mu g/m^3$ increase in BS at lag 0, lag 1, and the 5-day mean was associated with URS and cough among males. The strongest association in both cases was for the 5-day mean (OR for URS 1.43 [95% CI: 1.20-1.69]; OR for cough 1.16 [95% CI: 1.05-1.29]). The authors suggest that the sex differences observed may be explained by differential daily exposure to traffic exhaust experienced by men compared to women (Boezen et al., 2005, 087396).

As part of the multicenter ULTRA study, de Hartog et al. (2003, 001061) enrolled 131 older adults with coronary artery disease in three cities (Amsterdam, Erfurt [Germany], and Helsinki). Pooling data from all 3 cities, associations were observed between $PM_{2.5}$ and shortness of breath and phlegm: each 10 $\mu g/m^3$ increase in the 5-day avg $PM_{2.5}$ was associated with an increased risk of symptoms (OR for shortness of breath 1.12 [95% CI: 1.02-1.24]; OR for phlegm 1.16 [95% CI: 1.03-1.32]). Unlike fine particles, UFPs were not consistently associated with symptoms.

In a study that took place in Erfurt, Germany, von Klot et al. (2002, 034706) examined daily, winter time exposure to ambient $PM_{10-2.5}$, $PM_{2.5-0.01}$ and $PM_{0.1-0.01}$ and respiratory health effects in 53 adult asthmatics. The authors examined associations between wheeze, use of inhaled, short-acting β_2-agonists or inhaled corticosteroids and exposure to particles in single and multipollutant models. Particle exposure metrics examined included same-day, 5-day and 14-day average concentrations. No effects were observed for wheeze and exposure to $PM_{10-2.5}$ for any averaging time. The strongest association between wheeze and exposure to UFPs was for a 14-day avg: each 7,700 increase in the $NC_{0.01-0.1}$ increased the risk of wheeze by 27% (OR 1.27 [95% CI: 1.13-1.43]). The effect was attenuated in copollutant models that also included $PM_{2.5-0.01}$ (OR 1.12 [95% CI: 1.01-1.24]), NO_2 (OR 1.12 [95% CI: 0.99-1.26]), CO (OR 1.05 [95% CI: 0.92-1.19]) or SO_2 (OR 1.14 [95% CI: 1.04-1.26]). The correlations between UFPs and two gaseous pollutants, NO_2 and CO, were high: 0.66 for each.

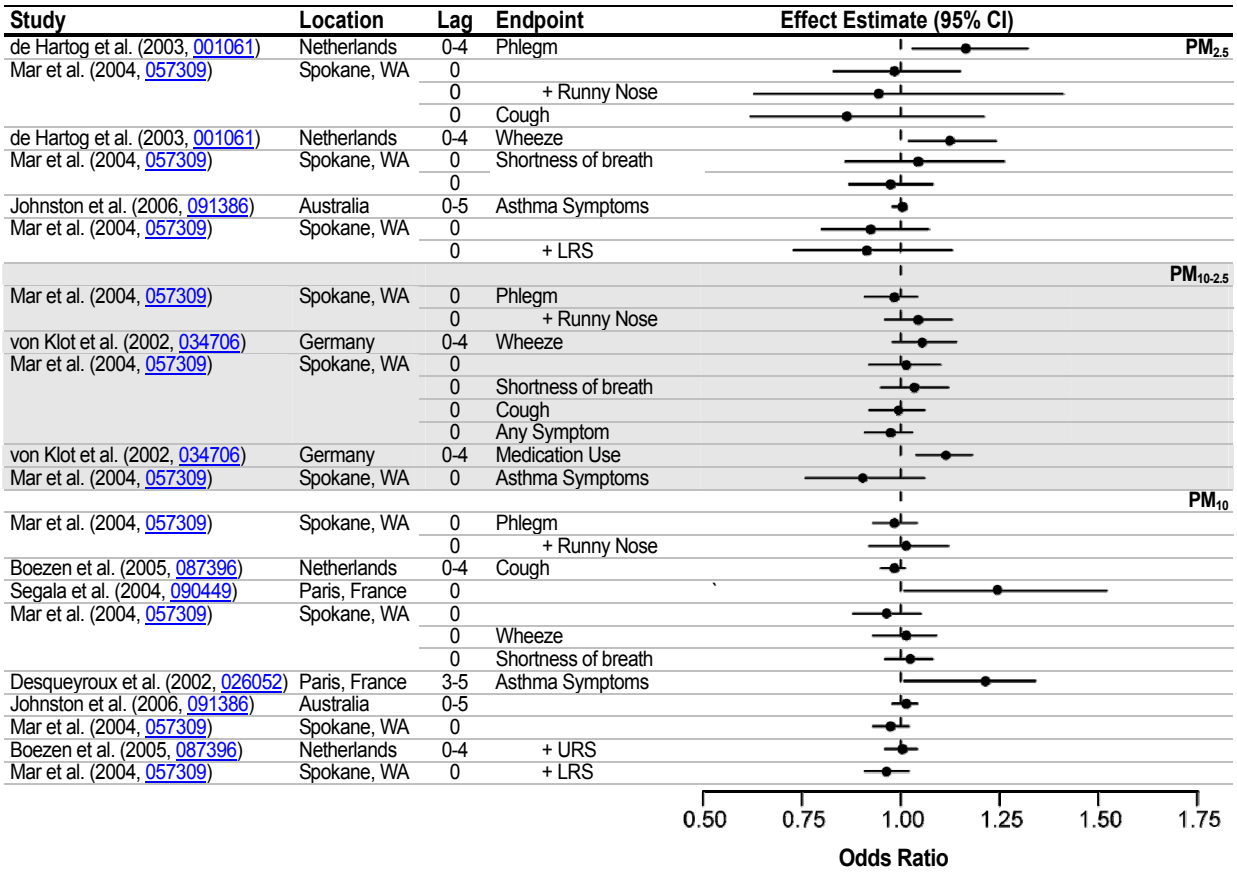


Figure 6-8. Respiratory symptoms and/or medication use among asthmatic adults following acute exposure to particles. Summary of studies using 24-h avg of PM_{10}, $PM_{2.5}$, $PM_{10-2.5}$. ORs and 95% CIs were standardized to increments of 10 µg/m^3.

In the same study, no association was found between exposure to $PM_{10-2.5}$,, $PM_{2.5}$, or UFPs and use of short-acting inhalers, though there was an association with maintenance medication. Increased likelihood of maintenance medication was significantly associated with PM of all sizes and all averaging times (same-day, 5- and 14-day avg) and gaseous copollutants in single or copollutant models. The strongest effects were seen for 14-day avg of $PM_{10-2.5}$ (for each 10 µg/m^3 increase OR 1.43 [95% CI: 1.28-1.60]), $PM_{2.5-0.01}$ (for each 20 µg/m^3 increase OR 1.54 [95% CI: 1.43-1.66]), $NC_{0.01-0.1}$ (for each 7,700 increase OR 1.45 [95% CI: 1.29-1.63]). For $PM_{2.5-0.01}$, effects were unchanged in copollutant models, including a model with UFPs. The authors conclude that this is evidence for independent effects of $PM_{2.5}$ and UFPs (Von et al., 2002, 034706).

In Paris, Segala et al. (2004, 090449) recruited 78 adults from an otolaryngology clinic and followed them for three months. Both PM_{10} and BS (which were highly correlated [r =.88]) were associated with cough: OR 1.24 (95% CI: 1.01-1.52) for a 10 µg/m^3 increase in mean 0-4 day PM_{10} and OR 1.18 (95% CI: 1.02-1.39) for a 10 µg/m^3 increase in BS.

Also in Paris, 60 severe asthmatics were followed for 13 months and the relationship between daily air quality (including 24-h PM_{10} as measured at the site nearest to the subject's home) and asthma attack (defined as the need to increase rescue medication use and one or more positive signs on clinical exam of wheezing, expiratory brake, thoracic distention, hypertension with tachycardia, polypnea) were examined with GEE models (Desqueyroux et al., 2002, 026052). Each 10 µg/m^3 increase in PM_{10} increased the risk of asthma attack, but only after lags of 3-5 days. The strongest effect was seen for the mean lag of days 3-5 (OR 1.21 [95% CI: 1.04-1.40]). Effect sizes were larger among patients not on regular oral steroid therapy: for PM_{10} lag 3-5 (OR 1.41 [95% CI: 1.15-1.73]). This effect persisted in copollutant models for winter time levels of PM_{10} and SO_2 (OR 1.51 [95%

CI: 1.20-1.90]) or NO_2 (OR 1.43 [95% CI: 1.16-1.76]), but not in summer time models with O_3 (OR 1.09 [95% CI: 0.71-1.67]).

Copollutant Models

A limited number of respiratory symptoms studies reported results of copollutant models. Generally, the associations between respiratory symptoms and PM were robust to the inclusion of copollutants (Figure 6-9), though Desqueyroux et al. (2002, 026052) indicate the effects of PM may be potentiated by NO_2 and SO_2 during the winter months. Gent et al. (2003, 052885) also reported the results of copollutant models, though the categorical exposure groups used in the analysis did not allow these results to be included in Figure 6-9. As reported above, the investigators found that effects were attenuated in models including O_3.

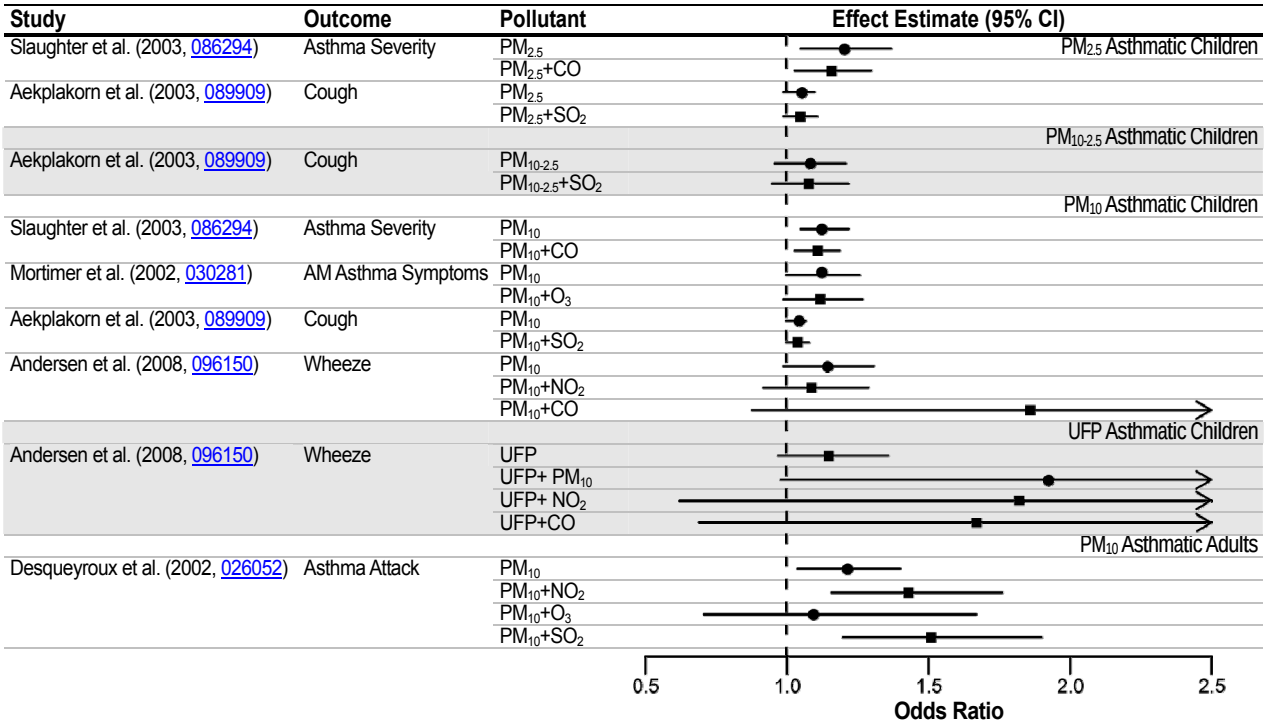


Figure 6-9. Respiratory symptoms following acute exposure to particles and additional criteria pollutants. Circles represent single pollutant effect estimates and squares represent copollutant effect estimates.

6.3.1.2. Controlled Human Exposure Studies

CAPs

Neither new controlled human exposure studies nor studies cited in the 2004 PM AQCD (U.S. EPA, 2004, 056905) have found significant effects of CAPs on respiratory symptoms among healthy or asthmatic adults, or among older adults with COPD (Gong et al., 2000, 155799; 2003, 042106; 2004, 087964; 2004, 055628; 2005, 087921; 2008, 156483; Petrovic et al., 2000, 004638).

Urban Traffic Particles

One new study reported an increase in respiratory symptoms (upper and lower airways) among healthy volunteers (19-59 yr) during a 2-h exposure to road tunnel traffic ($PM_{2.5}$ concentration 46-81 $\mu g/m^3$) (Larsson et al., 2007, 091375). However, information on specific respiratory symptoms (e.g., throat irritation, wheeze or chest tightness) was not provided. In addition, this study only evaluated respiratory symptoms pre- versus post-exposure, and did not compare response with a filtered air control exposure.

Diesel Exhaust

Respiratory symptoms including mild nose and throat irritation have been reported following controlled exposure to DE; however, other symptoms such as cough, wheeze and chest tightness have not been observed (Mudway et al., 2004, 180208).

Model Particles

Pietropaoli et al. (2004, 156025) found no association between exposure to UF carbon particles and respiratory symptoms in healthy adults at concentrations between 10 and 50 $\mu g/m^3$, or asthmatics at a concentration of 10 $\mu g/m^3$. Beckett et al. (2005, 156261) exposed healthy subjects to UF and fine ZnO (500 $\mu g/m^3$) and observed no difference in respiratory symptoms compared to filtered air control 24 h following exposure. In a study evaluating respiratory effects of exposure to ammonium bisulfate or aerosolized H_2SO_4 (200 and 2,000 $\mu g/m^3$) among healthy and asthmatic adults, Tunnicliffe et al. (2003, 088744) observed no change in respiratory symptoms with either particle type or concentration relative to filtered air. This finding is in agreement with many similar older studies which have generally reported no increase in respiratory symptoms following exposure to acid aerosols at concentrations <1,000 $\mu g/m^3$ (U.S. EPA, 1996, 079380; 2004, 056905).

Summary of Controlled Human Exposure Study Findings for Respiratory Symptoms

These new studies confirm previous reports that have found no association between PM exposure and respiratory symptoms.

6.3.2. Pulmonary Function

Epidemiologic studies cited in the 2004 PM AQCD (U.S. EPA, 2004, 056905) observed small decrements in pulmonary function associated with both $PM_{2.5}$ and PM_{10} (U.S. EPA, 2004, 056905). The majority of controlled human exposure studies reported no effect of PM on pulmonary function, while the results from toxicological studies were mixed, with some evidence of changes in tidal volume and respiratory rate following exposure to CAPs. Epidemiologic studies published since the 2004 PM AQCD (U.S. EPA, 2004, 056905) have reported an association between $PM_{2.5}$ concentration and decrements in forced expiratory volume in one second (FEV_1), particularly among asthmatic children. These findings are coherent with recent toxicological evidence of AHR following CAPs exposure. Results from recent controlled human exposure studies have been inconsistent, with some studies demonstrating small decreases in arterial oxygen saturation, FEV_1 or maximal mid-expiratory flow following exposure to CAPs or EC. It is interesting to note that these effects appear to be more pronounced among healthy adults than adults with asthma or COPD. A number of recent animal toxicological studies demonstrated alterations in respiratory frequency following short-term exposure to CAPs.

6.3.2.1. Epidemiologic Studies

The 2004 PM AQCD (U.S. EPA, 2004, 056905) concluded that both $PM_{2.5}$ and PM_{10} appeared to affect lung function in asthmatics. A limited number of studies evaluated UFPs and found them to be associated with a decrease in peak expiratory flow (PEF). Few analyses were able to clearly distinguish the effects of $PM_{2.5}$ and PM_{10} from other pollutants. Results for PM_{10} PEF analyses in non-asthmatic studies were inconsistent, with fewer studies reporting strong associations.

Asthmatic Children

Several recent panel studies have been conducted in the U.S. examining the association of exposure to ambient PM and lung function in asthmatic children (Allen et al., 2008, 156208 in Seattle; Lewis et al., 2003, 088413 in Southern California; 2004, 097498; Lewis et al., 2005, 081079 in Detroit; O'Connor et al., 2008, 156818; Rabinovitch et al., 2004, 096753 in Denver). Mean concentration data from these studies are summarized in Table 6-10. In the Inner-City Asthma Study (ICAS), FEV_1 and PEF tidal were statistically related to the 5-day avg of $PM_{2.5}$ but not to the 1-day avg concentration (O'Connor et al., 2008, 156818). The risk of experiencing a percent-predicted FEV_1 more than 10% below personal best was related to the 5-day avg concentration of $PM_{2.5}$ (1.14 [95% CI: 1.01-1.29]). The risk of experiencing a percent-predicted PEF rate more than 10% below personal best was related to $PM_{2.5}$ (1.18 [95% CI: 1.03-1.35]). This effect remained robust in copollutant models with O_3 and NO_2 for the FEV_1 effect, but not the PEF rate effect.

The Denver study (Rabinovitch et al., 2004, 096753), described in Section 6.3.1.1, also examined daily FEV_1 and PEF in 86 asthmatic children over the course of three winters (some subjects participated in more than one winter). Lung function measurements were performed under supervision daily at the elementary school where all subjects attended, and without supervision every evening and on nonschool days. As described above, the authors chose to use a 3-day moving average of 24-h $PM_{2.5}$ or PM_{10} as the exposure metric. No statistical associations were observed between morning or afternoon FEV_1 or PEF and particle exposure. The same group of researchers (Strand et al., 2006, 089203) used regression calibration to estimate personal exposures to ambient $PM_{2.5}$ and found that a 10 $\mu g/m^3$ increase in $PM_{2.5}$ was associated with a 2.2% (95% CI: 0.0-4.3) decrease in FEV_1 at a 1-day lag as compared with the estimate of a 1.0% decrease in FEV_1 using ambient $PM_{2.5}$ concentrations from fixed monitors. These results underscore the effects of exposure error on epidemiologic study results; the effect estimate using an estimate of personal exposure to ambient $PM_{2.5}$ was twice that for central site $PM_{2.5}$.

From winter 2001 to the spring of 2002, the same number (n = 86) of primary school-age asthmatic children participated in six 2-wk seasonal assessments of lung function in Detroit (Lewis et al., 2005, 081079). Using a protocol similar to that used in Rabinovitch et al. (2004, 096753), morning lung function measurements (FEV_1, PEF) were self-administered at school under supervision by research staff. Evening and weekend measurements were recorded by subjects at home, without supervision from research staff. Community-level exposure was assessed using monitors placed on a school roof top of both of the communities. Most of the subjects (82 of 86) lived within 5 km of their respective community monitors. In single-pollutant models using GEE and only among children reporting the use of maintenance medication (corticosteroids), each 10 $\mu g/m^3$ increase in lag 2 PM_{10} was associated with a decrease in the lowest daily percent predicted FEV_1 (a reduction of 1.15%, [95% CI: -2.1 to -0.25]). Among children reporting presence of URI on the day of lung function measurement, increases in the average of lag 3-5 of either $PM_{2.5}$ or PM_{10} resulted in a decrease in the lowest daily FEV_1 (for a 10 $\mu g/m^3$ increase in $PM_{2.5}$ the reduction was 2.24% [95% CI: -4.4 to -0.25]; and for a 10 $\mu g/m^3$ increase in PM_{10} the reduction was 2.4% [95% CI: -4.5 to -0.3]). In copollutant models that included one particle pollutant and O_3, and among children using maintenance medication, lag 3-5 $PM_{2.5}$ continued to be associated with lowest daily FEV_1 as well as diurnal FEV_1 variability: each 10 $\mu g/m^3$ increase was associated with a 2.23% decrease in FEV_1 (95% CI: -3.92 to -0.57) and a 2.22% increase in FEV_1 variability (95% CI: 1.0 to 3.50). Increases in lag 1 or lag 2 of PM_{10} were associated with FEV_1 and FEV_1 diurnal variability in copollutant models. The strongest association was with lag 2 for diurnal variability (for each 10 $\mu g/m^3$ increase variability increased by 7.0% [95% CI: 4.2-9.6). It is unclear what role the lack of supervision during the evening and weekend measures may have had on these diurnal results.

Two panel studies in southern California examined the association of PM exposure on lung function in asthmatic children (Delfino et al., 2003, 050460; 2004, 056897). In Delfino et al. (2003,

050460), described above, no association between exposure to particles and PEF was found for 22 Hispanic, asthmatic children living in an area of relatively high pollution. In Delfino et al. (2004, 056897) 19 asthmatic children, aged 9-17 yr, were followed for 2 weeks and daily, self-administered FEV_1 measurements were taken. Particle exposures studied included central-site PM_{10} in addition to personal PM (in the range of 0.1-10 μm range, with the highest response in the fine PM range), and home stationary measurements of both $PM_{2.5}$ and PM_{10}. The authors report inverse associations between percent expected FEV_1 and PM indicators. The strongest association for exposure to personal PM was for a 5-day moving average of 12-h daytime PM: for each 10 $\mu g/m^3$ increase, FEV_1 decreased by 7.1% (95% CI: -9.9 to -2.9). Effects for all stationary sites (inside and outside of residence, central site) for $PM_{2.5}$ were on the order of 1-2% reductions in FEV_1, with the strongest associations for the 5-day moving average (presented in figures only). Likewise for PM_{10} measured at stationary sites, the strongest effects were for the 5-day moving average and ranged from approximately 3.8% reduction associated with indoor monitors to about 1.5% for both the outdoor and central site monitors (presented in figures only). A helpful comparison among all 24-h measures is given for 10 $\mu g/m^3$ increases in personal PM and $PM_{2.5}$ associated with decreases in percent predicted FEV_1: an increase of 10 $\mu g/m^3$ personal PM is associated with a decrease in FEV_1 of 3.0% (95% CI: -5.6 to -0.5); 10 $\mu g/m^3$ increase in indoor PM with 2.4% decrease (95% CI: -4.2 to -0.6); 10 $\mu g/m^3$ increase in outdoor PM with 1.5% decrease (95% CI: -3.4 to 0.1); 10 $\mu g/m^3$ increase in central site PM with 0.9% decrease (95% CI: -2.6 to 0.5).

Trenga et al. (2006, 155209) reported associations among personal, residential, and central site $PM_{2.5}$ and lung function in 17 asthmatic children in Seattle. The only statistical association with decline in FEV_1 was with indoor measurements of $PM_{2.5}$: each 10 $\mu g/m^3$ increase in lag 1 indoor $PM_{2.5}$ was associated with a decline in FEV_1 of 64.8 mL (95% CI: -111.3 to 18.3) (a 3.4% decline from the mean of 1.9 L). Indoor $PM_{2.5}$ (lag 1) was also associated with declines in PEF (by 9.2 L/min [95% CI: -17.5 to -0.9], a 3.6% decline from the 254 L/min avg) and in maximal mid-expiratory flow (MMEF) for the six subjects not taking anti-inflammatory medication (by 12.6 L/min [95% CI: -20.7 to -4.6], a 13.7% decline from the 92 L/min avg). Personal $PM_{2.5}$ (lag 1) was only statistically associated with PEF for the six subjects not on anti-inflammatory medication: each 10 $\mu g/m^3$ increase resulted in a 10.5 L/min ([95% CI: -18.7 to -2.3], a 4.5% decline from the 233 L/min avg) reduction in PEF. Anti-inflammatory medication use attenuated associations with $PM_{2.5}$.

Also in Seattle, Allen et al. (2008, 156208) evaluated the effect of different $PM_{2.5}$ exposure metrics in relation to lung function among children in wood smoke-impacted areas. The authors found that the ambient-generated component of $PM_{2.5}$ exposure was associated with decrements in lung function only among children not using inhaled corticosteroids, whereas no association was reported with the nonambient exposure component. All of the ambient concentrations were associated with decrements in both PEF and maximal expiratory flow (MEF). There were no associations between any exposure metrics and forced vital capacity (FVC). The authors suggest that lung function may be especially sensitive to the combustion-generated component of ambient $PM_{2.5}$, whereas airway inflammation may be more closely related to some other source.

In a longitudinal study, Liu et al. (2009, 192003) examined the association between acute increases in ambient air pollutants and pulmonary function among children (ages 9-14 yr) with asthma. FEV_1 and $FEF_{25-75\%}$ exhibited a consistent trend of negative associations with $PM_{2.5}$ across lag days 0, 1, 0-1, and 0-2, with the strongest effects for $FEF_{25-75\%}$ on lag day 0 (-1.12% [95% CI: -2.06 to -0.18]) and lag days 0-1 (-1.18% [95% CI: -2.24 to -0.12]). Copollutant models including O_3, SO_2 or NO_2 did not result in marked changes in the $PM_{2.5}$ risk estimates for FEV_1 or $FEF_{25-75\%}$.

Moshammer and Neuberger (2003, 041956) used a novel technique for assessing exposure to PM in a study they conducted in Austria. They employed a diffusion charging particle sensor (model LQ 1-DC, Matter Engineering AG, Wohlen, Switzerland) and a photoelectric aerosol sensor (model PAS 2000 CE, EcoChem Analytics, League City, TX) to relate the spirometry scores of Upper Austrian children, aged 7-10 yr, to particle surface area and particle-bound PAH concentration, respectively. Details on these methods for measuring surface area and PAH can be found in Shi et al. (2001, 078292) and Burtscher (2005, 155710), respectively. By measuring the surface area distribution, it was possible to understand potential for contact area with respiratory tract cells. The authors found that acute decrements of pulmonary function (FVC, FEV_1, MEF_{50}) were related to the active surface of particles after adjustment for PM_{10}. For short-term lung impairments, this indicates that active particle surface is a better index of exposure than PM mass.

A number of additional panel studies conducted outside of the U.S. and Canada also examined lung function using more traditional exposure metrics. Several European and Asian studies reported

associations with PM measurements and decrements in pulmonary function (FEV_1, FVC, FEF, MEF, PEF rate) (Hogervorst et al., 2006, 156559; Hong et al., 2007, 091347; Moshammer et al., 2006, 090771; Odajima et al., 2008, 192005; Peacock et al., 2003, 042026; Peled et al., 2005, 156015). Others found little evidence for a relationship between PM and daily changes in PEF after correction for the confounding effects of weather, trends in the data, and autocorrelation (Fischer et al., 2002, 025731; Holguin et al., 2007, 099000; Just et al., 2002, 035429; Preutthipan et al., 2004, 055598; Ranzi et al., 2004, 089500; Ward, 2003, 157111).

Adults

Trenga et al. (2006, 155209) examined personal, residential, and central site monitoring of particles and the relationship with lung function in Seattle. In models controlling for gaseous copollutants (CO, NO_2), adults, regardless of COPD status, experienced a decline in FEV_1 associated only with measurements of $PM_{2.5}$ at the central site: each 10 $\mu g/m^3$ increase in lag 0 $PM_{2.5}$ was associated with a 35.3 mL (95% CI: -70 to -1.0) decrease in FEV_1. This represents a 2.2% decline in mean FEV_1 (mean 1.6 L during the study). Results for personal, indoor and outdoor measures of $PM_{2.5}$ were inconsistent. No statistical associations were reported with outdoor $PM_{10-2.5}$.

Girardot et al. (2006, 088271) assessed the effects of $PM_{2.5}$ on the pulmonary function of adult day hikers in the Great Smoky Mountains National Park. Hikers performed spirometry both before their hike and when they returned from their hike. The authors reported no statistically significant responses in pulmonary function with an average of five hours of outdoor exercise at ambient $PM_{2.5}$ levels that were below the current NAAQS. Specifically, post-hike percentage changes in FVC, FEV_1, FEV_1/FVC, FEF_{25-75}, and PEF were not associated with $PM_{2.5}$ exposure.

Ebelt et al. (2005, 056907) developed an approach to separately estimate exposures to PM of ambient and non-ambient origin based on a mass balance model. These exposures were linked with respiratory and cardiovascular health endpoints for 16 patients with COPD in Vancouver, Canada (mean age 74 yr). Effect estimates for estimated ambient exposure were generally equal to or larger than those for the respective ambient concentration levels for post-FEV and ΔFEV_1, and were statistically significant for all ΔFEV_1 comparisons (estimated from figure).

Several studies outside of the U.S. and Canada examined the relationship between PM concentrations and lung function and all reported a decrease in lung function in adults (FEV_1, FVC, PEFR) associated with PM exposure (Boezen et al., 2005, 087396; Bourotte et al., 2007, 150040; Lagorio et al., 2006, 089800; Lee et al., 2007, 093042; McCreanor et al., 2007, 092841; Penttinen et al., 2006, 087988).

Measures of Oxygen Saturation

Oxygen saturation measures the percentage of hemoglobin binding sites in the bloodstream occupied by oxygen. DeMeo et al. (2004, 087346) estimated the change in oxygen saturation and mean $PM_{2.5}$ concentration in the previous 24 h in a panel of elderly subjects. They used the same panel of elderly Boston residents (n = 28) and study protocol and analytic methods (12 wk of repeated oxygen saturation measurements) as Gold et al. (2005, 087558) and Schwartz et al. (2005, 074317) in studies of ST-segment depression and HRV, respectively. At each clinic visit, subjects had 5 min each of rest, standing, post-exercise rest, and 20 cycles of paced breathing. The median $PM_{2.5}$ concentration during the study period was 10.0 $\mu g/m^3$ (Schwartz et al., 2005, 074317). Each 10 $\mu g/m^3$ increase in the mean $PM_{2.5}$ concentration in the previous 6 h was associated with a 0.15% decrease in oxygen saturation (95% CI: -0.22 to 0.0) during the baseline rest period. Each 10 $\mu g/m^3$ increase in mean 6-h $PM_{2.5}$ concentration was also associated with a decline in oxygen saturation during the post-exercise period (-0.15% [95% CI: -0.22 to 0.0]), and post-exercise paced breathing period (-0.07% [95% CI: -0.22 to 0.0]), but not during the exercise period. The authors suggest that these oxygen saturation reductions may result from pulmonary vascular and inflammatory changes.

In a similar study, Goldberg et al. (2008, 180380) examined the association between oxygen saturation, pulse rate, and ambient $PM_{2.5}$, NO_2, and SO_2 concentrations in a panel of 31 subjects in Montreal, with NYHA Class II or III heart failure who were aged 50-85 yr. Although each 10 $\mu g/m^3$ increase in $PM_{2.5}$ on lag day 0 was associated with a -0.119 (95% CI = -0.196 to -0.042) change in oxygen saturation in unadjusted models, once adjusted for temperature and barometric pressure, the estimated change was smaller and no longer significant (-0.077 [95% CI = -0.160 to 0.007). Only

SO_2 was significantly associated with reduced oxygen saturation in copollutant models. None of the pollutants examined, including $PM_{2.5}$, were associated with a change in pulse rate.

6.3.2.2. Controlled Human Exposure Studies

As with respiratory symptoms, there is little evidence from controlled human exposure studies of PM-induced changes in pulmonary function. One study cited in the 2004 PM AQCD (U.S. EPA, 2004, 056905) noted a significant decrement in thoracic gas volume in healthy adults following a 2-h exposure to $PM_{2.5}$ CAPs (92 μg/m^3); however, no significant changes were observed in spirometric measurements, diffusing capacity (DLCO), total lung capacity, or airways resistance (Petrovic et al., 2000, 004638). Other studies found no significant changes in pulmonary function in healthy adults following exposure to inhaled iron oxide particles (Lay et al., 2001, 020613) or UF EC (Frampton, 2001, 019051), or in healthy and asthmatic adults following exposure to CAPs (Ghio et al., 2000, 012140; Gong et al., 2000, 155799; 2003, 087365). Rudell et al. (1996, 056577) reported a significant increase in specific airways resistance following exposure to DE, an effect that was not attenuated by reducing the particle number by 46% (2.6×10^6 particles/cm^3 compared with 1.4×10^6 particles/cm^3) using a particle trap. The particle trap did not affect the concentrations of other measured diesel emissions including NO_2, NO, CO, or total hydrocarbons. As described below, more recent controlled human exposure studies provide limited and inconsistent evidence of changes in lung function following exposure to particles from various sources.

CAPs

Among a group of healthy and asthmatic adults exposed to UFPs (Los Angeles, mean concentration 100 μg/m^3), Gong et al. (2008, 156483) observed small, yet statistically significant decrements in arterial oxygen saturation immediately following exposure, 4 h post-exposure, and 22 h post-exposure (0.5% mean decrease relative to filtered air across all time points, $p < 0.05$). A statistically significant decrease in FEV_1 was also observed, but only at 22 h post-exposure (2% decrease relative to filtered air, $p < 0.05$). The responses demonstrated in this study were not affected by health status. No such effects were observed in a similar study conducted in Chapel Hill, NC which exposed healthy adults to a lower concentration of UF CAPs (49.8 μg/m^3) (Samet et al., 2009, 191913). In addition, two studies evaluating effects of exposure to $PM_{10-2.5}$ CAPs (average concentration 89-157 μg/m^3) on lung function observed no changes in spirometric measurements, DLCO or arterial oxygen saturation 0-22 h post-exposure in asthmatic or healthy adults (Gong et al., 2004, 055628; Graff et al., 2009, 191981). While Gong et al. (2004, 087964) did not observe a significant association between exposure to $PM_{2.5}$ CAPs and spirometry in older subjects (60-80 yr), the investigators did report a decrease in oxygen saturation immediately following CAPs exposure. This effect was observed more consistently in healthy older adults than in older adults with COPD. These findings were confirmed by a subsequent study conducted by the same laboratory (Gong et al., 2005, 087921). The authors also observed a small decrease in MMEF following a 2-h exposure to $PM_{2.5}$ CAPs (200 μg/m^3) which was more pronounced in healthy subjects.

Urban Traffic Particles

Neither short-term exposure to relatively high levels of urban traffic particles nor longer exposures to lower concentrations of urban particles have been observed to alter pulmonary function in controlled exposures among healthy adults. Larsson et al. (2007, 091375) exposed 16 adults for 2 h to $PM_{2.5}$ concentrations of 46-81 μg/m^3 in a room adjacent to a busy road tunnel, with concomitant exposure to NO_2 (0.12 ppm), NO (0.71 ppm), and CO (5 ppm). Although respiratory effects in this study were not compared to filtered air control, no difference in lung function was observed 14 h after exposure to traffic particles relative to lung function measured on a day following typical activities that did not include transit though a road tunnel. In a study of 24-h exposures to urban traffic particles ($PM_{2.5}$ 9.7 μg/m^3), no change in lung function was reported at 2.5 h after the start of exposure relative to filtered air (Brauner et al., 2009, 190244).

Diesel Exhaust

Mudway et al. (2004, 180208) exposed 25 healthy adults to DE with an average particle concentration of 100 μg/m^3 and observed mild bronchoconstriction (airways resistance) immediately following exposure relative to filtered air. No changes were observed in FEV_1 or FVC following DE exposure in these subjects, or in a group of 15 asthmatics exposed using the same protocol (Mudway et al., 2004, 180208; Stenfors et al., 2004, 157009).

Model Particles

Pietropaoli et al. (2004, 156025) observed a reduction in MMEF and DLCO in healthy adults 21 h after a 2-h exposure to UF carbon particles (50 μg/m^3). This reduction in DLCO may reflect a PM-induced vasoconstrictive effect on the pulmonary vasculature. Tunnicliffe et al. (2003, 088744) did not observe any significant change in lung function following exposure to ammonium bisulfate or aerosolized H_2SO_4 (200 and 2,000 μg/m^3) in healthy or asthmatic adults, which is consistent with findings of the majority of studies of controlled exposures to acid aerosols presented in the last two PM AQCDs (U.S. EPA, 1996, 079380; 2004, 056905).

Summary of Controlled Human Exposure Study Findings for Pulmonary Function

Taken together, the majority of controlled human exposure studies do not provide evidence of PM-induced changes in pulmonary function; however, some investigators have observed slight decreases in DLCO, MMEF, FEV_1, oxygen saturation, or increases in airways resistance following exposure to CAPs, DE, or UF EC.

6.3.2.3. Toxicological Studies

The 2004 PM AQCD (U.S. EPA, 2004, 056905) included three animal toxicological studies which measured pulmonary function following multiday short-term inhalation exposure to CAPs. A decreased respiratory rate was noted in the one study involving dogs. Increased tidal volume was observed in one study involving rats while no changes were observed in the other rat study. AHR was found in four studies of mice, healthy rats or SH rats exposed to ROFA by IT instillation or inhalation. Studies conducted since the last review are discussed below.

CAPs

SH rats exposed to Tuxedo, NY CAPs via nose-only inhalation for 4 h (mean concentration 73 μg/m^3; single-day concentrations 80 and 66 μg/m^3; 2/2001 and 5/2001, respectively) had a statistically significant decreased respiratory rate compared with air-exposed controls (Nadziejko et al., 2002, 087460). This measure was obtained from BP fluctuations using radiotelemetry. The decrease in respiratory rate of 25-30 breaths/min was an immediate response to CAPs, beginning shortly after the exposure began and ceasing with the end of exposure. It was accompanied by a decrease in HR (Section 6.2.1.3). Rats were also exposed to fine (MMAD 160 nm; 49-299 μg/m^3) and UF H_2SO_4 (MMAD 50-75 nm; 140-750 μg/m^3) (Nadziejko et al., 2002, 087460) because H_2SO_4 aerosols have the potential to activate irritant receptors. Irritant receptors, found at all levels of the respiratory tract, include rapidly-adapting receptors and sensory C-fiber receptors (Alarie, 1973, 070967; Bernardi et al., 2001, 019040; Coleridge and Coleridge, 1994, 156362; Widdicombe, 2003, 157145; Widdicombe, 2006, 155519). Activation of trigeminal afferents in the nose causes CNS reflexes resulting in decreases in respiratory rate through a lengthened expiratory phase, closure of the glottis, closure of the nares with increased nasal airflow resistance and effects on the cardiovascular system such as bradycardia, peripheral vasoconstriction and a rise in systolic arterial blood pressure. Sneezing, rhinorrhea and vasodilation with subsequent nasal vascular congestion are also nasal reflex responses involving the trigeminal nerve (Sarin et al., 2006, 191166). Activation of vagal afferents in the tracheobronchial and alveolar regions of the respiratory tract causes CNS reflexes resulting in bronchoconstriction, mucus secretion, mucosal vasodilation, cough, and apnea

followed by rapid shallow breathing. Besides effects on the respiratory system, effects on the cardiovascular system can also occur including bradycardia and hypotension or hypertension. Fine H_2SO_4 induced an overall decrease in respiratory rate, with UF H_2SO_4 resulting in elevated respiratory rate compared to control (Nadziejko et al., 2002, 087460). The authors suggested that both CAPs and fine H_2SO_4 aerosols activated sensory irritant receptors in the upper airways, resulting in a decreased respiratory rate. The response to UF H_2SO_4 aerosols differed from the other responses and was thought to be due to deposition of UFPs deeper into the lung with the subsequent activation of pulmonary irritant receptors which trigger an increase in respiratory rate. Since irritant receptors in nasal, tracheobronchial and alveolar regions act via trigeminal- and vagal-mediated pathways, this study indicates a role for neural reflexes in respiratory responses to CAPs.

Kodavanti et al. (2005, 087946) measured respiratory frequency 1 day after a 2-day exposure of SH and WKY rats to CAPs from RTP, NC (mean mass concentration range 144-2,758 $\mu g/m^3$; <2.5 µm in size; 8/27-10/24/2001) for 4 h/day. Increases in inspiratory and expiratory times were seen in SH, but not WKY rats, exposed to CAPs compared with filtered air controls.

Effects of CAPs on pulmonary function were also investigated in a rat model of pulmonary hypertension using SD rats pre-treated with monocrotaline (Lei et al., 2004, 087999). In this study, rats were exposed to CAPs from an urban high traffic area in Taiwan (mean mass concentration 371 $\mu g/m^3$) for 6 h/day on three consecutive days and pulmonary function was evaluated 5 h post-exposure using whole-body plethysmography. A statistically significant decrease in respiratory frequency and an increase in tidal volume were observed following CAPs exposure, along with an increase in airway responsiveness (measured as Penh) following Mch challenge.

In many animal studies changes in ventilatory patterns are assessed using whole body plethysmography, for which measurements are reported as enhanced pause (Penh). Some investigators report increased Penh as an indicator of AHR, but these are inconsistently correlated and many investigators consider Penh solely an indicator of altered ventilatory timing in the absence of other measurements to confirm AHR. Therefore use of the terms AHR or airway responsiveness has been limited to instances in which the terminology has been similarly applied by the study investigators.

Diesel Exhaust

Li et al. (2007, 155929) exposed BALB/c and C57BL/6 mice to clean air or to low dose DE (containing 100 $\mu g/m^3$ particles) for 7 h/day and 5 days/wk for 1, 4 and 8 wk. Average gas concentrations were reported to be 3.5 ppm CO, 2.2 ppm NO_2, and <0.01 ppm SO_2. AHR was evaluated by whole-body plethysmography at day 0 and after 1, 4 and 8 wk of exposure. Exposure to DE for 1 wk resulted in an increased sensitivity of airways to Mch, measured as Penh, in C57BL/6 but not BALB/c, mice. Other short-term responses of this study are discussed in Sections 6.3.3.3 and 6.3.4.2.

McQueen et al. (2007, 096266) investigated the role of vagally-mediated pathways in respiratory responses to PM. Respiratory minute volume (RMV) was increased in anesthetized Wistar rats 6 h after treatment with 500 µg DE particles (SRM2975) by IT instillation. This response was blocked by severing the vagus nerve or pretreatment with atropine. The absence of a respiratory response with vagotomy or atropine indicated that the increase in RMV following DE particle exposure involved a neural reflex acting via vagal afferents. No statistically significant changes in mean BP, HR or HRV were observed in response to DE particles in this study. Vagally-mediated inflammatory responses to DEP were also observed in this study and are discussed in Section 6.3.3.3.

Model Particles

In a study by Last et al. (2004, 097334), BALB/c mice were exposed to 250 $\mu g/m^3$ laboratory-generated iron-soot (size range 80-110 nm; about 200 $\mu g/m^3$ as soot) for 4 h/day and 3 days/wk for 2 wk. Pulmonary function was measured by whole-body plethysmography after challenge with Mch. No AHR, as measured by Penh, was observed following 2-wk exposure to iron-soot. Other findings of this study are reported in Sections 6.3.3.3 and 6.3.5.3.

Summary of Toxicological Study Findings for Pulmonary Function

Several recent studies demonstrated alterations in respiratory frequency and in airway responsiveness following short-term exposure to CAPs and DE. Two studies provide evidence for the involvement of irritant receptors and vagally-mediated neural reflexes in mediating changes in respiratory functions.

6.3.3. Pulmonary Inflammation

The discussion of the effects of PM on pulmonary inflammation in the 2004 PM AQCD (U.S. EPA, 2004, 056905) was limited by a relative lack of information from controlled human exposure and toxicological studies. Although no epidemiologic studies of pulmonary inflammation were described in the 2004 PM AQCD (U.S. EPA, 2004, 056905), several recent studies have observed a positive association between PM concentration and exhaled NO (eNO). New controlled human exposure and toxicological studies have also generally observed an increase in markers of inflammation in the pulmonary compartment following exposure to PM.

6.3.3.1. Epidemiologic Studies

No epidemiologic studies of pulmonary inflammation were described in the 2004 PM AQCD (U.S. EPA, 2004, 056905).

Exhaled Nitric Oxide – Asthmatic Children

Exhaled NO, a biomarker for airway inflammation, was the outcome studied in panels of asthmatic children in southern California (Wu et al., 2006, 157156) and Seattle (Allen et al., 2008, 156208; Koenig et al., 2003, 156653; 2005, 087384; Mar et al., 2005, 088759). Mean concentration data from these studies are summarized in Table 6-10. Delfino et al. (2006, 157156) followed 45 asthmatic children for ten days with offline fractional eNO and examined the associations with exposures to personal $PM_{2.5}$ and 24-h $PM_{2.5}$, EC and OC as well as ambient $PM_{2.5}$, EC and OC. The strongest associations were between eNO and 2-day avg pollutant concentrations: for a 10 $\mu g/m^3$ increase in personal $PM_{2.5}$, eNO increased by 0.46 ppb (95% CI: 0.04-0.79); for 0.6 $\mu g/m^3$ personal EC, eNO increased by 0.7 ppb (95% CI: 0.3-1.1). An association with exposure to ambient $PM_{2.5}$ was only statistically significant in 19 subjects taking inhaled corticosteroids: for each 10 $\mu g/m^3$ increase in $PM_{2.5}$, eNO increased by 0.77 ppb (95% CI: 0.07-1.47).

In a panel of 19 asthmatic children in Seattle, effects were observed only among the ten non-users of inhaled corticosteroids. For each 10 $\mu g/m^3$ increase in personal, outdoor, indoor, or central site $PM_{2.5}$, eNO increased from 3.82 ppb (associated with central site, 95% CI: 1.22-6.43) to 4.48 ppb (with personal $PM_{2.5}$, 95% CI: 1.02-7.93) (Koenig et al., 2003, 156653). Further analysis examining the association between eNO and outdoor and indoor-generated particles suggested that eNO was associated more strongly with ambient particles, but only for non-users of medication: each 10 $\mu g/m^3$ increase in estimated ambient $PM_{2.5}$ results in an increase in eNO of 4.98 ppb (95% CI: 0.28-9.69) (Koenig et al., 2005, 087384).

Also in Seattle, WA, Mar et al. (2005, 088759) examined the association between eNO and ambient $PM_{2.5}$ concentration among children (aged 6-13 yr) recruited from an asthma/allergy clinic. Fractional exhaled nitric oxide (FeNO) was associated with hourly averages of $PM_{2.5}$ up to 10-12 h after exposure. Each 10 $\mu g/m^3$ increase in 1-h mean $PM_{2.5}$ concentration was associated with a 6.99 ppb increase in eNO (95% CI: 3.43-10.55) among children not taking inhaled corticosteroids, but associated with only a 0.77 ppb decrease in eNO (95% CI: -4.58 to 3.04) among those taking inhaled corticosteroids.

Allen et al. (2008, 156208), in a reanalysis of data from Koenig et al. (2005, 087384), evaluated the effect of different $PM_{2.5}$ exposure metrics in relation to airway inflammation among children in wood smoke-impacted areas of Seattle. The authors found that for the nine non-users of inhaled corticosteroids, the ambient-generated component of $PM_{2.5}$ exposure was associated with respiratory responses, both airway inflammation and decrements in lung function, whereas the non-ambient $PM_{2.5}$ exposure component was not. They did note, however, different relationships for

airway inflammation and decrements in lung function, with the former significantly associated with total personal $PM_{2.5}$, personal light-absorbing carbon (LAC), and ambient generated personal $PM_{2.5}$ and the latter related to ambient $PM_{2.5}$ and its combustion markers. The different results between FeNO and lung function were not unexpected; epidemiologic data show that airway inflammation indicated by FeNO does not correlate strongly with either respiratory symptoms or lung function (Smith and Taylor, 2005, 192176). The authors conclude that lung function decrements may be associated with the combustion-generated component of ambient $PM_{2.5}$, whereas airway inflammation may be related to some other component of the ambient $PM_{2.5}$ mixture.

In a longitudinal study, Liu et al. (2009, 192003) examined the association between acute increases in ambient air pollutants and FeNO among children (ages 9-14 yr) with asthma. FeNO had a trend of positive associations with $PM_{2.5}$, with the strongest association on lag day 0 (3.12% [95% CI: -2.12 to 8.82]). Copollutant models including O_3, SO_2 or NO_2 did not result in marked changes in the $PM_{2.5}$ risk estimates for FeNO.

A few studies outside of the U.S. examined eNO in relation to PM exposure among children. Fischer et al. (2002, 025731) and Murata et al. (2007, 189159) found a statistical association between increases in PM and increases in the percent of eNO. Holguin et al. (2007, 099000) found no association between exposure to PM and eNO. However, they did see statistical associations between increases in eNO for the 95 asthmatic subjects and measures of road density of roads 50- and 75-m from the home.

Exhaled Nitric Oxide – Adults

Three recent panel studies examined the effects of particle exposure on eNO measured in older adults (Adamkiewicz et al., 2004, 087925 in Steubenville, OH; Adar et al., 2007, 001458; Jansen et al., 2005, 082236 in Seattle). Mean concentration data from these studies are characterized in Table 6-10. Breath samples were collected weekly for 12 weeks from a group of 29 elderly adults in Steubenville, OH (Adamkiewicz et al., 2004, 087925). In single-pollutant models, each 10 $\mu g/m^3$ increase in 24-h ambient $PM_{2.5}$ increased eNO by 0.82 ppb (95% CI: 0.19-1.45), a change of 15% compared to mean eNO (9.9 ppb). Effects were essentially unchanged in copollutant models that included ambient and/or indoor NO. The effect estimates for the seven COPD subjects were higher than for normal subjects (2.20 vs. 0.45 ppb, $p = 0.03$) (Adamkiewicz et al., 2004, 087925).

In the Seattle panel of older adults (aged 60-86 yr), seven subjects were asthmatic and nine had a diagnosis of COPD (five with asthma and four without) (Jansen et al., 2005, 082236). Exhaled NO was measured daily for 12 days, along with personal, indoor, outdoor and central site PM_{10}, $PM_{2.5}$ and BC. The strongest associations between 24-h avg PM and eNO were found for the asthmatic subjects: 10 $\mu g/m^3$ increases in outdoor levels (measured outside the subjects' homes) of $PM_{2.5}$ or PM_{10} were associated with increases in eNO of 4.23 ppb (95% CI: 1.33-7.13), an increase of 22% above the group mean of 19.2 ppb, and 5.87 ppb (95% CI: 2.87-8.88), an increase of 31%, respectively. BC measured indoors, outdoors or personally was also associated with increases in eNO (of 3.97, 2.32, and 1.20 ppb, respectively) (Jansen et al., 2005, 082236).

Adar et al. (2007, 001458) conducted a panel study of 44 non-smoking senior citizens residing in St. Louis, MO. As part of the study, subjects were taken on group trips to a theater performance, Omni movie, outdoor band concert, and a Mississippi River boat cruise. Subjects were driven to and from each event aboard a diesel bus. Before and after each bus trip, eNO was measured on each subject. Two carts containing continuous air pollution monitors were used to measure group-level micro-environmental exposures to $PM_{2.5}$, BC, and size-specific particle counts (0.3-2.5 µm and 2.5-10 µm) on the day of each trip. Each 10 $\mu g/m^3$ increase in 24-h mean $PM_{2.5}$ concentration was associated with a 36% increase in eNO pre-trip (95% CI: 5-71). Each 10 $\mu g/m^3$ increase in micro-environmental $PM_{2.5}$ concentration (i.e., during the bus ride) was associated with a 27% increase in eNO post-trip (95% CI: 17-38).

These studies all demonstrated an association between increased levels of eNO and increases in PM in the previous 4-24 h. Further, three studies demonstrated effects in elderly populations (Adamkiewicz et al., 2004, 087925; Adar et al., 2007, 001458; Jansen et al., 2005, 082236) while four others reported a similar acute increase in eNO among children (Delfino et al., 2006, 090745; Koenig et al., 2003, 156653; 2005, 087384; 2005, 088999).

Outside of the U.S., one study examined eNO in a panel of 60 adult asthmatic subjects in London. McCreanor et al. (2007, 092841) reported that 1 $\mu g/m^3$ increase in personal exposure to EC

was associated with increases of approximately 1.75-2.25% in eNO (results were presented graphically only) for up to 22 h post-exposure.

Other Biomarkers of Pulmonary Inflammation and Oxidative Stress

Other biomarkers of respiratory distress that have been examined in recent panel studies include urinary leukotriene E4 (LTE_4) in asthmatic children (Rabinovitch et al., 2006, 088031); two oxidative stress markers: TBARS and 8-isoprostane in asthmatic children (Liu et al., 2009, 192003) and breath acidification in adolescent athletes (Ferdinands et al., 2008, 156433). Mean concentration data from these studies are characterized in Table 6-10.

In Rabinovitch et al. (2006, 088031), LTE_4, an asthma-related biological mediator, was used to study the response to short-term particle exposure. In the second winter of their 2-yr study of asthmatic children (described above in Section 6.3.1.1), urine samples were collected at approximately the same time of day from 57 subjects for eight consecutive days. Controlling for days with URI symptoms, each 10 $\mu g/m^3$ increase in morning maximum $PM_{2.5}$ (measured by TEOM), was associated with an increase in LTE_4 levels by 5.1% (95% CI: 1.6-8.7). No statistically significant effects were observed on the same day or up to 3 days later based on 24-h averaged concentrations from the TEOM monitor or from the FRM central site monitor.

In a longitudinal study conducted in Windsor, Ontario, Liu et al. (2009, 192003) examined the association between acute increases in ambient air pollutants and TBARS and 8-isoprostane among children (ages 9-14 yr) with asthma. TBARS, but not 8-isoprostane, was positively associated with $PM_{2.5}$ (percent change in TBARS 40.6% [95% CI: 11.8-81.3], lag 0-2 days). The association with TBARS persisted for at least three days. Adverse changes in pulmonary function (Section 6.3.2.1) were consistent with those of TBARS in response to $PM_{2.5}$ with a similar lag structure, suggesting a coherent outcome for small airway function and oxidative stress.

The effects of vigorous outdoor exercise during peak smog season in Atlanta, GA on breath pH, a biomarker of airway inflammation, in adolescent athletes (n = 16, mean age = 14.9 yr) were examined by Ferdinands et al. (2008, 156433). Median pre-exercise breath pH was 7.58 (range 4.39-8.09) and median post-exercise breath pH was 7.68 (range 3.78-8.17). The authors observed no significant association between ambient PM and post-exercise breath pH. However both pre- and post-exercise breath pH were strikingly low in these athletes when compared to 14 relatively sedentary healthy adults and to published values of breath pH in healthy subjects. The authors speculate that repetitive vigorous exercise may induce airway acidification.

Effect of Measurement Location on Studies of Pulmonary Function and Inflammation

A number of studies examining exposure to $PM_{2.5}$ and pulmonary function and inflammation have compared the results of exposure assessment based on concentrations recorded from personal, indoor, outdoor, and/or ambient monitors (Allen et al., 2008, 156208; Delfino et al., 2004, 056897; Delfino et al., 2006, 090745; Koenig et al., 2005, 087384; Trenga et al., 2006, 155209). Two investigations evaluated $PM_{2.5}$ concentrations from indoor, outdoor, personal and central site monitors and the relationship with FEV_1. Delfino et al. (2004, 056897) reported that personal exposure estimates showed a stronger association with FEV_1 than any of the stationary exposures, and that indoor exposure estimates were associated with a stronger effect than either outdoor or central site exposure estimates. However, Trenga et al. (2006, 155209) reported the largest declines in FEV_1 associated with central site exposure estimates, though the most consistent association with declines in FEV_1 came from the exposure estimates measured by indoor monitors. Delfino et al. (2006, 090745) used personal and ambient exposure estimates in a study of FeNO among asthmatic children and found that the personal exposure estimates were more robust than the ambient exposure estimates. Two studies conducted in Seattle, WA partitioned personal exposure to $PM_{2.5}$ into its ambient-generated and indoor-generated components. Koenig et al. (2005, 087384) reported that ambient-generated $PM_{2.5}$ was consistently associated with an increase in FeNO, while the indoor-generated component of $PM_{2.5}$ was less strongly associated with FeNO. This could reflect the difference in composition of indoor-generated $PM_{2.5}$ as compared to ambient-generated $PM_{2.5}$. Similarly, Allen et al. (2008, 156208) found that FeNO was associated with the ambient-generated

component of personal $PM_{2.5}$ exposure, but not with ambient $PM_{2.5}$ concentrations measured by central site monitors. Overall, these studies provide a unique perspective on how measurement location influences the findings of epidemiologic studies. This small group of studies indicates that effects are associated with all types of PM measurement, suggesting health effects of both ambient-generated and indoor-generated particles. It is likely that variability in season, meteorology, topography, geography, behavior and exposure patterns contribute to the observed differences.

6.3.3.2. Controlled Human Exposure Studies

Studies of controlled human exposures presented in the 2004 PM AQCD (U.S. EPA, 2004, 056905) provided evidence of pulmonary inflammation induced by exposure to PM. Lay et al. (1998, 007683) found that instillation of iron oxide particles (2.6 μm) produced an increase in alveolar macrophages and neutrophils in bronchoalveolar lavage fluid (BALF) collected 24 h post-instillation. Ghio and Devlin (2001, 017122) evaluated the inflammatory response following bronchial instillation of particles extracted from filters collected in the Utah Valley both prior to and after the closure of an area steel mill. Subjects who underwent pulmonary instillation of particles (500 μg) collected while the steel mill was operating (n = 16) had significantly higher levels of neutrophils 24 h post-instillation compared with either saline instillation or with subjects (n = 8) who were instilled with the same mass of PM collected during the mill's closure. This finding indicates that metals may be an important PM component for this health outcome. In an inhalation study of exposure to $PM_{2.5}$ CAPs (23-311 $\mu g/m^3$) from Chapel Hill, NC, Ghio et al. (2000, 012140) observed an increase in airway and alveolar neutrophils 18 h after the 2-h exposure. A similar finding was reported by Rudell et al. (1999, 001964) following exposure to DE among healthy adults. In this study, reducing the particle number from 2.6×10^6 particles/cm^3 to 1.3×10^6 particles/cm^3 while maintaining the concentration of gaseous diesel emissions was not observed to attenuate the response. One study of controlled exposures to UF EC among healthy adults did not report particle-related effects on eNO (Frampton, 2001, 019051). As summarized below, several recent studies of controlled exposures have provided some additional evidence of pulmonary inflammation associated with PM.

CAPS

A series of exposures to UF, $PM_{2.5}$, and $PM_{10-2.5}$ CAPs from Los Angeles with average particle concentrations between 100 and 200 $\mu g/m^3$ have not been shown to have a significant effect on markers of airway inflammation in healthy or health-compromised adults (Gong et al., 2004, 087964; 2004, 055628; 2005, 087921; 2008, 156483). However, two recent studies conducted in Chapel Hill, NC reported significant increases in percent PMNs and concentration of IL-8 in BALF among healthy adults 18-20 h following controlled exposures to $PM_{10-2.5}$ (89 $\mu g/m^3$) and UF (49.8 $\mu g/m^3$) CAPs, respectively (Graff et al., 2009, 191981; Samet et al., 2009, 191913). As discussed above, the same laboratory previously reported a mild inflammatory response in the lower respiratory tract following exposure to $PM_{2.5}$ CAPs (Ghio et al., 2000, 012140). In a follow-up analysis, Huang et al. (2003, 087377) found the increase in BALF neutrophils demonstrated by Ghio et al. (2000, 012140) to be positively associated with the Fe, Se, and SO_4^{2-} content of the particles.

Alexis et al. (2006, 154323) recently evaluated the effect of $PM_{10-2.5}$ on markers of airway inflammation, specifically focusing on the impact of biological components of $PM_{10-2.5}$. Healthy men and women (n = 9) between the ages of 18 and 35 inhaled nebulized saline (0.9%) as well as aerosolized $PM_{10-2.5}$ collected from ambient air. Subjects were exposed to $PM_{10-2.5}$ on two separate occasions, once using $PM_{10-2.5}$ that had been heated to inactivate biological material and once using non-heated $PM_{10-2.5}$. Approximately 0.65 mg $PM_{10-2.5}$ was deposited in the respiratory tract of subjects during the exposures. Markers of inflammation and immune function were analyzed in induced sputum collected 2-3 h after inhalation of saline or $PM_{10-2.5}$. Both heated and non-heated $PM_{10-2.5}$ were observed to increase the neutrophil response compared with saline. Exposure to non-heated $PM_{10-2.5}$ was found to increase levels of monocytes, eotaxin, macrophage TNF-α mRNA, and was also associated with an upregulation of macrophage cell surface markers. No such effects were observed following exposure to biologically inactive $PM_{10-2.5}$. These results suggest that while $PM_{10-2.5}$-induction of neutrophil response is not dependent on biological components, heat sensitive

components of $PM_{10-2.5}$ (e.g., endotoxin) may be responsible for PM-induced alveolar macrophage activation.

Traffic Particles

Larsson et al. (2007, 091375) exposed 16 healthy adults to air pollution in a road tunnel for 2 h during the afternoon rush hour in Stockholm, Sweden. The median $PM_{2.5}$ and PM_{10} concentrations during the road tunnel exposures were 64 μg/m^3 and 176 μg/m^3, respectively. Bronchial biopsies were obtained and bronchoscopy and BAL were performed 14 h after the exposure. The results were compared with a control exposure which consisted of exposure to urban air during normal activity. The authors reported significant BALF increases in percentage of lymphocytes, total cell number, and alveolar macrophages following exposure to road tunnel exposure versus control. These results provide evidence of a significant association between exposure to road tunnel air pollution and airway inflammation. However, unlike other controlled exposure studies, the control exposure was not a true clean air control, but only a lower exposure group with no characterization of personal exposure. In addition, it is not possible to separate out the contributions of each air pollutant, including PM, on the observed inflammatory response.

Diesel Exhaust

In a recent study evaluating the effect of DE exposure on markers of airway inflammation, Behndig et al. (2006, 088286) exposed healthy adults (n = 15) for 2 h with intermittent exercise to filtered air or DE with a reported PM_{10} concentration of 100 μg/m^3. Eighteen hours after exposure to DE, the authors found significant increases in neutrophil and mast cell numbers in bronchial tissue, as well as significant increases in neutrophil numbers and IL-8 in BALF compared with filtered air control. Similarly, Stenfors et al. (2004, 157009) observed an increase in pulmonary inflammation (e.g., airways neutrophilia and an increase in IL-8 in BALF) among healthy adults 6 h following exposure to DE (PM_{10} average concentration 108 μg/m^3). It is interesting to note, however, that no such inflammatory effects were observed in a group of mild asthmatic subjects in the same study. The DE-induced neutrophil response in the airways of healthy subjects observed in these two studies (Behndig et al., 2006, 088286; Stenfors et al., 2004, 157009) is qualitatively consistent with the findings of Ghio et al. (2000, 012140) who exposed healthy subjects to Chapel Hill $PM_{2.5}$ CAPs. In a group of healthy volunteers, Bosson et al. (2007, 156286) demonstrated that exposure to O_3 (2 h at 0.2 ppm) may enhance the airway inflammatory response of DE relative to clean air (1-h exposure to 300 μg/m^3). Exposure to O_3 was conducted 5 h after exposure to DE, and resulted in an increase in the percentage of neutrophils in induced sputum collected 18 h after exposure to O_3. In a subsequent study using a similar protocol at the same concentrations, prior exposure to DE was shown to increase the inflammatory effects of O_3 exposure, demonstrated as an increase in neutrophil and macrophage numbers in bronchial wash (Bosson et al., 2008, 196659).

Wood Smoke

Barregard et al. (2008, 155675) examined the effect of a short-term exposure (4 h) to wood smoke (240-280 μg/m^3) on markers of pulmonary inflammation in a group of healthy adults. Exposure to wood smoke increased alveolar NO compared to filtered air (2.0 ppb versus 1.3 ppb) 3 h after exposure. Although these results provide some evidence of a PM-induced increase in pulmonary inflammation, the physiological significance of the relatively small increase in alveolar NO is unclear.

Model Particles

Pietropaoli et al. (2004, 156025) observed a lack of airway inflammatory response 21 h after exposure to UF EC particles (10-50 μg/m^3) among healthy and asthmatic adults. The same laboratory reported no effect of exposure to UF or fine ZnO (500 μg/m^3) on total or differential sputum cell

counts 24 h after exposure in a group of healthy adults (Beckett et al., 2005, 156261). Tunnicliffe et al. (2003, 088744) measured levels of eNO as a marker of airway inflammation following 1-h controlled exposures to ammonium bisulfate or aerosolized H_2SO_4 (200 and 2,000 μg/m^3) in a group of healthy and asthmatic adults. While exposure to ammonium bisulfate increased the concentration of eNO immediately following exposure in asthmatics, no such effect was observed in healthy adults, or in either healthy or asthmatic adults following exposure to aerosolized H_2SO_4.

Instillation

Schaumann et al. (2004, 087966) investigated the inflammatory response of human subjects instilled with $PM_{2.5}$ (100 μg) collected from two different cities in Germany, Hettstedt and Zerbst. Although endobronchial instillation of PM from both cities were shown to induce airway inflammation, instillation of PM from the more industrial area (Hettstedt) resulted in greater influxes of BALF monocytes compared to PM collected from Zerbst. The authors postulated that the difference in response between PM from the two cities may be due to the higher concentration of transition metals observed in the samples collected from Hettstedt. Another study reported no change in inflammatory markers in nasal lavage fluid 4 and 96 h following intranasal instillation of DEP (300 μg/nostril) in asthmatics and healthy adults (Kongerud et al., 2006, 156656). Pre-exposure of DEP to O_3 was not shown to have any effect on the response. Although not a cross-over design, these findings suggest that exposure to DEP without the gaseous component of DE may have little effect on inflammatory responses in human subjects.

Summary of Controlled Human Exposure Study Findings for Pulmonary Inflammation

These new studies strengthen the evidence of PM-induced pulmonary inflammation; however, the response appears to vary significantly depending on the source and composition of the particles.

6.3.3.3. Toxicological Studies

The 2004 PM AQCD (U.S. EPA, 2004, 056905) discussed numerous studies investigating pulmonary inflammation in response to CAPs, ROFA, DEPs, metals and acid aerosols. A wide variety of responses was reported depending on the type of PM and route of administration. In general, IT instillation exposure to fly ash and metal PM resulted in notable pulmonary inflammation. In contrast, inhalation of sulfates and acid aerosols had minimal, if any, effect on pulmonary inflammation. More recent animal toxicological studies using CAPs, DE and other relevant PM types are summarized below.

CAPs

The 2004 PM AQCD (U.S. EPA, 2004, 056905) found that exposure to $PM_{2.5}$ CAPs at concentrations of 100-1,000 μg/m^3 for 1-6 h/day and 1-3 days generally resulted in minimal to mild inflammation in rats and dogs. Somewhat enhanced inflammation was observed in a model of chronic bronchitis. Since the last review, numerous studies have investigated inflammatory responses to $PM_{2.5}$ and UF CAPs in both healthy and compromised animal models.

In one study of healthy animals, SD rats were exposed to CAPs for 4 h/day on 3 consecutive days in Fresno, CA, in fall 2000 and winter 2001 ($PM_{2.5}$ mean mass concentration 190-847 μg/m^3) (Smith et al., 2003, 042107). The particle concentrator used in these studies was capable of enhancing the concentration of UF as well as fine particles. Immediately after exposure on the third day, BALF was collected and analyzed for total cells and neutrophils. Statistically significant increases were observed in numbers of neutrophils during the first week of the fall exposure period and in numbers of total cells, neutrophils and macrophages during the first week of the winter exposure period. CAPs concentrations were >800 μg/m^3 during both of those weeks.

Two studies were conducted using CAPs in Boston. In a study by Godleski et al. (2002, 156478), healthy SD rats were exposed for 5 h/day for 3 consecutive days to CAPs ranging in

concentration from 73.5-733.0 μg/m^3. BALF and lung tissue were collected for analysis 1 day later. Neutrophilic inflammation was indicated by a statistically significant increase in percent neutrophils in BALF. Microarray analysis of RNA from lung tissue and BALF cells demonstrated increased gene expression of pro-inflammatory mediators, markers of vascular activation and enzymes involved in organic chemical detoxification. This study overlapped in part with previously described studies by Saldiva et al. (2002, 025988) and Batalha et al. (2002, 088109) (Section 6.2.4.3). In another study (Rhoden et al., 2004, 087969), healthy SD rats were exposed for 5 h to CAPs (mean mass concentration 1228 μg/m^3; June 20-August 16, 2002). A statistically significant increase in BALF neutrophils was observed 24 h following CAPs exposure. Histological analysis confirmed the influx of inflammatory cells (Section 6.3.5.3). Inflammation was accompanied by injury which is discussed in Section 6.3.5.3.

Kodavanti et al. (2005, 087946) reported two sets of studies involving $PM_{2.5}$ CAPs exposure during fall months in RTP, NC. In the first study, SH rats were exposed to filtered air or CAPs (mean mass concentration range 1,138-1,765 μg/m^3; <2.5 μm) for 4 h and analyzed 1-3 h later. No increase in BALF inflammatory cells or other measured parameter was observed. In the second study, SH and WKY rats were exposed to filtered air or CAPs (mean mass concentration range 144-2,758 μg/m^3; <2.5 μm) for 4 h/day on 2 consecutive days and analyzed 1 day afterward. Differences in baseline parameters were noted for the two rat strains since SH rats had greater numbers of BALF neutrophils than WKY rats. Following the 2-day CAPs exposure, increased BALF neutrophils were observed in the WKY rats but not in the SH rats compared with filtered air controls. Inflammation was not accompanied by increases in BALF markers of injury (Section 6.3.5.3).

Two CAPs studies involving SH rats were conducted in the Netherlands. In the first, SH rats were exposed by nose-only inhalation to CAPs (ranging in concentration from 270-3,660 μg/m^3 and in size from 0.15-2.5 μm) from three different sites in the Netherlands (suburban, industrial and near-freeway) for 6 h (Cassee et al., 2005, 087962). Increased numbers of neutrophils were observed in BALF 2 days post-exposure compared to air controls. When CAPs exposure was used as a binary term, the relationship between CAPs concentration and number of PMN in BALF was statistically significant. In contrast, Kooter et al. (2006, 097547) reported no changes in markers of pulmonary inflammation measured 18 h after a 2-day exposure (6 h/day) of SH rats to $PM_{2.5}$ or $PM_{2.5}$+UFP CAPs from sites in the Netherlands (mean mass concentration range 399-3613 and 269-556 μg/m^3, respectively; $PM_{2.5}$ CAPs site in Bilthoven and $PM_{2.5}$+UF CAPs site in freeway tunnel in Hendrik-Ido-Ambacht).

Pulmonary inflammation was investigated in two studies using a rat model of pulmonary hypertension (i.e., SD rats pre-treated with monocrotaline). In the first study, rats were exposed to $PM_{2.5}$ CAPs from an urban high traffic area in Taiwan (mean mass concentration of 371 μg/m^3) (Lei et al., 2004, 087999) for 6 h/day on 3 consecutive days and BALF was collected 2 days later. A statistically significant increase in total cells and neutrophils was observed in BALF. Levels of TNF-α and IL-6 in the BALF were not altered by CAPs exposure. In the second study, rats were exposed to $PM_{2.5}$ CAPs (mean mass concentration 315.6 and 684.5 μg/m^3 for 6 and 4.5 h, respectively; Chung-Li area, Taiwan) during a dust storm event occurring March 18-19, 2002 (Lei et al., 2004, 087884). Only one animal served as control during the 6-h exposure (from 2100-300 on the first exposure day) so results from that one animal were combined with that of three control animals from the 4.5-h exposure (from 300-730) on the second exposure day. A statistically significant increase in total cells and neutrophils in BALF occurred in both CAPs-exposed groups. In addition, increases in BALF IL-6 and markers of injury (Section 6.3.5.3) were observed as a function of CAPs exposure.

In summary, pulmonary inflammation was noted in all three studies involving multiday exposure of healthy rats to CAPs from different locations. No pulmonary inflammation was seen in one study of SH rats exposed to CAPs for 4 h and analyzed 1-3 h later. In studies involving multiday exposure of SH rats, one demonstrated pulmonary inflammation while two did not. In the rat monocrotaline model of pulmonary hypertension, both single-day and multiday exposures to CAPs resulted in mild pulmonary inflammation.

On-Road Exposures

In a study by Elder et al. (2004, 087354) old rats (21 mo) were exposed to on-road highway aerosols (particle concentration range 0.95-3.13×10^5 particles/cm^3; mass concentration estimated to be 37-106 μg/m^3; Interstate 90 between Rochester and Buffalo, NY) for 6 h on one or three

consecutive days. No increase in BALF inflammatory cells was observed 18 h post-exposure in any of the treatment groups.

Urban Air

To evaluate inflammatory responses to ambient particles from vehicles, Wistar rats were exposed to ambient urban air from a high traffic site (concentration range 22-225 μg/m^3 PM_{10}; Porto Alegre, Brazil) or to the same air which was filtered to remove the PM (Pereira et al., 2007, 156019). Concentrations of gases were not reported. Compared with controls exposed to filtered urban air, a significant increase in total number of BALF cells was observed 24 h following the 20 h continuous exposure, but not following the 6 h of exposure to unfiltered urban air.

Diesel Exhaust

The 2004 PM AQCD (U.S. EPA, 2004, 056905) summarized findings of the 2002 EPA Diesel Document regarding the health effects of DE. Short-term inhalation exposure to low levels of DE results in the accumulation of diesel PM in lung tissue, pulmonary inflammation and alveolar macrophage aggregation and accumulation near the terminal bronchioles. More recent studies are summarized below.

Pulmonary inflammatory responses were investigated in C57BL/6 mice exposed to DE 7 h/day for 6 consecutive days (Harrod et al., 2003, 097046). Compared with controls, inflammatory cell counts in BALF were increased in mice exposed to the higher concentration of DE (1,000 μg/m^3 PM) but not in mice exposed to the lower concentration of DE (30 μg/m^3 PM). Concentrations of gases present in the higher dose DE were reported to be 43 ppm NO_X, 20 ppm CO and 364 ppb SO_2.

In a second study evaluating DE effects on BALF inflammatory cells, no increases in numbers of neutrophils, lymphocytes or eosinophils were observed in BALB/c mice exposed by inhalation to 500 or 2,000 μg/m^3 DE particles for 4 h/day on 5 consecutive days (Stevens et al., 2008, 157010). Concentrations of gases reported in this study were 4.2 ppm CO, 9.2 ppm NO, 1.1 ppm NO_2, and 0.2 ppm SO_2 for the higher concentration of DE. Transcriptional microarray analysis demonstrated upregulation of chemokine and inflammatory cytokine genes, as well as genes involved in growth and differentiation pathways, in response to the higher concentration of DE. No gene expression results were reported for the lower concentration of DE. Sensitization and challenge with ovalbumin (OVA) significantly altered these findings (Section 6.3.6.2). These results demonstrate that changes in gene expression can occur in the absence of measurable pulmonary inflammation or injury markers (Section 6.3.5.3).

Li et al. (2007, 155929) exposed mice to clean air or to low dose DE (100 μg/m^3 PM) for 7 h/day and 5 days/wk for 1, 4 and 8 wk as described in Section 6.3.2.3. Analysis of BALF and histology of lung tissues was carried out at day 0 and after 1, 4 and 8 wk of exposure. Total numbers of cells and macrophages in BALF were significantly increased in C57BL/6 mice, but not in BALB/c mice, after 1-wk exposure to DE compared with 0 day controls. Neutrophils and lymphocytes were increased after 1-wk exposure to DE in both strains compared with 0 day controls. Differences in BALF cytokines were also noted between the two strains after 1-wk exposure to DE. No changes were observed by histological analysis. Pulmonary function and oxidative responses were also evaluated (Sections 6.3.2.3 and 6.3.4.2). Long-term exposure responses are discussed in Sections 7.3.2.2, 7.3.3.2 and 7.3.4.1.

Healthy F344 rats and A/J mice were exposed to DE containing 30, 100, 300 and 1,000 μg/m^3 PM by whole body inhalation for 6 h/day, 7 days/wk for either 1 wk or 6 months in a study by Reed et al. (2004, 055625). Concentrations of gases were reported to be from 2.0-45.3 ppm NO, 0.2-4.0 ppm NO_2, 1.5-29.8 ppm CO and 8-365 ppb for SO_2 in these exposures. One week of exposure resulted in no measurable effects on pulmonary inflammation. Long-term exposure responses are discussed in Section 7.3.3.2.

In a study by Wong et al. (2003, 097707), also reported by Witten et al. (2005, 087485), F344/NH rats were exposed nose-only to filtered room air or to DE at concentrations of 35.3 μg/m^3 and 669.3 μg/m^3 PM (particle size range 7.2-294.3 nm) for 4 h/day and 5 days/wk for 3 wk. Gases associated with the high dose exposure were reported to be 3.59 ppm NO, 3.69 ppm NO_X, 0.1 ppm NO_2, 2.95 ppm CO, 518.96 ppm CO_2 and 0.031 ppm total hydrocarbon. The focus of this study was

on the possible role of neurogenic inflammation in mediating responses to DE. Neurogenic inflammation is characterized by both the influx of inflammatory cells and plasma extravasation into the lungs following the release of neuropeptides from bronchopulmonary C-fibers. Pulmonary inflammation was evaluated by histological analysis of lung tissue at the end of the 3-wk exposure period. Following high, but not low, concentration exposure to DE, a large number of alveolar macrophages was found in the lungs. Small black particles, presumably DE particles, were found in the cytoplasm of these alveolar macrophages. Perivascular cuffing consisting of mononuclear cells was also observed in high dose-exposed animals. Influx of neutrophils or eosinophils was not seen, although mast cell number was increased in high-dose exposed animals. Pulmonary plasma extravasation was measured by the ^{99m}Technecium-albumin technique and found to be dose-dependently increased in the bronchi and lung parenchyma. Alveolar edema was also observed by histology in high concentration-exposed animals. A significant decrease in substance P content in lung tissue was reported in DE-exposed rats. These responses initially suggested that DE resulted in stimulation of C-fibers and activation of a local axon reflex resulting in the repeated release of the stored neuropeptide substance P. Subsequent experiments were conducted using capsaicin pretreatment, which inhibits neurogenic inflammation by activating C-fibers and causing the depletion of neuropeptide stores. Pretreatment with capsaicin was found to reduce the influx of inflammatory cells, but not plasma extravasation, in response to DE. Hence, DE is unlikely to act through bronchopulmonary C-fibers to cause neurogenic edema in this model, although there may be a different role for bronchopulmonary C-fibers in mediating the inflammatory cell influx.

Stimulation of bronchopulmonary C-fibers can result in activation of both local and CNS reflexes through vagal parasympathetic pathways. McQueen et al. (2007, 096266) investigated the role of vagally-mediated pathways in acute inflammatory responses to DE particles. A statistically significant increase in BALF neutrophils was observed 6 h after IT instillation treatment of anesthetized Wistar rats with 500 µg DE particles (SRM2975). This response was blocked by severing the vagus nerve or pretreatment with atropine (McQueen et al., 2007, 096266). Similarly, atropine treatment blocked the increase in BALF neutrophils seen 6 h after DE particle exposure in conscious Wistar rats. These results provide evidence for the involvement of a pulmonary vagal reflex in the inflammatory response to DE particles.

In summary, several studies demonstrate that short-term inhalation exposure to DE (100-1,000 µg/m^3 PM) causes pulmonary inflammation in rodents. No attempt was made in these studies to determine whether the responses were due to PM components or to gaseous components. However, PM from DE was found to be capable of inducing an inflammatory response, as demonstrated by the one IT instillation study described above. Evidence was presented suggesting that DEP may act through bronchopulmonary C-fibers to stimulate pulmonary inflammation.

Gasoline Emissions and Road Dust

Healthy male Swiss mice were exposed to gasoline exhaust (635 µg/m^3 PM and associated gases) or filtered air for 15 min/day for 7, 14, and 21 days (Sureshkumar et al., 2005, 088306). BALF was collected for analysis 1 h after the last exposure. Histological analysis was also carried out at 7, 14, and 21 days. The number of leukocytes in BALF was increased after exposure to gasoline exhaust, but this increase did not achieve statistical significance. However, levels of the pro-inflammatory cytokines TNF-α and IL-6 were significantly increased in BALF following 14 and 21 days of exposure. Furthermore, inflammatory cell infiltrate in the peribronchiolar and alveolar regions were observed by histology. Evidence of lung injury was also found (Section 6.3.5.3). In this study, BALF analysis of inflammatory cells was a less sensitive indicator of pulmonary inflammation than BALF analysis of cytokines and histological analysis of lung tissue. Results of this study cannot entirely be attributed to the presence of PM in the gasoline exhaust since 0.11 mg/m^3 SO_X, 0.49 mg/m^3 of NO_X and 18.7 ppm of CO were also present during exposure.

Using ApoE$^{-/-}$ mice on a high-fat diet, Campen et al. (2006, 096879) studied the impact of inhaled gasoline emissions and road dust (6 h/day×3 day) on pulmonary inflammation. For gasoline emissions, the PM-containing atmosphere (PM mean concentration 61 µg/m^3; NO_X mean concentration 18.8 ppm; CO mean concentration 80 ppm) failed to increase numbers of inflammatory cells in BALF collected 18 h after the last exposure. However, a statistically significant increase in total cells and macrophages was observed in response to resuspended road dust ($PM_{2.5}$) at 3,500 µg/m^3, but not at 500 µg/m^3.

Model Particles

In a study by Elder et al. (2004, 055642), pulmonary inflammation was investigated in two compromised, aged animal models (11-14 mo old SH and 23 mo old F344) exposed by inhalation to UF CB (count median diameter = 36 nm) at a relevant concentration (150 $\mu g/m^3$). No changes in BALF cells were seen 24 h post-exposure in either model.

An increase in BALF neutrophils was observed at 24 h, but not at 4 h, in WKY rats exposed to UF carbon particles (median particle size 38 nm; mass concentration 180 $\mu g/m^3$; mean number concentration 1.6×10^7 particles/cm^3) for up to 24 h (Harder et al., 2005, 087371). Changes in HR and HRV demonstrated in this study (Section 6.2.1.3) occurred much more rapidly than the inflammatory response.

No evidence of pulmonary inflammation was found by analysis of BALF or histology one or three days following 24-h exposure of SH rats to UF carbon particles under similar conditions (median particle size 31 nm; mass concentration 172 $\mu g/m^3$; mean number concentration 9.0×10^6 particles/cm^3) (Upadhyay et al., 2008, 159345). However increased expression of HO-1, ET-1, ET_A and ET_B, tPA and, plasminogen activator-1 was found in lung tissue three days following exposure.

In a study by Gilmour et al. (2004, 054175), adult Wistar rats were exposed for 7 h to fine and UF CB particles (mean mass concentration 1,400 and 1,660 $\mu g/m^3$ for fine and UF CB, respectively; mean number concentration 3.8×10^3 and 5.2×10^4 particles/cm^3, respectively; count median aerodynamic diameter 114 nm and 268 nm, respectively). Both treatments resulted in increased BALF neutrophils 16 h post-exposure, with the UFPs having the greater response. UFPs also increased total BALF leukocytes and macrophage inflammatory protein-2 (MIP-2) mRNA in BALF cells. Although these exposures may not be relevant to ambient exposures, this study demonstrated the greater propensity of UF CB particles to cause a pro-inflammatory response compared with fine CB particles.

In a study by Last et al. (2004, 097334), mice were exposed to 250 $\mu g/m^3$ laboratory-generated iron-soot over a 2-wk period as described in Section 6.3.2.3. BALF was collected 1-h after the last exposure and analyzed for total cells. No increase in total cell number was observed following iron-soot exposure. Other findings of this study are described in Sections 6.3.2.3 and 6.3.5.3.

Pinkerton et al. (2008, 190471) exposed young adult male SD rats to filtered air, iron, soot or iron-soot for 6 h/day for 3 days. The iron particles were mainly less than 100 nm aerodynamic diameter, while the soot particles were initially 20-40 nm in diameter but formed clusters of 100-200 nm in diameter. The size-distribution of iron-soot particles was bimodal over 10-250 nm and averaged 70-80 nm in diameter. Rats were exposed to 45, 57 and 90 $\mu g/m^3$ iron or to 250 $\mu g/m^3$ soot alone or in combination with 45 $\mu g/m^3$ iron. Increased levels of the pro-inflammatory cytokine IL-1β were observed in lung tissue of rats exposed for 6 h/day for 3 days to 90 $\mu g/m^3$, but not 57 $\mu g/m^3$, iron. No change in BALF inflammatory cells was observed after exposure to 57 $\mu g/m^3$ or 90 $\mu g/m^3$ iron. Exposures to 250 $\mu g/m^3$ soot in combination with 45 $\mu g/m^3$ iron also resulted in increased levels of lung IL-1β and activation of the transcription factor NF-κB. Levels of lung IL-1β were increased in neonatal rats exposed to 250 $\mu g/m^3$ soot in combination with 100, but not 30, $\mu g/m^3$ iron. Other endpoints of this study are described in Section 6.3.4.2.

Summary of Toxicological Study Findings for Pulmonary Inflammation

New studies involving short-term exposures to CAPs and urban air strengthen the evidence of PM-induced pulmonary inflammation. In addition, several studies demonstrated pulmonary inflammation in response to diesel and gasoline exhaust; however it is not known whether PM or gaseous components of the exhaust were responsible for these effects. Mixed results were obtained in studies using model particles such as CB and iron-soot.

6.3.4. Pulmonary Oxidative Responses

The results of a small number of controlled human exposure and toxicological studies presented in the 2004 PM AQCD (U.S. EPA, 2004, 056905) provided some initial evidence of an association between exposure to PM and pulmonary oxidative stress. Recent controlled human

exposure studies have provided support for previous findings of an increase in markers of pulmonary oxidative stress following exposure to DE, and one new study has observed a similar effect following controlled exposure to wood smoke. New findings from toxicological studies provide further evidence that oxidative species are involved in PM-mediated effects. No epidemiologic studies have evaluated the association between PM concentration and pulmonary oxidative response.

6.3.4.1. Controlled Human Exposure Studies

Two studies cited in the 2004 PM AQCD (U.S. EPA, 2004, 056905) observed effects on markers of airway oxidative response in healthy adults following controlled exposures to fresh DE or resuspended DE particles (Blomberg et al., 1998, 051246; Nightingale et al., 2000, 011659). Several recent studies are described below which have further evaluated the oxidative response following exposure to particles in human volunteers.

Diesel Exhaust

Pourazar et al. (2005, 088305) exposed 15 adults (11 males and four females) for 1 h to air or DE (PM_{10} concentration 300 μg/m^3) in a controlled cross-over study. Bronchoscopy with airway biopsy was performed 6 h after exposure. The expression of NF-κB, AP-1 (c-jun and c-fos), p38, and JNK in bronchial epithelium was quantified using immunohistochemical staining. DE was observed to significantly increase nuclear translocation of NF-κB, AP-1, phosphorylated p38, and phosphorylated JNK; however, the findings of this study require confirmation with more quantitative methods such as Western blot analysis. The observed activation of redox-sensitive transcription factors by DE may result in the induction of pro-inflammatory cytokines. There is some evidence to suggest that this bronchial response to DE is mediated through the epidermal growth factor receptor signaling pathway (Pourazar et al., 2008, 156884). Behndig et al. (2006, 088286) evaluated the upregulation of endogenous antioxidant defenses following exposure to DE (100 μg/m^3 PM_{10}) in a group of 15 healthy adults. Increases in urate and reduced GSH were observed in alveolar lavage, but not bronchial wash, 18 h after exposure. In a study utilizing the same exposure protocol, Mudway et al. (2004, 180208) observed an increase in GSH and ascorbate in nasal lavage fluid 6 h following exposure to DE in a group of 25 healthy adults.

Wood Smoke

Barregard et al. (2008, 155675) observed a significant increase in malondialdehyde levels in breath condensate of healthy volunteers (n = 13) immediately following and 20 h after a 4-h exposure to wood smoke (240-280 μg/m^3 PM).

Endobronchial Instillation

Schaumann et al. (2004, 087966) demonstrated an increased oxidant radical generation of BALF cells following endobronchial instillation of urban particles compared with instillation of particles collected in a rural area. The authors suggested that this difference was likely due to the greater concentration of transition metals found in the urban particles.

Summary of Controlled Human Exposure Study Findings for Pulmonary Oxidative Responses

Taken together, these studies suggest that short-term exposure to PM at near ambient levels may produce mild oxidative stress in the lung. Limited data suggest that proximal and distal lung regions may be subject to different degrees of oxidative stress during exposures to different pollutant particles.

6.3.4.2. Toxicological Studies

The 2004 PM AQCD (U.S. EPA, 2004, 056905) reported one study which provided evidence that ROS were involved in PM-mediated responses. This particular study used pre-treatment with the antioxidant DMTU to block the neutrophilic response to ROFA. More recently, several studies evaluated the effects of PM exposure on pulmonary oxidative stress. Oxidative stress can be directly determined by measuring ROS or oxidation products of lipids and proteins. An indirect assay involves measurement of the enzyme HO-1 or of the antioxidant enzymes SOD or catalase, all of which can be induced by oxidative stress. Antioxidant interventions which inhibit or prevent responses are a further indirect measure of oxidative stress playing a role in the pathway of interest.

CAPs

Gurgueira et al. (2002, 036535) measured oxidative stress as in situ CL. Immediately following a 5-h $PM_{2.5}$ CAPs exposure (mean mass concentration range 99.6-957.5 $\mu g/m^3$; Boston, MA) increased CL was observed in lungs of CAPs-exposed SD rats. CL evaluated after CAPs exposure durations of 3 h was also increased but did not achieve statistical significance compared to the filtered air group. When animals were allowed to recover for 24 h following the 5-h CAPs exposure, CL levels returned to control values. Interestingly, a decrease in lung CL was observed in rats breathing filtered air for three days compared with rats breathing room air for the same duration. To compare potential particle-induced differences in in situ CL, rats were exposed to ROFA (1.7 mg/m^3 for 30 min) or CB (170 $\mu g/m^3$ for 5 h). Only the ROFA-treated animals exhibited increased CL in lung tissue. Additionally, levels of antioxidant enzymes in the lung (MnSOD and catalase) were increased in CAPs-exposed rats. A CAPs-associated increase in CL was also seen in the heart (Section 6.2.9.3), but not the liver.

In a similar study, Rhoden et al. (2004, 087969) exposed SD rats for 5 h to $PM_{2.5}$ CAPs from Boston (mean mass concentration 1,228 $\mu g/m^3$) or to filtered air. Significant increases in TBARS and protein carbonyl content (a measure of protein oxidation) were observed 24 h post-exposure to CAPs. Pretreatment with the thiol antioxidant NAC (50 mg/kg i.p.) 1-h prior to exposure prevented not only the lipid and protein oxidation observed in response to CAPs, but also the increase in BALF neutrophils and pulmonary edema in this model (Sections 6.3.3.3 and 6.3.5.3). Results of this study demonstrate the key role played by oxidative stress in these CAPs-mediated effects.

A later study by Rhoden et al. (2008, 190475) investigated the role of superoxide in mediating pulmonary inflammation following exposure to ambient air particles. In this study, adult SD rats were exposed by IT instillation to 1 mg of SRM1649. Two hours prior to exposure, half of the rats were pretreated with the membrane-permeable SOD mimetic MnTBAP (10 mg/kg, i.p.). MnTBAP abrogated the inflammatory response, measured by increased BALF inflammatory cells, and the increase in lung superoxide, measured by CL, observed 4 h following exposure to urban air particles.

Kooter et al. (2006, 097547) reported an increase in HO-1 in BALF and lung tissue measured 18 h after a 2-day exposure (6 h/day) of SH rats to $PM_{2.5}$ or $PM_{2.5}$+UF CAPs (mean mass concentration range 399-3613 and 269-556 $\mu g/m^3$, respectively; $PM_{2.5}$ CAPs site in Bilthoven and $PM_{2.5}$+UF site in freeway tunnel in Hendrik-Ido-Ambacht, the Netherlands). This occurred in the absence of any measurable pulmonary inflammation (Section 6.3.3.3).

Urban Air

To evaluate oxidative stress responses to ambient particles from vehicles, Wistar rats were exposed to ambient urban air from a high traffic site (concentration range 22-225 $\mu g/m^3$ PM_{10}; Porto Alegre, Brazil) or to the same air which was filtered to remove the PM (Pereira et al., 2007, 156019). Several exposure regimens were carried out: 6- and 20-h continuous exposures or to intermittent exposures of 5 h/day for four consecutive days. A significant increase in lipid peroxidation (measured as malondialdehyde) was seen in lung tissue immediately following the 20-h continuous exposure, but not following the 6-h exposure or the intermittent exposures. Inflammation-related endpoints are described in Section 6.3.3.3.

Diesel Exhaust

Li et al. (2007, 155929) exposed mice to clean air or to low dose DE (100 μg/m^3 PM) for 7 h/day and 5 days/wk for 1, 4 and 8 wk as described in Section 6.3.2.3. HO-1 mRNA and protein were increased in lung tissues of both mouse strains after 1 wk of DE exposure. In addition, AHR and changes in BALF cells and cytokines were observed (Sections 6.3.2.3 and 6.3.3.3). Pretreatment with the thiol antioxidant NAC (320 mg/kg, i.p.) on days 1-5 of DE exposure greatly attenuated the AHR and inflammatory response seen after 1 wk of DE exposure. Long-term responses are discussed in Sections 7.3.2.2, 7.3.3.2 and 7.3.4.1.

A study by Whitekus et al. (2002, 157142) investigated the adjuvant effects of DE particles in an allergic animal model and is discussed in detail below (Section 6.3.6.3). Intervention with the thiol antioxidants bucillamine and NAC inhibited the increases in allergen-specific IgE and IgG_1 as well as the increases in protein carbonyl and lipid hydroperoxides in the lung following DE particle exposure.

Gasoline Exhaust

Pulmonary oxidative stress was evaluated by measurement of CL and TBARS following exposure of SD rats to gasoline engine exhaust (Seagrave et al., 2008, 191990). Animals were exposed for 6 h in a nose-only inhalation exposure system. PM mass concentration was reported to be 60 μg/m^3; count median diameter 20 nm; mass median diameter 150 nm; while the concentrations of gaseous copollutants were 104 ppm CO, 16.7 ppm NO, 1.1 ppm NO_2 and 1.0 ppm SO_2. A statistically significant increase in lung CL was observed without a concomitant increase in lung TBARS. Discordant results were also observed for road dust exposures in the heart (Section 6.2.9.3). The discrepancy between oxidative stress indicators suggests that the responses may follow different time courses. Furthermore, no CL was seen when the gasoline exhaust was filtered to remove the particulate fraction.

Model Particles

Increased expression of HO-1 was observed in lung tissue three days following 24-h exposure of SH rats to UF carbon particles (median particle size 31 nm; mass concentration 172 μg/m^3; mean number concentration 9.0×10^6 particles/cm^3) despite no evidence of pulmonary inflammation (Section 6.3.3.3) (Upadhyay et al., 2008, 159345)

In a study conducted by Pinkerton et al. (2008, 190471), young adult male SD rats were exposed to filtered air, soot, iron or iron-soot for 6 h/day for three days as described in Section 6.3.3.3. A statistically significant decrease in total antioxidant power and a statistically significant increase in glutathione-S-transferase activity were observed in lung tissue from rats exposed to 90 μg/m^3 iron. This high concentration iron exposure also resulted in increased levels of ferritin protein in lung tissue, indicating the presence of free iron which has the potential to redox cycle and cause oxidative stress. Lung tissue total antioxidant power was decreased and glutathione redox ratio was increased by the combined exposure to 250 μg/m^3 soot and 45 μg/m^3 iron. The iron-soot exposure also increased oxidized glutathione in BALF and lung tissue. These results demonstrate that co-exposure to soot enhanced iron-mediated oxidative stress. Furthermore, co-exposure to soot and iron resulted in increased expression of cytochrome P450 isozymes CYP1A1 and CYP2E1 in lung tissue, an effect not observed in response to either agent alone. Inflammation-related endpoints observed in this study are described in Section 6.3.3.3.

In a parallel study, Pinkerton et al. (2008, 190471) exposed neonatal male SD rats to iron-soot or filtered air 6 h/day for three days during the second and fourth week of life. Both 30 μg/m^3 and 100 μg/m^3 iron in combination with 250 μg/m^3 soot resulted in increased BALF oxidized glutathione, glutathione redox ratio and glutathione-S-transferase activity and decreased total antioxidant power. The higher concentration exposure resulted in increased ferritin expression in lung tissue. Effects on cellular proliferation in specific regions of the lung were also noted as described in Section 6.3.5.3.

Nurkiewicz et al. (2009, 191961) exposed SD rats to fine (count median diameter 710 nm) and UF (count median diameter 100 nm) TiO_2 particles via aerosol inhalation at concentrations of 1.5-16

mg/m^3 for 240-720 min. These exposures were chosen in order to produce deposition of 4-90 μg/rat, which was demonstrated in a previous study to result in different degrees of impaired microvascular function (Nurkiewicz et al., 2008, 156816). Histological analysis of lung tissue did not find any significant inflammation, although particle accumulation in alveolar macrophages and a frequent association of alveolar macrophage with the alveolar wall was observed 24 h following exposure (Nurkiewicz et al., 2008, 156816). Although the main focus of the more recent study was on effects of TiO_2 on NO production and microvascular reactivity in the spinotrapezius muscle (Section 6.2.4.3), the presence of nitrotyrosine was determined in both lung tissue and spinotrapezius muscle as a measure of peroxynitrite formation. Peroxynitrite formation occurs mainly as a result of the rapid reaction of NO with superoxide and suggests an increase in local superoxide production. The area of lung tissue containing nitrotyrosine immunoreactivity increased three-fold 24 h following exposure to 10 μg UF TiO_2. Nitrotyrosine immunoreactivity was localized in inflammatory cells found in the alveolar region of the lung.

Summary of Toxicological Study Findings for Pulmonary Oxidative Responses

New studies involving short-term exposure to CAPs, urban air, diesel and gasoline exhaust, and model particles such as CB, iron-soot and TIO_2 consistently demonstrate pulmonary oxidative responses. Furthermore, antioxidant treatment ameliorated effects observed in response to CAPs, DE and DE particles.

6.3.5. Pulmonary Injury

The 2004 PM AQCD (U.S. EPA, 2004, 056905) presented evidence from several toxicological studies of small PM-induced increases in markers of pulmonary injury including thickening of alveolar walls and increases in BALF protein. These findings are consistent with the results of recent toxicological and controlled human exposure studies demonstrating mild pulmonary injury accompanying inflammatory responses to CAPs and wood smoke. One recent epidemiologic study has also observed a positive association between PM and urinary concentrations of lung Clara cell protein.

6.3.5.1. Epidemiologic Studies

One epidemiologic study examined biomarkers of pulmonary injury. The mean concentration data from this study are characterized in Table 6-10. Timonen et al. (2004, 087915) enrolled subjects with coronary heart disease in Amsterdam (n = 37), Erfurt, Germany (n = 47) and Helsinki (n = 47) to study daily variation in PM and urinary concentrations of lung Clara cell protein (CC16). No associations were seen between the PNC of the smallest particles ($NC_{0.01-0.1}$) and CC16. Significant associations with $NC_{0.1-1}$ and $PM_{2.5}$ (which were strongly correlated with each other [r = 0.8]) were seen only for Helsinki subjects: same day, lag 3 and 5-day mean $NC_{0.1-1}$ increases of 1000 particles/cm^3 were associated with increases in ln (CC16/creatinine) of 15.5% (95% CI: 0.001-30.9), 17.4% (95% CI: 3.4-31.4), and 43.2% (95% CI: 17.4-69.0), respectively. Similar associations were seen for 10 μg/m^3 increases in $PM_{2.5}$: lag 0 and 5-day mean $PM_{2.5}$ were associated with increases in ln (CC16/creatinine) of 23.3% (95% CI: 6.3-40.3) and 38.8% (95% CI: 15.8-61.8), respectively.

6.3.5.2. Controlled Human Exposure Studies

No studies of controlled human exposures presented in the 2004 PM AQCD (U.S. EPA, 2004, 056905) specifically examined the effect of PM on pulmonary injury. However, several recent studies have evaluated changes in markers of injury and increased alveolar permeability following exposures to various types of particles.

Urban Traffic Particles

Bräuner et al.(2009, 190244) evaluated the effect of exposure to urban traffic particles (24-h exposure, $PM_{2.5}$ 9.7 μg/m^3) on the integrity of the alveolar epithelial membrane in a group of 29 healthy adults, with and without exercise. Following 2.5 h of exposure, alveolar epithelial permeability was assessed by measuring the pulmonary clearance of ^{99m}Tc-DTPA, which was administered as an aerosol during 3 min of tidal breathing. While pulmonary clearance of ^{99m}Tc-DTPA was observed to increase following exercise, there was no significant difference in clearance between exposure to urban traffic particles and filtered air. In addition, PM exposure was not observed to affect the level of CC16 in plasma or urine at 6 or 24 h after the start of exposure.

Diesel Exhaust

Relative to filtered air, exposure for 1 h to DE (300 μg/m^3 PM) was not observed to affect the plasma CC16 concentration at 6 or 24 h post exposure in a group of 15 former smokers with COPD (Blomberg et al., 2005, 191991).

Wood Smoke

In a study examining the respiratory effects of wood smoke, Barregard et al. (2008, 155675) exposed two groups of healthy adults in separate 4-h sessions to wood smoke with median particle concentrations of 243 and 279 μg/m^3. At 20 h post-exposure, the mean serum CC16 concentration was significantly higher after exposure to wood smoke when compared with filtered air. However, when the analysis was stratified by exposure session, a statistically significant effect of wood smoke on serum CC16 was observed in the subjects in session 1 but not those in session 2. It is interesting to note that while the mean particle concentration was only slightly higher in session 1, the mean particle number in session 1 was almost 90% higher than the particle number in session 2, with geometric mean particle diameters of 42 and 112 nm, respectively.

Summary of Controlled Human Exposure Study Findings for Pulmonary Injury

The findings from these studies provide limited evidence to suggest that exposures to particles may increase markers of pulmonary injury in healthy adults.

6.3.5.3. Toxicological Studies

The 2004 PM AQCD (U.S. EPA, 2004, 056905) reported mild increases in BALF protein, a marker of pulmonary injury, in several studies involving inhalation exposure to CAPs. In addition, histological analysis demonstrated that the bronchoalveolar junction was the site of the greatest inflammation following CAPs exposure. Low level exposure to DE was associated with Type 2 cell proliferation and thickening of alveolar walls near alveolar macrophages according to the 2002 EPA Diesel Document (U.S. EPA, 2002, 042866). In addition, IT instillation of fly ash and metal-containing PM generally caused pulmonary injury as measured by increases in BALF protein, LDH and albumin. Proliferation of bronchiolar epithelium was also noted. More recent studies of BALF markers of pulmonary injury and histological analysis of lung tissue are summarized below.

BALF Markers of Pulmonary Injury and Increased Permeability

CAPs

Kodavanti et al. (2005, 087946) exposed SH and WKY rats to filtered air or $PM_{2.5}$ CAPs from RTP, NC as described in Section 6.3.3.3. Differences in baseline parameters were noted for the two rat strains since SH rats had greater levels of protein and lower levels of LDH, NAG, ascorbate and

uric acid in the BALF compared with WKY rats. One day after the 2-day CAPs exposure, increased levels of GGT were observed in BALF (a marker of epithelial injury) of SH rats, but not WKY rats, compared with filtered air controls. Injury was not accompanied by inflammation (Section 6.3.3.3).

In a study by Cassee et al. (2005, 087962), SH rats were exposed for 6 h by nose-only inhalation to CAPs from three different sites in the Netherlands as described in Section 6.3.3.3. The pulmonary injury marker CC16 was increased in BALF two days following CAPs exposure. Inflammation was also observed (Section 6.3.3.3).

Gurgueira et al. (2002, 036535) exposed SD rats to Boston, MA CAPs as described in Section 6.3.4.2 and reported a small but statistically significant increase in lung wet/dry ratios after 3 and 5 h of exposure, indicating the presence of mild edema. This response was accompanied by increased oxidative stress as measured by in situ CL (Section 6.3.4.2). In a similar study, Rhoden et al. (2004, 087969) reported an increase in lung wet/dry ratio in rats 24 h following a 5-h exposure to Boston CAPs which was diminished by pre-treatment of the antioxidant NAC (Section 6.3.4.2).

Pulmonary injury was investigated in two studies using a rat model of pulmonary hypertension (SD rats pre-treated with monocrotaline) which is described in greater detail in Section 6.3.3.3 (Lei et al., 2004, 087999). Significant increases in BALF LDH and protein were observed in response to CAPs. Pulmonary inflammation was observed in both of these studies (Section 6.3.3.3).

Diesel Exhaust

In a study evaluating the effects of DE, no changes were observed in BALF protein and LDH in mice exposed by inhalation to concentrations of 50 and 2000 μg/m^3 DE particles for 4 h/day on 5 consecutive days as described in Section 6.3.3.3 (Stevens et al., 2008, 157010). Changes in gene expression were observed in the higher exposure group. This study demonstrates that changes in gene expression can occur in the absence of measurable markers of injury or pulmonary inflammation.

In a study by Wong et al. (2003, 097707), also reported by Witten et al. (2005, 087485), rats were exposed nose-only to filtered room air or to DE over a 3-wk period. This study, focusing on neurogenic inflammation, is described in greater detail in Section 6.3.3.3. Pulmonary plasma extravasation was measured by the ^{99m}Technecium-albumin technique and found to be dose-dependently increased in the bronchi and lung. Pretreatment with capsaicin, which inhibits neurogenic inflammation by activating C-fibers and causing the depletion of neuropeptide stores, did not reduce plasma extravasation following DE exposure. Hence, DE is unlikely to act through bronchopulmonary C-fibers to cause neurogenic edema in this model. Inflammatory responses measured in this study are discussed in Section 6.3.3.3.

Gasoline Exhaust

Healthy male Swiss mice were exposed to gasoline exhaust (635 μg/m^3 PM and associated gases) or filtered air for 15 min/day for 7, 14, and 21 days as described in Section 6.3.3.3 (Sureshkumar et al., 2005, 088306). BALF was collected for analysis 1-h after the last exposure. Statistically significant increases in BALF markers of lung injury, alkaline phosphatase, gamma-glutamyl transferase and LDH, were observed at all time points studied. Alveolar edema was noted following 14 and 21 days of exposure. Other findings of this study, including inflammation and histopathological changes, are discussed in Section 6.3.3.3 and below.

Histopathology

CAPs

Histopathological changes were demonstrated in rats exposed for 5 h to Boston CAPs as described in Section 6.3.3.3 (Rhoden et al., 2004, 087969). Slight bronchiolar inflammation and thickened vessels at the bronchiole were observed 24 h post-exposure, consistent with the influx of polymorphonuclear leukocytes observed in BALF (Section 6.3.3.3).

Diesel Exhaust

In a study by Wong et al. (2003, 097707), also reported by Witten et al. (2005, 087485), rats were exposed nose-only to filtered room air or to DE over a 3-wk period. This study, focusing on neurogenic inflammation, is described in greater detail in Section 6.3.3.3. Pulmonary inflammation was evaluated by histological analysis of lung tissue. Following high, but not low, concentration-exposure to DE, a large number of alveolar macrophages was found in the lungs. Small black particles, presumably DE particles, were found in the cytoplasm of these alveolar macrophages. Perivascular cuffing consisting of mononuclear cells was also observed in the high exposure animals. Influx of neutrophils or eosinophils was not seen although mast cell number was increased. Other indices of injury demonstrated in this study are described above.

Gasoline Exhaust

Another study, which is described in greater detail in Section 6.3.3.3, demonstrated histopathological responses to gasoline exhaust in mice exposed to gasoline exhaust or filtered air for 15 min/day for 7, 14, and 21 days (Sureshkumar et al., 2005, 088306). Histological observations showed inflammatory cell infiltrate in the peribronchiolar and alveolar region, alveolar edema and thickened alveolar septa at 14 and 21 days post-exposure. Levels of pro-inflammatory cytokines and marker enzymes of lung damage were also increased in BALF. The numbers of inflammatory cells in BALF was increased but not significantly, demonstrating that BALF analysis of inflammatory cells was a less sensitive indicator of pulmonary inflammation in this study than histological analysis. Other indices of injury found in this study are described above.

Model Particles

In a study investigating the effects of iron-soot, mice were exposed to 250 $\mu g/m^3$ laboratory-generated iron-soot as described in Sections 6.3.2.3 and 6.3.3.3 (Last et al., 2004, 097334). Analysis of airway collagen content was conducted by histology and by biochemical analysis of microdissected airways. No increases in airway collagen content were found by either method in mice exposed to iron-soot for two weeks. Furthermore, no goblet cells were observed in airways of air or iron-soot exposed animals. Other findings of this study are described in Sections 6.3.2.3 and 6.3.3.3.

One study demonstrating histopathological responses to PM in neonatal rats was reported by Pinkerton et al. (2004, 087465). Rat pups (10 days old) were exposed to soot and iron particles (mean mass concentration of 243 $\mu g/m^3$; iron concentration 96 $\mu g/m^3$; size range 10-50 nm) for 6 h/day on 3 consecutive days. Cell proliferation in different lung regions was evaluated following bromodeoxyuridine injection 2 h prior to necropsy. The rate of cell proliferation in the proximal alveolar region (immediately beyond the terminal bronchioles) was significantly reduced in iron-soot exposed animals compared to controls. This was a region-specific response since the rate of cell proliferation was not altered in the terminal bronchioles or the general lung parenchyma. However alveolar septation, the process by which alveoli are formed during development, and alveolar growth were not altered by iron-soot exposure. Decreased cell viability and increased LDH was also noted in BALF of neonatal rats (Pinkerton et al., 2008, 190471). The authors suggest the possibility of greater susceptibility to air pollution during the critical postnatal lung development period which occurs in animals and humans and that neonatal exposure to PM may contribute to impaired lung growth seen in children.

Summary of Toxicological Study Findings for Pulmonary Injury

New studies involving short-term exposure to CAPs and diesel and gasoline exhaust demonstrate mild pulmonary injury, including enhanced BALF markers of injury, pulmonary edema and histopathology. In general, injury responses were accompanied by inflammatory responses. In addition, altered cellular proliferation in the proximal alveolar region was observed in neonatal rats exposed to iron-soot, suggesting the possibility of greater susceptibility to PM during postnatal lung development.

Relative Toxicity of PM Size Fractions

Ambient PM Studies

A recently undertaken multinational project entitled "Chemical and biological characterization of ambient thoracic coarse ($PM_{10-2.5}$), fine ($PM_{2.5-0.2}$), and UFPs ($PM_{0.2}$) for human health risk assessment in Europe" (PAMCHAR) takes a systematic approach to expanding the present knowledge about the physiochemical and toxicological effects of these three PM size fractions. Six European cities were selected that represented contrasting ambient PM profiles: Helsinki, Duisburg, Prague, Amsterdam, Barcelona, and Athens. For PM collected at all sites, $PM_{10-2.5}$ induced the greatest pulmonary effects in C57BL/6J mice IT instilled with 1, 3, or 10 mg/kg of particles (Happo et al., 2007, 096630). Dose-response relationships in BALF parameters measured 24 h post-IT instillation exposure, including cell number and protein, were observed for all sites following $PM_{10-2.5}$, and neutrophils were the predominant cell type present in the BALF (Happo et al., 2007, 096630). Prague $PM_{10-2.5}$ exposure resulted in decreased macrophages in BALF at 12 h, and Amsterdam, Barcelona, and Athens $PM_{10-2.5}$ induced lymphoplasmacytic cells in BALF (Happo et al., 2007, 096630). No inflammatory responses were observed for UFPs measured 12-h after exposure. Protein was elevated for $PM_{10-2.5}$ for all locations with the 10 mg/kg dose; Athens UFPs induced protein release only at the two lowest doses 12 h post-exposure. For TNF-α and IL-6, the greatest response was observed with $PM_{10-2.5}$ 4 h following exposure (Happo et al., 2007, 096630). Exposure to UFPs from Duisburg resulted in elevated TNF-α for the 1 and 3 mg/kg doses. Only the Helsinki sample appeared to induce the same level of IL-6 release for $PM_{10-2.5}$ and $PM_{0.2}$ at 10 mg/kg, albeit the collection times differed. In vitro TNF-α and IL-6 responses did not always reflect in vivo effects (Table 6-11), as the Duisburg $PM_{10-2.5}$ sample was the most potent in vivo compared to the other sites and elicited much lower cytokine release compared to other cities (except Helsinki) in vitro (Happo et al., 2007, 096630; Jalava et al., 2006, 155872; Jalava et al., 2008, 098968). Helsinki PM was collected in the spring and generally had the lowest in vivo and in vitro activity for $PM_{10-2.5}$ compared to the other cities (Happo et al., 2007, 096630; Jalava et al., 2006, 155872; Jalava et al., 2008, 098968). Spring-time samples were collected because episodes of resuspended road dust occur frequently during this season (Pennanen et al., 2007, 155357). There was a high correlation between EC content in $PM_{2.5}$ and $PM_{10-2.5}$, indicating that traffic impacted both size fractions (Sillanpaa et al., 2005, 156980). Duisburg PM collected in fall had the greatest amounts of Mn and Zn compared to PM samples from other locations (Pennanen et al., 2007, 155357). Metals industries in Duisburg are likely contributors to the observed PM metals concentrations. For the Prague winter PM samples, the As content was higher than at any other location (Pennanen et al., 2007, 155357). Prague also had the highest PAH levels in all three size fractions, possibly attributable to stable atmosphere conditions and incomplete combustion of coal and biomass in residential heating (Pennanen et al., 2007, 155357). High levels of ammonium and nitrate in PM samples from Amsterdam suggest traffic as a large source of air pollution (Pennanen et al., 2007, 155357). Approximately one-third of $PM_{10-2.5}$ mass from Amsterdam was comprised of sea salt (Sillanpaa et al., 2005, 156980), double that of any other city. In Barcelona and Athens, high calcium or Ca^{2+} contents in spring and summer $PM_{2.5}$ and $PM_{10-2.5}$ are indicative of resuspended soil-derived particles (Pennanen et al., 2007, 155357).

Table 6-11. PAMCHAR $PM_{10-2.5}$ inflammation results with ambient PM.

City and Season	In Vivo[a] (mg/kg)						In Vitro[b] (µg/mL)		
	BALF protein	BALF TNF-α	BALF IL-6	BALF KC	BALF PMN	BALF AM	TNF-α	IL-6	MIP-2
Helsinki spring	+10	+10	+10	[+3 10]	+10	--	+150,300	+150,300	+150,300
Duisburg fall	+10	+10	+10	+10	+10	--	+150,300	+150,300	+300
Prague winter	+10	[+3 10]	+10	[+3 10]	+10	+10	+150,300	+150,300	+150,300
Amsterdam winter	+10	+10	+10	+10	+10	--	+150	+150,300	+150,300
Barcelona spring	+10	+10	[+3 10]	+10	+10	--	+150,300	+150,300	+150,300
Athens summer	+10	[+3 10]	[+3 10]	[+3 10]	+10	--	+150,300	+150,300	+150,300

[a]Source: Happo et al. (2007, 096630); 2 cell lines used for in vitro study were RAW264.7
[b]Source: Jalava et al. (2006, 155872); + indicates increased response and numbers that follow indicate at which dose the response was observed

Schins et al. (2004, 054173) employed PM from two cities in Germany, Duisburg and Borken, in another study. In contrast to the PAMCHAR study where animals were administered PM suspended in pathogen-free water (Happo et al., 2007, 096630), animals received PM via IT instillation suspended in saline at a dose of 320 µg (Schins et al., 2004, 054173). In female Wistar rats, neutrophils in BALF were significantly elevated for $PM_{10-2.5}$ from Duisburg and Borken (Table 6-12), albeit the percent of neutrophils with the $PM_{10-2.5}$ from Borken was nearly double that of Duisburg. The responses with $PM_{2.5}$ were much smaller. When these $PM_{10-2.5}$ particles were introduced into whole blood to determine overall inflammogenic capacity, IL-8 and TNF-α were released in greater quantities than in response to $PM_{2.5}$. Furthermore, $PM_{10-2.5}$ from Borken induced higher cytokine responses than Duisburg $PM_{10-2.5}$.

An in vivo study involving SH rats was conducted using $PM_{10-2.5}$ and $PM_{2.5}$ from six different European locations with varying traffic densities (3 or 10 mg/kg IT instillation; UFPs were not collected) (Gerlofs-Nijland et al., 2007, 097840). It was reported that $PM_{10-2.5}$ generally induced greater responses than $PM_{2.5}$. IT instillation of $PM_{10-2.5}$ from a location with high traffic influence in Munich, Germany, demonstrated the greatest response in terms of LDH activity, protein, total cells, neutrophils, and lymphocytes in BALF 24 h post-exposure. $PM_{10-2.5}$ collected from a low traffic site in Munich induced the greatest cytokine response for TNF-α and MIP-2. Some correlations were observed between $PM_{10-2.5}$ components (Ba and Cu) and BALF parameters, but were largely driven by one location (Gerlofs-Nijland et al., 2007, 097840).

Table 6-12. Other ambient PM – in vivo $PM_{10-2.5}$ studies – BALF results, 18-24 h post-IT exposure.

Location	Endotoxin (~ Values)	Dose (mg/kg)	Cell Differentials	Cytokines	Injury Biomarkers	Reference
Germany, Borken; rural Feb-May 2000	6.6 EU/mg	0.58-0.91	↑* % PMN	↑ TNF-α		Schins et al. (2004, 054173)
Germany, Duisburg; heavy industry Feb-May 2000	5.0 EU/mg	0.58-0.91	↑ % PMN	↑ MIP-2		Schins et al. (2004, 054173)
USA, Seattle, WA Feb-March 2004	6.0 EU/mg	1.25, 5.0				Gilmour, et al. (2007, 096433)
USA, Salt Lake City, UT Apr-May 2004	6.3 EU/mg	1.25, 5.0			↑ protein	Gilmour, et al. (2007, 096433)
USA, South Bronx, NY Dec 2003-Jan 2004	2.8 EU/mg	1.25, 5.0	↑ PMN	↑ MIP-2		Gilmour, et al. (2007, 096433)
USA, Sterling Forest, NY Dec 2003-Jan 2004	2.9 EU/mg	1.25, 5.0				Gilmour, et al. (2007, 096433)

Location	Endotoxin (~ Values)	Dose (mg/kg)	Cell Differentials	Cytokines	Injury Biomarkers	Reference
USA, RTP, NC Oct-Nov 1996	0.96 EU/mg	0.5, 2.5, 5.0	↑↑ PMN	↑ IL-6		Dick (2003, 088776)
Germany, Munich Ost Bahnhof; high traffic A Aug 2002	2.9 EU/mg	3, 10	↑↑* total cells ↑↑ AM ↑↑*PMN ↑↑* Lymph	↑↑ MIP-2 ↑↑ TNF-α	↑↑* LDH ↑* protein	Gerlofs-Nijland, et al. (2007, 097840)
Netherlands, Hendrik-Ido-Ambacht; high traffic Sept 2002	6.5 EU/mg	3, 10	↑↑ total cells ↑↑*AM ↑↑ PMN ↑↑ Lymph	↑ MIP-2 ↑↑ TNF-α	↑↑ LDH ↑ protein	Gerlofs-Nijland, et al. (2007, 097840)
Italy, Rome; high traffic Apr 2002	1.5 EU/mg	3, 10	↑ total cells ↑↑ AM ↑↑ PMN ↑↑ Lymph	↑↑ MIP-2 ↑↑ TNF-α	↑↑ LDH	Gerlofs-Nijland, et al. (2007, 097840)
Netherlands, Dordrecht; moderate traffic Apr 2002	0.6 EU/mg	3, 10	↑↑ total cells ↑ AM ↑↑ PMN ↑ Lymph		↑↑ LDH ↑ protein	Gerlofs-Nijland, et al. (2007, 097840)
Germany, Munich Grosshadern Hospital; low traffic Jun-Jul 2002	2.9 EU/mg	3, 10	↑ total cells ↑↑ AM ↑↑ PMN ↑↑ Lymph	↑↑* MIP-2 ↑↑* TNF-α	↑↑* LDH ↑ protein	Gerlofs-Nijland, et al. (2007, 097840)
Sweden, Lycksele; low traffic Feb-March 2002	0.9 EU/mg	3, 10	↑↑ total cells ↑ AM ↑↑ PMN ↑ Lymph		↑↑ LDH ↑ protein	Gerlofs-Nijland, et al. (2007, 097840)

For Gerlofs-Nijland study, composition data were averaged across seasons. ↑ significant only at highest dose.
↑↑ Significant at lowest and highest dose.
* Greatest potency for that endpoint and study. Gilmour et al. (2007, 096433)exposure was via aspiration.

A more recent study by these investigators (Gerlofs-Nijland et al., 2009, 190353) compared responses to PM from three different European cities based on size fraction and content of metals and PAH. SH rats were IT instilled with 7 mg/kg PM, and markers of toxicity and inflammation were measured in BALF 24 h later. Blood markers of coagulation were also measured and are described in Section 6.2.8.3. In the first part of the study, both $PM_{2.5}$ and $PM_{10-2.5}$ from Duisburg were found to have dramatic effects on inflammatory cell influx and activation as well as on the injury markers LDH, protein and albumin in the BALF. The antioxidant species uric acid was increased in BALF from rats exposed to both size fractions and was interpreted as an adaptive response to oxidative stress. Statistical analysis demonstrated that $PM_{10-2.5}$ was more potent in eliciting these responses than $PM_{2.5}$. In the second part of the study, responses to metal-rich PM from Duisburg and metal-poor PM from Prague were determined. A statistically significant greater enhancement of BALF markers of inflammation and injury was observed for the Duisburg PM compared with the Prague PM. Furthermore, responses to PAH-rich $PM_{10-2.5}$ from Prague and PAH-poor $PM_{10-2.5}$ from Barcelona were determined. $PM_{10-2.5}$ from Prague was found to have statistically significant greater effects compared with $PM_{10-2.5}$ from Barcelona. However, organic extracts of these $PM_{10-2.5}$ fractions had very little capacity to produce inflammation or toxicity in this model. These findings suggest an important role for specific components associated with $PM_{10-2.5}$ in mediating the pro-inflammatory effects.

In another study investigating specific components of $PM_{10-2.5}$, BALB/c mice were IT instilled with 25 and 50 µg $PM_{10-2.5}$ from a rural area of the San Joaquin Valley, California (Wegesser and Last, 2008, 190506). Inflammatory cell influx into BALF began at 6 h and peaked at 24 h following IT instillation with 50 µg PM, with the increase in neutrophils preceding the increase in macrophages. Pro-inflammatory effects were found to be mainly due to insoluble components of PM. Furthermore, heat-treatment, which was capable of inactivating endotoxin, had no effect on inflammation. Numbers of neutrophils in the BALF were found to correlate with the content of MIP-2, a known neutrophil chemoattractant released from macrophages and epithelial cells. Taken together, these results demonstrate that the pro-inflammatory effect of this $PM_{10-2.5}$ was associated with insoluble components and not with endotoxin.

In an in vivo study that employed ambient PM collected in fall 1996 from RTP, NC, neutrophilic influx was observed in BALF of female CD1 mice 18 h post-IT instillation (10, 50 or 100 µg) of coarse PM (3.5-20 µm), although a dose-response relationship was not evident (Dick et al., 2003, 088776). Mice were also exposed to fine (1.7-3.5 µm) and fine/ultrafine (<1.7 µm) PM fractions. Only the two highest doses of PM for the smaller size fractions induced elevated neutrophils. Significant responses in albumin and TNF-α were only observed for the fine PM (1.7-3.5 µm) exposure group. Total protein, LDH and NAG responses were unchanged from control levels for all PM size fractions. Levels of IL-6 were elevated in mice exposed to 100 µg for coarse, fine, and fine/ultrafine (<1.7 µm) PM. When dimethylthiourea (DMTU) was administered intravenously prior to exposure, the neutrophil response was attenuated in all groups to levels below control.

Another study compared $PM_{10-2.5}$, $PM_{2.5}$, and UFPs collected in Seattle, WA, Salt Lake City, UT, South Bronx, NY, and Sterling Forest, NY (Gilmour et al., 2007, 096433). In female BALB/c mice, the 100 µg dose of $PM_{10-2.5}$ (approximately 5 mg/kg) from Salt Lake City induced a significant increase in protein in BALF, and the level released was almost as high as that observed after LPS exposure. $PM_{10-2.5}$ from the South Bronx resulted in dose-related increases in neutrophil number and MIP-2 levels in BALF. In contrast, no effects were observed with $PM_{10-2.5}$ from Sterling Forest. The greatest amount of LPS was observed in the Salt Lake City and Seattle $PM_{10-2.5}$ samples. There was a less discernable pattern of response with fine and UFPs.

Coal Fly Ash

Coal fly ash of differing size fractions and composition was administered to female CD1 mice via oropharyngeal aspiration (25 or 100 µg) to assess lung inflammation and injury 18 h following exposure (Gilmour et al., 2004, 057420). Montana (low-sulfur subbituminous; 0.83% sulfur, 11.72% ash content) or western Kentucky (high-sulfur bituminous; 3.11% sulfur, 8.07% ash content) coal was combusted using a laboratory-scale down-fired furnace. Interestingly, no significant effects on BALF neutrophils, TNF-α, MIP-2, albumin, total protein, LDH activity, or NAG activity were observed 18 h post-exposure to $PM_{10-2.5}$ from either coal fly ash. However, the UF fraction ($PM_{0.2}$) of combusted Montana coal induced greater numbers of neutrophils than $PM_{10-2.5}$ or $PM_{2.5}$ at both doses. TNF-α was only elevated in animals exposed to 100 µg of the Montana UFPs; MIP-2 was also increased at both doses. The $PM_{2.5}$ western Kentucky coal fly ash caused increased BALF neutrophils, MIP-2, albumin, and protein (Gilmour et al., 2004, 057420).

In a similar study employing Montana subbituminous coal fly ash particles >2.5 µm, C57BL/6J mice were IT instilled with PM alone or PM+LPS and BALF was obtained 18 h post-exposure (Finnerty et al., 2007, 156434). TNF-α and IL-6 in lung homogenates were only elevated in the animals exposed to PM+100 µg LPS, although it appeared that there was a greater-than additive effect. Total cells and cell differentials were not measured.

Summary of Toxicological Study Findings for Relative Toxicity of PM Size Fractions

Biomarkers of injury and inflammation were measured in in vivo and in vitro studies comparing the toxicity of different size fractions of ambient PM from various locations. Responses were measured in BALF from rodents following IT instillation or aspiration of PM. In general, the $PM_{10-2.5}$ size fraction was more potent than $PM_{2.5}$ or UFPs and endotoxin levels did not appear responsible. In one study, rural $PM_{10-2.5}$ from Germany induced a greater inflammatory and cytokine response than $PM_{10-2.5}$ from an industrial location. In contrast, $PM_{10-2.5}$ from Sterling Forest, NY did not lead to any change in BALF inflammation or injury markers. A study that employed coal fly ash

indicated that the UF fraction was the most inflammogenic. All of these studies were conducted using high doses of PM (0.58-10 mg/kg) and it is unclear if similar effects would be observed at lower doses.

6.3.6. Allergic Responses

A large number of toxicological and controlled human exposure studies cited in the 2004 PM AQCD (U.S. EPA, 2004, 056905) reported an exacerbation of existing allergic airway disease following exposure to laboratory-generated and ambient particles. In addition, numerous studies have demonstrated that PM can alter the immune response to challenge with specific antigens and suggest that PM may act as an adjuvant to promote allergic sensitization. Recent toxicological studies have provided evidence of enhanced allergic responses and allergic sensitization following exposure to CAPs and DE that is consistent with the findings presented in the 2004 PM AQCD. PM can enhance allergic responses by facilitating delivery of allergenic material and promoting subsequent immune reactivity. The initiation or exacerbation of allergic responses has important implications for allergic asthma, the most common form of asthma. Additionally, PM has been shown to alter ventilatory measures in non-allergic animal models, suggesting a possible role in other forms of asthma.

6.3.6.1. Epidemiologic Studies

Allergy contributes to a number of respiratory morbidity outcomes, including asthma. However, relatively few epidemiologic studies of PM have specifically examined indicators of allergy. The 2004 PM AQCD (U.S. EPA, 2004, 056905) presented one study (Hajat et al., 2001, 016693) showing an association between doctor visits for allergic rhinitis and PM_{10} among children in London. This association was strongest at a lag of 3 or 4 days. Similar results were obtained in a new study by Tecer et al. (2008, 180030), which found significant associations between $PM_{2.5}$, $PM_{10\text{-}2.5}$, and PM_{10} with hospital admissions for allergic rhinitis in Turkish children, particularly at lag day 4. While exacerbation of allergic symptoms may occur relatively rapidly, repeated or longer exposures may be required for allergic sensitization to develop; a number of studies associating long-term exposure to PM with specific indicators of allergic sensitization are described in Chapter 7.

6.3.6.2. Controlled Human Exposure Studies

Exacerbation of Allergic Responses

Diesel Exhaust and Diesel Exhaust Particles

Exposure to DE particles was shown to increase the allergic response among atopic individuals in several controlled human exposure studies cited in the 2004 PM AQCD (U.S. EPA, 2004, 056905). Nordenhall et al. (2001, 025185) found that exposure to DE significantly decreased the concentration of Mch required to induce a 20% decrease in FEV_1 in a group of atopic asthmatics 24 h post-exposure. In addition, Diaz-Sanchez et al. (1997, 051247) demonstrated an increase in allergen-specific IgE following exposure via intranasal spray to ragweed plus DE particles (0.3 mg) relative to ragweed allergen alone. Decreases in IFN-γ and IL-2, as well as increases in IL-4, IL-5, IL-6, IL-10, and IL-13 were also observed when ragweed allergen was administered with DE particles. It should be noted that the DE particles used in this study were collected during a cold start of a light-duty Isuzu diesel engine, and thus contained relatively high levels of incomplete combustion materials and semi-volatiles organics (e.g., PAHs). One new study using the same source of DE particles (Bastain et al., 2003, 098690) also observed an increase in IL-4 and allergen specific IgE, as well as a decrease in IFN-γ following intranasal administration of ragweed allergen with DE particles (0.3 mg) in atopic adults. The protocol was repeated in this study for all subjects, and the enhancement of allergic response by coexposure to DE particles was observed to be highly reproducible within individuals. In addition, Gilliland et al. (2004, 156471) demonstrated that GST

polymorphisms may alter the adjuvant effects of DE particles on allergic response, with individuals with GSTM1 null or GSTP1 I105 wild type genotypes showing the largest effects.

Allergic Sensitization

Diesel Exhaust Particles

One controlled human exposure study has demonstrated that de novo sensitization to a neoantigen can be induced by exposure to DE particles. In this study, Diaz-Sanchez et al. (1999, 011346) dosed 25 atopic adults intranasally with 1 mg keyhole limpet hemocyanin (KLH), followed by two biweekly challenges with 100 μg KLH. In 15 of the 25 subjects, cold-start DE particles (0.3 mg) were administered intranasally 24 h prior to each KLH exposure, while in the other ten subjects, no DE particles were administered. No KLH-specific IgE was observed in the nasal lavage fluid of any of the subjects exposed to KLH without exposure to DE particles. However, KLH-specific IgE was present in the nasal lavage fluid of 9 out of 15 subjects 28-32 days after the initial KLH immunization when exposures were preceded by administration of DE particles.

CAPs

Increased levels of eotaxin, a marker of allergic activation, were observed in healthy adult volunteers after inhalation of nebulized ambient Chapel Hill $PM_{10-2.5}$ (Alexis et al., 2006, 154323). This particular effect was found to be due to endotoxin, based on its elimination by heat-inactivation; study details are provided in Section 6.3.3.2.

6.3.6.3. Toxicological Studies

Exacerbation of Allergic Responses

Increased use of actual ambient air particle mixes in toxicological studies since the 2004 CD has greatly expanded evidence relevant to assessing these and other immunotoxic effects. A number of studies have also included ambient-level concentrations, although many still include relatively high doses of questionable relevance compared to the doses inhaled by humans. Recent dosimetric models reveal that a small fraction of epithelial cells located at the carinal ridges of airway bifurcations can receive massive doses that may be even a few hundred times higher than the average dose for the whole airway (Chapter 4). These areas, coincidentally, are locations of bronchus associated lymphoid tissues (BALT) which are sites at which interaction of T and B lymphocytes with antigen presenting cells (APC) occurs. Hence the deposited particles are in near-ideal proximity to immunologically active tissues. Doses used for assessing PM immunotoxicity should be viewed with this perspective. In many animal studies, changes in ventilatory patterns are assessed using whole body plethysmography, for which measurements are reported as enhanced pause (Penh). Some investigators report increased Penh as an indicator of AHR, but these are inconsistently correlated and many investigators consider Penh solely an indicator of altered ventilatory timing in the absence of other measurements to confirm AHR. Therefore use of the terms AHR or airway responsiveness has been limited to instances in which the terminology has been similarly applied by the study investigators.

CAPs

Existing allergic sensitization confers susceptibility to the effects of PM in rodent models. For example, studies in allergic rats (Harkema et al., 2004, 056842; Morishita et al., 2004, 087979) suggest that allergic sensitization enhances the retention of PM in the airways. Recovery of anthropogenic trace elements (La, V, Mn, S) from lung tissue was greater for Detroit $PM_{2.5}$ CAPs exposed OVA sensitized/challenged BN rats than for air exposed or non-allergic CAPs exposed controls (24 h post-exposure for 4 or 5 consecutive 10-h days during July or September; time weighted avg mass concentration of 676 ± 288 or 313 ± 119 $\mu g/m^3$, respectively) (Harkema et al.,

2004, 056842). Interestingly, despite lower avg mass concentration, increases in these elements were observed in September, when the avg number concentration of UFPs was nearly double that of July (10,879 ± 5,126 vs. 5,753 ± 2,566 particles/cm^3). September CAPs was associated with eosinophil influx and BALF protein content, as well as significantly increased airway mucosubstances, and the authors speculated that the high concentration of UFPs facilitated particle penetration into the alveolar region of the lungs. IT instillation of fractionated insoluble $PM_{2.5}$ collected from this period resulted in a mild pulmonary neutrophilic inflammation in healthy BN rats, but no differential effects were obtained after IT instillation of total, soluble, or insoluble $PM_{2.5}$ in allergic rats.

Research has also been conducted to determine the effect of proximity to the roadway on exacerbation of existing allergic disease. OVA-allergic BALB/c mice were exposed to $PM_{2.5}$ or UF (≤0.15 μm) CAPs, (avg total concentration 400 μg/m^3) for five 4-h days a week over 2 wk at 50 or 150 m downwind of a heavily trafficked road (Kleinman et al., 2005, 087880). Markers of allergy (serum OVA-specific IgE and IgG1, lung IL-5 and eosinophils) were significantly higher in mice exposed to CAPs ($PM_{2.5}$ or UF) than in air-exposed mice after OVA challenge. IL-5, IgG1, and eosinophils were higher in mice closer to the roadway (50 m) than in mice 150 m downwind. The authors suggest that the enhanced responses closer to the roadway may reflect a greater proportion of UFPs in this vicinity, given that the concentrations of sub-25-nm particles decrease rapidly with distance from the roadway and the $PM_{2.5}$ CAPs closer to the roadway contained a greater number of particles for a similar mass, a portion of which were UF. Animal-to-animal variability among the biomarkers tested made it necessary to combine values from two exposures spanning two years for statistical power (determined prior to the start of the experiment). A subsequent publication (Kleinman et al., 2007, 097082) included a third exposure regimen as well as compositional analysis. $PM_{2.5}$ CAPs mass concentration was intentionally adjusted to an avg concentration of approximately 400 μg/m^3, ranging from 163 to 500 μg/m^3, with an estimated particle number of 2.1×10^5 particles/cm^3 at 50 m and 1.6×10^5 particles/cm^3 at 150 m. UFPs ranged from 146 to 430 μg/m^3, with particle counts of $4.9 \pm 1.4\times10^5$ particles/cm^3 at 50 m, and $4.4 \pm 2.1\times10^5$ particles/cm^3 at 150 m. Analysis of results from the three exposures indicated that OVA-sensitized mice exposed 50 m downwind of the roadway exhibited increased levels of IL-5 and IgG_1 compared to mice exposed 150 m downwind or exposed to air. No markers of allergy-related responses were observed in the 150 m exposure groups, and very little difference was seen between $PM_{2.5}$ and UF CAPs responses, perhaps because $PM_{2.5}$ contained 20-32% UF components. The strongest associations between component concentrations and biological markers of allergy (IL-5 and IgG1) were with EC and OC. These studies demonstrate that CAPs can enhance allergic responses, and that proximity to a source may be an important factor.

In a BN rat model for allergic asthma (Heidenfelder et al., 2009, 190026), thirteen 8-h days of exposure to Grand Rapids, MI $PM_{2.5}$ CAPs alone did not result in differential gene expression or indicators of asthmatic pathology in the lung, but the combination of CAPs and OVA resulted in differential expression of genes predominantly related to inflammation and airway remodeling, along with significant increases in IgE, mucin, and total protein in BALF. Consistent with these changes in gene expression and BALF markers, OVA with CAPs also induced a more severe allergic bronchopneumonia (distribution and severity of bronchiolitis and alveolitis) and increased mucus cell metaplasia/hyperplasia and mucosubstances, indicating exacerbation of allergic or asthmatic disease. CAPs was collected in July and characterized as having an average mass of 493±391, OC 244±144, EC 10±4, SO_4^{2-} 79±131 (13 day avg was only about 10% of the CAPs, but a spike occurred during the first week), nitrate 39±67, ammonium 39±59, and urban dust (estimated from Fe, Al, Ca, and Si) 18±6 (mean ± SD in μg/m^3).

Diesel Exhaust Particles

Resuspended DE particles influences airway responses in mice with existing allergic sensitization. A single 5-h nose-only exposure to 870 μg/m^3 aerosolized filter-collected DE particles ($PM_{2.5}$) increased Mch-induced increases in ventilatory timing (Penh) in OVA sensitized/challenged C57BL/6J mice (Farraj et al., 2006, 088469). Intranasal pretreatment with an antibody against the pan neurotrophin receptor p75 attenuated the DE particle-induced increase in airflow obstruction, indicating a role for neurotrophins. Neurotrophins are expressed by various structural, nerve and immune cells within the respiratory tract and are linked to the etiology of asthma in both humans and animal models. DE particles alone in unsensitized mice caused a significant increase in lung macrophages; this response was also inhibited by anti-p75, which may suggest mediation of macrophage influx by neurotrophin or alternatively may reflect anti-p75 dependent depletion of

macrophages due to expression of the p75 receptor. Aside from increased macrophages, the single exposure to DE particles had little effect on other markers of airway inflammation. In a similar subsequent study, these authors demonstrate neurotrophin-mediated DE particle-induced airflow obstruction in OVA sensitized and challenged BALB/c mice (Farraj et al., 2006, 141730), in this case using a higher 2000 μg/m^3 single 5-h exposure to aerosolized filter-collected $PM_{2.5}$. Differences between whole body plethysmography and tracheal ventilation measurements indicated that airflow obstruction may have originated in the nasal passages. Again, very few indices of inflammation were increased; however, similar neurotrophin-dependent increases in lung macrophages were observed after DE particle exposure alone, and BALF IL-4 protein levels were increased 5-fold in sensitized, challenged, DE particle-exposed mice. This neurotrophin-dependent IL-4 response was not evident in the first study, and may be related to the higher dose used in the second study or the characteristic allergic/Th2 bias of the BALB/c strain. Airflow obstruction in the absence of airway inflammation in OVA-sensitized animals seen in both studies by Farraj et al. (2006, 088469; 2006, 141730) may reflect DE particle-induced acute enhancement of neurogenic as opposed to immunologic inflammation.

Diesel Exhaust

Exposure to relatively low doses of DE has been shown to exacerbate asthmatic responses in OVA sensitized/challenged BALB/c mice (Matsumoto et al., 2006, 098017). Mice were intranasally challenged one day prior to chamber exposure to DE (100 μg/m^3 PM; CO, 3.5 ppm; NO_2, 2.2 ppm; SO_2 <0.01 ppm) for 1 day or 1, 4, or 8 wk (7h/day, 5 days/wk, endpoints 12-h post-DE exposure). Results from the 8 wk study are described in Section 7.3.6.2. It should be noted that control mice were left in a clean room as opposed to undergoing chamber exposure to filtered air. Significant AHR upon Mch challenge was observed after 1 and 4 wk of exposure, and airway sensitivity (provocative concentration of Mch causing a 200% increase in Penh) was significantly increased after 1 wk of exposure but not 4 wk. DE had no effect on total cells in BALF, but transiently increased expression of IL-4, IL-5, and IL-13 after 1 day of exposure, MDC after 1 wk, and RANTES after 2 and 3 wk. Eotaxin, TARC, and MCP-1 were elevated without statistical significance after short-term (1 day or wk) exposure. Statistical power may have been lacking due to few animals in the exposure group (n=3). Protein levels of IL-4 and RANTES were significantly elevated after one day of DE exposure. DE had no effect on OVA challenge-induced peribronchial inflammatory or mucin positive cells. Therefore DE-induced AHR was observed in the absence of neutrophilic inflammation, similar to the responses described for aerosolized or nebulized DE particles by Farraj et al. (2006, 088469; 2006, 141730) and Hao et al. (2003, 096565).

Gasoline Exhaust

Acute exposure to fresh gasoline engine exhaust PM does not appear to exacerbate allergic responses (Day et al., 2008, 190204). BALB/c mice were exposed to whole exhaust diluted 1:10 (H), 1:15 (M), or 1:90 (L), filtered exhaust at the 1:10 (HF), or clean air for 6 h/day over three days. Analytes for the high (H) and high filtered (HF) concentrations were: PM mass (μg/m^3) 59.1±28.3 (H) and 2.3±2.6 (HF); PM number (particles/cm^3) 5.0×10^5 and 1.1×10^4; CO (mg/m^3) 102.8±33.0 and 99.5±1.6; NO (mg/m^3) 18.4±2.8 and 17.2±1.9; NO_2 (mg/m^3) 1.4±0.3 and 1.7±0.2; SO_2 (μg/m^3) 1366.8±56.0 and 1051.1±43.0; NH_3 (μg/m^3) 1957.7±8.1 and 1241.5±6.1; NMHC (mg/m^3) 15.9 and 25.9. Particles represented only 0.04% of the total exposure mass and particle size in the H exposure ranged from 5.5 to 150 nm with the majority between 5-20 nm (MMD 150 nm) (McDonald et al., 2008, 191978). Although particles were filtered out, it should be noted that NMHC (non-methane volatile organics) increased by 62%. Mice were exposed with or without prior sensitization to OVA, after one aerosol challenge and with or without secondary challenge. Acute gasoline engine exhaust exposure had variable effects on inflammatory and allergic markers depending on the exposure protocol, but there were no statistically significant differences between the H and HF exposure results, suggesting that the PM fraction of gasoline engine exhaust does not appear to contribute significantly to observed health effects.

Hardwood Smoke

One study indicated that hardwood smoke exposure only minimally exacerbated indices of allergic airway inflammation in an OVA-sensitized BALB/c mouse model and did not alter Th1/Th2

cytokine levels (Barrett et al., 2006, 155677). Trend analysis indicated increasing BALF eosinophils with increasing dose of hardwood smoke, becoming significantly elevated at 300 μg/m^3 (CO, 1.6±0.3 ppm; total vapor hydrocarbon, 0.6±0.2 ppm; NO_X, below limit of quantitation, PM MMAD 0.35±2.0 μm), and increasing, but not significantly, OVA-specific IgE levels with hardwood smoke up to 1,000 μg/m^3.

Model Particles

Exposures to an aerosol of soot and iron oxide generated from ethylene (0.235 mg/m^3 $PM_{2.5}$) were conducted to test whether the sequence of exposure to OVA aerosol challenge and PM affected the observed response of OVA sensitized BALB/c mice (Last et al., 2004, 097334). Though called $PM_{2.5}$, the authors characterized the PM material as UF, 80-110 nm, with the iron oxide crystals often spatially segregated from the soot (200 μg/m^3 soot, remainder iron oxide, CO <0.8 ppm, NO_X <0.4 ppm, PAH below detection). Mice were exposed to PM via chamber inhalation for 2 wk (4h/day, 3 days/wk) before or after 4 wk of OVA inhalation, or simultaneously to PM and OVA for 6 wk. Among endpoints (BALF cells, Penh, airway collagen, and goblet cells) only goblet cell counts were significantly increased with PM exposure in any combination with OVA. There was a trend toward increased Penh responses with exposure to PM alone or with OVA, particularly when PM exposure immediately preceded Mch challenge (after or during OVA challenge). Results from this study are difficult to interpret due to the varied elapsed times between cessation of PM or OVA treatment and endpoint determination. The mild responses to PM may be related to the intraperitoneal sensitization protocol used, reputed to generate a highly allergic mouse in which any additive effects of PM may be obscured by maximal responses to antigen challenge (Deurloo et al., 2001, 156396; Hao et al., 2003, 096565).

Residual Oil Fly Ash

Arantes-Costa and colleagues (2008, 187137) estimated that 60 μg of ROFA would be inhaled by a mouse during one day of exposure to Sao Paulo air. This dose, given intranasally every other day for 4 days, increased AHR in both nonsensitized and OVA sensitized/challenged BALB/c mice upon Mch challenge 2 days after the last exposure. ROFA had no significant impact on eosinophil or macrophage numbers in the lung, nor did it increase the chronic lung inflammation or thickening induced by OVA. In many studies, particular effects such as airway obstruction are only evident when allergic sensitization precedes exposure, but this study and a few others demonstrate allergen-independent AHR after exposure to PM including CAPs (Lei et al., 2004, 087999) and DE or DE particles (Hao et al., 2003, 096565; Li et al., 2007, 155929).

Allergy in Pregnancy or Early Life

Pregnancy or in utero exposure may confer susceptibility to PM-induced asthmatic responses. Exposure of pregnant BALB/c mice to aerosolized ROFA leachate by inhalation or to DE particles intranasally increased asthma susceptibility in their offspring (Fedulov et al., 2008, 097482; Hamada et al., 2007, 091235). The offspring from dams exposed for 30 min to 50 mg/mL ROFA 1, 3, or 5 days prior to delivery responded to OVA immunization and aerosol challenge with AHR and increased antigen-specific IgE and IgG1 antibodies. AHR was also observed in the offspring of dams intranasally instilled with 50 μg of DE particles or TiO_2, or 250 μg CB, indicating that the same effect could be demonstrated using relatively "inert" particles. Pregnant mice were particularly sensitive to exposure to DE particles or TiO_2 particles, and genetic analysis indicated differential expression of 80 genes in response to TiO_2 on the pregnant background. Thus pregnancy may enhance responses to PM, and exposure to even relatively inert particles may result in offspring predisposed to asthma.

Allergic Sensitization

A large number of in vivo animal studies and in vitro studies have demonstrated that particles can alter the immune response to challenge with specific antigens and suggest that PM acts as an adjuvant to promote allergic sensitization. This phenomenon was introduced in the 2002 Diesel

Document, and has been noted in multiple animal and human studies by the 2004 PM AQCD (U.S. EPA, 2004, 056905). Adjuvants enhance the immune response to antigens through various means, including chemoattraction, cytokines, or enhanced antigen presentation and costimulation, and may act on a number of cell types. Importantly, adjuvants may be major contributors to the development of inappropriate immune responses. These immune responses, mediated by T helper cells, fall along a continuum from T helper type 1 (Th1) to T helper type 2 (Th2). Th1 responses, characterized by IFN-γ, are inflammatory and in excess can lead to tissue damage. Alternatively, Th2 responses are characterized by IL-4, IL-5, IL-13, eosinophils, and IgE, and are associated with allergy and asthma. Autoimmune diseases may be driven by Th1, Th2, or mixed responses, but allergic diseases are predominantly Th2 mediated, and many of the immunologic effects observed for PM fall into the Th2 category.

It has been suggested that the capacity of particles to enhance allergic sensitization is associated more strongly with particle number and surface area than particle mass, and several studies comparing size fractions of the same material show greater adjuvant activity for an equivalent mass dose of smaller particles (de Haar et al., 2006, 144746; Inoue et al., 2005, 088625; Nygaard et al., 2004, 058558). This is particularly true of inert or homogeneous materials, such as carbon, polystyrene, and TiO_2, which vary little in composition with size fraction. Studies using CAPs have also observed that adjuvancy and allergic exacerbation are more strongly associated with the UF fraction, possibly due to greater oxidative potential (Kleinman et al., 2005, 087880; Kleinman et al., 2007, 097082; Li et al., 2009, 190457). In some studies of ambient PM, however, $PM_{10-2.5}$ or PM_{10} have demonstrated equal or greater adjuvancy compared to $PM_{2.5}$ (Nygaard et al., 2004, 058558; Steerenberg et al., 2004, 096024; Steerenberg et al., 2005, 088649). More inhalation studies to compare size fractions are needed in order to elucidate the role of particle size in mediating adjuvancy, but this may prove difficult given the influence of composition, e.g., combustion related materials (Steerenberg et al., 2006, 088249) and metal content (Gavett et al., 2003, 053153), which differs among various size fractions and sources.

CAPs

As little as 0.1 µg of UF Los Angeles CAPs administered intranasally with OVA was able to significantly boost allergic antibody responses in BALB/c mice (Li et al., 2009, 190457). A comparison of UFPs (aerodynamic diameter <0.15 µm) with a mix of sub-2.5 µm particles ($PM_{2.5}$/UFP) collected 200 m from a major freeway delivered intranasally five times over the course of nine days showed that UFP but not $PM_{2.5}$/UFP were associated with significant adjuvant effects. 0.5 µg of UFP with OVA (but not alone) led to an increase in BALF eosinophils, allergic cytokines, inflammatory mediators, and serum OVA-specific IgE/IgG1, as well as allergic tissue inflammation in the upper and lower airways. Adjuvant effects of UFP were observed with two independently collected samples (1/2007 and 9/2006) and could not be replicated by administering the same amount of endotoxin measured in the particles, indicating that the effects were not unique to the sampling period nor mediated by contaminating endotoxin. UFP had a greater OC and PAH content than $PM_{2.5}$/UFP, and induced greater oxidative stress in vitro. Partial blocking of the adjuvant effects by antioxidant administration implicates redox potential as a key factor in mediating these effects. The authors suggest that the lack of adjuvancy for UF carbon particles (being mostly EC) is due to a lack of redox cycling compounds, but this was not tested. In contrast, UF (30-50 nm) CB particles have demonstrated intranasal adjuvant activity in other studies (de Haar et al., 2005, 097872) when administered with OVA over three consecutive days. A 200-µg dose increased serum OVA-specific IgE, local lymph node dendritic cells and OVA-specific Th2 lymphocytes in the lung draining lymph nodes and lung, as well as post-challenge airway eosinophilia. Doses as low as 20 µg were able to activate adoptively transferred OVA-specific T cells.

Diesel Exhaust Particles

Resuspended DE particles have been shown to enhance OVA-specific IgG1 and IgE in BALB/c mice exposed via inhalation to doses as low as 200 and 600 $\mu g/m^3$, respectively (Whitekus et al., 2002, 157142). Mice were exposed to DE particles (200, 600 and 2,000 $\mu g/m^3$) for 1 h daily for 10 days prior to aerosol OVA challenge. Compared with responses to OVA alone, antibody levels were increased by all OVA+DE particle exposures. Statistical significance was reached for IgG1 at all DE particle exposure levels, whereas OVA specific IgE was significantly increased at the 600 and 2,000 $\mu g/m^3$ doses and total IgE was significantly elevated at 2,000 $\mu g/m^3$. Although strong adjuvant

effects were observed, no general markers of inflammation such as eosinophils, IL-5, GM-CSF, mucin, morphological changes, or eosinophilic major basic protein (MBP) deposition in the airways were observed in exposed mice. In vitro experiments using the RAW 264.7 macrophage-like cell line indicated a DE particle-induced lipid peroxidation and protein oxidation, which could be inhibited by a variety of antioxidants. Also observed was a decrease in the GSH:GSSG ratio and an increase in HO-1 expression, both of which were inhibited only by the thiol antioxidants NAC and BUC. These same thiol antioxidants were able to completely block DE particle-related increases in IgE and IgG1, as well as lipid peroxides and oxidized proteins recovered from BALF at the 2,000 $\mu g/m^3$ dose. Thus solid correlations between in vivo and in vitro antioxidant activities were found, and the reversal of adjuvant effects by antioxidants in vivo clearly indicates a link between oxidative stress and DE particle adjuvancy. However, the intranasal adjuvant activity of Ottawa, Canada, dust (EHC-93) in the same strain of mice was not inhibited by NAC pretreatment (Steerenberg et al., 2004, 087981), suggesting that disparate pathways may be utilized by different materials to exert immune stimulation.

Diesel Exhaust

DE inhalation during allergen exposure has been shown to augment IgE production and alter methylation of T helper genes in BALB/c mice (Liu et al., 2008, 156709) Animals were exposed to DE (1280 $\mu g/m^3$ PM) over a 3-wk period, 5 h per day, concurrent with periodic intranasal sensitization to the common fungus *Aspergillus fumigatus*. Gas concentrations were not reported. Total IgE and BALF eosinophils were elevated with *A. fumigatus* sensitization and further increased by concomitant DE exposure. Greater methylation of the IFN-γ promoter was observed following DE and *A. fumigatus* exposure (but not DE alone) compared to *A. fumigatus* alone, indicating that combined DE and allergen exposure might induce methylation and thus suppress expression of Th1 genes. Furthermore, hypomethylation of the IL-4 promoter was detected after exposure to *A. fumigatus* and DE compared with exposure to *A. fumigatus* or DE alone, suggesting pro-allergic Th2 gene activation upon combined exposure to allergen and DE. The changes in methylation status of these genes were associated with alterations in IgE levels in individual animals, indicating that modifications at the genetic level could result in predicted downstream effects. This study shows for the first time that DE exposure can exert pro-allergic in vivo effects on the mouse immune system at the epigenetic level.

A toxicogenomic approach to investigate early response mechanisms of DE adjuvancy was taken by Stevens et al. (2008, 157010). BALB/c mice were chamber exposed to filtered air, 500 or 2,000 $\mu g/m^3$ PM in DE for 4 h/day over 5 consecutive days and intranasally exposed to OVA on each of the first 3 days. In the low (500 $\mu g/m^3$) vs. high (2,000 $\mu g/m^3$) DE exposures, CO, NO, NO_2, and SO_2 were <0.1 versus 4.3, <2.5 vs. 9.2, <0.25 vs. 1.1 and <0.06 vs. 0.2 ppm; particle number median diameters were 80 and 86 nm, and volume median diameters were 184 and 195 nm, respectively. Lung tissues were assessed for alterations in global gene expression (n = 4) 4 h after the last DE exposure on day 4. Mice were intranasally challenged with OVA or saline on day 18 and then with OVA on day 28. Post-challenge results demonstrated mild adjuvancy with antigen and DE exposure as evidenced by significant increases in eosinophils, neutrophils, lymphocytes, and IL-6 in the BALF. Antibody responses were not significantly affected by DE exposure, although a slight increase in IgE after high concentration exposure was observed. DE alone only increased neutrophils, indicating the need for combined exposure to DE and antigen in the development of allergic outcomes. Comparison of low DE /OVA vs. air/OVA resulted in no significant changes in gene sets associated with this treatment. Comparison of the high DE/OVA versus air/OVA, however, showed significant changes in 23 gene sets, including neutrophil homing and other chemokines, inflammatory cytokines, numerous interleukins and TNF subtypes, and growth/differentiation pathways.

Summary of Toxicological Study Findings for Allergic Responses

Studies conducted since the last review confirm and extend the 2004 PM AQCD's (U.S. EPA, 2004, 056905) finding that PM can modulate immune reactivity in both humans and animals to promote allergic sensitization and exacerbate allergic responses. Numerous forms of PM, including inert materials, have been shown to function as adjuvants, and although toxicological studies of relatively homogeneous materials demonstrate greater adjuvancy for smaller particles, some analyses

of ambient PM do not. Recent toxicological studies comparing size fractions of well-characterized ambient PM for adjuvant activity in a direct, controlled fashion via inhalation exposure suggest a role for oxidative potential, but thus far the relative contributions of size and composition are not entirely clear. Although epidemiologic studies examining specific allergic outcomes and short-term exposure PM are relatively rare, the available studies, conducted primarily in Europe, positively associate various PM size fractions with allergic rhinitis. Similar findings from a number of long term studies are described in Chapter 7.

6.3.7. Host Defense

The normal and very important role of respiratory immune defense is the detection and/or destruction of pathogens that enter the lung via inhalation and removal of damaged, transformed (cancerous), or infected cells. Innate immune defenses of the respiratory tract include mucociliary clearance, release of toxic antimicrobial proteins into airway surface liquid, and activation of alveolar macrophages. The innate immune system is the earliest responder to irritation or infection, initiating the normal inflammatory response including the majority of detrimental inflammatory processes discussed. Activated macrophages and epithelial cells release cytokines and chemokines that can bring into play the adaptive immune system, which in turn can produce long-lasting pathogen-specific immune responses critical for resolving and preventing infections.

6.3.7.1. Epidemiologic Studies

Collectively, results from multicity studies of hospital admissions and ED visits for respiratory infection as well as single-city studies conducted in the U.S. and Canada (summarized in Figure 6-14) show a positive association between PM and respiratory infections. Lag structure was not investigated in most studies and effects have been observed in association with current day concentration (Zanobetti and Schwartz, 2006, 090195) as well as with concentrations modeled using a 14-day distributed lag function (Peel et al., 2005, 056305). Of studies examining multiple lag times, associations with increasing lag times were observed (Dominici et al., 2006, 088398; Peel et al., 2005, 056305; Peng et al., 2008, 156850). Although no significant positive associations were reported, Slaughter et al. (2005, 073854) observed a trend of increasing association with increasing lag for acute respiratory infection ED visits with PM_1, $PM_{2.5}$, PM_{10} and $PM_{10-2.5}$. This delay in the onset of disease may reflect the time necessary for an infection to become established and symptomatic. The majority of toxicological evidence, described below and in the 2004 PM AQCD (U.S. EPA, 2004, 056905), suggests that PM impairs innate immunity, the first line of defense in preventing infection.

6.3.7.2. Toxicological Studies

Several toxicological studies were cited in the 2004 PM AQCD (U.S. EPA, 2004, 056905) that demonstrated increased susceptibility to infectious agents following exposure to PM. A limited number of new studies have evaluated the effect of PM on host defense in rodents. Two recent studies have observed an increase in susceptibility to influenza infection and respiratory syncytial virus in mice. However, one new study found that wood smoke had no effect on bacterial clearance in rodents.

Bacterial Infection

Several studies included in the 2004 PM AQCD (U.S. EPA, 2004, 056905) demonstrated increased susceptibility to infectious agents following exposure to various forms of PM. CAPs exposed aged rats demonstrated increased *S. pneumoniae* burdens when a 24-h exposure (65 $\mu g/m^3$) followed infection (Zelikoff et al., 2003, 039009). In another study, IT instillation exposure to ROFA was found to affect bacterial clearance (Antonini et al., 2002, 035342). Examinations of mechanisms related to PM interference with host defenses have demonstrated impaired mucociliary clearance and modified macrophage phagocytosis and chemotaxis. Prolonged exposure to inhaled particles at sufficiently high concentrations can lead to diminished clearance of PM from the alveolar region of

the lung, resulting in the accumulation of retained particles and an accompanying chronic alveolar inflammation. Diminished clearance of PM may also increase susceptibility to pulmonary infection by impeding clearance of pathogens. Impaired phagocytosis by alveolar macrophages may contribute to a decrease in the lung's capacity to deal with increased particle loads (as occurs during high-pollution episodes) or infections and affect the local and systemic responses through the release of biologically active compounds (cytokines, ROS, NO, isoprostanes).

Diesel Exhaust

Since the last review, several additional studies have reported impairment of pathogen clearance following exposure to various sources of PM. All levels of DE (30, 100, 300 or 1,000 $\mu g/m^3$) decreased lung bacterial clearance in C57BL/6 mice exposed for 1 wk (7 days/wk, 6 h/day) prior to infection with *Pseudomonas aeruginosa* (Harrod et al., 2005, 088144). This effect appeared concentration dependent up to 100 $\mu g/m^3$ and was not enhanced at higher concentrations. Lung inflammation was not induced by DE in the absence of infection, but infection-induced inflammation was exacerbated by DE at all concentrations without apparent concentration dependency. Measures of histopathology in infected animals were increased by DE exposure in a concentration-dependent manner, peaking at 100 $\mu g/m^3$ and leveling off or decreasing with higher concentrations. Particle deposition was readily apparent in the lungs after exposure to the lowest concentration of 30 $\mu g/m^3$. A loss of ciliated cells was observed at 30 $\mu g/m^3$ and 100 $\mu g/m^3$ in large airways and in small airways at the higher concentration. Alterations in Clara cell morphology and function were observed at both concentrations as well. Concentrations of gases were reported to be 2.0-45.3 ppm NO, 0.2-4.0 ppm NO_2, 1.5-29.8 ppm CO and 8-365 ppb for SO_2 (McDonald et al., 2004, 055644). PM mass median diameter was ~100-150 nm at all exposure levels (>90% below 1 µm in aerodynamic diameter), with lower exposure concentrations having a slightly smaller size distribution (Reed et al., 2004, 055625).

Gasoline Exhaust

In a study by Reed et al. (2008, 156903), short or long-term exposure to fresh gasoline exhaust (6h/day, 7day/wk for 1 wk or 6 mo) did not affect clearance of *P. aeruginosa* from the lungs of C57BL/6 mice. Atmospheric characterizations are described above for the Day et al. (2008, 190204) and McDonald et al. (2008, 191978) studies in Section 6.3.6.3.

Hardwood Smoke

Similar to gasoline exhaust, hardwood smoke does not appear to have significant impact on pathogen clearance. C57BL/6 mice were exposed to 30-1,000 $\mu g/m^3$ hardwood smoke by whole-body inhalation for 1 wk and 6 months (Reed et al., 2006, 156043). Long-term responses are discussed in Sections 7.3.3.2 and 7.3.7.2. Concentrations of gases ranged from 229.0-14,887.6 mg/m^3 for CO, 54.9-139.3 $\mu g/m^3$ for ammonia, and 177.6-3,455.0 $\mu g/m^3$ for nonmethane volatile organic carbon in these exposures. Bacterial clearance of instilled *P. aeruginosa* was unaffected by hardwood smoke.

Intratracheal Instillation

Studies demonstrate that ROFA impairs host defenses and that soluble metals are important contributors. Antonini et al. (2004, 097199) compared sources of ROFA in SD rats. Precipitator ROFA induced an inflammatory response and diminished pulmonary clearance of *L. monocytogenes* while air heater ROFA had no effect on lung bacterial clearance at the same IT dose of 1 mg/100g body weight. Precipitator ROFA generated a metal-dependent hydroxyl radical suggesting that differences in metal composition were a determinant of the immunotoxicity of ROFA. Subsequent studies using soluble extracts of ROFA with or without a chelating agent confirmed that soluble metals were responsible for weakening defenses against bacterial infection and impairing both innate and adaptive lung immune responses (Roberts et al., 2004, 196994; Roberts et al., 2007, 097623) ROFA has also been shown to result in ciliated cell loss in BALB/c mice after intranasal administration of 60 µg every other day for 4 days (Arantes-Costa et al., 2008, 187137).

Viral Infection

Diesel Exhaust

Viral respiratory infections in early life are associated with increased incidence of childhood asthma and other pulmonary diseases. DE exposure can enhance the progression of influenza infection. BALB/c mice that were chamber exposed to DE 4 h/day for 5 days and subsequently IT instilled with influenza A/Bangkok/1/79 virus had increased susceptibility to influenza infection (Ciencewicki et al., 2007, 096557). Exposures to two concentrations of DE were conducted: 500 μg/m^3 (0.9 ppm CO, <0.25 ppm NO_2, <2.5 ppm NO, and 0.06 ppm SO_2) and 2,000 μg/m^3 (5.4 ppm CO, 1.13 ppm NO_2, 10.8 ppm NO, and 0.32 ppm SO_2). Responses were greater for animals exposed to 500 μg/m^3 DE than to 2,000 μg/m^3, and were associated with a significant increase in IL-6 protein and mRNA expression and IFN-β expression. The authors present the possibility that damage to the epithelium at the higher exposure prevented viral infection and replication. After exposure to 500 μg/m^3 DE alone or prior to infection, decreased expression of surfactant proteins (SP) A and D was observed. These proteins are part of the IFN-independent defense against influenza.

Similarly, Harrod et al. (2003, 097046) demonstrated decreased SP-A expression in the lungs following DE exposure and linked it to increased susceptibility to respiratory syncytial virus (RSV), the most common cause of respiratory infection in young children. C57BL/6 mice, a relatively RSV-resistant strain, were exposed via inhalation to DE at a concentration of 30 or 1,000 μg/m^3 PM 6h/day for 7 consecutive days prior to intratracheal viral inoculation. Gaseous copollutants ranged from 2.0-43.3 ppm for NO_X (~ 90% NO), 0.94-29.0 ppm CO, and 8.3-364.9 ppb SO_2. Exposure to 30 μg/m^3 DE did not induce a statistically significant increase in BALF cell numbers compared to air-treated, infected animals. However, distinct consolidated inflammatory infiltrates were observed in the peribronchial regions of RSV-infected animals exposed to this concentration, along with alterations in Clara cell morphology, decreased CCSP production by these cells, and occasional regional myofibril layer thickening. These changes were more pronounced in RSV-infected animals exposed to 1000 μg/m^3, and the higher concentration also resulted in significant increases in inflammatory cells, predominantly macrophages, in both uninfected and infected mice compared to air-exposed controls. Both doses elicited significant levels of TNF-α and IFN-γ in the lungs of infected animals, but decreased levels of SP-A. Consistent with this study's finding of decreased SP-A and increased viral gene and inflammatory cytokine expression after DE exposure, SP-A$^{-/-}$ mice demonstrate decreased clearance of RSV concordant with increased lung inflammation (Levine et al., 1999, 156687). Thus, DE may enhance susceptibility to respiratory viral infections by reducing the expression and production of SP (Ciencewicki et al., 2007, 096557; Harrod et al., 2003, 097046), although the contribution of gaseous copollutants, in some instances concentrated 1,000 times, should be considered for both studies. SP are also essential for clearance of other pathogens, including group *B Streptococcus* (GBS), *Haemophilus influenzae*, and *P. aeruginosa* (LeVine and Whitsett, 2001, 155928).

A reduction in host defense molecules and an increase in viral entry sites was observed by Gowdy et al. (2008, 097226) after BALB/c mice were exposed to HEPA filtered room air or DE at 0.5 or 2.0 mg/m^3 for 4hr/day for one or five consecutive days [O_2 (%) 21.0±0.10 or 20.7±0.09, CO (ppm) 1.7±0.15 or 5.4±0.07, NO_X (ppm) 2.0±0.36 or 7.4±0.61, SO_2 (ppm) 0.0±0.0 or 0.4±0.3, number median (nm) 96.2±2 or 97±2, volume median (nm) 238±2 or 249±2, OC/EC (wt ratio) 0.4±0.04 or 0.4±0.07 for the 0.5 or 2.0 mg/m^3 exposures, respectively]. One of the more notable features of this study was the observation that effects of extended exposure to the lower concentration (0.5 mg/m^3 for 5 days) tended to persist beyond 18 h post-exposure. Exposure to DE significantly increased BALF neutrophils in the higher exposure group, and this response persisted beyond 18 h only after the five day exposure. An increase in ICAM-1 expression (a viral entry site) was observed in both exposure groups, and was persistent in the lower concentration group after a 5-day exposure. Persistently elevated expression of pro-inflammatory cytokines IL-6 and TNF-α and pro-allergic cytokine IL-13 was observed after five days of low concentration exposure. Non-statistically significant effects of either concentration or exposure regimen included increased IFN-γ and MIP-2. Host defense molecules CCSP, SP-A and SP-D were decreased after either exposure regimen, persisting beyond 18 h in the low concentration group.

Taken together, these data suggest that exposure to DE can weaken host defenses, in some cases persistently. A role for PM in these responses is supported by studies demonstrating changes in host defense molecules and viral entry sites in vitro consistent with those observed in vivo. In lung epithelial cells, DE particles increased the mRNA expression of ICAM-1, LDL and platelet-activating factor (PAF) receptors, which can act as receptors for viruses or bacteria (Ito et al., 2006, 096648). DE particles may therefore enhance the susceptibility to infection by the upregulation of bacterial and viral invasion sites in the lungs. Expression of the β-defensin-2 gene, which is one antimicrobial mechanism of host defense in the airway, was significantly inhibited by V and not Ni or Fe in airway epithelial cells incubated with aqueous leachate of ROFA (Klein-Patel et al., 2006, 097092).

Immunosuppressive Effects of PM

Diesel Exhaust

DE may affect systemic immunity. Decreased thymus weight was observed in female F344 rats exposed to 300 μg/m^3 DE for 1 wk by Reed et al. (2004, 055625). Concentrations of gases for this PM concentration were reported to be approximately 16.1 ppm for NO, 0.8 ppm for NO_2, 9.8 ppm for CO, and 115 ppb for SO_2. Long-term responses are discussed in Section 7.3.8.

Summary of Toxicological Study Findings for Host Defense

Toxicological studies demonstrate that short-term inhalation exposures to CAPs and DE, but not gasoline exhaust or wood smoke, can increase susceptibility to infection by bacterial and viral pathogens. While gaseous copollutants may be contributing factors, a role for particles is demonstrated by studies utilizing IT instillation exposure and in vitro studies of PM where biomarkers parallel those observed in vivo. Although ethical considerations limit controlled exposure studies in humans, epidemiologic evidence reflects an association between most PM size fractions and hospital admissions for respiratory infections. Importantly, toxicological studies demonstrate impaired host defense against the etiological agents of influenza, pneumonia (*S. pneumoniae*), and bronchiolitis (RSV), which are commonly reported respiratory morbidities associated with PM.

6.3.8. Respiratory ED Visits, Hospital Admissions and Physician Visits

The epidemiologic evidence presented in the 2004 PM AQCD (U.S. EPA, 2004, 056905) linking short-term increases in PM concentration with respiratory hospitalizations and ED visits was consistent across studies. Recent investigations provide further support for this relationship, with larger effect estimates observed among children and older adults. However, effect estimates are clearly heterogeneous, with evidence of both regional and seasonal differences at play.

Excess risk estimates for hospitalizations or ED visits for all respiratory diseases combined, reported in studies reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905) fell within the range of approximately 1-4% per 10 μg/m^3 increase in PM_{10}. On average, excess risks for asthma were higher than excess risks for COPD and pneumonia. Associations with $PM_{2.5}$ (including PM_1) and $PM_{10-2.5}$ were also reported in the limited body of evidence reviewed in the 2004 AQCD. Excess risk estimates fell within the range of approximately 2.0-6.0% per 10 μg/m^3 increases in $PM_{2.5}$ or $PM_{10-2.5}$ for all respiratory diseases combined as well as COPD admissions. Larger estimates were reported for asthma admissions. Many of the associations of respiratory admissions and ED visits with short-term $PM_{2.5}$ concentration were statistically significant. The associations with $PM_{10-2.5}$ were less precise with fewer reaching statistical significance (U.S. EPA, 2004, 056905). Finally, several studies reviewed in the 2004 AQCD reported associations of PM with outpatient physician visits, suggesting that the population impacted by short-term increases in PM is not restricted to those admitted to the hospital or seeking medical attention through an ED.

Table 6-13. Description of ICD-9 and ICD-10 codes for diseases of the respiratory system.

Description	ICD 9 Codes	ICD 10 Codes
Diseases of the Respiratory System	460-519	J00-J99
Asthma	493	J45
COPD and allied conditions	490-496 (asthma, chronic bronchitis, emphysema, bronchiectasis, extrinsic allergic alveolitis)	
Chronic lower respiratory diseases		J40-J47 (bronchitis, emphysema, other COPD, asthma, status asthmaticus, bronchiectasis)
Acute Respiratory Infections	460-466 (common cold, sinusitis, pharyngitis, tonsillitis, laryngitis & tracheitis, bronchitis & bronchiolitis)	
Acute Upper Respiratory Infections		J00-J06 (common cold, sinusitis, pharyngitis, tonsillitis, laryngitis & tracheitis, croup & epiglottitis)
Acute bronchitis and bronchiolitis	466	J20-J22
Allergic Rhinitis	477	J30.1
Pneumonia	480-486	J13-J18
Wheezing	786.09	

Hospital admissions or ED visits for respiratory diseases and ambient concentrations of PM have been the subject of more than 90 peer-reviewed research publications since 2002 (Annex E). Included among these new publications are several large single-city and multicity studies. These new studies complement those reviewed in the 2004 AQCD by examining the effect of several PM size fractions and components on increasingly specific disease endpoints, as well as evaluating the presence of effect modification by factors such as season and region.

Specific design and methodological considerations of the large and multicity studies included in this review were discussed previously (Section 6.2.10). Like the CVD endpoints discussed, the respiratory endpoints examined in these studies were heterogeneous and approaches to selecting cases for inclusion in the studies were varied. ICD codes commonly used in hospital admission and ED visits studies for diseases of the respiratory system are found in Table 6-13.

6.3.8.1. All Respiratory Diseases

Findings from new studies of PM and respiratory hospitalization and ED visits among children are summarized in Figure 6-10. Results from new studies of adults are summarized in Figure 6-11. Information on the PM concentrations during the relevant study periods is found in Table 6-14.

Children

Barnett et al. (2005, 087394) used a case-crossover design to study respiratory hospital admissions (ICD-9 460-519) of children (age groups 0, 1-4, and 5-14 yr) in seven cities in Australia and New Zealand from 1998 to 2001. All respiratory diseases (ICD10 J00-J99) except Mendelson's Syndrome, post-procedural disorders, asphyxia and certain other symptoms (ICD10 codes J95.4-J95.9, R09.1, R09.8) were included in the study. In addition, scheduled admissions and transfers from other hospitals were excluded. Using an a priori lag (0- to 1-day avg), increases in respiratory hospital admissions of 2.0% (95% CI: -0.13 to 4.3) among infants <1 yr old, 2.3% (95% CI: 1.9-7.3) among children 1-4 yr old and 2.5% (95% CI: 0.1-5.1) among children 5-14 yr old per 10 $\mu g/m^3$ increase in 24-h avg PM_{10} were observed. Increases of 6.4% (95% CI: 2.7-10.3) among infants <1 yr and 4.5% (95% CI: 1.9-7.3) among children 1-4 yr per 10 $\mu g/m^3$ increase in $PM_{2.5}$ were observed.

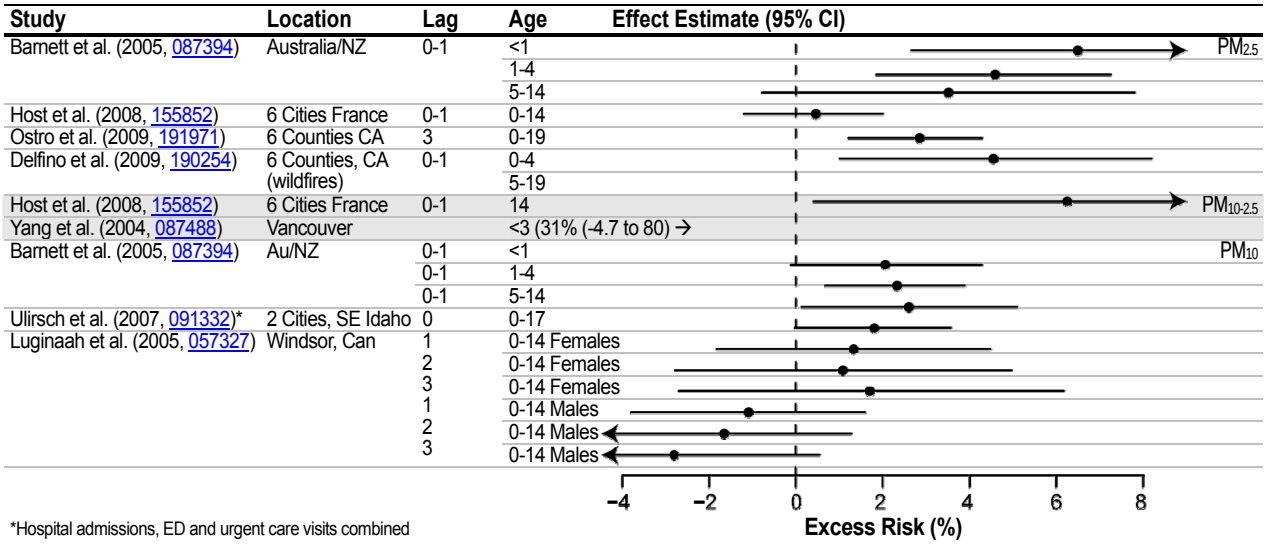
Ostro et al. (2009, 191971) studied the effect of $PM_{2.5}$ and components on respiratory disease (ICD9 460-519) hospitalizations among children <19 yr from 2000 to 2003 in six counties in California. The nine components examined (EC, OC, nitrates, sulfates, Cu, Fe, K, Si and Zn), were chosen because they made up relatively large proportion of $PM_{2.5}$, had a signal to noise ratio >2, or

the majority of their values were greater than the level of detection. Single day lags of 0-3 days were evaluated. The largest risks were observed at lag 3 days for $PM_{2.5}$ (2.8% [95%CI: 1.2-4.3] per 10 $\mu g/m^3$), EC (5.4% [95% CI: 0.8-10.3] per IQR) and Fe (4.7% [95% CI: 2.2-7.2] per IQR increase). Although not as great, positive associations were also observed for OC, SO_4^{2-}, nitrate, Cu and Zn.

In a study of $PM_{2.5}$ from wildfires in California during 2003, Delfino et al. (2009, 191994) evaluated conducted stratified analyses comparing $PM_{2.5}$ associations pre-, post- and during the wildfires. Four age groups (0-4, 5-19, 20-64 and ≥65 yr) were considered in these analyses. Authors found increased respiratory disease admissions in the periods before (2.6% [95%CI: -5.4 to 11.3]) and during (2.7% [95%CI: -1.6 to 7.6]) the wildfires among children 5-19 yr old, but not after the wildfire period. Among younger children (0-4 yr), hospital admissions were increased during fire periods (4.5% [95% CI: 1-8.2]), but not before or after the wildfire period. Estimated zip code level $PM_{2.5}$ concentrations were 90 $\mu g/m^3$ and 75 $\mu g/m^3$ during heavy and light smoke conditions, respectively, compared to 20 $\mu g/m^3$ during non-fire periods.

In the study of six cities in France described previously (PSAS), investigators report a change of 0.4% (95%CI: -1.2 to 2) per 10 $\mu g/m^3$ increases in $PM_{2.5}$ for all respiratory diseases combined (ICD-10: J00-J99) among children from 0-14 yr old (Host et al., 2008, 155852). The same study reported a larger increase associated with $PM_{10-2.5}$ of 6.2% (95% CI: 0.4-12.3, 0-1 day avg) per 10 $\mu g/m^3$ increase among children. A relatively large effect for $PM_{10-2.5}$ (31% [95% CI: -4.7 to 80]) was also observed in a single-city study of children <3 yr in Vancouver (Yang et al., 2004, 087488). The non-significant $PM_{2.5}$ effect estimates were not presented in the publication. Luginaah et al. (2005, 057327) did not observe significant increases in respiratory hospitalizations with increasing PM_{10} concentrations among male or female children in Ontario Canada, while Ulirsch et al. (2007, 091332) reported increased admissions for respiratory hospitalizations, ED and urgent care visits combined among children <17 yr in association with PM_{10}.

As shown in Figure 6-10, studies of respiratory hospitalizations or ED visits reported increased risks to children in association with all size fractions. However, increased risk among boys was not observed in Ontario (Luginaah et al., 2005, 057327). Estimates are imprecise and it is not clear if associations with $PM_{2.5}$, $PM_{10-2.5}$, or both are driving associations observed with PM_{10}.



*Hospital admissions, ED and urgent care visits combined

Figure 6-10. Excess risk estimates per 10 $\mu g/m^3$ 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10} concentration for ED visits and HAs for respiratory diseases in children. Studies represented in the figure include all multicity studies as well as single-city studies conducted in the U.S. or Canada.

Adults and All Ages Combined

In the study of four million ED visits from 31 hospitals in Atlanta described previously, SOPHIA investigators reported an excess risk of 1.3% (95% CI: 0.4-2.1, lag 0-2) per 10 $\mu g/m^3$ increase in 24-h avg PM_{10} for ED visits for respiratory causes combined (ICD-9: 460-466, 477, 480-486, 491-493, 496, 786.09) among all ages during January 1993-August 2000 (Peel et al., 2005, 056305). $PM_{2.5}$, $PM_{10-2.5}$, UF number count and $PM_{2.5}$ components (SO_4^{2-}, acidity, EC, OC, and an index of water-soluble transition metals) were available for inclusion in analyses beginning August 1, 1998. Excess risks of 1.6% (95% CI: -0.003 to 3.5) per 10 $\mu g/m^3$ increase in 24-h avg $PM_{2.5}$ and 0.6% (95% CI: -3.6 to 5.1) per 10 $\mu g/m^3$ increase in $PM_{10-2.5}$ were reported. Weaker, less precise associations with components were reported and no increase with UF PNC was observed.

Analyses with four additional years of data were conducted and more recently reported by SOPHIA investigators (Tolbert et al., 2007, 090316). Single-pollutant results are included in Figure 6-11. The effect of PM_{10} remained with the additional years of data, while the effect of $PM_{2.5}$ was diminished and a decrease in ED visits with $PM_{10-2.5}$ was observed. The association of PM_{10} with respiratory disease ED visits was robust to adjustment for O_3, CO and NO_2. In another recent analysis using SOPHIA data from 1998 through 2002 to compare source apportionment methods, Sarnat et al. (2008, 097972) reported that $PM_{2.5}$ from mobile sources, $PM_{2.5}$ from biomass burning and SO_4^{2-}-rich secondary $PM_{2.5}$ were associated with respiratory ED visits and associations were robust to the choice of the method. Excess risks were statistically significant, ranging from approximately 2-4%, depending on the method.

In a French multicity study, larger increases were observed in association with 24-h avg $PM_{10-2.5}$ concentration compared to $PM_{2.5}$ concentration among adults as well as children. Among adults 15-64 yr, investigators reported increases in respiratory hospitalizations of 0.8% (95%CI: -0.7 to 2.3) and 2.6% (95%CI: -0.5 to 5.8) per 10 $\mu g/m^3$ for $PM_{2.5}$ and $PM_{10-2.5}$, respectively (lag 0-1 days) (Host et al., 2008, 155852).

In a study of respiratory hospital admission and ED visits (ICD-9 Codes 460-519) among all ages conducted in Spokane, Washington, no associations were observed with any size fraction of PM considered (e.g., PM_1, $PM_{2.5}$, $PM_{10-2.5}$, PM_{10}) (Slaughter et al., 2005, 073854). Furthermore, several of the same investigators conducted a source apportionment analysis using daily $PM_{2.5}$ filter samples from the same residential monitor in Spokane (Schreuder et al., 2006, 097959). In this investigation, $PM_{2.5}$ from vegetative burning in the previous day (lag 1) was associated with respiratory hospital admissions (2.3% [95% CI: 0.9-3.8] per interquartile range increase in the source marker). In a study of $PM_{2.5}$ from wildfires in California during 2003, associations with respiratory hospitalizations were generally stronger relative to associations in the periods before and after the fires (Delfino et al., 2009, 191994). Among adults 20-64 yr, an increase of 2.4% (95% CI: 0.5-4.4 per 10 $\mu g/m^3$) was reported during the wildfire period compared to 0.9% (95%CI: -0.1 to 1.8 per 10 $\mu g/m^3$) for all periods combined (pre-, post- and during wildfires).

Luginaah et al. (2005, 057327) examined respiratory hospital admissions in relation to PM_{10} concentration across strata for age and gender and compared time series to case-crossover approaches. The results for all ages combined, which were relatively precise, stratified by gender and all lags are presented in Figure 6-11; the largest estimates for PM_{10} were for adult males (15-64 yr old). Fung et al. (2005, 093262) did not report evidence of an association between respiratory admissions and 24-h PM_{10} concentration among adults <65 yr, in a study in Ontario, Canada, while Ulirsch et al. (2007, 091332) reported a significant positive association among all ages and adults (18-64 yr) in two Southeast Idaho cities for hospitalizations, ED and urgent care visits combined. This estimate was robust to adjustment for gaseous pollutants.

Older Adults

Among older adults, MCAPS investigators observed largely null findings for $PM_{2.5}$ and respiratory hospitalizations (ICD-9: 490-492, 464-466, 480-487) for the U.S. as a whole, but reported heterogeneity in effect estimates across the country that were explained by regional and seasonal factors (Bell et al., 2008, 156266). The nationwide excess risk of respiratory admissions with $PM_{2.5}$ was 0.22% (95% PI: -0.12 to 0.56, lag 0) (Bell et al., 2008, 156266). The largest increase was observed during the winter in the Northeast (1.76% [95% PI: 0.60-2.93], lag 0). Significant increases in respiratory admissions were also observed at lag 2. In an analysis of $PM_{10-2.5}$, MCAPS

investigators observed small imprecise increases in respiratory admissions with 24-h $PM_{10-2.5}$ concentration (0.33% [95% PI: -0.21 to 0.86, per 10 μg/m^3, lag 0]) (Peng et al., 2008, 156850), which decreased after adjustment for $PM_{2.5}$ (0.26% [95% PI: -0.32 to 0.84 per 10 μg/m^3 lag 0]). Associations with $PM_{2.5}$ increased (0.7% [95% PI: 0-1.5, lag 0]) or persisted (0.6% [95% PI: -0.2 to 1.25, lag 2]), after adjustment for $PM_{10-2.5}$.

Two recent MCAPS analyses evaluate the effect of $PM_{2.5}$ components on respiratory hospital admissions. Bell et al. (2009, 191997) analyzed a subset of MCAPS data restricted to 106 counties with data available for both long-term average concentrations of $PM_{2.5}$ components (Bell et al., 2007, 155683) and $PM_{2.5}$ total mass (1999-2005). The components evaluated included 20 chemicals with demonstrated toxicity or that contribute a large proportion of $PM_{2.5}$ mass (Al, NH_4^+, As, Ca, Cl, Cu, EC, OCM, Fe, Pb, Mg, Ni, NO_3^-, K, Si, Na^+, Ti, V, Zn). Increases in effect estimates of 511% (95% PI: 80.7-941) for EC, 223% (95% PI: 36.9-410) for Ni and 392% (95% CI: 46.3-738) for V per IQR increases in county-specific component fraction were observed. Associations were somewhat reduced and non-significant in two-pollutant models. When Queens or New York County were excluded, the association of V with hospital admissions lost significance. Associations were also diminished when alternative lag structures were considered.

Peng et al. (2009, 191998) linked data on hospital admissions for respiratory causes among older adults from 2000-2006 to daily air levels from the STN in 119 counties in which both sets of data were available. Chemical constituents evaluated were SO_4^{2-}, nitrate, Si, EC, OCM, sodium and ammonium ions. Single-day lags of 0-2 days were considered. These investigators found a 0.82% increase (95% PI: 0.22-1.44) per IQR increase in same day OCM. After adjustment for the other components, a 1.01% (95% PI: 0.04-1.98, lag 0) increase in respiratory admissions per IQR increase OCM was observed.

French PSAS investigators reported a non-significant increase in hospitalizations for respiratory diseases (ICD-10 J00-J99) with 24-h avg $PM_{10-2.5}$ among older adults. $PM_{2.5}$ estimates were also not significant (Host et al., 2008, 155852). Adjusted estimates from two-pollutant models were not presented. Positive associations of first hospitalization, overall hospitalizations and readmission for respiratory diseases and $PM_{10-2.5}$ were also reported among older adults in Vancouver (Chen et al., 2005, 087555). $PM_{10-2.5}$ was associated with an increase of 15% (95% CI: 4.8-22.8) in overall admissions per 10 μg/m^3. Increases associated with $PM_{10-2.5}$ were larger for readmissions compared to overall admissions. The association for $PM_{2.5}$ with overall admissions was 5.1% (95% CI: -4.9 to 13) and the association with readmissions was not larger. In this study, effect estimates for $PM_{10-2.5}$ and PM_{10} lost precision, but were robust to adjustment for gaseous pollutants, while the estimate for $PM_{2.5}$ was null after adjustment for gaseous pollutants. In Vancouver, Fung et al. (2006, 089789) report increased admissions of 1.8% (95% CI: -2.5 to 5.8) per 10 μg/m^3 increase in $PM_{2.5}$ and 3.8% (95% CI: 0-7.6) per 10 μg/m^3 increase in $PM_{10-2.5}$ (lag 0-1 day avg) among adults ≥65 yr.

In a multicity Australian study, Simpson et al. (2005, 087438) examined the association between $PM_{2.5}$ measured by nephelometry and respiratory hospital admissions (ICD-9 460-519) among older adults (≥65 yr) and reported significant associations (1.055 [95% CI: 1.008-1.1045], lag 0-1 day avg) from a meta-analysis combining effect estimates from all cities. Results from three statistical models were considered, including standard GAM, which produced similar results.

Delfino et al. (2009, 191994) reported that $PM_{2.5}$ from wildfire in California was associated with respiratory hospital admissions among older adults (3% 95% CI: 1.1-4.9 per 10 μg/m^3). In two analyses of data collected in Copenhagen, Denmark between 1999 and 2004, several size fractions including UF and accumulation mode (Andersen et al., 2008, 189651) and PM_{10} sources (Andersen et al., 2007, 093201) were investigated in relation to respiratory hospitalizations (J41-42, J43, J44-46) among adults >65 yr of age. Of the size fractions examined (NC total, NC median diameter of 12 nm [NC_{a12}], NC_{a23}, NC_{a57}, NC_{a100}, NC_{a212}, PM_{10}, $PM_{2.5}$) NC_{a212}, typically aged secondary long-range transported, NC_{a57} and PM_{10} were significantly associated with respiratory hospitalizations (Andersen et al., 2008, 189651). PM_{10} sources including biomass combustion, secondary inorganic compounds, oil combustion, and crustal were associated with respiratory hospitalizations (excess risks ranged from 3.5% to 5.4% per interquartile range, respectively) (Andersen et al., 2007, 093201). PM_{10} associations were diminished somewhat in two-pollutant models (Andersen et al., 2007, 093201; 2008, 189651); the authors note that it was difficult to separate the effects of PM_{10} and NC_{a212}, which were highly correlated in these data. $PM_{2.5}$ was not associated with respiratory hospitalizations in these data.

Results from other single-city studies offer somewhat consistent evidence for the effect of PM_{10} on respiratory admissions among older age groups. Ulirsch et al. (2007, 091332) found

increases in hospitalizations, ED and urgent care visits combined among this age group in two cities of Southeast Idaho. Two studies in Vancouver report increased admissions for respiratory causes with the largest effects observed for a 3-day ma (0-2 days) (Chen et al., 2005, 087555; Fung et al., 2006, 089789). Fung et al. (2005, 093262) observed non-significant increases in admissions with PM_{10} among older adults in Ontario, Canada, while another study conducted in Ontario (Luginaah et al., 2005, 057327) did not provide compelling evidence for an effect that was robust to method selection, although some increases among males were observed. Finally, a study of hospital admissions for cardiopulmonary conditions combined among older adults (≥ 65 yr) in Allegheny County, PA found a positive association with PM_{10} at lag 0 (Arena et al., 2006, 088631).

Effect estimates for adults (and combined age groups) as well as older adults are found in Figure 6-11. Effects observed in single-city studies are generally imprecise but most studies report positive associations. Regional and seasonal variation was observed with the largest effect estimate reported by Bell et al. (2008, 156266) in the Northeast during the winter. Although the number of studies examining components or sources was limited, EC, OC, Ni, V, and $PM_{2.5}$ from mobile sources were associated with increased respiratory admissions. Several additional studies conducted outside the U.S. and Canada reported positive associations of respiratory hospitalizations with PM_{10} for different age groups and lags (Bedeschi et al., 2007, 090712; Chen et al., 2005, 087555; Chen et al., 2006, 087947; Hanigan et al., 2008, 156518; Lai and Cheng, 2008, 180301; Larrieu et al., 2009, 180294; Middleton et al., 2008, 156760; Oftedal et al., 2003, 055623), $PM_{2.5}$ (Hinwood et al., 2006, 088976; Neuberger et al., 2004, 093249; Vigotti et al., 2007, 090711), BS (Bartzokas et al., 2004, 093252; Tecer et al., 2008, 180030) and with $PM_{10-2.5}$ (Tecer et al., 2008, 180030). Other studies reported no associations with PM_{10} (Vegni and Ros, 2004, 087448) or TSP (Llorca et al., 2005, 087825).

6.3.8.2. Asthma

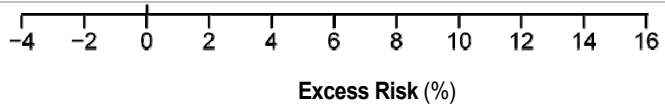
Results from multicity studies of hospital admissions and ED visits for asthma as well as single-city studies conducted in the U.S. and Canada are summarized in Figure 6-12. Studies reviewed in the 2004 AQCD are included for continuity. Concentrations of PM for the relevant study period are found in Table 6-14.

Children

SOPHIA investigators (Peel et al., 2005, 056305) reported that, of the PM mass indicators examined, the largest effect estimate observed using the a priori lag (0- to 2-day avg) was the association of PM_{10} with pediatric (2-18 yr) asthma ED visits (1.6% [95% CI: -0.2 to 3.4]). ED visits for both asthma (ICD-9: 493) and wheezing (ICD-9: 786.09) were included in their study. New York State DOH (2006, 090132) conducted a study comparing effect estimates for ED visits for asthma and 24-h $PM_{2.5}$ and 1-h $PM_{2.5}$ across two communities in New York City (the Bronx and Manhattan). No associations with 24-h $PM_{2.5}$ were reported for either borough for age categories 0-4 or 5-18 yr. Non-significant increases with 1-h maximum $PM_{2.5}$ were reported for the Bronx. Asthma hospital admissions (ICD-10 J45, J46, J44.8) in children <14 yr were examined in the Australia/New Zealand multicity study (Barnett et al., 2005, 087394). In this study, associations for asthma hospital admissions with $PM_{2.5}$ and PM_{10} were increased but imprecise.

Lin et al. (2002, 026067) used both time series and case-crossover approaches to investigate the influence of PM on asthma hospitalization in children, 6-12 yr old, in Toronto from 1981 to 1993. These authors report relatively small differences in results obtained through bi-directional case crossover and time series approaches, but indicate that unidirectional case-crossover methods may overestimate the relative risks. Single- to 7-day avg lags were investigated and estimates appeared to increase and then level off at the longer lags (0- to 2-day and 0- to 5-day lags are shown in Figure 6-12). Effect estimates for $PM_{2.5}$ are not easily distinguished from the null, but $PM_{10-2.5}$ is significantly associated with asthma admissions among boys and among girls. These associations were imprecise, but robust to adjustment for gaseous pollutants, among all children combined.

Study	Location	Lag	Age	Gender	Effect Estimate (95% CI)	
ADULTS OR ALL AGES COMBINED						
Peel et al. (2005, 056305)*	Atlanta, GA	0-2	All			$PM_{2.5}$
Tolbert et al. (2007, 090316)*	Atlanta, GA	0-2	All			
Slaughter et al. (2005, 073854)*	Spokane, WA	1	All			
Host et al. (2008, 155852)	6 Cities, France	0-1	15-64			
Delfino et al. (2009, 191994)	California Wildfires	0-1	20-64			
Peel et al. (2005, 056305)*	Atlanta, GA	0-2	All			$PM_{10-2.5}$
Tolbert et al. (2007, 090316)*	Atlanta, GA	0-2	All			
Slaughter et al. (2005, 073854)*	Spokane, WA	1	All			
Host et al. (2008, 155852)	6 Cities, France	0-1	15-64			
Peel et al. (2005, 056305)*	Atlanta, GA	0-2	All			PM_{10}
Tolbert et al. (2007, 090316)*	Atlanta, GA	0-2	All			
Luginaah et al. (2005, 057327)	Windsor, Can	1	All	Female		
		2	All	Female		
		3	All	Female		
		1	All	Male		
		2	All	Male		
		3	All	Male		
Slaughter et al. (2005, 073854)*	Spokane, WA	1	All			
		2	All			
		3	All			
Ulirsch et al. (2007, 091332)**	Idaho	0	All			
		0	18-64			
Fung et al. (2005, 093262)	Ontario, Can	0	<65			
		0-1	<65			
		0-2	<65			
OLDER ADULTS (65+ YR)						
Bell et al. (2008, 156266)	202 Counties, US	0				$PM_{2.5}$
		1				
		2				
	Winter, US	0				
	Winter, Northeast	0				
Host et al. (2008, 155852)	6 Cities, France	0-1				
Fung et al. (2006, 089789)	Vancouver, Can	0				
		0-2				
		0-4				
		0-6				
Chen et al. (2005, 087555)	Vancouver, Can	1				
		0-1				
		0-2				
Delfino et al. (2009, 191994)	California Wildfires	0-1				
Host et al. (2008, 155852)	6 Cities, France	0-1				$PM_{10-2.5}$
Peng et al. (2008, 156850)	108 Counties, US	0				
		1				
		2				
Fung et al. (2006, 089789)	Vancouver, Can	0				
		0-2				
		0-4				
		0-6				
Chen et al. (2005, 087555)	Vancouver, Can	1				
		0-1				
		0-2				
Fung et al. (2006, 089789)	Vancouver, Can	0				PM_{10}
		0-2				
		0-4				
		0-6				
Ulirsch et al. (2007, 091332)**	2 Cities in ID	0				
Chen et al. (2005, 087555)	Vancouver, Can	0				
		0-1				
		0-2				
Fung et al. (2005, 093262)	Ontario, Can	0				
		0-1				
		0-2				



Studies represented in the figure include all multicity studies as well as single-city studies conducted in the U.S. or Canada

* ED Visits

** Hospitalization, ED, and Urgent Care Visits Combined

Figure 6-11. Excess risks estimates per 10 µg/m^3 increase in 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10} for ED visits and HAs for respiratory diseases among adults.

Although Ostro et al. (2009, 191971) presented estimates for all respiratory diseases combined, these authors note that $PM_{2.5}$ and its components were associated with asthma hospitalizations among the children in six counties of Los Angeles studied. Delfino et al. (2009, 191994) examined the association of $PM_{2.5}$ before, during, and after wildfires in California with asthma hospitalizations among age and gender subgroups. Associations were observed for children 0-4 yr among children during the wildfire period (8.3% [95% CI: 2.1-14.9] per 10 $\mu g/m^3$), but not before or after the wildfire period. For older children, 5-19 yr, non-significant increases in asthma hospitalizations were found before the wildfire period, but not during or after the fires.

Hirshon et al. (2008, 180375) studied hospital admissions and ED visits by children 0-17 yr old in Baltimore, MD from June 2002-November 2002, in relation to Zn as a component in $PM_{2.5}$. Single day lags from 0-2 days were tested with the highest estimates observed for the previous day. A 23% (95% CI: 7-41) increase in admissions was observed comparing medium (8.63-20.76 ng/m^3) concentrations on the previous day to low concentrations (<8.63 ng/m^3) on the previous day. Previous day high concentration (>20.76 ng/m^3) was associated with an increase in admissions of 16% (95% CI: -3 to 39) compared to previous day low concentration. Zinc associations were robust to adjustment for EC, CO, NO_2, Ni, and Cr. However, evidence of effect modification by EC and NO_2 at lags 1 and 2 was observed.

Mohr et al. (2008, 180215) used measurements of EC, O_3, SO_2, and total NO_X from the EPA supersite in St. Louis for June 2001-May 2003, to examine the association of EC, temperature and season with asthma ED visits among children 2-17 yr old. The association of EC with asthma ED visits varied by age, season and weekday versus weekend. The largest associations were observed for 2-5 yr olds during the fall weekends (3% [95% CI: 1-5] per 0.1 $\mu g/m^3$) and 11-17 yr olds during winter weekdays (3% [95% CI: 0-5] per 0.1 $\mu g/m^3$) and summer weekends (9% [95% CI: 2-17] per 0.1 $\mu g/m^3$). Investigators also report that temperature modified the effect of EC after adjusting for gaseous copollutants, such that the association of ED visits with EC increased with increasing temperature during the summer and increased with decreasing temperature during the winter. Authors attribute the temperature modification to time-activity patterns among this age group.

Sinclair and Tolsma (2004, 088696) investigated respiratory ambulatory care visits using ARIES data in Atlanta, GA (also used by SOPHIA investigators) and health insurance records. These authors evaluated three 3-day ma lags (0-2, 2-5 and 6-8 days) and reported relative risks, with no confidence intervals, for significant results only (not included in Figure 6-12). For childhood asthma outpatient visits, OHC, $PM_{10-2.5}$, PM_{10}, EC and OC were significantly associated with ambulatory care visits at lags 0-2 or 2-5 days.

A study in Anchorage used medical records to examine effects of particle exposure on pediatric asthma outpatient visits, inpatient visits and prescriptions for short-acting inhalers (Chimonas and Gessner, 2007, 093261). Authors examined Medicaid claims for asthma-related and lower respiratory infection visits among children less than 20 yr of age for 5 yr (approximately 25,000 children were enrolled in Medicaid each year between 1999 and 2003). Citing work done in the mid-1980's, the authors describe their city's particles as arising primarily from natural, geologic sources (PM_{10}), and to a lesser extent from local automotive emissions ($PM_{2.5}$) (Pritchett and Cooper, 1985, 156886). Using GEE in a time-series analysis of daily and weekly effects of particle exposure on health outcomes, the authors found that each 10 $\mu g/m^3$ increase in 24-h avg PM_{10} was associated with a 0.6% increase (95% CI: 0.1-1.3) in outpatient visits for asthma. The same increase in weekly PM_{10} concentration resulted in a 2.1% increase (95% CI: 0.4-3.8) in asthma visits, after adjustment for gaseous pollutants. No meaningful associations were observed for $PM_{2.5}$.

In Copenhagen, Denmark, Anderson et al. (2007, 093201) found an association between PM_{10} attributed to vehicle emissions and asthma hospitalizations among children 5-18 yr (5.4% 95% CI: 0.57-22.9 per 10 $\mu g/m^3$, 0- to 5-day avg). In an analysis of size distribution and number concentration, accumulation mode particles were most strongly associated with asthma admissions (8% [95% CI: 0-17] per 495 particles/cm^3, lag 0-5). (Andersen et al., 2008, 189651). In Helsinki, Halonen et al. (2008, 189507) examined the association of various size fractions of PM (e.g., Aitken, accumulation mode, $PM_{2.5}$, $PM_{10-2.5}$) with ED visits for asthma among children <15 yr. These authors evaluated lags 0-5 and noted a different lag structure depending on age with children experiencing greater effects at lags 3-5 days compared to adults at lag 0. Aitken, accumulation mode particles and traffic-related PM were significantly and most strongly associated with asthma visits among children, while no association with $PM_{10-2.5}$ was observed in this age group.

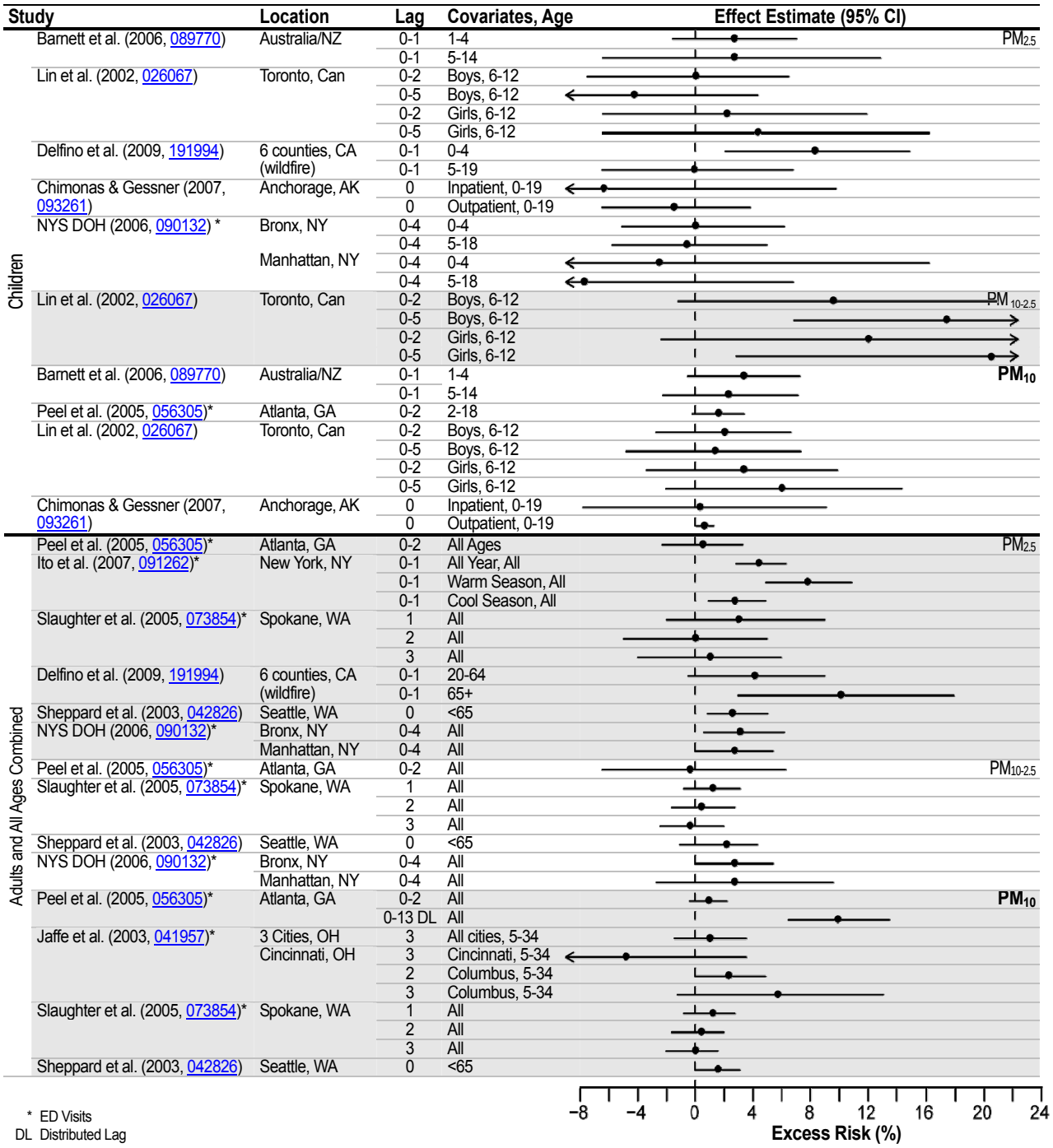


Figure 6-12. Excess risk estimates per 10 µg/m^3 increase in 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10} for asthma ED visits and HAs. Studies represented in the figure include all multicity studies as well as single-city studies conducted in the U.S. or Canada.

Adults and All Ages Combined

Results from the Atlanta SOPHIA study based on the a priori models examining a 3-day ma (lag 0-2 days) revealed no statistically significant associations with asthma (ICD-9 493, 786.09)

among all ages for any of the PM metrics studied (e.g., $PM_{2.5}$, $PM_{10-2.5}$, PM_{10}, UF PNC, PM components) (Peel et al., 2005, 056305). However, the 14-day unconstrained distributed lag model produced an excess risk of 9.9% (95% CI: 6.5-13.5 per 10 μg/m^3 PM_{10}). The authors note that associations of $PM_{2.5}$ and OC with asthma tended to be stronger during the warmer months. Sinclair and Tolsma (2004, 088696) report a significant association between adult outpatient visits for asthma and UFPs, but not other PM size fractions (not included in Figure 6-12 because only significant results were presented).

Jaffe et al. (2003, 041957) examined the effects of ambient pollutants (PM_{10}, O_3, NO_2 and SO_2) during the summer months (June through August) on the daily number of ED visits for asthma among Medicaid recipients aged 5-34 yr from 1991 to 1996 in Cincinnati, Columbus, and Cleveland. Lags 1 to 3 were tested and only statistically significant lags were presented. For all cities combined, the overall effect estimate for 24-h avg PM_{10} was 1.0% (95% CI: -1.44 to 3.54 per 10 μg/m^3 increase). The effect estimate for Cleveland was the only significantly elevated estimate (2.3% [95% CI: 0.0-4.9] per 10 μg/m^3 increase) when the cities were examined independently. The authors reported results from analyses indicating a possible concentration response for O_3, but no consistent effects for PM_{10}.

In New York City, Ito et al. (2007, 156594) examined numbers of ED visits for asthma among all ages (ICD-9 493) in relation to pollution levels from 1999 to 2002; several weather models were evaluated. Although the association with NO_2 was the strongest, $PM_{2.5}$ was significantly associated with asthma ED visits in each weather model (strongest during the warm months) and remained significant after adjustment for O_3, NO_2, CO and SO_2. Slaughter et al. (2005, 073854) reported no associations with ED visits or hospitalizations for asthma, among all ages, in Spokane, Washington for the PM size fractions studied (PM_1, $PM_{2.5}$, PM_{10}, $PM_{10-2.5}$). An association with CO, which the authors attribute to combustion related pollution in general, was observed. The effect of 24-h avg and 1-h max $PM_{2.5}$, $PM_{10-2.5}$, EC and OC on ED visits for asthma among all ages combined, comparing two communities in New York City was investigated (ATSDR, 2006, 090132). In the Bronx, an increase in visits of 3.1% (95% CI: 0.6-6.2 per 10 μg/m^3) was observed in relation to 24-h avg $PM_{2.5}$. For $PM_{10-2.5}$, an increase of 2.7% (95% CI: 0.0-5.4) was observed in the Bronx. Smaller, less precise estimates were observed for Manhattan. Increased asthma visits were observed with OC, EC and total metals. In the Bronx, the association of 1-h max $PM_{2.5}$ with ED visits was larger than the association with 24-h $PM_{2.5}$ when standardized to the mean concentration for both communities and was generally robust to adjustment for copollutants.

Delfino et al. (2009, 191994) examined the association of $PM_{2.5}$ before, during and after wildfires in California with asthma hospitalizations among age and gender subgroups. The increase among older adults >65 yr of 10% (95% CI: 3-17.8 per 10 μg/m^3) was larger than the increase among adults 20-64 yr of 4.1% (95% CI: -0.5 to 9 per 10 μg/m^3). For older adults, the association was stronger during the wildfire period compared to the pre-wildfire period and did not diminish during the post-wildfire period.

Effect estimates from studies of hospital admissions and ED visits for asthma are summarized in Figure 6-12. Associations with $PM_{2.5}$ concentration among children are imprecise and not consistently positive across different age groups and lags. Findings from two studies of $PM_{10-2.5}$ (Sinclair and Tolsma, 2004, 088696), as well as PM_{10} studies both show positive associations, although estimates lack precision. Among adults and adults and children combined, associations of asthma hospital admissions and ED visits with $PM_{2.5}$ concentration were observed in most studies. Positive, non-significant associations of $PM_{10-2.5}$ concentration with asthma admissions and ED visits were observed in some studies of adults. Again, PM_{10} estimates are more consistently positive and precise compared to other size fractions. Associations were observed with several $PM_{2.5}$ components (e.g., EC, OC and Zn) and sources (e.g., traffic, wildfires). Many factors (e.g., the underlying distribution of individual sensitivity and severity, medication use and other personal behaviors) can influence the lag time observed in observational studies (Forastiere et al., 2008, 186937). Excess risk estimates for asthma were generally sensitive to choice of lag and increase with longer or cumulative lags times. Most additional single-city studies conducted in Europe, South America and Asia, have investigated the associations of asthma hospitalizations, ED visits or doctor visits and most have reported evidence of an association with TSP (Arbex et al., 2007, 091637; Migliaretti and Cavallo, 2004, 087425; 2005, 088689), PM_{10} (Bell et al., 2008, 156266; Bell et al., 2008, 091268; Chardon et al., 2007, 091308; Chen et al., 2006, 087947; Erbas et al., 2005, 073849; Galan et al., 2003, 087408; Jalaludin et al., 2004, 056595; Kim et al., 2007, 092837; Ko et al., 2007, 091639; Kuo et al., 2002, 036310; Lee et al., 2002, 034826; Lee et al., 2006, 090176) and $PM_{2.5}$ (Chardon et al., 2007, 091308;

Ko et al., 2007, 091639; Ko et al., 2007, 092844) while a few have not shown an association with PM_{10} (Larrieu et al., 2009, 180294; Masjedi et al., 2003, 052100; Tsai et al., 2006, 089768; Yang and Chen, 2007, 092847; Yang et al., 2007, 092848).

6.3.8.3. Chronic Obstructive Pulmonary Disease

Results from multicity studies of hospital admissions and ED visits for COPD as well as single-city studies conducted in the U.S. and Canada are summarized in Figure 6-13. Studies reviewed in the AQCD are included in the figure for continuity. Concentrations of PM for the relevant study period are found in Table 6-14.

In a study of Medicare recipients in 204 U.S. counties, Dominici et al. (2006, 088398) reported an overall increase of about 1% in COPD hospitalizations (ICD-9 490-492) associated with 24-h avg $PM_{2.5}$, with the largest effects at lags 0 and 1. In this study effect estimates were heterogeneous across the U.S. with a significant increase of about 4% observed in the Southeast at lag 0. In another study using Medicare data in 36 U.S. cities (1986-1999) short-term exposure to PM_{10} was associated with an increase in COPD hospital admissions (ICD-9 490-496, excluding 493) of 1.47% (95% CI: 0.93-2.01, lag 1) during the warm season (Medina-Ramon et al., 2006, 087721). A smaller effect was observed during the cold season.

In Atlanta, SOPHIA investigators reported a comparably sized effect estimate for COPD (ICD-9 491, 492, 496) and 24-h avg $PM_{2.5}$ (1.5% [95% CI: -3.1 to 6.3], 0- to 2-day avg]). The association of PM_{10} with COPD reported by Peel et al. (2005, 056305) was 1.8% (95% CI: -0.6 to 4.3). No associations were observed for $PM_{10-2.5}$, UF or $PM_{2.5}$ components. Slaughter et al. (2005, 073854) reported no associations between any size fraction of PM in Spokane, Washington ($PM_{2.5}$, $PM_{10-2.5}$, PM_{10}) and COPD (ICD-9 491, 492, 494, 496). In contrast, Chen et al. (2004, 087262) reported increases in COPD admissions (ICD-9 490-492, 494, 496) for $PM_{2.5}$ (17.1% [95% CI: 4.6-31.0], 0- to 2-day avg), $PM_{10-2.5}$ (10.0% [95% CI: -1.2 to 22.8, 0- to 2-day avg]), and PM_{10} (16.5% [95% CI: 6.88-27.02], 0- to 2-day avg]). However, the estimates for PM metrics were diminished after adjustment for NO_2.

Delfino et al. (2009, 191994) examined the association of $PM_{2.5}$ from the wildfires of 2003 in California with COPD hospitalizations among age and gender subgroups. Among older adults (≥65 years), associations were similar across pre-, post- and wildfire periods with none reaching significance. The increase for all periods combined in this age group was 1.9% (95% CI: -0.6 to 4.4, per 10 $\mu g/m^3$). Michaud et al. (2004, 188530) reported an association for asthma and COPD ED visits combined with PM_1 (lag 1) in Hilo, Hawaii in a study designed to investigate the effect of volcanic fog.

Halonen et al. (2008, 189507) conducted a study of ED visits for COPD and asthma combined (J41, J44-J46) among adults 15-64 yr and older adults >65 yr. These authors examined the effects of Aitken mode particles, accumulation mode particles, $PM_{2.5}$ and $PM_{10-2.5}$ as well as several sources of $PM_{2.5}$ (traffic, long range transported particles, road dust and coal/oil combustion). Concentrations, lagged from 0-5 days, were examined and the largest effects among older adults were observed in association with concurrent day $PM_{2.5}$, $PM_{10-2.5}$, accumulation mode particles, NO_2, and CO concentrations. The $PM_{2.5}$ association was diminished with adjustment for UFPs, NO_2 and CO. A similar diminishment was observed when $PM_{10-2.5}$ was adjusted for $PM_{2.5}$, NO_2 and CO. However, traffic related particles and long range transported particles (e.g., accumulation mode particles such as carbon compounds, sulfates and nitrates from central Europe and Russia) were associated with COPD and asthma among older adults. This same research group conducted additional analyses of hospital admissions using the same PM metrics focusing on older adults (≥65 yr) (Halonen et al., 2009, 180379). The $PM_{2.5}$ results and lag structure were similar to the earlier ED visit study. The strongest effect was for accumulation mode particles with COPD/asthma admissions. Traffic related $PM_{2.5}$ was associated with COPD/asthma admissions at lag 1 while no effect was observed with concurrent day concentration. Long range transported particles and road dust were also associated with admissions for asthma and COPD.

With the exception of one study conducted in Spokane Washington (Slaughter et al., 2005, 073854), associations have been consistently observed for $PM_{2.5}$ and PM_{10} with COPD in multicity and single-city studies conducted in the U.S. and Canada. Associations with $PM_{10-2.5}$ are fewer and less consistent. A study that examined seven single-day lags in association with pooled COPD and asthma ED visits in Finland reported that $PM_{2.5}$, $PM_{10-2.5}$, traffic sources as well as gaseous pollutants

had a more immediate effect in older adults (lags 0 and 1) compared to children experiencing asthma (3- to 5-day lags) (Halonen et al., 2008, 189507). Larger estimates at shorter lags were not observed consistently across other studies. Most single-city studies conducted outside of the U.S. or Canada focused on PM_{10} (Chiu et al., 2008, 191989; Hapcioglu et al., 2006, 093263; Ko et al., 2007, 091639; Ko et al., 2007, 092844; Martins et al., 2002, 035059; Masjedi et al., 2003, 052100; Sauerzapf et al., 2009, 180082; Yang and Chen, 2007, 092847).

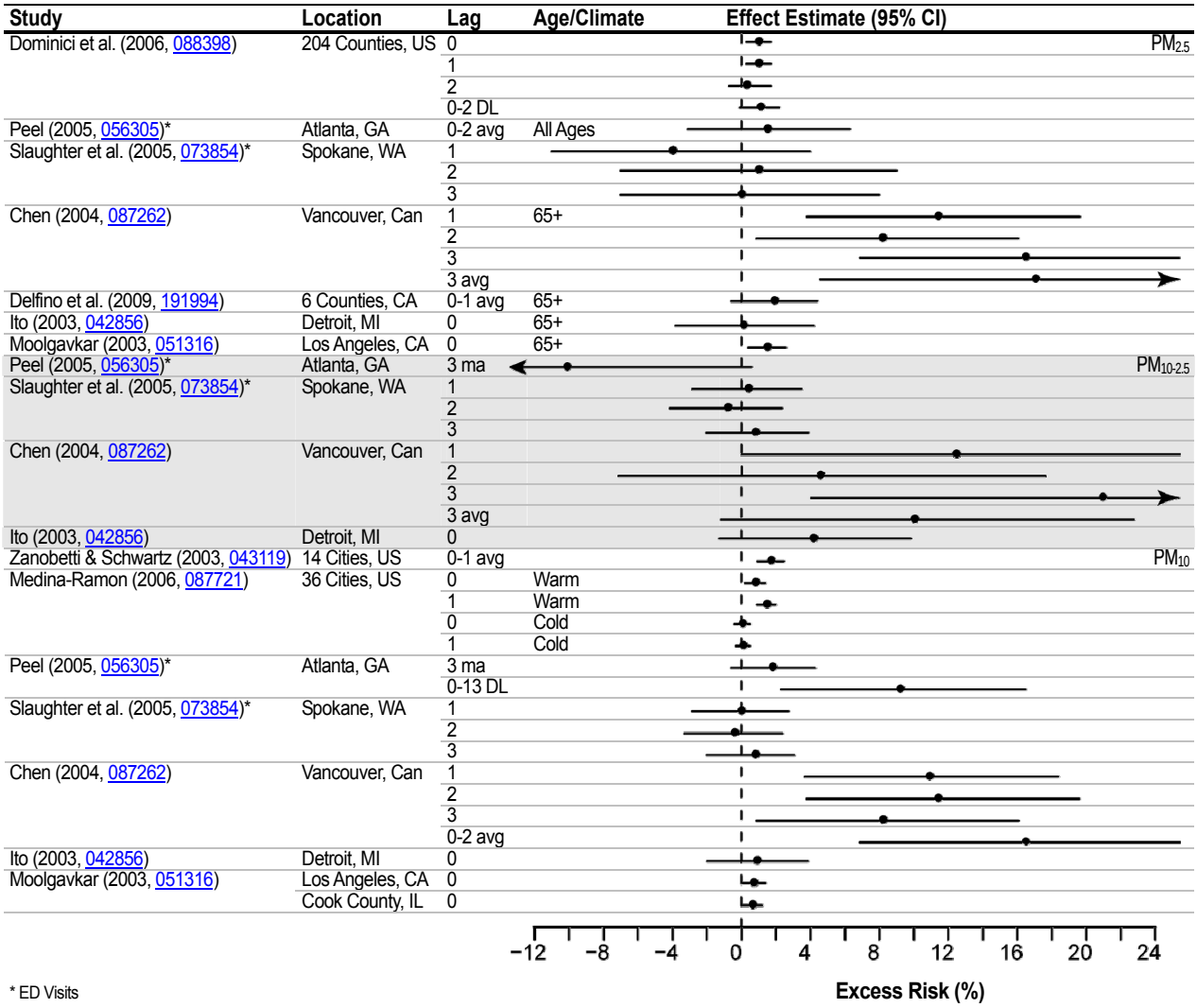


Figure 6-13. Excess risks estimates per 10 µg/m^3 increase in 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10} for COPD ED visits and HAs among older adults (65+ yr, unless other age group is noted). Studies represented in the figure include all multicity studies as well as single-city studies conducted in the U.S. or Canada.

6.3.8.4. Pneumonia and Respiratory Infections

Results from multicity studies of hospital admissions and ED visits for respiratory infection as well as single-city studies conducted in the U.S. and Canada are summarized in Figure 6-14. The figure includes studies of respiratory infection reviewed in the 2004 AQCD. Concentrations of PM for the relevant study period are found in Table 6-14.

Children

In the study of seven cities in Australia and New Zealand, associations of $PM_{2.5}$ with pneumonia and acute bronchitis (ICD-10 J12-J17, J18.0, J18.1, J18.8, J18.9, J20, J21) were observed among infants <1 yr old (4.54% [95% CI: 0.00-9.20]) and children 1-4 yr old (6.44% [95% CI: 0.26-12.85]) (Barnett et al., 2005, 087394). Although quantitative results were only presented for all respiratory diseases combined, Ostro et al. (2009, 191971) examined several specific respiratory diseases including acute bronchitis and pneumonia. They reported that $PM_{2.5}$ and its components were more strongly associated with these endpoints compared to other respiratory diseases. Delfino et al. (2009, 191994) reports imprecise increases in admissions among children during wildfire periods for acute bronchitis and bronchiolitis, as well as pneumonia.

Inpatient and outpatient visits for lower respiratory tract infections among children in Anchorage, Alaska, were not associated with $PM_{2.5}$ or PM_{10} (Chimonas and Gessner, 2007, 093261). Lin et al. (2005, 087828) observed associations of respiratory infections (ICD-9 464, 466, 480-487) with $PM_{10-2.5}$ and PM_{10} that persisted after adjustment for gaseous pollutants among subjects <15 yr old living in Toronto. Analyses were stratified by gender and both single and multiple day lags were examined (4- and 6-day avg were presented). The largest significant effect estimates were for $PM_{10-2.5}$. The size of the $PM_{2.5}$ estimate varied by gender and was sensitive to the choice of lag. $PM_{2.5}$ results were not generally robust to adjustment for gases.

All Ages and Older Adults

SOPHIA investigators examined ED visits for upper respiratory tract infections (URI) (ICD-9 460-466, 477) and pneumonia (ICD-9 480-486) among all ages. An excess risk of 1.4% (95% CI: 0.4-2.5 per 10 $\mu g/m^3$, lag 0- to 2-day avg) for PM_{10} was associated with URI visits. With the exception of a small increase in risk for OC of 2.8% (95% CI: 0.4-5.3 per 2 $\mu g/m^3$, 0- to 2-day avg) with pneumonia visits, Peel et al. (2005, 056305) reported no association with other PM size fractions or components evaluated. However, Sinclair and Tolsma (2004, 088696), who also used ARIES data in their analysis, reported significant associations with outpatient visits for LRI. These associations were generally observed for 3- to 5-day ma lags, in association with $PM_{10-2.5}$, PM_{10}, EC, OC, and $PM_{2.5}$ water soluble metals (not pictured in figure because only significant lags were reported). No associations with pneumonia for any size fractions were observed among all ages in a study conducted in Spokane, Washington (effect estimates were not reported) (Slaughter et al., 2005, 073854).

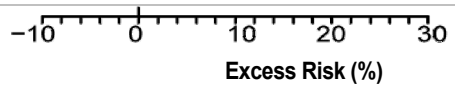
French PSAS investigators examined the effect of $PM_{2.5}$ and $PM_{10-2.5}$ on hospital admissions for respiratory infection (ICD-10: J10-22) among all ages. Increases of 2.5% (95% CI: 0.1-4.8) and 4.4% (95%CI: 0.9-8.0) per 10 $\mu g/m^3$ were observed in association with $PM_{2.5}$ and $PM_{10-2.5}$, respectively (Host et al., 2008, 155852). In a multicity study of older adults (≥65 yr) Medina-Ramon et al. (2006, 087721) examined hospital admissions for pneumonia (ICD-9 480-487) in 36 U.S. cities in relation to 24-h avg PM_{10} concentration. An increase in pneumonia admissions of 0.84% (95% CI: 0.50-1.19 per 10 $\mu g/m^3$, lag 0) was reported by these investigators during the warm season. Cold season associations were weaker (0.30% [95% CI: 0.07-0.53] per 10 $\mu g/m^3$, lag 0) as were lag 1 associations. Dominici et al. (2006, 088398) investigated hospital admissions for all respiratory infections including pneumonia (ICD-9 464-466, 480-487) among older adults in 204 urban U.S. counties in relation to $PM_{2.5}$ and reported a significant increased risk only at lag 2. Heterogeneity in effect estimates was observed across the U.S. with the largest associations reported for the South and Southeast.

In Boston, excess risks of pneumonia hospitalization in association with $PM_{2.5}$, BC, and CO were observed among older adults (Zanobetti and Schwartz, 2006, 090195). A measure of non-traffic PM, e.g., the residuals from the regression of $PM_{2.5}$ on BC, was not associated with pneumonia hospitalization in these data. In a California study (Delfino et al., 2009, 190254), effect estimates were of similar magnitude for pneumonia admissions associated with $PM_{2.5}$ from wildfires among all ages combined and older adults (2.8% [95% CI: 0.7-5.0] per 10 $\mu g/m^3$, all ages combined). The $PM_{2.5}$ association with acute bronchitis and bronchiolitis admissions during the wildfire period for all age groups showed an approximately 10% increase (9.6% 95% CI: 1.8-17.9, per 10 $\mu g/m^3$). The increase was not larger during the wildfire period compared to the pre-fire period for either outcome.

In a study of four cities in Australia, statistically significant associations of pneumonia and acute bronchitis with particles measured by nephelometry (but not $PM_{2.5}$ mass) and NO_2 were observed among older adults (Simpson et al., 2005, 087438). Halonen et al. (2009, 180379) examined pneumonia among older adults (ICD10 J12-J15) in their most recent analysis. Associations of $PM_{2.5}$ (5.0% [95% CI: 1.0-9.3] per 10 µg/m^3, lag 5-day mean), as well as accumulation mode particles, with pneumonia admissions were observed.

Although the body of literature is small, several studies of children reported associations of $PM_{2.5}$, $PM_{10-2.5}$ and PM_{10} with respiratory infections but the outcomes studied are heterogeneous and effect estimates are imprecise. Studies of adults show a similar pattern of increased risk for each of these size fractions. Several other single-city studies conducted outside the U.S. and Canada reported associations for PM_{10} (Cheng et al., 2007, 093034; Hwang and Chan, 2002, 023222; Nascimento et al., 2006, 093247) and $PM_{2.5}$ (Hinwood et al., 2006, 088976) with hospitalization or ED visits for respiratory infections.

Study	Location	Lag	Age	Outcome	Effect Estimate (95% CI)	
CHILDREN						
Barnett et al. (2006, 089770)	7 Cities, Australia/NZ	0-1	<1	Pneumonia		$PM_{2.5}$
		0-1	1-4	Pneumonia		
Chimonas & Gessner (2007, 093261)	Anchorage, AK	0	0-19	LRI	Outpatient	
		0	0-19	LRI	Inpatient	
Delfino et al. (2009, 191994)	6 Counties, S. CA	0-1	0-4	Bronchitis, Bronchiolitis	Wildfire	
		0-1	0-4	Pneumonia	Wildfire	
		0-1	5-19	Pneumonia	Wildfire	
Lin et al. (2005, 087828)	Ontario, Can	0-3	<15	RTI		
Lin et al. (2005, 087828)	Ontario, Can	0-3	<15	RTI		$PM_{10-2.5}$
Barnett et al. (2006, 089770)	7 Cities, Australia/NZ	0-1	<1	Pneumonia, Acute Bronchitis		PM_{10}
		0-1	1-4	Pneumonia, Acute Bronchitis		
Chimonas & Gessner (2007, 093261)	Anchorage, AK	0	0-19	LRI	Outpatient	
		0-1	0-19	LRI	Inpatient	
Lin et al. (2005, 087828)	Ontario, Can	0-3	<15	RTI		
ALL AGES COMBINED OR OLDER ADULTS						
Dominici et al. (2006, 088398)	204 Counties, US	0	65+	RTI		$PM_{2.5}$
		1	65+	RTI		
		2	65+	RTI		
Dominici et al. (2006, 088398)	90 Counties, US	0-2 DL	65+	RTI		
Zanobetti & Schwartz (2006, 090195)	Boston, MA	0	65+	Pneumonia		
		0-1	65+	Pneumonia		
Peel et al. (2005, 056305)*	Atlanta, GA	0-3	All	URI		
		0-3	All	Pneumonia		
Host et al. (2008, 155852)	6 Cities, France	0-1	All	RTI		
Delfino et al. (2009, 191994)	6 Counties, S.CA	0-1	All	Pneumonia	Wildfire	
		0-1	All	Bronchiolitis	Wildfire	
Ito (2003, 042856)	Detroit, MI	0	65+	Pneumonia		
Peel et al. (2005, 056305)*	Atlanta, GA	0-3	All	Pneumonia		$PM_{10-2.5}$
		0-3	All	URI		
Host et al. (2008, 155852)	6 Cities, France	0-1	All	RTI		
Ito (2003, 042856)	Detroit, MI	0	65+	Pneumonia		
Medina-Ramon et al. (2006, 087721)	36 Cities, US	0	65+	Pneumonia	Warm	PM_{10}
		1	65+	Pneumonia	Warm	
		0	65+	Pneumonia	Cold	
		1	65+	Pneumonia	Cold	
Peel et al. (2005, 056305)*	Atlanta, GA	0-3	All	URI		
		0-13 DL	All	URI		
		0-3	All	Pneumonia		
		0-13 DL	All	Pneumonia		
Zanobetti (2003, 043119)	14 Cities, US	0-1	65+	Pneumonia		
Ito (2003, 042856)	Detroit, MI	0	65+	Pneumonia		



*ED Visits
DL = Distributed Lag

Figure 6-14. Excess risks estimates per 10 µg/m^3 increase in 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10} for respiratory infection ED visits* and HAs. Studies represented in the figure include all multicity studies as well as single-city studies conducted in the U.S.

Table 6-14. PM concentrations in epidemiologic studies of respiratory diseases.

Study	Location	Mean Concentration ($\mu g/m^3$)	Upper Percentile concentrations ($\mu g/m^3$)
$PM_{2.5}$			
Andersen et al. (2007, 093201)	Copenhagen, Denmark	10	99th: 28
Barnett et al. (2005, 087394)	7 Cities Australia, NZ	8.1-11	Max: 29.3-122.8
Bell et al. (2008, 156266)	202 U.S. counties	12.92	98th: 34.16
Chardon et al. (2007, 091308)	Paris, France	14.7	75th: 18.2
Chen et al. (2004, 087262; 2005, 087555)	Vancouver, Canada	7.7	Max: 32
Chimonas and Gessner (2007, 093261)	Anchorage, AK	6.1	Max: 69.8
Delfino et al. (2009, 191994)	6 counties, CA	18.4-32.7	45.3-76.1 (mean during wildfire period)
Dominici et al. (2006, 088398)	204 U.S. counties	13.4	75th: 15.2
Fung et al. (2006, 089789)	Vancouver, Canada	7.72	Max: 32
Halonen et al. (2008, 189507)	Helsinki, Finland	NR; Median = 9.5	Max: 69.5
Host et al. (2008, 155852)	6 Cities France	13.8-18.8	95th: 25.0-33.0
Ito et al. (2007, 091262)	New York, NY	All yr: 15.1	All yr: 95th: 32
Lin et al. (2002, 026067)	Toronto Canada	17.99	Max: 89.59
Lin et al. (2005, 087828)	Ontario, Canada	9.59	Max: 73
Moolgavkar (2003, 051316)	Los Angeles, CA	22 (median)	Max: 86
New York State DOH (2006, 090132)	Bronx/Manhattan	15.0/16.7	NR
Peel et al. (2005, 056305)	Atlanta, GA	19.2	90th: 32.3; 98th: 39.8
Sinclair and Tolsma (2004, 088696)	Atlanta, GA	17.62	NR
Sheppard et al. (2003, 042826)	Seattle, WA	16.7	98th: 46.6
Slaughter et al. (2005, 073854)	Spokane, WA	NR	Max: 20.2 (using 90% of concentrations)
Tolbert et al. (2007, 090316)	Atlanta, GA	17.1	90th: 28.8; 98th: 38.7
Yang et al. (2004, 087488)	Vancouver, Canada	7.7	Max: 32.0
Zanobetti and Schwartz (2006, 090195)	112 U.S. cities	11.1 (Median)	95th: 26.31
$PM_{10-2.5}$			
Chen et al. (2004, 087262; 2005, 087555)	Vancouver, Canada	5.6	Max: 24.6
Fung et al. (2006, 089789)	Vancouver, Canada	5.6	Max: 27.07
Halonen et al. (2008, 189507)	Helsinki, Finland	NR; Median: 9.9	Max: 101.4
Host et al. (2008, 155852)	6 Cities France	7.0-11.0	95th: 12.5-21.0
Lin et al. (2002, 026067)	Toronto, Canada	12.17	Max: 68.00
Lin et al. (2005, 087828)	Ontario, Canada	10.86	Max: 45
New York State DOH	Bronx/Manhattan	7.69/7.10	NR
Peel et al. (2005, 056305)	Atlanta, GA	9.7	90th: 16.2
Peng et al. (2008, 156850)	108 U.S. counties	NR; Median: 9.8	75th: 15.0
Sinclair and Tolsma (2004, 088696)	Atlanta, GA	9.67	NR
Sheppard et al. (2003, 042826)	Seattle, WA	16.2	Max: 88
Slaughter et al. (2005, 073854)	Spokane, WA	NR	NR
Tolbert et al. (2007, 090316)	Atlanta, GA	9	90th: 15.1; Max: 50.3
Yang et al. (2004, 087488)	Vancouver, Canada	7.7	Max: 24.6
PM_{10}			
Andersen et al. (2007, 093201)	Copenhagen, Denmark	25/24	75th: 30 / 99th: 72
Barnett et al. (2005, 087394)	7 Cities, Australia, NZ	16.5-20.6	Max: 50.2-156.3
Chardon et al. (2007, 091308)	Paris, France	23	Max: 97.3
Chen et al. (2004, 087262; 2005, 087555)	Vancouver, Canada	13.3	Max: 52.2
Chimonas and Gessner (2007, 093261)	Anchorage, AK	27.6	Max: 421
Fung et al. (2005, 093262)	Ontario, Canada	38	Max: 248
Fung et al. (2006, 089789)	Vancouver, Canada	13.3	Max: 52.17
Gordian and Choudhury (2003, 054842)	Anchorage, AK	36.11	Max: 210.0
Jaffe et al. (2003, 041957)	Cincinnati, OH	43	Max: 90

Study	Location	Mean Concentration ($\mu g/m^3$)	Upper Percentile concentrations ($\mu g/m^3$)
Jalaludin et al. (2004, 056595)	Sydney, Australia	22.8	Max: 44.9
Lin et al. (2002, 026067)	Toronto, Canada	30.16	Max: 116.20
Lin et al. (2005, 087828)	Ontario, Canada	20.41	Max: 73
Luginaah et al. (2005, 057327)	Ontario, Canada	50.6	Max: 349
Medina-Ramon et al. (2006, 087721)	36 U.S. Cities	15.9-44.0	NR
Moolgavkar (2003, 051316)	Los Angeles, CA	22 (median)	Max: 86
Moolgavkar (2003, 051316)	Cook County, IL	35 (median)	Max: 365
Peel et al. (2005, 056305)	Atlanta, GA	27.9	Max: 44.7
Sinclair and Tolsma (2004, 088696)	Atlanta, GA	29.03	NR
Slaughter et al. (2005, 073854)	Spokane, WA	NR	Max: 41.9 (using 90% of concentrations)
Tolbert et al. (2007, 090316)	Atlanta, GA	26.6	90th: 42.8
Ulirsch et al. (2007, 091332)	Idaho	23.2	Max: 183.0
Yang et al. (2004, 087488)	Vancouver, Canada	13.3	Max: 52.2
Zanobetti (2003, 043119);Samet et al. (2000, 010269)	14 U.S. Cities	24.4-45.3	Max 94.8-605.8
UFP			
Andersen et al. (2008, 189651)	Copenhagen, Denmark	Mean particles/cm^3: 6847	99th: 19,895 particles/cm^3
Halonen et al. (2008, 189507)		NR: Median particles/cm^3: 8,203	Max: 50,990 particles/cm^3

6.3.8.5. Copollutant Models

Some studies have investigated potential confounding by copollutants through the application of multipollutant models (Figure 6-15). Several Canadian studies of respiratory hospital admissions reported larger effects for $PM_{10-2.5}$ compared to $PM_{2.5}$ that were robust to adjustment for gaseous pollutants (Chen et al., 2005, 087555; Lin et al., 2002, 026067; Yang et al., 2004, 087488). The COPD associations between $PM_{2.5}$ and $PM_{10-2.5}$ reported by Chen et al. (2004, 087262) remained positive but were diminished slightly after adjustment for NO_2. The associations reported by Ito et al. (2003, 042856) of $PM_{2.5}$ and $PM_{10-2.5}$ with pneumonia hospital admissions remained after adjustment for gases, while the association of $PM_{10-2.5}$ with COPD admissions was not robust to adjustment for O_3. Associations reported by Burnett et al. (1997, 084194), Moolgavkar et al. (2003, 042864) and Delfino et al. (1998, 093624) were not consistently robust to adjustment for gaseous copollutants. In the MCAPS study, the effect of $PM_{2.5}$ was robust to adjustment for $PM_{10-2.5}$, while the $PM_{10-2.5}$ effect on respiratory admissions was diminished after adjustment for $PM_{2.5}$ (Peng et al., 2008, 156850). Effect estimates for PM_{10} were robust to adjustment for gases in several recent studies (Andersen et al., 2007, 093201; Tolbert et al., 2007, 090316; Ulirsch et al., 2007, 091332).

Multiple pollutant analyses for other size fractions and components have been conducted in a some additional studies. PM_{10} associations with respiratory disease did not change in models also containing total PNC, nor did the association of ACP diminish after adjustment for UFP concentration(Andersen et al., 2008, 189651). Peng et al. (2009, 191998) reports an OCM effect that was robust to adjustment for other components while the associations with Ni, V, and EC were somewhat diminished in models containing multiple components.

Inconsistency across these study findings is likely due to differences in the correlation structure among pollutants as well as differing degrees of exposure measurement error.

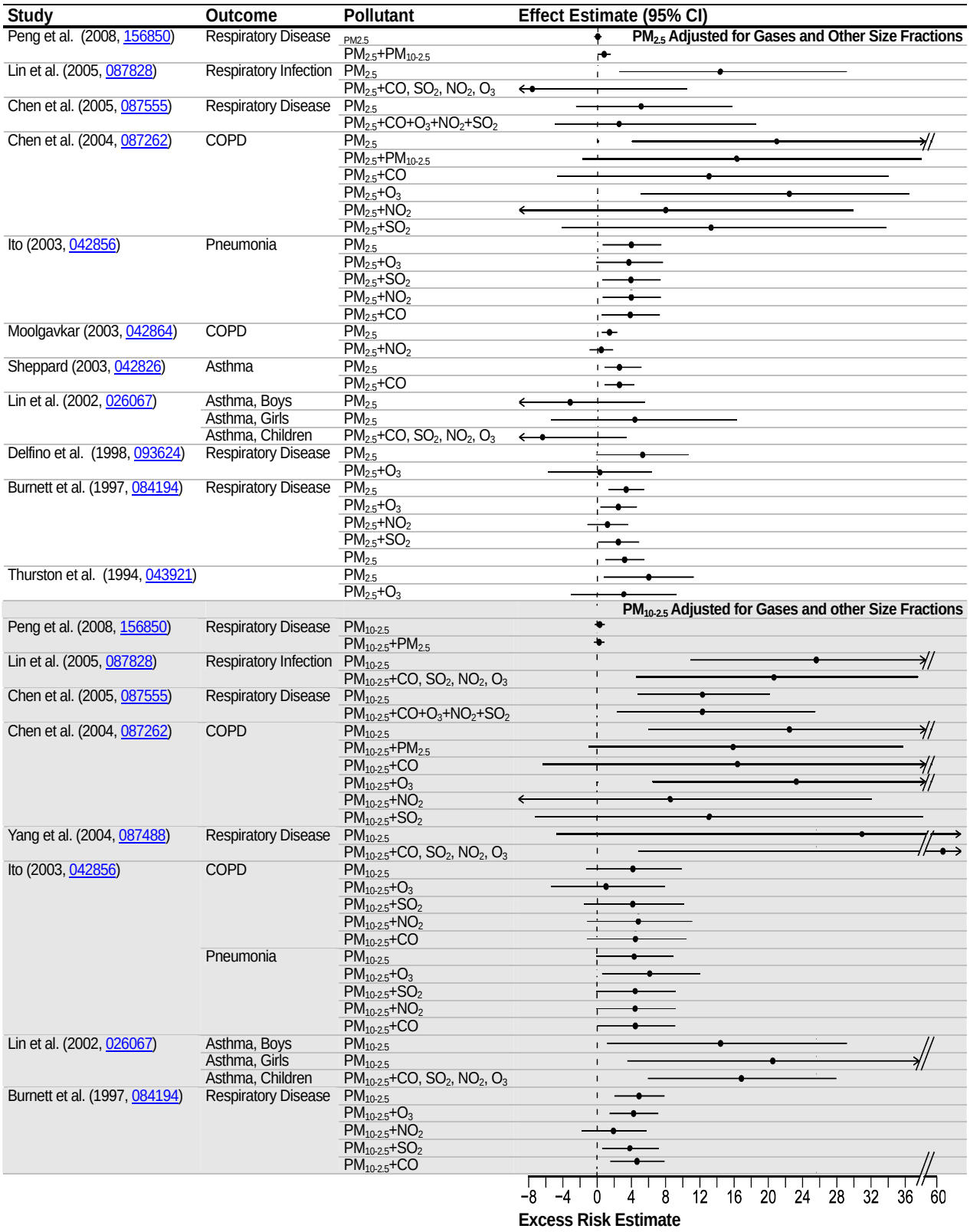


Figure 6-15. Excess risk estimates per 10 μg/m^3 increase in 24-h avg $PM_{2.5}$, and $PM_{10-2.5}$ for respiratory disease ED visits or HAs, adjusted for co-pollutants.

6.3.9. Respiratory Mortality

An evaluation of studies that examined the association between short-term exposure to $PM_{2.5}$ and $PM_{10-2.5}$ and mortality provides additional evidence for PM-related respiratory health effects. Although the primary analysis in the majority of mortality studies evaluated consists of an examination of the relationship between $PM_{2.5}$ or $PM_{10-2.5}$ and all-cause (nonaccidental) mortality, some studies have examined associations with cause-specific mortality including respiratory-related mortality.

Multicity mortality studies that examine the PM-respiratory mortality relationship on a national scale – Franklin et al. (2007, 091257): 27 U.S. cities and Zanobetti and Schwartz (2009, 188462): 112 U.S. cities – have found consistent positive associations between short-term exposure to $PM_{2.5}$ and respiratory mortality of approximately 1.68% per 10 $\mu g/m^3$ at lag 0-1 (Section 6.5). The associations observed on a national scale are consistent with those presented by Ostro et al. (2006, 087991) in a study that examined the $PM_{2.5}$-mortality relationship in nine California counties (2.2% [95% CI: 0.6-3.9] per 10 $\mu g/m^3$). An evaluation of studies that examined additional lag structures of associations found smaller respiratory mortality effect estimates when using the average of lag days 1 and 2 (1.01% [95% CI: -0.03 to 2.05] per 10 $\mu g/m^3$) (Franklin et al., 2008, 097426), and associations consistent with those observed at lag 0-1 when examining single-day lags, specifically lag 1 (1.78% [95% CI: 0.2-3.36]). Although the overall effect estimates reported in the multicity studies evaluated are consistently positive, it should be noted that a large degree of variability exists between cities when examining city-specific effect estimates potentially due to differences between cities and regional differences in $PM_{2.5}$ composition (Figure 6-25). Only a limited number of studies that examined the $PM_{2.5}$-mortality relationship have conducted analyses of potential confounders, such as gaseous copollutants, and none examined the effect of copollutants on $PM_{2.5}$ respiratory mortality risk estimates. Although the recently evaluated multicity studies did not extensively examine whether $PM_{2.5}$ mortality risk estimates are confounded by gaseous pollutants, evidence from the limited number of single-city studies evaluated in the 2004 PM AQCD (U.S. EPA, 2004, 056905) suggest that gaseous copollutants do not confound the $PM_{2.5}$-respiratory mortality association. This is further supported by studies that examined the PM_{10}-mortality relationship in both the 2004 PM AQCD (U.S. EPA, 2004, 056905) and this review. Overall, the respiratory $PM_{2.5}$ effects observed in the new studies evaluated were larger, but less precise than those reported for all-cause (nonaccidental) mortality (Section 6.5), and are consistent with the effect estimates observed in the single- and multicity studies evaluated in the 2004 PM AQCD (U.S. EPA, 2004, 056905).

Zanobetti and Schwartz (2009, 188462) also examined $PM_{10-2.5}$ mortality associations in 47 U.S. cities and found evidence for respiratory mortality effects (1.16% [95% CI: 0.43-1.89] per 10 $\mu g/m^3$ at lag 0-1), which are somewhat larger than those reported for all-cause (nonaccidental) mortality (0.46% [95% CI: 0.21-0.671] per 10 $\mu g/m^3$). In addition, Zanobetti and Schwartz (2009, 188462) reported seasonal (i.e., larger in spring) and regional differences in $PM_{10-2.5}$ respiratory mortality risk estimates. However, single-city studies conducted in Atlanta, GA (Klemm et al., 2004, 056585) and Vancouver, Canada ((Villeneuve et al., 2003, 055051) reported no associations between short-term exposure to $PM_{10-2.5}$ and respiratory mortality. The difference in the results observed between the multi- and single-city studies could be due to a variety of factors including differences between cities and compositional differences in $PM_{10-2.5}$ across regions (Figure 6-30). Only a small number of studies have examined potential confounding by gaseous copollutants or the influence of model specification on $PM_{10-2.5}$ mortality risk estimates, but the effects are relatively consistent with those studies evaluated in the 2004 PM AQCD (U.S. EPA, 2004, 056905).

6.3.10. Summary and Causal Determinations

6.3.10.1. $PM_{2.5}$

Several studies of the effect of $PM_{2.5}$ on hospital admissions for respiratory diseases reviewed in the 2004 AQCD (U.S. EPA, 2004, 056905) reported positive associations for several diseases. The 2004 AQCD (U.S. EPA, 2004, 056905) presented limited epidemiologic evidence of $PM_{2.5}$ being associated with respiratory symptoms (including cough, phlegm, difficulty breathing, and bronchodilator use); observations for $PM_{2.5}$ were positive, with slightly larger effects for $PM_{2.5}$ than

for PM_{10}. In addition, mortality studies reported relatively higher $PM_{2.5}$ risk estimates for respiratory-related mortality compared to all-cause (nonaccidental) mortality. Controlled human exposure studies did not provide support for effects of CAPs on respiratory symptoms. Small decrements in peak flow for both $PM_{2.5}$ and PM_{10} in asthmatics and nonasthmatics were reported in epidemiologic studies included in the 2004 PM AQCD (U.S. EPA, 2004, 056905), whereas controlled human exposure and animal toxicological studies reported few or no effects on pulmonary function with inhalation of CAPs. In addition, the 2004 PM AQCD (U.S. EPA, 2004, 056905) presented a number of controlled human exposure and toxicological studies that reported mild pulmonary inflammation following exposure to $PM_{2.5}$ CAPs and DE or DE particles, as well as ROFA or other metal-containing PM in animals. The 2004 PM AQCD (U.S. EPA, 2004, 056905) described controlled human exposure studies showing increases in allergic responses among previously sensitized atopic subjects after short-term exposure to DE particles. These observations were supported by many toxicological studies that added to existing evidence demonstrating that various types of PM could promote allergic disease and exacerbate allergic asthma in animal models. Toxicological studies also indicated that $PM_{2.5}$ increased susceptibility to respiratory infection.

Overall, in recent studies $PM_{2.5}$ effects on respiratory hospitalizations and ED visits have been consistently observed. Most effect estimates were in the range of ~1-4% and were observed in areas with mean 24-h $PM_{2.5}$ concentrations between 6.1 and 22 $\mu g/m^3$. Further, recent studies have focused on increasingly specific disease endpoints such as asthma, COPD, and respiratory infection. The strongest recent evidence of an association comes from large multicity studies of COPD, respiratory tract infection, and all respiratory diseases among Medicare recipients (≥65 yr) (Bell et al., 2008, 156266; Dominici et al., 2006, 088398). Studies of children have also found evidence of an effect of $PM_{2.5}$ on hospitalization for all respiratory diseases, including asthma and respiratory infection. However, many of these effect estimates are imprecise, their magnitude and statistical significance are sensitive to choice of lag, and some null associations were observed. Although the association of $PM_{2.5}$ with pediatric asthma was not examined specifically, it is noteworthy that one of the strongest associations observed in the Atlanta-based SOPHIA study was between PM_{10} and pediatric asthma visits; $PM_{2.5}$ makes up a large proportion of PM_{10} in Atlanta (Peel et al., 2005, 056305). Positive associations between $PM_{2.5}$ (or PM_{10}) and hospital admissions for respiratory infection (Figure 6-14) are supported by animal toxicological studies which add to previous findings of increased susceptibility to infection following exposure to $PM_{2.5}$. These include studies demonstrating reduced clearance of bacteria (*Pseudomonas, Listeria*) or enhanced pathogenesis of viruses (influenza, RSV) after exposure to DE or ROFA.

Epidemiologic studies that examined the association between $PM_{2.5}$ and mortality provide additional evidence for $PM_{2.5}$-related respiratory effects (Section 6.3.9). The multicity studies evaluated found consistent, precise positive associations between short-term exposure to $PM_{2.5}$ and respiratory mortality ranging from 1.67 to 2.20% increases at mean 24-h $PM_{2.5}$ avg concentrations above 13 $\mu g/m^3$. Although only a limited number of studies examined potential confounders of the $PM_{2.5}$-respiratory mortality relationship, the studies evaluated in both this review and the 2004 PM AQCD (U.S. EPA, 2004, 056905) support an association between short-term exposure to $PM_{2.5}$ and respiratory mortality.

Epidemiologic studies of asthmatic children have observed increases in respiratory symptoms and asthma medication use associated with higher $PM_{2.5}$ or PM_{10} concentrations. Associations with respiratory symptoms and medication use are less consistent among asthmatic adults, and there is no evidence to suggest an association between respiratory symptoms with $PM_{2.5}$ among healthy individuals. In addition, respiratory symptoms have not been reported following controlled exposures to $PM_{2.5}$ among healthy or health-compromised adults (Section 6.3.1.2).

Although more recent epidemiologic studies of pulmonary function and $PM_{2.5}$ have yielded somewhat inconsistent results, the majority of studies have found an association between $PM_{2.5}$ concentration and FEV_1, PEF, and/or MMEF. In asthmatic children, a 10 $\mu g/m^3$ increase in $PM_{2.5}$ is associated with a decrease in FEV_1 ranging from 1-3.4% (Section 6.3.2.1). A limited number of controlled human exposure studies have reported small decreases in arterial oxygen saturation and MMEF following exposure to $PM_{2.5}$ CAPs with more pronounced effects observed in healthy adults than in asthmatics or older adults with COPD (Section 6.3.2.2). In toxicological studies, changes in pulmonary function have been observed in healthy and compromised rodents after inhalation exposures to CAPs from a variety of locations or DE. A role for the PM fraction of DE is supported by altered pulmonary function in healthy rats after IT instillation of DE particles (Section 6.3.2.3).

Several lines of evidence suggest that $PM_{2.5}$ promotes and exacerbates allergic disease, which often underlies asthma (Section 6.3.6). Although epidemiologic studies examining specific allergic outcomes and short-term exposure to PM are relatively rare, the available studies, conducted primarily in Europe, positively associate $PM_{2.5}$ and PM_{10} with allergic rhinitis or hay fever and skin prick reactivity to allergens. Short-term exposure to DE particles in controlled human exposure studies has been shown to increase the allergic response among previously sensitized atopic subjects, as well as induce de novo sensitization to an antigen. Toxicological studies continue to provide evidence that $PM_{2.5}$, in the form of CAPs, resuspended DE particles, or DE, but not wood smoke, spurs and intensifies allergic responses in rodents. Proposed mechanisms for these effects include mediation by neurotrophins and oxidative stress, and one study demonstrated that effects were mediated at the epigenetic level (Liu et al., 2008, 156709).

A large body of evidence, primarily from toxicological studies, indicates that various forms of PM induce oxidative stress, pulmonary injury, and inflammation. Notably, CAPs from a variety of locations induce inflammatory responses in rodent models, although this generally requires multiday exposures. The toxicology findings are consistent with several recent epidemiologic studies of $PM_{2.5}$ and the inflammatory marker eNO, which reported statistically significant, positive effect estimates with some inconsistency in the lag times and use of medication. In asthmatic children, a 10 $\mu g/m^3$ increase in $PM_{2.5}$ is associated with an increase in eNO ranging from 0.46 to 6.99 ppb. Several new controlled human exposure studies report traffic or DE-induced increases in markers of inflammation (e.g., neutrophils and IL-8) in BALF from healthy adults. Recent studies have provided additional evidence in support of a pulmonary oxidative response to DE in humans, including induction of redox-sensitive transcription factors and increased urate and GSH concentrations in nasal lavage. In addition, exposure to wood smoke has recently been demonstrated to increase the levels of eNO and malondialdehyde in breath condensate of healthy adults (Barregard et al., 2008, 155675). Preliminary findings indicate little to no pulmonary injury in humans following controlled exposures to $PM_{2.5}$ urban traffic particles or DE, in contrast to a number of toxicological studies demonstrating injury with CAPs or DE (Sections 6.3.5.2 and 6.3.5.3, respectively).

Recent studies have reported associations of hospital admissions, ED or urgent care visits for several respiratory diseases with $PM_{2.5}$ components and sources including Ni, V, OC and EC, wood smoke and traffic emissions, in studies of both children and adults. Delfino et al. (2003, 090941; 2006, 090745) found positive associations between EC and OC components of PM and asthma symptoms and between EC and eNO. Particle composition and/or source also appears to heavily influence the increase in markers of pulmonary inflammation demonstrated in studies of controlled human exposures to $PM_{2.5}$. For example, whereas exposures to $PM_{2.5}$ CAPs from Chapel Hill, NC have been shown to increase BALF neutrophils in healthy adults, no such effects have been observed in similar studies conducted in Los Angeles. In addition, differential inflammatory responses have been observed following bronchial instillation of particles collected at different times or from different areas (Section 6.3.3.2). One new study found that the increased airway neutrophils previously observed by Ghio et al. (2000, 012140) in human volunteers after Chapel Hill CAPs exposure could be largely attributed to the content of sulfate, Fe, and Se in the soluble fraction (Huang et al., 2003, 087377).

In summary, new evidence of ED visits and hospital admissions builds upon the positive and statistically significant evidence presented in the 2004 PM AQCD to support a consistent association with ambient concentrations of $PM_{2.5}$. Most effect estimates with respiratory hospitalizations and ED visits were in the range of ~1-4% and were observed in areas with mean 24-h $PM_{2.5}$ concentrations between 6.1 and 22 $\mu g/m^3$. The evidence for $PM_{2.5}$-induced respiratory effects is strengthened by similar hospital admissions and ED visit associations for PM_{10}, along with the consistent positive associations observed between $PM_{2.5}$ and respiratory mortality in multicity studies. Panel studies also indicate associations with $PM_{2.5}$ and respiratory symptoms, pulmonary function, and pulmonary inflammation among asthmatic children. Further support for these observations is provided by recent controlled human exposure studies in adults demonstrating increased markers of pulmonary inflammation following DE and other traffic-related exposures, oxidative responses to DE and wood smoke, and exacerbations of allergic responses and allergic sensitization following exposure to DE particles. Although not consistent across studies, some controlled human exposure studies have reported small decrements in various measures of pulmonary function following exposures to $PM_{2.5}$. Numerous toxicological studies demonstrating a wide range of responses provide biological plausibility for the associations between $PM_{2.5}$ and respiratory morbidity observed in epidemiologic studies. Altered pulmonary function, mild pulmonary inflammation and injury, oxidative responses,

AHR in allergic and non-allergic animals, exacerbations of allergic responses and increased susceptibility to infections were observed in a large number of studies involving exposure to CAPs, DE, other traffic-related PM, and wood smoke. The evidence for an effect of $PM_{2.5}$ on respiratory outcomes is somewhat restricted by limited coherence between some of the findings from epidemiologic and controlled human exposure studies for the specific health outcomes reported and the sub-populations in which those health outcomes occur. For instance, although there is evidence for respiratory symptoms among asthmatic children in epidemiologic panel studies, the studies of hospital admissions and ED visits provide more evidence for effects from COPD and respiratory infections than for asthma. Additionally, controlled human exposure studies report greater effects in healthy adults when compared to asthmatics or those suffering from COPD. Finally, there is limited information which could explain the relationship between the clinical and subclinical respiratory outcomes observed and the magnitude of the $PM_{2.5}$-respiratory mortality associations reported. Therefore, the evidence is sufficient to conclude that a **causal relationship is likely to exist between short-term $PM_{2.5}$ exposures and respiratory effects.**

6.3.10.2. $PM_{10-2.5}$

The 2004 PM AQCD (U.S. EPA, 2004, 056905) presented the results from several epidemiologic studies of respiratory symptoms and $PM_{10-2.5}$, which provided limited evidence for cough and effects on morning PEF. Toxicology data for $PM_{10-2.5}$ were extremely limited, and there were no controlled human exposure studies presented in the 2004 PM AQCD (U.S. EPA, 2004, 056905) that evaluated the effect of $PM_{10-2.5}$ on respiratory symptoms, pulmonary function, or inflammation. Epidemiologic studies of the effect of $PM_{10-2.5}$ on hospitalizations or ED visits for respiratory diseases (i.e., pneumonia, COPD and respiratory diseases combined) reviewed in the 2004 AQCD (U.S. EPA, 2004, 056905) reported positive associations. Additionally, the few mortality studies that examined cause-specific mortality suggested somewhat larger risk estimates for respiratory mortality compared to all-cause (nonaccidental) mortality.

Several new studies report associations between $PM_{10-2.5}$ and respiratory hospitalizations with the most consistent evidence among children (Figure 6-10 through Figure 6-14), however, effect estimates are imprecise. Although a number of studies provide evidence of respiratory effects in older adults, a recent analysis of MCAPS data reports that weak associations of $PM_{10-2.5}$ with respiratory hospitalizations are further diminished after adjustment for $PM_{2.5}$. It is not clear that $PM_{10-2.5}$ estimates across all populations and regions are confounded by $PM_{2.5}$. An examination of $PM_{10-2.5}$ mortality associations on a national scale found a strong association between $PM_{10-2.5}$ and respiratory mortality, but this association varied when examining city-specific risk estimates (Zanobetti and Schwartz, 2009, 188462). The regional variability in $PM_{10-2.5}$ mortality risk estimates is further confirmed by the negative associations reported in the single-city studies evaluated. However, there is greater spatial heterogeneity in $PM_{10-2.5}$ compared to $PM_{2.5}$ and consequently greater potential for exposure measurement error in epidemiologic studies relying on central site monitors. This exposure measurement error may bias effect estimates toward the null and could explain some of the regional variability in the observed associations between $PM_{10-2.5}$ and respiratory morbidity and mortality.

Mar et al. (2004, 057309) provide evidence for an association with increased respiratory symptoms in asthmatic children, but not asthmatic adults. Consistent with this, controlled human exposures to $PM_{10-2.5}$ have not been observed to affect lung function or respiratory symptoms in healthy or asthmatic adults. However, increases in markers of pulmonary inflammation have been demonstrated in healthy volunteers. In these studies, an increase in neutrophils in BALF or induced sputum was observed, with additional evidence of alveolar macrophage activation associated with biological components of $PM_{10-2.5}$ (i.e., endotoxin). Toxicological studies using inhalation exposures are still lacking, but pulmonary injury and inflammation have been observed in animals after IT instillation exposure and both rural and urban $PM_{10-2.5}$ have induced these responses. In some cases, $PM_{10-2.5}$ from urban air was more potent than $PM_{2.5}$ (Section 6.3.3.3). $PM_{10-2.5}$ respiratory effects may be due to components other than endotoxin (Wegesser and Last, 2008, 190506).

Overall, the most compelling new evidence comes from a number of recent epidemiology studies conducted in Canada and France showing significant associations between respiratory ED visits or hospitalization and short-term exposure to $PM_{10-2.5}$. Effects have been observed in areas where the mean 24-h avg $PM_{10-2.5}$ concentrations ranged from 7.4 to 13.0 $\mu g/m^3$. The strongest relationships were observed among children, whereas studies of adults and older adults show less

consistent evidence of an association. While controlled human exposure studies have not observed an effect on lung function or respiratory symptoms in healthy or asthmatic adults in response to exposure to $PM_{10-2.5}$, healthy volunteers have exhibited increases in markers of pulmonary inflammation. Toxicological studies using inhalation exposures are still lacking, but pulmonary injury has been observed in animals after IT instillation exposure to both rural and urban $PM_{10-2.5}$, which may not be entirely attributed to endotoxin. Overall, epidemiologic studies, along with the limited number of controlled human exposure and toxicological studies that examined $PM_{10-2.5}$ and respiratory outcomes, provide evidence that is **suggestive of a causal relationship between short-term $PM_{10-2.5}$ exposures and respiratory effects.**

6.3.10.3. UFPs

The 2004 PM AQCD (U.S. EPA, 2004, 056905) included a few epidemiologic and controlled human exposure studies that examined the effect of UFPs on respiratory morbidity. Collectively these studies provided limited evidence of an association between UFPs and respiratory symptoms, medication use, inflammation, and decreased pulmonary function. Evidence from toxicological studies presented in the 2004 AQCD, although limited, suggested that exposure via inhalation to high concentrations of UF TiO_2 may increase pulmonary inflammation in healthy rodents. Since the publication of the 2004 AQCD there has been an increased focus among the scientific community on gaining a better understanding of the potential health effects associated with exposure to UFPs (U.S. EPA, 2004, 056905). A number of recent controlled human exposure and toxicological studies have evaluated respiratory responses following exposures to UF CAPs, model particles, and fresh diesel or gasoline exhaust. While DE contains both $PM_{2.5}$ and UFPs, the MMAD is typically $\leq$ 100 nm, and therefore the results of these studies may be used to support findings from studies utilizing other sources of UFP.

UFPs were associated with incident wheezing symptoms among infants (<1 yr) in a study conducted in Copenhagen, Denmark, where the mean UFP number concentration was 8,092 particles/cm^3, though this association did not persist for children between ages 1-3 yr (Andersen et al., 2008, 096150). Recent epidemiologic studies conducted in Copenhagen, Denmark and Helsinki, Finland, reported associations between UFPs and hospital admissions or ED visits for respiratory diseases, including childhood asthma and pneumonia in adults (Andersen et al., 2008, 189651; Halonen et al., 2008, 189507). The median UFP number concentrations in Copenhagen and Helsinki were 6,243 particles/cm^3 and 8,203 particles/cm^3, respectively. Associations between UFP and ED visits for respiratory diseases were not observed in the Atlanta-based SOPHIA study, where the mean UFP number concentration was 38,000 particles/cm^3.

A single recent epidemiologic study has examined associations between UFP and pulmonary function, and observed that asthmatic adults exhibited decreased lung function after exposure to diesel traffic pollution in London (McCreanor et al., 2007, 092841). Two new controlled human exposure studies have reported small decreases in pulmonary function among healthy adults approximately following exposure to Los Angeles UF CAPs or UF EC (Gong et al., 2008, 156483; Pietropaoli et al., 2004, 156025). Exposures to lower concentrations of UF CAPs from Chapel Hill, NC did not result in any changes in pulmonary function (Samet et al., 2009, 191913). However, while Gong et al. (2008, 156483) did not observe any effect of exposure to UF CAPs on markers of pulmonary inflammation, Samet et al. (2009, 191913) reported an UF CAPs-induced increase in IL-8 in BALF at 18 hours post-exposure. A limited number of controlled human exposure studies have also demonstrated increases in the pulmonary inflammatory response following exposure to UF and $PM_{2.5}$ from DE, which may be enhanced by exposure to O_3 (Section 6.3.3.2).

Altered pulmonary function and inflammation have also been observed in toxicological studies of DE and UF model particles (Sections 6.3.2.3 and 6.3.3.3). In one rat model, pulmonary inflammation was observed after exposure to UF CB at concentrations as low as 180 $\mu g/m^3$ (Harder et al., 2005, 087371). However, inflammatory responses vary considerably depending on the animal model, dose, test material, and exposure duration. In cases where pulmonary inflammation was not observed, oxidative stress was often evident (Section 6.3.4.2). Oxidative stress is a major mechanism by which PM may exert effects (Chapter 5), and some toxicological studies suggest that UFPs are more potent than $PM_{2.5}$, possibly due to a higher proportion of pro-oxidative OC and PAH content and greater surface area with which to deliver these components.

The relationship between exposure to UFP and pulmonary injury has not been widely examined. No association with pulmonary injury biomarkers was found for UFP in a European

multicity epidemiologic study (Timonen et al., 2004, 087915). In controlled human exposure studies, UFP from wood smoke resulted in significantly increased markers of injury in healthy adults, but this effect was not evident in COPD sufferers exposed to DE (Section 6.3.5.2). Exposure of neonatal rats to UF iron-soot particles resulted in a significantly reduced rate of cell proliferation in the proximal alveolar region, which suggests that postnatal lung development may be susceptible to air pollution, consistent with impaired lung function growth observed in children (Pinkerton et al., 2004, 087465). In contrast, no histopathological responses were evident in adult mice exposed to UF iron-soot particles (Last et al., 2004, 097334). Some toxicological studies have reported pulmonary injury after inhalation of DE or gasoline exhaust (Section 6.3.5.3). In studies that evaluated ambient PM size fractions from a variety of European and U.S. cities for relative toxicity in rodents following IT instillation exposure, UFPs were generally less injurious than the larger size fractions. However, the UF fraction of Montana coal fly ash induced greater injury and inflammation than the $PM_{10-2.5}$ fraction (Gilmour et al., 2004, 057420).

In rodent studies, UF CAPs appeared to be more potent than $PM_{2.5}$ CAPs in inducing and exacerbating allergic responses (Section 6.3.6.3). In addition to CAPs, UF CB or iron-soot particles, but not particles from fresh gasoline exhaust, have been shown to induce or exacerbate allergic responses in mice. Bacterial clearance appears unaffected by hardwood smoke or gasoline engine exhaust. However, host defenses are impaired by DE, which has been shown to reduce bacterial clearance, impair defenses against viral infection, and reduce thymus weight, indicating systemic immunosuppression.

Several toxicological studies demonstrated oxidative, inflammatory, and allergic responses following exposure to a number of different UFP types, including model particles (i.e., CB, iron-soot particles), CAPs, and DE. Although the respiratory effects of controlled exposures to UFPs have not been extensively examined in humans, two controlled human exposure studies have observed small UFP-induced decreases in pulmonary function; however, no increases in respiratory symptoms have been reported. In a limited number of studies, markers of pulmonary inflammation were increased following controlled human exposures to UFP, which has been most consistently observed in studies using fresh DE. In both controlled human exposure and animal toxicological studies using fresh DE, the relative contributions of gaseous copollutants to the observed effects remain unresolved. However, similar effects are reported using resuspended DE particles, and although not UFPs, these particles can be assumed to have similar composition. A limited number of epidemiologic studies have provided some evidence of an association between short-term exposure to UFPs and respiratory symptoms, as well as asthma hospitalizations. However, the interpretation of these findings is difficult due to the spatial variability of UFPs. Thus, the current collective evidence is **suggestive of a causal relationship between short-term UFP exposure and respiratory effects.**

6.4. Central Nervous System Effects

While evidence of an effect of PM on the CNS was not presented in the 2004 PM AQCD (U.S. EPA, 2004, 056905), a limited number of recent epidemiologic, controlled human exposure and toxicological studies provide some evidence that exposure to PM may be associated with changes in neurological function. The majority of studies included in this section are of short-term exposure, however, there are also a few studies of long-term exposure. As CNS effects of PM are a newly emerging area, and since there are so few studies, all studies that evaluate CNS responses are included in this section.

6.4.1. Epidemiologic Studies

Chen and Schwartz (2009, 179945) used extant data on CNS function from the Third National Health and Nutrition Examination Survey (NHANES III) to characterize the association between cognitive function in adults (ages 20-59 yr) and exposure to ambient air pollution. Three computerized neurobehavioral tests were used: a simple reaction time test (SRTT), a basic measure of visuomotor speed; a symbol digit substitution test (SDST) on coding ability; and a serial digit learning test (SDLT) on attention and short-term memory. The authors used annual PM_{10} concentrations to approximate the long-term exposure to ambient air pollution prior to the

NHANES-III examination. Increased PM_{10} levels were associated with reduced performance in all three neurobehavioral tests, and were particularly strong for SDST and SDLT scores in models adjusted for age and sex. However, after additional adjustment for race/ethnicity or SES, the magnitudes of these associations were greatly diminished and largely null. It is possible that the observed associations disappeared after adjustment for race/ethnicity and SES due to the potential confounding by residential segregation of ethnic minorities and poorer people in areas with high levels of ambient PM_{10} concentrations.

Two additional epidemiologic studies evaluated the effect of ambient PM on the CNS (Calderón-Garcidueñas et al., 2008, 156317; Suglia et al., 2008, 157027). These studies examined long-term exposure to non-specific PM indicators and are detailed in Annex E.

6.4.2. Controlled Human Exposure Studies

In a recent controlled human exposure study, Cruts et al. (2008, 156374) exposed 10 healthy males (18-39 yr) to filtered air and dilute DE (300 μg/m^3 PM) for 1 h using a randomized crossover study design. Changes in brain activity were measured during and following exposure using quantitative electroencephalography (QEEG). Exposure to DE was observed to significantly increase the median power frequency (MPF) in the frontal cortex during exposure, as well as in the hour following the completion of the exposure. While this study does provide some evidence of an acute cortical stress response to DE, it is important to note that the QEEG findings are very nonspecific, and could have been caused by factors other than diesel PM such as DE gases (e.g., CO, NO and NO_2) or the odor of the DE.

6.4.3. Toxicological Studies

Evidence is mounting that the CNS may be a critical target of PM and that adverse health effects may result from PM exposure. Whether these health effects are a direct or indirect effect of PM has not yet been established. One hypothesis suggests that UFPs which deposit onto nasal olfactory epithelium enter the CNS by axonal olfactory transport to the olfactory bulb and lead to a cascade of effects involving inflammatory cytokines and ROS. An increased potential for neurodegenerative processes may ensue. Evidence for translocation of UFPs to the olfactory bulb via olfactory neurons is discussed in Chapter 4, but its relevance to CNS health effects is unknown. Another hypothesis suggests that brain inflammation occurs secondarily to PM-mediated systemic inflammation. Finally, it has been suggested that PM-stimulation of the ANS via respiratory tract receptors results in inflammatory or other effects in the CNS. This is an emerging field with many unknowns.

6.4.3.1. Urban Air

Calderon-Garciduenas et al. (2003, 156316) conducted a long-term observational study in mongrel dogs from Mexico City and Tlaxcala. DNA damage and inflammation in the brain and respiratory tract were evaluated in dogs living in Mexico City (exposed group) and dogs living in Tlaxcala (control group). These cities are similar in altitude but differ in air pollutant levels. Measurements of air pollutant levels were presented only for Mexico City, the more polluted city. Statistically significant greater levels of apurinic/apyrimidinic sites (an indicator of DNA damage) were observed in the olfactory bulbs and hippocampus of Mexico City dogs compared with controls. These differences were not seen in other brain regions examined or in nasal respiratory epithelium. In addition, Mexico City dogs demonstrated greater histopathological changes in the respiratory and olfactory epithelium of the nasal cavity compared with controls. Immunohistochemical staining of brain tissue from the Mexico City dogs demonstrated greater immunoreactivity for NF-κB, iNOS, cyclooxygenase-2, glial fibrillatory acidic protein (GFAP), ApoE, amyloid precursor product and β-amyloid compared with controls. These results are indicative of inflammation and stress protein responses. This study has several limitations given that the dogs were of mixed breeds and of variable ages and that there was no standardization of exposures or diets. However results suggest a possible relationship between air pollution and brain inflammation.

6.4.3.2. CAPs

Several new inhalation studies have provided evidence of CNS effects due to ambient PM exposures. In one study, Campbell et al. (2005, 087217) exposed OVA-sensitized BALB/c mice to filtered air or near-highway Los Angeles CAPs (a 20-fold concentration of $PM_{2.5}$+UFPs or UFPs only; mean exposure concentration UFPs 282.5 μg/m^3 and $PM_{2.5}$ 441.7 μg/m^3) for 4 h/day and 5 days/wk over a 2-wk period. The animals were subsequently challenged with OVA to elicit an allergic response in the lungs; brain tissue was obtained one day later. Exposure to CAPs, but not filtered air, resulted in activation of the immune-related transcription factor NF-κB and upregulation of the cytokines TNF-α, and IL-1α in the brain, demonstrating pro-inflammatory responses that could contribute to neurodegenerative disease. While this study demonstrates CAPs effects in an allergic animal model, it is not known whether these responses also occur in non-allergic animals.

In a second study, control or OVA-sensitized and challenged Brown Norway rats were exposed for 8 h to filtered air or $PM_{2.5}$ CAPs (500 μg/m^3) in Grand Rapids, MI (Sirivelu et al., 2006, 111151). Brain tissue was obtained 1 day later. CAPs exposure resulted in brain region-specific modulation of neurotransmitters. In animals which were not pretreated with OVA, statistically significant increases in norepinephrine were observed in the paraventricular nucleus and olfactory bulb of CAPs-exposed rats compared with filtered air controls. In animals which were pretreated with OVA, a statistically significant increase in dopamine was observed in the medial preoptic area in CAPs-exposed rats compared with controls. Furthermore, exposure to CAPs resulted in a statistically significant increase in serum corticosterone. These data suggest that the hypothalamo-pituitary-adrenal axis (i.e., stress axis) may be activated by PM exposure, causing aggravation of allergic airway disease. The authors discuss the possible role of the olfactory bulb in mediating neuroendocrine control of autonomic activities involved in respiratory and cardiovascular functions; however these relationships require clarification.

Pro-inflammatory responses were examined in a subchronic CAPs study involving normal (C57BL/6J) and ApoE$^{-/-}$ mice (Kleinman et al., 2008, 190074). Mice were exposed to filtered air or to two concentrations of UF CAPs from a near-highway area of central Los Angeles (average of 30.4 and 114.2 μg/m^3) for 5 h/day and 3 days/wk over a 6-wk period. Brain tissue was harvested one day after the last exposure and cortical samples prepared. CAPs exposure resulted in activation of transcription factors, with a dose-dependent increase observed for AP-1 and an increase in NF-κB observed at the higher concentration. Increased levels of GFAP (representing activation of astrocytes) and phosphorylated JNK (representing MAP kinase activation) were observed at the lower but not higher concentration of CAPs. No changes were observed in levels of or activation of the other MAP kinases p38 and ERK or of IκB. These findings provide evidence that inhalation of CAPs can lead to activation of cell signaling pathways involved in upregulation of pro-inflammatory cytokine genes in the cortical region of the mouse brain.

In another study utilizing normal (C57BL/6) and ApoE$^{-/-}$ mice, brain histopathology was examined following a 4-month chronic exposure to $PM_{2.5}$ CAPs from Tuxedo, NY (March, April or May through September 2003) (Veronesi et al., 2005, 087481). The average $PM_{2.5}$ exposure concentration was 110 μg/m^3. CAPs exposure resulted in a statistically significant decrease in dopaminergic neurons, measured by tyrosine hydroxylase immunoreactivity, in the substantia nigra of ApoE$^{-/-}$ mice but not in control mice. This population of neurons is targeted in neurodegenerative diseases such as Parkinson's. Furthermore, a statistically significant increase in GFAP immunoreactivity, a marker for astrocytes, was observed in the nucleus compacta of CAPs-exposed ApoE$^{-/-}$ mice compared to air-exposed ApoE$^{-/-}$ mice. These results suggest that the ApoE$^{-/-}$ mice, a genetic model involving increased oxidative stress, are susceptible to PM-induced neurodegeneration. Evidence for brain oxidative stress has also been found in normal animals following IT instillation of high concentrations of $PM_{2.5}$ from Taiyuan, China (Liu and Meng, 2005, 088650) and of gasoline exhaust (Che et al., 2007, 096460) and following chronic exposure to ROFA by intranasal instillation (Zanchi et al., 2008, 157173).

6.4.3.3. Diesel Exhaust

A recent study tested the effects of DE inhalation on spatial learning and memory function-related gene expression in the hippocampus (Win-Shwe et al., 2008, 190146). Male BALB/c mice were exposed to DE (148.86 μg/m^3 PM) for 5 h/day and 5 day/wk over a 4-wk period. Particle size was 26.21±1.50 nm and PNC was $1.92\times10^6 \pm 6.18\times10^4$ particles/m^3. Concentrations of gases were

3.27 ppm CO, 0.01 ppm SO_2, 0.53 ppm NO_2, 0.98 ppm NO and 0.07 ppm CO_2. Half of the animals were injected i.p. once per week with lipoteichoic acid (LTA), a bacterial cell wall component used to induce systemic inflammation. The ability of the mice to perform spatial learning tasks was examined the day after the final exposure to DE and on two subsequent days. Impaired acquisition of spatial learning was observed in DE-exposed mice on the first day and on all three days in DE-exposed mice that had also been treated with LTA. LTA by itself had no effect. Since the NMDA (a type of neurotransmitter) receptors in the hippocampus play an important role in spatial learning ability, mice were sacrificed and total RNA from hippocampus was extracted and analyzed for expression of NMDA receptor subunits. DE exposure resulted in a statistically significant increase in the expression of one subunit while the combined exposure to DE and LTA resulted in statistically significant increases in the expression of three subunits compared with controls. The expression of pro-inflammatory cytokines was also examined in the hippocampus. DE exposure resulted in a statistically significant increase in TNF-α mRNA, while LTA exposure resulted in a statistically significant increase IL-1β mRNA compared with controls. Neither exposure altered the expression of HO-1. These results demonstrated that subchronic exposure to UF-rich DE resulted in impaired spatial learning and altered expression of hippocampal genes involved in memory function and inflammation. These responses were modulated by systemic inflammation.

6.4.3.4. Summary of Toxicological Study Findings of CNS Effects

In summary, PM may produce adverse effects in the CNS by direct or indirect mechanisms which are at present incompletely understood. Two recent short-term $PM_{2.5}$ CAPs inhalation studies demonstrated pro-inflammatory responses in the brain and brain region-specific modulation of neurotransmitters and suggest the involvement of neuroimmunological pathways. One recent chronic $PM_{2.5}$ CAPs inhalation study demonstrated loss of dopaminergic neurons in the substantia nigra and suggested that oxidative stress contributes to neurodegeneration. Veronesi et al. (2005, 087481) have noted that the brain is very vulnerable to the oxidative stress induced by PM due to the brain's high energy demands, low levels of endogenous free radical scavengers, and high content of lipids and proteins. PM-mediated upregulation of inflammatory cytokines and mediators may also contribute to neurodegeneration. In fact, a recent subchronic study involving UF CAPs demonstrated the activation of cell signaling pathways associated with upregulation of pro-inflammatory cytokines in brain cortical regions. Furthermore, a subchronic study involving UF-rich DE demonstrated impaired spatial learning and altered expression of pro-inflammatory and neurotransmitter receptor genes in the hippocampus. Further investigations are required to delineate mechanisms involved in these responses.

6.4.4. Summary and Causal Determination

Recent animal toxicological studies involving acute or chronic CAPs exposure have demonstrated pro-inflammatory responses in the brain, brain region-specific modulation of neurotransmitters and loss of dopaminergic neurons in the substantia nigra (Campbell et al., 2005, 087217; Kleinman et al., 2008, 190074; Sirivelu et al., 2006, 111151; Veronesi et al., 2005, 087481). However, the mechanisms underlying these effects need to be delineated. A single controlled human exposure study provides some evidence of an acute cortical stress response to DE, though these findings are nonspecific and could have been caused by DE gases rather than DE particles (Cruts et al., 2008, 156374). Similar consideration is warranted for the single animal toxicological study involving DE which demonstrated impaired spatial learning and altered expression of pro-inflammatory and neurotransmitter genes in the hippocampus following subchronic exposure (Win-Shwe et al., 2008, 190146). The single epidemiology study that examined CNS outcomes did not find associations between long-term exposure to PM_{10} and cognitive function in adults after adjustment for race/ethnicity or SES (Chen and Schwartz, 2009, 179945). Though the effect of ambient air pollution on CNS outcomes has recently begun to draw more attention, the evidence for a PM-induced CNS effect is limited. While most available studies have evaluated the effects of fine particle exposures, there is insufficient evidence to draw conclusions regarding effects of specific PM size fractions. Overall, the **evidence is inadequate to determine if a causal relationship exists between short-term exposures to $PM_{2.5}$, $PM_{10-2.5}$, or UFPs and CNS effects.**

6.5. Mortality

The relationship between short-term exposure to PM and mortality has been extensively addressed in previous PM assessments (U.S. EPA, 1982, 017610; 1996, 079380; 2004, 056905). A positive association between PM concentration and mortality was consistently demonstrated across studies cited in the 2004 PM AQCD (U.S. EPA, 2004, 056905); these results are summarized below in Section 6.5.1. Numerous studies have been published since the previous review, including a number of multicity analyses and many single-city studies. The current body of evidence examines the association between short-term exposure to PM of various size fractions (i.e., PM_{10}, $PM_{10-2.5}$, $PM_{2.5}$, and UFPs) and mortality through the use of time-series and/or case-crossover studies. Both study designs aim to disentangle the PM-mortality effect through either complex modeling (i.e., time-series) or matching strategies (i.e., case-crossover). Overall, the results of the more recent studies build upon the conclusions from the previous review, showing consistent positive associations between mortality and short-term exposure to $PM_{2.5}$ and $PM_{10-2.5}$.

Section 6.5.2 reviews and summarizes the results of recent studies that examined mortality associations with the four PM size classes listed above. Each section integrates the results of recent studies with those available in previous PM reviews. This assessment first focuses on multicity studies that examined mortality associations with PM_{10} because this is an important body of literature that provides information on potential effect modifiers, potential confounding by copollutants, evaluation of concentration-response relationships, and the influence of different modeling approaches on the PM-mortality relationship (Section 6.5.2.1). The PM_{10} studies have provided the most data among the PM indices thus far; therefore this evaluation begins with the consideration of those findings as they relate to the general association between PM and mortality. It is difficult to interpret the extent to which these studies inform an evaluation of the effects of $PM_{2.5}$ or $PM_{10-2.5}$, since data are combined from multiple cities with different PM composition. Interpretations of the PM size fraction that contributes the most to the PM_{10} effects observed are provided when appropriate in the following review. The multicity studies that examine the association between PM_{10} and mortality also offer new evidence on regional and seasonal differences in effect estimates, building upon observations made in the 2004 PM AQCD (U.S. EPA, 2004, 056905).

Recent study findings on associations with $PM_{2.5}$, $PM_{10-2.5}$, and UFPs are evaluated in Sections 6.5.2.2, 6.5.2.3, and 6.5.2.4, respectively. For $PM_{2.5}$, the focus of the assessment remains on multicity study findings; however, for $PM_{10-2.5}$ and UFPs, some additional emphasis is placed on single-city studies, due to the relative sparseness of peer-reviewed literature on these size fractions. Some studies have also evaluated relationships between mortality and specific components and sources of PM, and the results are summarized in Sections 6.5.2.4 and 6.5.2.5. Finally, Section 6.5.2.6 assesses evidence on the concentration-response relationship between short-term PM exposure and mortality.

6.5.1. Summary of Findings from 2004 PM AQCD

The 2004 PM AQCD (U.S. EPA, 2004, 056905) found strong evidence that PM_{10} and $PM_{2.5}$, or one or more $PM_{2.5}$ components, acting alone and/or in combination with gaseous copollutants, are associated with total (nonaccidental) mortality and various cause-specific mortality outcomes. For PM_{10}, several multicity studies in the U.S., Canada, and Europe provided strong support for this conclusion, reporting associations with total mortality highlighted by effect estimates ranging from ~0.2 to 0.7% (per 10 $\mu g/m^3$ increase in PM_{10}) (U.S. EPA, 2004, 056905). Numerous studies also reported PM_{10} associations with cause-specific mortality, specifically cardiovascular- and respiratory-related mortality. For $PM_{2.5}$, the strength of the evidence varied across categories of cause-specific mortality, with relatively stronger evidence for associations with cardiovascular compared to respiratory mortality. The resulting effect estimates reported from the U.S.- and Canadian-based studies (both multi- and single-city) analyzed for these two categories ranged from 1.2 to 2.7% for cardiovascular-related mortality and 0.8 to 2.7% for respiratory-related mortality, per 10 $\mu g/m^3$ increase in $PM_{2.5}$ (U.S. EPA, 2004, 056905). In regards to $PM_{10-2.5}$, the PM AQCD found a limited body of evidence that was suggestive of associations between short-term exposure to ambient $PM_{10-2.5}$ and various mortality outcomes (e.g., 0.08-2.4% increase in total [nonaccidental] mortality per 10 $\mu g/m^3$ increase in $PM_{10-2.5}$). The positive effect estimates obtained from studies that analyzed the association between $PM_{10-2.5}$ and mortality resulted in the conclusion that $PM_{10-2.5}$, or some

constituent component(s) (including those on the surface) of $PM_{10-2.5}$, may contribute, in certain circumstances, to increased human health risks.

Some additional studies examined the association between specific $PM_{2.5}$ chemical components and mortality. These studies observed associations for SO_4^{2-}, NO_3^-, and CoH, but not crustal particles. The strength of the association for each component varied from city to city (U.S. EPA, 2004, 056905). Source-oriented analyses were also conducted to identify specific source-types associated with mortality. These studies implicate $PM_{2.5}$ from anthropogenic origin, such as motor vehicle emissions, coal combustion, oil burning, and vegetative burning, as being important in contributing to increased mortality (U.S. EPA, 2004, 056905).

6.5.2. Associations of Mortality and Short-Term Exposure to PM

The recent literature examines the association between short-term exposure to various PM size fractions (i.e., PM_{10}, $PM_{10-2.5}$, $PM_{2.5}$, UFPs, or species [e.g., OC, EC, transition metals, etc.]) and mortality. This ISA, similar to previous AQCDs, focuses more heavily on multicity studies, and especially those conducted in the U.S. and Canada (Table 6-15). By using this approach it is possible to: (1) obtain a more representative sample of or insight into the PM-mortality relationship observed across the U.S.; (2) analyze the association between mortality and short-term exposure to PM at or near ambient conditions observed in the U.S.; (3) examine the potential heterogeneity in effect estimates between cities and regions; and (4) analyze the confounders and/or effect modifiers that may explain the PM-mortality relationship in the U.S. Although this section focuses on mortality outcomes in response to short-term exposure to PM, it does not evaluate studies that examine the association between PM and infant mortality. These studies are evaluated in Section 7.5,,although it is possible that short- and long-term in utero exposures may contribute to infant mortality. In addition, the exposure windows of interest for this unique health outcome can be difficult to characterize and may span both short- and long-term exposure periods.

Table 6-15. Overview of U.S. and Canadian multicity PM studies of mortality analyzed in the 2004 PM AQCD and the PM ISA[b].

Study	Location	Mean Concentration ($\mu g/m^3$)	98th; 99th Percentiles ($\mu g/m^3$)	Upper Percentile: Concentrations ($\mu g/m^3$)
PM_{10}				
Dominici et al. (2003, 156407)[a]	90 U.S. cities	15.3-53.2	---	NR
Burnett and Goldberg (2003, 042798)[a]	8 Canadian cities	25.9	---	95th: 54; Maximum: 121
Peng et al. (2005, 087463)	100 U.S. cities	13-49	---	50th: 27.1; 75th: 32.0 Maximum: 48.7
Dominici et al. (2007, 097361)[f]	100 U.S. cities	13-49	---	50th: 27.1; 75th: 32.0 Maximum: 48.7
Welty and Zeger (2005, 087484)[f]	100 U.S. cities	13-49	---	50th: 27.1; 75th: 32.0 Maximum: 48.7
Bell et al. (2009, 191007)	84 U.S. urban communities	NR	---	NR
Burnett et al. (2004, 086247)	12 Canadian cities	NR	---	NR
Samoli et al. (2008, 188455)	12 Canadian cities 90 U.S. cities[e] 22 European cities	NR	---	NR
Schwartz (2004, 078998)	14 U.S. cities	23-36[d]	---	75th: 31-57
Schwartz (2004, 053506)	14 U.S. cities	23-36[d]	---	75th: 31-57
Zeka et al. (2005, 088068)	20 U.S. cities	15-37.5	---	NR
Zeka et al. (2006, 088749)	20 U.S. cities	15.9-37.5	---	NR

Study	Location	Mean Concentration ($\mu g/m^3$)	98th; 99th Percentiles ($\mu g/m^3$)	Upper Percentile: Concentrations ($\mu g/m^3$)
$PM_{2.5}$				
Burnett and Goldberg (2003, 042798)[a]	8 Canadian cities	13.3	38.9; 45.4	95th: 32; Maximum: 86
Dominici et al. (2007, 097361)	96 U.S. cities	NR	---	NR
Zanobetti and Schwartz (2009, 188462)	112 U.S. cities	13.2	34.3; 38.6	Maximum: 57.4
Franklin et al. (2007, 091257)	27 U.S. cities	15.6	45.8; 54.7	Maximum: 239
Franklin et al. (2008, 097426)[g]	25 U.S. cities	14.8	43.0; 50.9	Maximum: 239.2
Ostro et al. (2006, 087991)	9 California counties	19.9	68.2; 82.0	95th: 61.3; Maximum: 160.0
Ostro et al. (2007, 091354)	6 California counties	18.4	61.2; 70.1	Maximum: 116.1
Burnett et al. (2004, 086247)	12 Canadian cities	12.8	38.0; 45.0	Maximum: 86.0
$PM_{10-2.5}$				
Burnett and Goldberg (2003, 042798)[a]	8 Canadian cities	12.6	---	95th: 30; Maximum: 99
Zanobetti and Schwartz (2009, 188462)	47 U.S. cities	11.8	40.2; 47.2	Maximum: 88.3
Burnett et al. (2004, 086247)	12 Canadian cities	11.4	---	Maximum: 151
Villeneuve et al. (2003, 055051)	Vancouver, Canada	6.1	---	90th: 13.0; Maximum: 72.0
Klemm et al. (2004, 056585)	Atlanta, Georgia	9.7	20.7	50th: 9.34; 75th: 11.94 Maximum: 25.17
Slaughter et al. (2005, 073854)	Spokane, Washington	NR	---	NR
Wilson et al. (2007, 157149)	Phoenix, Arizona	NR	---	NR
Kettunen et al. (2007, 091242)	Helsinki, Finland	Cold season: 6.7[d] Warm season: 8.4[d]	---	Cold season: 50th: 6.7 75th: 12.5; Maximum: 101.4 Warm season: 50th: 8.4 75th: 11.8; Maximum: 42.0
Perez et al. (2008, 156020)	Barcelona, Spain	Saharan Dust Days: 16.4 Non-Saharan Dust Days: 14.9	---	Saharan Dust Days 50th: 14.8; 75th: 21.8 Maximum: 36.7 Non-Saharan Dust Days 50th: 12.6; 75th: 18.9 Maximum: 93.1

[a] Multicity studies examined in the 2004 PM AQCD (U.S. EPA, 2004, 056905)
[b] Because only two multicity study was identified that examined $PM_{10-2.5}$, single-city and international studies that examined $PM_{10-2.5}$ were analyzed in this ISA and are included in this table.
[c] The majority of multicity studies examined in the PM ISA provide the mean PM concentration of each individual city, not an overall PM concentration across all cities. As a result, the range of PM concentrations for a particular study are presented, which represents the lowest and highest mean PM concentrations reported across cities, if an overall mean is not provided within the study.
[d] Median PM concentration.
[e] The study included 90 U.S. cities in the 1-day lag analysis, but only 15 U.S. cities in the analysis of the average of lag days 0-1.
[f] The concentrations reported for these studies were estimated from Peng et al. (2005, 087463) because they used the same number of cities and years of data from NMMAPS.
[g] This study did not present an overall mean 24-h avg $PM_{2.5}$ concentration across all cities for each season. The range of mean 24-h avg concentrations reported in this table for each season represents the lowest mean 24-h avg $PM_{2.5}$ concentration and the highest 24-h avg $PM_{2.5}$ concentration reported across all cities included in the study.

6.5.2.1. PM_{10}

The majority of studies that examined the association between short-term exposure to PM and mortality focused on effects attributed to PM_{10}. Although these studies do not characterize the compositional differences in PM_{10} across the cities examined in each of the studies evaluated, they can provide an underlying basis for the overall pattern of associations observed when examining the relationship between $PM_{10-2.5}$ and $PM_{2.5}$ and mortality. The studies evaluated in this review analyzed the PM_{10}-mortality relationship through either a time-series or case-crossover design.[1]

[1] Schwartz (1981, 078988) used a case-crossover study design, but also conducted a time-series analysis to validate the results obtained using the case-crossover approach.

Time-Series Analyses

Mortality associations with short-term exposure to PM_{10} in the U.S. have been examined in several updated time-series analyses of the NMMAPS. In the previous NMMAPS analysis (Dominici et al., 2003, 156407; Samet et al., 2000, 005809; Samet et al., 2000, 010269) of the 1987-1994 data, which was reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905), the strongest association was found for nonaccidental mortality for 1-day lag, with a combined estimate across 90 cities of 0.21% (95% PI: 0.09-0.33) per 10 $\mu g/m^3$ increase in PM_{10}. The association was found to be robust to the inclusion of other gaseous copollutants in the regression models, but the investigators found heterogeneity across regions, with the strongest associations in northeastern cities. In the new updated analyses, the investigators examined additional issues surrounding the association between PM and mortality including: seasonal effect modification; change in risk estimates over time; sensitivity of results to alternative weather models; and effect modification by air conditioning use. The NMMAPS data has also been used to examine the PM concentration-response relationship using PM_{10} data from 20 cities (Section 6.5.2.7). A few multicity studies conducted in Canada and Europe provide additional information, which further clarifies and supports the association between PM and mortality presented in the NMMAPS analyses.

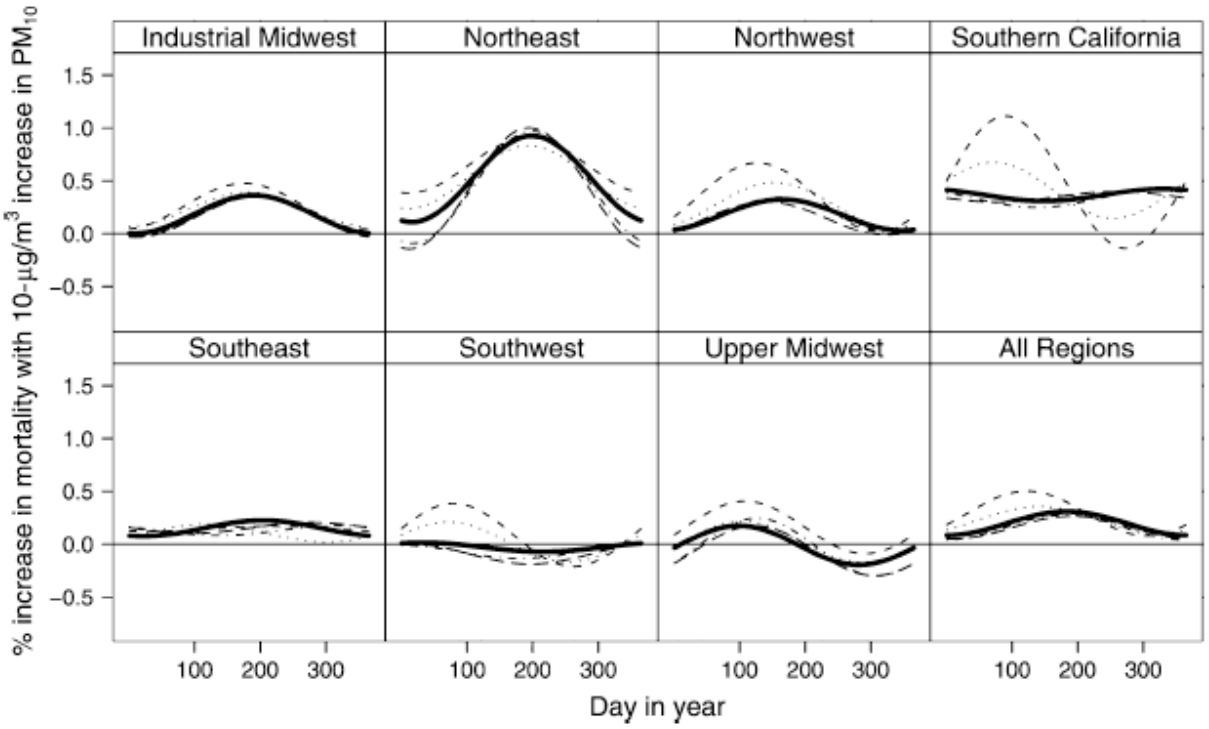
Seasonal Analyses of PM_{10}-Mortality Associations

Using the updated NMMAPS data, which consisted of 100 U.S. cities for the period 1987-2000, Peng et al. (2005, 087463) examined the effect of season on PM_{10}-mortality associations. In their first stage regression model, for each city, the PM_{10} effect was modeled to have a sinusoidal shape that completes a cycle in a year, but was constrained to be periodic across years using sine/cosine terms. The authors also considered a model that consisted of PM_{10}-season interactions using season indicators. Both of these models also included covariates that were used in their earlier NMMAPS analyses. In the second stage model, the seasonal patterns of PM_{10} mortality coefficients were estimated for seven geographic regions and on average for the entire U.S. Peng et al. (2005, 087463) found for 1-day lag, at the national level, season specific increases in nonaccidental mortality per 10 $\mu g/m^3$ increase in PM_{10} of: 0.15% (95% PI: -0.08 to 0.39), 0.14% (95% PI: -0.14 to 0.42), 0.36% (95% PI: 0.11-0.61), and 0.14% (95% PI: -0.06 to 0.34) for winter, spring, summer, and fall, respectively. The corresponding all-season estimate was 0.19% (95% PI: 0.10-0.28). After the inclusion of SO_2, O_3, or NO_2 in the model with PM_{10} in a subset of cities (i.e., 45 cities) for which data existed, PM_{10} risk estimates remained fairly robust. An analysis by geographic region found a strong seasonal pattern in the Northeast. Figure 6-16 presents the estimated seasonal pattern of PM_{10} risk estimates by region from Peng et al. (2005, 087463), which includes a sensitivity analysis aimed to determine the appropriate number of degrees of freedom for temporal adjustment. It is clear from Figure 6-16 that the Northeast has the strongest association with PM_{10} and mortality, which peaks in the summer and is robust to the extent of temporal adjustment. The industrial Midwest also shows the summer peak, but with smaller risk estimates. Other regions have either no seasonal pattern (Southeast) or a suggestion of a spring peak that appears to be sensitive to the extent of temporal adjustment. On a nationwide basis, the PM_{10} risk estimates appear to peak between spring and summer. Overall, this study identified an effect modifier that may be useful in identifying the specific chemical component(s) of PM that are related to specific regions and times of the year.

Change in PM_{10}-Mortality Associations over Time

Dominici et al. (2007, 097361) conducted an analysis of the extended NMMAPS data set (i.e., 1987-2000) to examine if short-term PM_{10}-mortality risk estimates changed during the course of the study period. The investigators estimated the average PM_{10} mortality risk coefficient for 1-day lag, using essentially the same model specification as in their 2003 analysis, separately for three time periods (i.e., 1987-1994, 1995-2000, and 1987-2000) the ‘‘eastern U.S.’’ (62 counties), the ‘‘western U.S.’’ (38 counties), and all 100 U.S. counties. To produce national and regional estimates, two-stage hierarchical models were used as in the previous NMMAPS studies. As shown in Table 6-16, the authors found a continuation of the PM_{10}-mortality association in the nationwide data for the entire study period. A comparison of the relative risk estimates for 1987-1994 vs. 1995-2000 suggests weak evidence (not a statistically significant difference) that short-term effects declined. Most of the decline in the national estimate appears to be attributable to the eastern U.S. counties. However, the decline in the risk estimate for all-cause mortality in the eastern U.S. appears to be

disproportionately influenced by the reduction in the risk estimate for the "other" mortality category (i.e., all-cause minus cardio-respiratory category, which may be 40-50% of all-cause deaths in U.S. cities). Likewise, the apparent increase in the risk estimate for all-cause mortality in the western U.S. appears to be affected by the increase in the risk estimate for the "other" mortality category. Because the study does not clearly identify the specific cause(s) in the "other" mortality category that are affected by PM, interpreting the reduction in risk estimates for all-cause mortality requires caution. In contrast, the apparent reductions (~23%) in PM_{10} risk estimates for cardio-respiratory deaths were more comparable between the two regions.



Source: Reprinted with Permission of Oxford University Press from Peng et al. (2005, 087463)

Figure 6-16. National and regional estimates of smooth seasonal effects for PM_{10} at a 1-day lag and their sensitivity to the degrees of freedom assigned to the smooth function of time in the updated NMMAPS data 1987-2000. Note: The degrees of freedom chosen were 3 df (short-dashed line), 5 df (dotted line), 7 df (solid line), 9 df (dotted-and-dashed line), and 11 df (long-dashed line) per year of data.

In addition, the investigators estimated time-varying PM_{10} mortality risk as a linear function of calendar time for the period 1987-2000, producing the percentage rate change in the PM_{10} risk estimate with a change in time of 1 yr. The estimated rate of decline in slope for all-cause mortality and the combination of cardiovascular and respiratory mortality were -0.012 (95% PI: -0.037 to 0.014) and -0.016 (95% PI: -0.058 to 0.027), respectively. The authors also estimated a $PM_{2.5}$ mortality risk for the period 1999-2000 (discussed in Section 6.5.2.2.).

Table 6-16. NMMAPS national and regional percentage increase in all-cause, cardio-respiratory, and other-cause mortality associated with a 10 μg/m^3 increase in PM_{10} at lag 1 day for the periods 1987-1994, 1995-2000, and 1987-2000.

	1987-1994	95% PI	1996-2000	95% PI	1987-2000	95% PI
ALL CAUSE						
East	0.29	0.12, 0.46	0.13	-0.19, 0.44	0.25	0.11, 0.39
West	0.12	-0.07, 0.30	0.18	-0.07, 0.44	0.12	-0.02, 026
National	0.21	0.10, 0.32	0.18	0.00, 0.35	0.19	0.10, 0.28
CARDIORESPIRATORY						
East	0.39	0.16, 0.63	0.30	-0.13, 0.73	0.34	0.15, 0.54
West	0.17	-0.07, 0.40	0.13	-0.23, 0.50	0.14	-0.05, 0.33
National	0.28	0.14, 0.43	0.21	-0.03, 0.44	0.24	0.13, 0.36
OTHER						
East	0.21	-0.03, 0.44	0.00	-0.49, 0.50	0.15	-0.09, 0.39
West	0.09	-0.21, 0.38	0.23	-0.15, 0.62	0.11	-0.10, 0.33
National	0.15	-0.02, 0.32	0.17	-0.07, 0.41	0.15	0.00, 0.29

Source: Reprinted with Permission of HEI from Dominici et al. (2007, 097361)

The objective of the Dominici et al. (2007, 097361) study described above was motivated by accountability research, the idea of measuring the impact of policy interventions. However, unlike the intervention studies conducted in Hong Kong (Hedley et al., 2002, 040284) and Dublin, Ireland (Clancy et al., 2002, 035270) that were reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905), this study was not designed to estimate a reduction in mortality in response to a sudden change in air pollution. In fact, the figure of observed trend in PM_{10} levels presented in the Dominici et al. (2007, 097361) study indicates that the decline in PM_{10} levels during the study period was very gradual, with much of the decline appearing in the first few years (median values of ~33 μg/m^3 in 1987 to ~25 μg/m^3 in 1992, then down to ~23 μg/m^3 in 2000). A flaw in the use of the time-series study design for this type of analysis is that it adjusts for long-term trends, and, therefore, does not estimate the change in mortality in response to the gradual change in PM_{10}. The apparent change, though weak, in the PM_{10} risk estimates may also reflect a potential change in the composition of PM_{10} (i.e., $PM_{10-2.5}$ or $PM_{2.5}$). The study listed a number of PM_{10}-related air pollution control programs that were implemented between 1987 and 2000. Some of these programs, such as the Acid Rain Control Program, did result in major reductions in emissions, and, therefore, could have contributed to the results observed, but the analytic approach used in the study does not allow for a systematic analysis of the effect of air pollution policies on the risk of mortality.

Sensitivity of PM-Mortality Associations to Alternative Weather Models

To examine the sensitivity of PM_{10}-mortality risk estimates to alternative weather models that consider longer lags, Welty and Zeger (2005, 087484) analyzed the updated NMMAPS 100 U.S. cities data. All of the previous NMMAPS analyses only considered temperature and dew point up to 3-day lags. In this analysis, the authors considered various forms of a constrained distributed lag model: (1) containing a step function of temperature with steps at lag 0, 2, 7 and extended to 14 days; (2) similar to (1) but with time-varying coefficients to change over season and study period; and, (3) containing a smooth function to account for non-linearity in the temperature-mortality relationship. With the combination of degrees of freedom for temporal trends and the number of distributed lags, more than 20 models were applied to each of the 3 lag days (0, 1, and 2) of PM_{10}. These city-specific risk estimates were then combined across the 100 cities in the second stage Bayesian model. The combined PM_{10} risk estimates were generally consistent within the lag. In particular, the risk estimates for nonaccidental mortality for lag 1 day ranged between 0.15% and

0.25% per 10 μg/m^3 increase in PM_{10}, and were always statistically significant regardless of the model used. In addition, the range of these point estimates across the models was found to be much narrower than the regression posterior intervals. Thus, the PM_{10} risk estimates at lag 1 day were robust to alternative temperature models that considered temperature effects lasting up to a 2-week period.

In summary, the above three analyses of the updated NMMAPS data provided useful information on PM-mortality risks, resulting in the following conclusions: (1) estimated PM_{10} mortality risk is particularly high in the northeast and in the summer; (2) there remains an overall PM_{10}-mortality association in the 1987-2000 time period as well as the 1995-2000 time period; (3) there is a weak indication that PM_{10}-mortality risk estimates are declining; and (4) PM_{10}-mortality risk estimates were not sensitive to alternative temperature models.

Effect Modification of PM_{10}-Mortality Associations by Air Conditioning Use

It has been hypothesized that air conditioning (AC) use reduces an individual's exposure to PM and subsequently modifies the PM-mortality association. Bell et al. (2009, 191007) investigated the role of AC use on the relationship between PM_{10} and all-cause mortality using the NMMAPS PM_{10} risk estimates from 84 U.S. urban communities from 1987-2000.[1] Bayesian hierarchical modeling was used to examine if AC prevalence (i.e., fraction of households with central or any AC) explained city-to-city variation in PM_{10} risk estimates. The authors calculated yearly, summer-only, and winter-only effect estimates stratified by housing stock that had either central AC or any AC, which includes window units. Risk estimates for lag 1 (previous day) were used in the analysis because this lag showed the strongest association with mortality in the original NMMAPS analyses. Community-specific AC prevalence was calculated from national survey U.S. Census American Housing Survey (AHS) data, which is available every two years. The investigators computed percent change in PM_{10} effect estimates per an additional 20% of the population acquiring AC.

The AC variables were not strongly correlated with socio-economic variables (poverty rate, unemployment, and education) from the U.S. Census (correlation ranged from -0.27 to 0.29). Bell et al. (2009, 191007) found that communities with higher AC prevalence had lower PM_{10} mortality risk estimates for all-cause mortality (-30.4% [95% PI: -80.4 to 19.6] per an additional 20% of the population acquiring any AC; -39.0% [95% PI: -81.4 to 3.3] for central AC), but results were not statistically significant. When restricting the analysis to the summer months and focusing on the 45 cities with summer-peaking PM_{10} concentrations, the authors reported positive, non-significant risk estimates (29.9% [95% PI: -84.0 to 144] per an additional 20% of the population acquiring any AC; -2.0% [95% PI: -60.3 to 64.3] for central AC). A similar analysis was conducted for winter months using data from six cities with winter peaking PM_{10} concentrations, but the confidence bands were too wide (due to the small sample size) for meaningful interpretation.

Although the estimated reductions in PM_{10} all-cause mortality risks from AC use reported in the Bell et al. (2009, 191007) study were not statistically significant, their large magnitude suggests that AC use may reduce an individual's exposure to PM. Given the expected additional increase in AC use in the future, and the results from recent multicity studies, which have reported stronger PM-mortality associations during the warm season, AC use may play a larger role in determining an individuals exposure to PM. Studies that have examined the effect of AC use on the $PM_{2.5}$-mortality association have reported similar results. For example, Franklin et al. (2007, 091257) (discussed in detail in Section 6.5.2.2) found that AC use non-significantly modified $PM_{2.5}$ mortality risk estimates, but the result was suggestive of higher $PM_{2.5}$ effects in cities with lower AC use, especially in cities with summer-peaking $PM_{2.5}$ concentrations. Overall, further investigation is needed to fully understand the relationship between AC use and mortality attributed to short-term exposure to PM.

PM_{10}-Mortality Associations in Canada and Europe

Burnett et al. (2004, 086247) examined the association between mortality and various air pollutants in 12 Canadian cities, and reported that the most consistent association was found for NO_2. For this analysis, PM was measured every 6th day for the majority of the study period, and the PM_{10} concentrations used in the study represent the sum of the $PM_{2.5}$ and $PM_{10\text{-}2.5}$, which were directly measured by dichotomous samplers. The authors found that the simultaneous inclusion of

[1] This study also examined risk estimates for cardiovascular and respiratory hospital admissions in older adults (≥ 65).

NO_2 and PM_{10} in a model, on those days with PM data, greatly reduced the PM_{10} association with nonaccidental mortality, from 0.47% (95% CI: 0.04-0.89) to 0.07% (95% CI: -0.44 to 0.58) per 10 μg/m^3 increase. The previous Canadian multicity analysis (Burnett and Goldberg, 2003, 042798), a re-analysis of Burnett et al. (2000, 010273) reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905), did not consider gaseous pollutants. Thus, PM_{10} risk estimates in the Canadian data appear to be more sensitive to NO_2 than those estimates reported in U.S. studies.

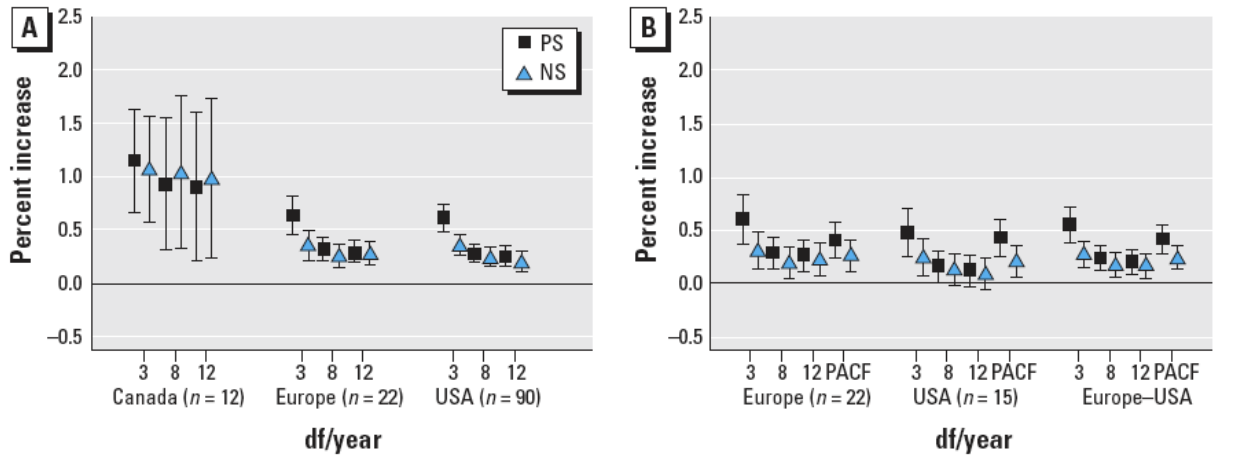
The association between PM_{10} and mortality in Europe was also reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905) through Katsouyanni et al. (2003, 042807), which presented results from the APHEA-2 study, a multicity study that examined PM_{10} effects on total mortality in 29 European cities. Analitis et al. (2006, 088177) published a brief report on effect estimates for cardiovascular and respiratory deaths also based on the 29 European cities, within the APHEA2 study. They reported for the average of 0- and 1-day lags, PM_{10} risk estimates per 10 μg/m^3 of 0.76% (95% CI: 0.47-1.05) for cardiovascular deaths and 0.71% (95% CI: 0.22-1.20) for respiratory deaths in random effects models.

Comparison of PM-Mortality Associations in Europe, Canada, and the U.S.

The APHENA study (Samoli et al., 2008, 188455) was a collaborative effort by the APHEA, NMMAPS, and the Canadian multicity study investigators to evaluate the coherence of PM_{10} mortality risk estimates across locations and possible effect modifiers of the PM-mortality relationship using a common protocol. To adjust for temporal trends, Samoli et al. (2008, 188455) used 3, 8, and 12 degrees of freedom (df) with natural splines and penalized splines, as well as the minimization of the sum of the absolute values of the partial auto-correlation function (PACF). The investigators also included a smooth function of temperature on the same day of death and the day before death. The study reported risk estimates for a 1-day lag (from all three data sets), the average of lag day 0 and 1 (all but for the Canadian data because PM data was collected every 6th day), and an unconstrained distributed lag model using lags of 0, 1, and 2 days (all but for the Canadian data). The second-stage regression included: (a) the average pollution level and mix in each city; (b) air pollution exposure characterization (e.g., number of monitors, density of monitors); (c) the health status of the population (e.g., cardio-respiratory deaths as a percentage of total mortality, crude mortality rate, etc.); and (d) climatic conditions (e.g., mean and variance of temperature). In addition, unemployment rate was examined for 14 European cities and all U.S. cities. Effect modification patterns were examined only for cities with complete time-series data and using the average of lags 0 and 1 day, resulting in the exclusion of the Canadian data.

Generally, the risk estimates from Europe and the U.S. were similar, but those from Canada were substantially higher.[1] For example, the percent excess risks per 10 μg/m^3 increase in PM_{10} for all ages using 8 df/yr and penalized splines were 0.84% (95% CI: 0.30-1.40), 0.33% (95% CI: 0.22-0.44), and 0.29% (95% CI: 0.18-0.40) for the Canadian, European, and U.S. data, respectively. Note that the risk estimate for the 90 U.S. cities is slightly larger than that reported in the original NMMAPS study (0.21%, using natural splines, and more temperature variables). In the all ages model, the average of lag days 0 and 1, and the distributed lag model with lags 0, 1, and 2 did not result in larger risk estimates compared to those for a 1 day lag. In copollutant models, PM_{10} risk estimates did not change when controlling for O_3. Figure 6-17 shows the risk estimates from the three data sets for alternative extent of temporal smoothing and smoothing methods. The Canadian data appear less sensitive to the extent of temporal smoothing or smoothing methods (Panel A of Figure 6-17). When stratifying by age the risk estimates for the older age group (≥ 75 yr) were consistently larger than those for the younger age group (<75 yr) (e.g., 0.47% vs. 0.12% for the U.S. data) for all the three data sets. Although the study did not quantitatively present the results from the effect modification analyses, some evidence of effect modification across the study regions was observed. The investigators reported that, in the European data, higher levels of NO_2 and a larger NO_2/PM_{10} ratio were associated with greater PM_{10} risk estimates, and that while this pattern was also present in the U.S. data, it was less pronounced. Additionally, in the U.S. data, smaller PM_{10} risk estimates were observed among older adults in cities with higher O_3 levels. Effect modification by temperature was also observed, but only in the European data.

[1] The risk estimate reported for the 12 Canadian cities examined in the APHENA study is higher than that reported by Burnett et al. (2004, 086247). This is because the APHENA study did not use the 12 cities data from Burnett et al. (2004, 086247), but instead used a composite of the data from three previous studies conducted by the same group by the same group (Burnett and Goldberg, 2003, 042798; 1998, 029505; Burnett et al., 2000, 010273).



Source: Samoli et al. (2008, 188455)

Figure 6-17. Percent increase in the daily number of deaths, for all ages, associated with a 10-μg/m^3 increase in PM_{10}: lag 1 (A) and lags 0 and 1 (B) for all three centers. PACF indicates df based on minimization of PACF.

In this study, the underlying basis for the larger PM_{10} risk estimates (by twofold) in the Canadian data compared to the European and U.S. data could not be identified, even when consistent statistical methods were applied across each of the data sets. Because the effect modification of PM_{10} risk estimates were not examined in the Canadian data, the potential influence of air pollution type or mixture could not be ruled out as a potential source of heterogeneity across the three data sets. It should be noted that both the original U.S. and European studies reported regional heterogeneity in PM risk estimates, and the U.S. data also demonstrated seasonal heterogeneity. In both of these cases the specific characteristics associated with the regions that contributed to the heterogeneity observed were not identified. Thus, further investigation is needed to identify factors that influence the heterogeneity in PM risk estimates observed between different countries and across regions.

Case-Crossover Analyses

Since the 2004 PM AQCD (U.S. EPA, 2004, 056905) investigators have used the case-crossover study design more frequently as an alternative to time-series analyses to examine the association between short-term exposure to PM and mortality. This study design allows for the control of seasonal variation, time trends, and slow time varying confounders without the use of complex models. However, similar to any study design, biases can be introduced into the study depending on the control (i.e., referent) period selected (Janes et al., 2005, 087535). The multicity case-crossover analyses discussed below match cases (i.e., days in which a death occurred) to controls (i.e., days in which a death did not occur), to control for (1) seasonal patterns and gaseous pollutants; or (2) temperature. In addition, the studies attempted to examine the heterogeneity of effect estimates through the analysis of individual-level and city-specific effect modification.

Controlling for Temperature

Schwartz (2004, 078998) investigated the PM_{10}-mortality association in 14 U.S. cities for the years 1986-1993 (some cities started in later years because of PM_{10} data availability) using a case-crossover study design. Note that in this analysis, four more cities (Boulder, CO; Cincinnati, OH; Columbus, OH; and Provo-Orem, UT) were added to the cities Schwartz (2003, 042800) previously analyzed using a time-series study design. These cities were chosen for this analysis because they collected daily PM_{10} data, unlike most U.S. cities, which only monitor PM_{10} every six days. Lag 1-day PM_{10} risk estimates were computed using several methods. Model 1 (i.e., the main model) and Model 2 were constructed from a case-crossover analysis with bidirectional control days

(7-15 days before and after the case). Model 1 obtained city-specific estimates in the first stage analysis, followed by a second stage random-effects model to obtain a combined estimate. Model 2 is the same as Model 1, but consisted of a single stage model, which included data from all 14 cities. Models 3 and 4 were also constructed from a case-crossover analysis, but used time-stratified control days (i.e., matched on season and temperature within the same degree in Celsius). Model 3 obtained single-city estimates in the first stage analysis, followed by a second stage random-effects model to obtain combined estimates. Model 4 used the same approach as Model 3, but consisted of a single stage model including data from all 14 cities. The final model, Model 5 consisted of a two-stage Poisson time-series model, which produced city-specific estimates in the first stage, and combined estimates across cities in the second stage. In the main model the estimated excess risk for nonaccidental mortality was 0.36% (95% CI: 0.22-0.50) per 10 $\mu g/m^3$ increase in PM_{10}. The other models yielded a similar magnitude of effect estimates, ranging from 0.32% (Model 2) to 0.53% (Model 4). Thus, the methods used to select control days and adjust for weather in the case-crossover design did not result in major differences in effect estimates, and in addition, were comparable to the estimates obtained from the time-series analysis, 0.40% (Model 5).

Controlling for Gaseous Pollutants

In a subsequent analysis, Schwartz (2004, 053506) analyzed the same 14 cities data described above, using a case-crossover design, to investigate the potential confounding effects of gaseous pollutants. For each case day, control days were selected from all other days of the same month of the same year. In addition, control days were selected if they had gaseous pollutant concentrations within: 1 ppb, 1 ppb, 2 ppb, or 0.03 ppm for SO_2, NO_2, 1-h max O_3, and CO, respectively, of the case day. Unlike the study described above (Schwartz, 2004, 078998) in this analysis, the excess risk was estimated for the average of 0- and 1-day lag PM_{10} (rather than 1-day lag). In addition, apparent temperature (a composite index of temperature and humidity) was used rather than temperature and humidity individually. The case-crossover analysis was conducted in each city, and a combined estimate was computed in a second-stage random effects model. The number of cities analyzed varied across pollutants depending on the availability of monitors. The study reported PM_{10} risk estimates for nonaccidental mortality of 0.81% (95% CI: 0.47-1.15), 0.78% (95% CI: 0.42-1.15), 0.45% (95% CI: 0.12-0.78), and 0.53% (95% CI: 0.04-1.02) per 10 $\mu g/m^3$ increase, for the analysis matched by SO_2 (10 cities), NO_2 (8 cities), O_3 (13 cities), and CO (13 cities), respectively.

Schwartz (2004, 053506) only presented PM_{10} risk estimates matched by gaseous pollutants, therefore, it is unclear in this analysis how matching by gaseous pollutants affected (i.e., reduced or increased) unmatched PM_{10} risk estimates. The estimates reported were computed using the average of 0- and 1-day lagged PM_{10} and, therefore, cannot be directly compared to the 1-day lag PM_{10} risk estimates obtained in the Schwartz (2004, 078998) 14-city study described above. The estimates reported in the case-crossover analysis that controlled for gaseous pollutants (Schwartz, 2004, 053506) are generally larger than those obtained in the analysis that controlled for temperature (Schwartz, 2004, 078998), which was expected since the Schwartz (2004, 053506) analysis used 2-day avg PM_{10}. However, the estimates reported in Schwartz (2004, 053506) are comparable to the average of 0- and 1-day lagged PM_{10} risk estimate for nonaccidental mortality (0.55% [95% CI: 0.39-0.70]) per 10 $\mu g/m^3$ increase from the 10-city study (Schwartz, 2003, 042800), which was reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905). Overall, Schwartz (2004, 053506) provided an alternative method to assess the influence of gaseous copollutants. The results suggest that PM_{10} is significantly associated with all-cause mortality after controlling for each of the gaseous copollutants.

City-Level Effect Modification

Zeka et al. (2005, 088068) expanded the 14 cities analyses conducted by Schwartz (2004, 078998; 2004, 053506) to 20 cities, added more years of data (1989-2000), and investigated PM_{10} effects on total and cause-specific mortality using a case-crossover design. Individual 0-, 1-, and 2-day lags as well as an unconstrained distributed lag model with 0, 1, and 2 lag days were examined. For each case day, control days were defined as every third day in the same month of the same year, to eliminate serial correlation. The authors also investigated potential effect modifiers in the second stage regression using city-specific variables including percent using AC, population density, standardized mortality rates, the proportion of elderly in each city, daily minimum apparent

temperature in summer, daily maximum apparent temperature in winter, and the estimated percentage of primary PM_{10} from traffic sources.

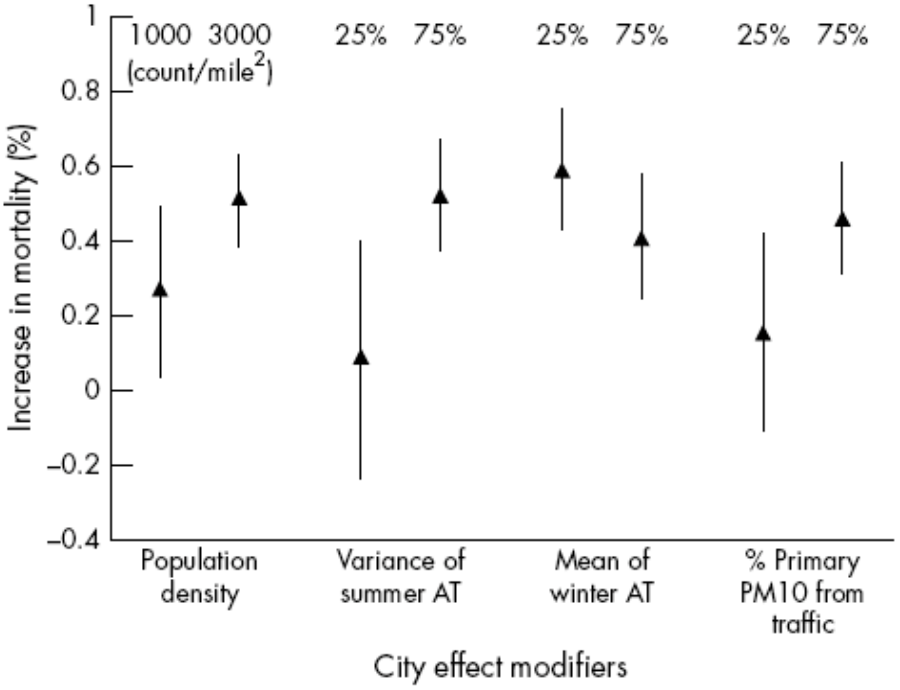


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Figure 6-18. Effect modification by city characteristics in 20 U.S. cities. Note: The two estimates and their CI for each of the modifying factors represent the percentage increase in mortality for a 10 μg/m³ increase in PM_{10}, for the 25th percentile, and 75th percentile of the modifier distribution across the 20 cities.

The investigators found that, for all-cause (nonaccidental) mortality, lag 1 day showed the largest risk estimate (0.35% [95% CI: 0.21-0.49] per 10 μg/m³) among the individual lags. Respiratory mortality exhibited associations at lag 0, 1, and 2 days (0.34%, 0.52%, and 0.51%, respectively), whereas cardiovascular mortality was most strongly associated with PM_{10} at lag day 2 (0.37%). The sum of the distributed lag risk estimates (e.g., 0.45% [95% CI: 0.25-0.65] for all-cause mortality) was generally larger than those for single-day lag estimates. The excess risk estimates for single-day lags for specific respiratory and cardiovascular causes had generally wider confidence intervals due to their smaller daily mortality counts, but some of the categories showed markedly larger estimates when included in the combined distributed lag model (e.g., pneumonia 1.24% [95% CI: 0.46-2.02]). As shown in Figure 6-18, Zeka et al. (2005, 088068) also found evidence indicative of several PM_{10} effect modifiers including higher population density and the estimated percentage of primary PM_{10} from traffic. When 25th versus 75th percentiles of these city-specific variables were evaluated, the estimated percent increase in mortality attributed to PM_{10} appears to contrast substantially (e.g., 0.09% vs. 0.52% for variance of summer time apparent temperature).

The effect modifiers investigated by Zeka et al. (2005, 088068) consisted of city-specific variables. Some of these variables are ecological in nature, and therefore, interpreting the meaning of "effect modification" requires some caution. As the investigators pointed out, the population density and the estimated percentage of primary PM_{10} from traffic were correlated in this data set ($r = 0.65$)[1]. These variables may also be a surrogate for another or composite aspects of "urban" characteristics.

[1] The correlation coefficient was calculated based on the numbers provided in Table 1 of Zeka et al. (2005, 088068).

Thus, the apparent effect modification by traffic-related PM_{10} needs further investigation. Interestingly, the percent of homes with central AC was not a significant effect modifier of PM_{10} risk estimates, which questions the impact of reduced building ventilation rates on PM exposure. Overall, this study presented PM_{10} risk estimates that are consistent with those found in other analyses, but also provided new information on the risk estimated for broad and specific respiratory and cardiovascular mortality designations, along with possible effect modifying city-specific characteristics.

Individual-level Effect Modification

In an additional analysis, Zeka et al. (2006, 088749) examined individual-level, instead of city-specific, effect modification of PM_{10}-mortality associations in the 20 U.S. cities described above using the same case-crossover design. City-specific estimates were obtained in the first stage model, followed by a second stage model which estimated the overall effects across all cities. Figure 6-19 shows PM_{10} excess risks by four of the individual characteristics examined in the study (i.e., gender, race, age group, and education). It should be noted that the lag and averaging of days for the associations reported varied across the outcomes: all-cause and heart disease deaths used the average of lag 1 and 2 days; respiratory deaths used the average of lag 0 through 2 days; MI deaths used lag 0 day; and stroke deaths used lag 1 day. PM_{10} risk estimates do not appear to differ by gender or by race. However, significant differences were found for the youngest vs. oldest age groups for all-cause and heart disease mortality. For all-cause mortality, the level of education appeared to be inversely related to the PM_{10} risk estimates (i.e., greater risk for lower education level), but this observation was not statistically significant. The study also examined effect modification by location of death ("out-of-hospital" versus "in-hospital") and season (Figure 6-20). The "out-of-hospital" deaths showed larger PM_{10} risk estimates than were found for "in-hospital deaths" with a significant difference per 10 $\mu g/m^3$ for all-cause (0.71% versus 0.22%) and heart disease (0.93% versus 0.15%) deaths. Stroke deaths also showed a significant difference (0.87% vs. 0.06%, not shown in Figure 6-20).

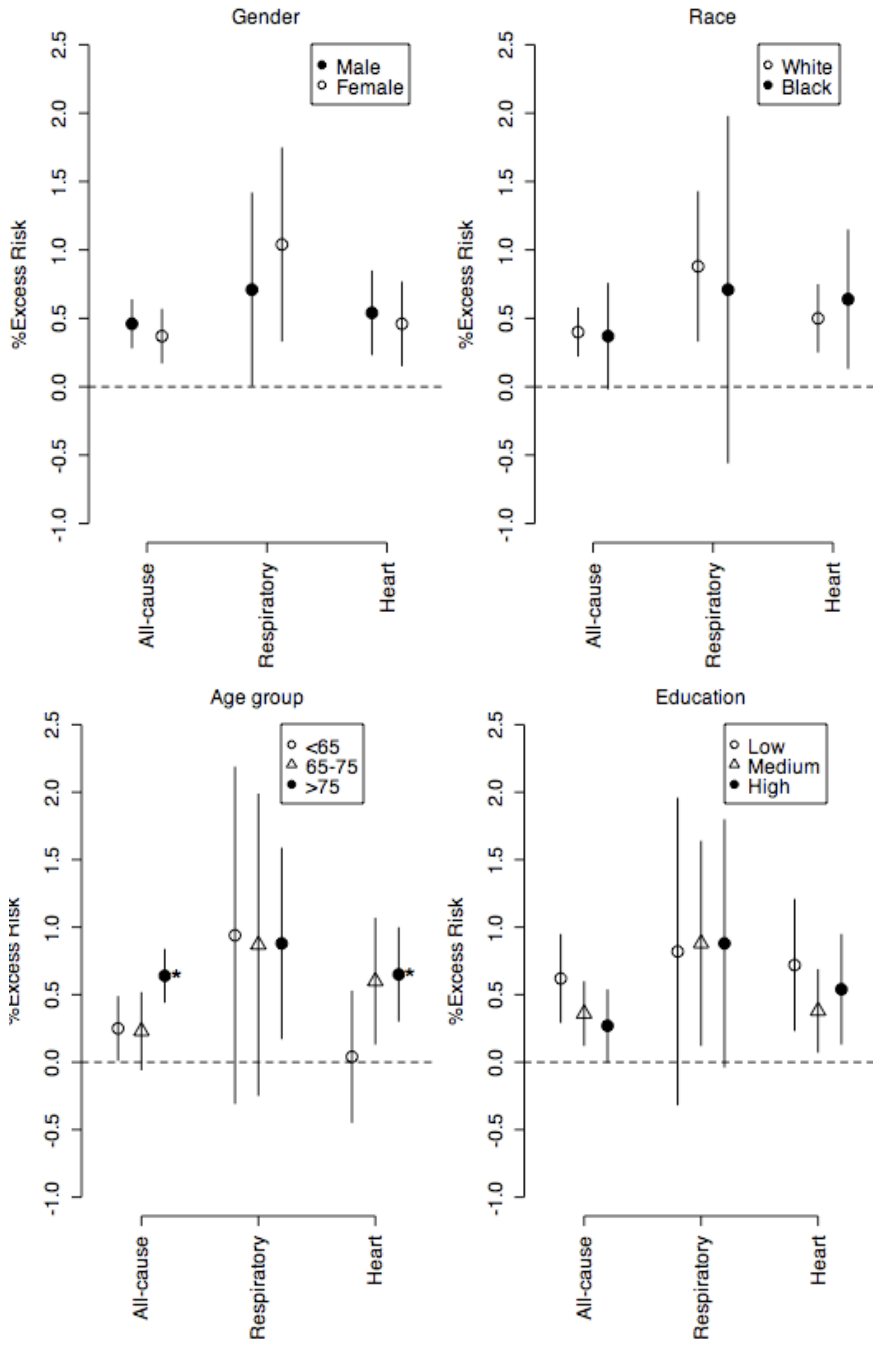


Figure 6-19. Percent excess risk in mortality (all-cause [nonaccidental] and cause-specific) per 10 µg/m^3 increase in PM_{10} by individual-level characteristics. The risk estimates and 95% confidence intervals were plotted using numerical results from tables in Zeka et al. (2006, 088749). The estimates with * next to them are significantly higher than the lowest estimate in the group.

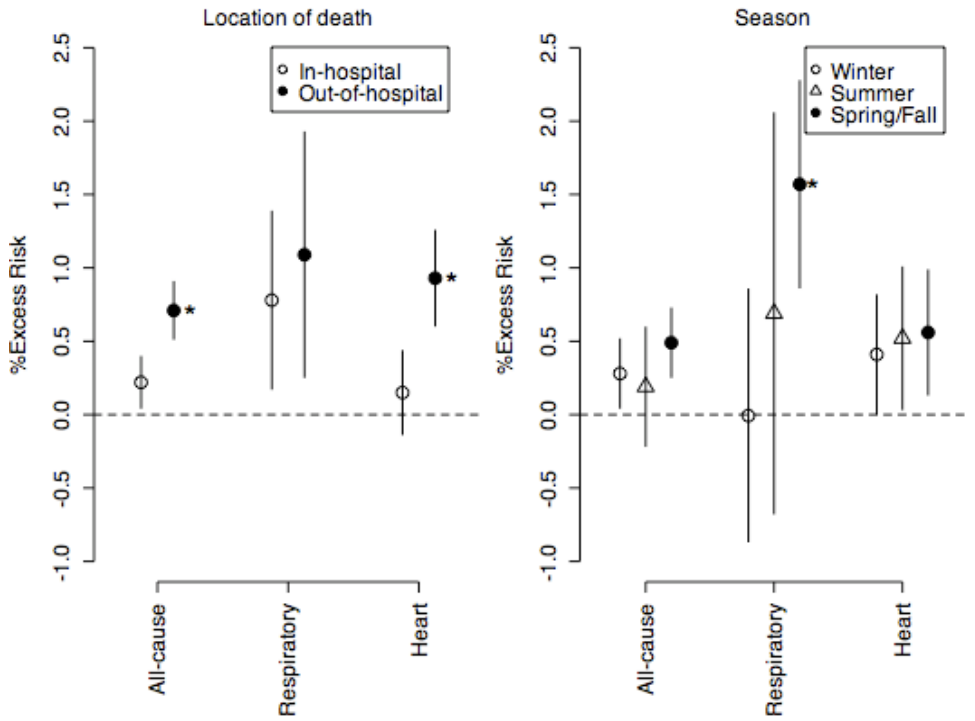
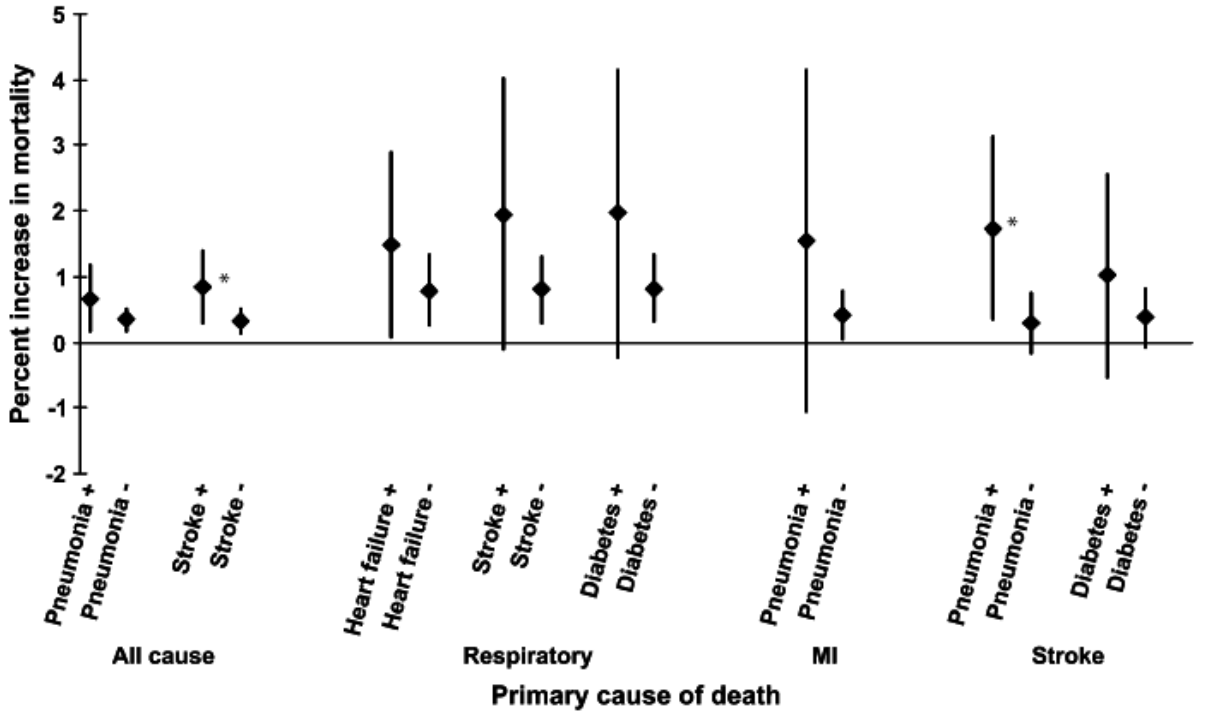


Figure 6-20. Percent excess risk in mortality (all-cause [nonaccidental] and cause-specific) per 10 µg/m^{3}increase in PM_{10} by location of death and by season. The risk estimates and 95% confidence intervals were plotted using numerical results from tables in Zeka et al. (2006, 088749). The estimates with * next to them are significantly higher than the lowest estimate in the group.

Overall, Zeka et al. (2006, 088749) showed a consistent pattern of effect modification by contributing causes of death (i.e., pneumonia, stroke, heart failure, and diabetes) on PM_{10} risk estimates for primary causes of death (Figure 6-21; not all results for contributing cause are shown). However, because the contributing causes of death counts were relatively small, as reflected by the wide confidence intervals in Figure 6-21, most of the differences observed did not achieve statistical significance.



Source: Adatped with Permission of Oxford University Press from Zeka et al. (2006, 088749)

Figure 6-21. Percent increase in mortality (all-cause [nonaccidental] and cause-specific) per 10 µg/m^3 increase in PM_{10} by contributing causes of death. The estimates with * (added to the original figure) indicates a significant difference.

In addition, when examining the other effect modifiers, the results that show no difference in PM_{10} risk estimates between gender or race for all-cause and cardiovascular deaths are important, given the relatively narrow confidence bands of these estimates. The effect modification by the location of death has been reported previously in smaller studies, but the large contrast found for all-cause and cardiovascular mortality in this large multicity analysis is noteworthy. The elevated PM_{10} risks reported by Zeka et al. (2006, 088749) for all-cause, heart disease (and stroke) "out-of-hospital" deaths are also consistent with the hypothesis of acute PM_{10} effects on "sudden deaths" brought on by systemic inflammation or dysregulation of the ANS. The finding regarding the seasonal effect modification, though significant only for respiratory deaths, is somewhat in contrast with the Peng et al. (2005, 087463) analysis of the extended NMMAPS data, which observed the greatest effects during the summer season. The apparent inconsistency may be due to the difference in geographic coverage (i.e., 20 versus 100 cities) or methodology (i.e., case-crossover with referent days in the same month of the same year vs. time-series analysis with adjustment for temporal trend in the regression model).

Summary of PM_{10} Risk Estimates

Overall, the recent studies continue to show an association between short-term exposure to PM and mortality. Although these studies do not examine mortality effects attributed to PM size fractions that compose PM_{10}, the regional, seasonal, and effect modification analyses conducted contribute to the evidence for the $PM_{2.5}$ and $PM_{10-2.5}$ associations presented in Sections 6.5.2.2and 6.5.2.3, respectively. Of the PM_{10} studies evaluated, depending on the lag/averaging time and the number of cities included, the estimates for all-cause (nonaccidental) mortality for all ages ranged from 0.12% (Dominici et al., 2007, 097361) to 0.84% (Samoli et al., 2008, 188455) per 10 µg/m^3 increase in PM_{10}, regardless of the study design used (i.e., time-series vs. case crossover). Although this range of PM mortality risk estimates is smaller than those reported for $PM_{10-2.5}$ and $PM_{2.5}$ they do support the

association between PM and mortality. The majority of studies examined present estimates for either a lag of 1 day or a 2-day avg (lag 0-1), both of which have been found to be strongly associated with the risk of death (Schwartz, 2004, 078998; 2004, 053506). The use of a distributed lag model (using lag 0, 1, and 2 days) was found to result in slightly larger (by ~30%) estimates compared to those for single-day lags in the 20 cities study (Zeka et al., 2005, 088068), but when using the 15 cities data from NMMAPS analyzed in the APHENA study (Samoli et al., 2008, 188455), the 1-day lag combined risk estimate was larger than the distributed lag (lag, 0, 1, and 2 days) estimate. Overall, an examination of the PM_{10} risk estimates stratified by cause-specific mortality and age, for all U.S.- and Canadian-based studies, further supports the findings of the multicity studies discussed in the 2004 PM AQCD (U.S. EPA, 2004, 056905) (i.e., consistent positive associations between short-term exposure to PM_{10} and mortality) and this ISA, however, it must be noted that a large degree of variability exists between cities when examining city-specific risk estimates.

The variability in PM_{10} mortality risk estimates reported within and between multicity studies may be due to the difference in the cities analyzed and the potential regional differences in PM composition. The NMMAPS studies have found that geographic regions and seasons are the two most important factors that determine the variability in risk estimates, with estimates being larger in the eastern U.S. and during the summer. These findings were fairly consistent across studies, but Zeka et al. (2006, 088749) observed the strongest association during the transition period (spring and fall); however, this may be due to the difference in geographic coverage or the difference in the model specification used compared to Peng et al. (2005, 087463).

Finally, examination of potential confounders showed that the size of PM_{10} risk estimates are fairly robust to the inclusion of gaseous copollutants in models (Peng et al., 2005, 087463) or by matching days with similar gaseous pollutant concentrations (Schwartz, 2004, 053506). These findings further confirmed that PM_{10} risk estimates are not, at least in a straightforward manner, confounded by gaseous copollutants.

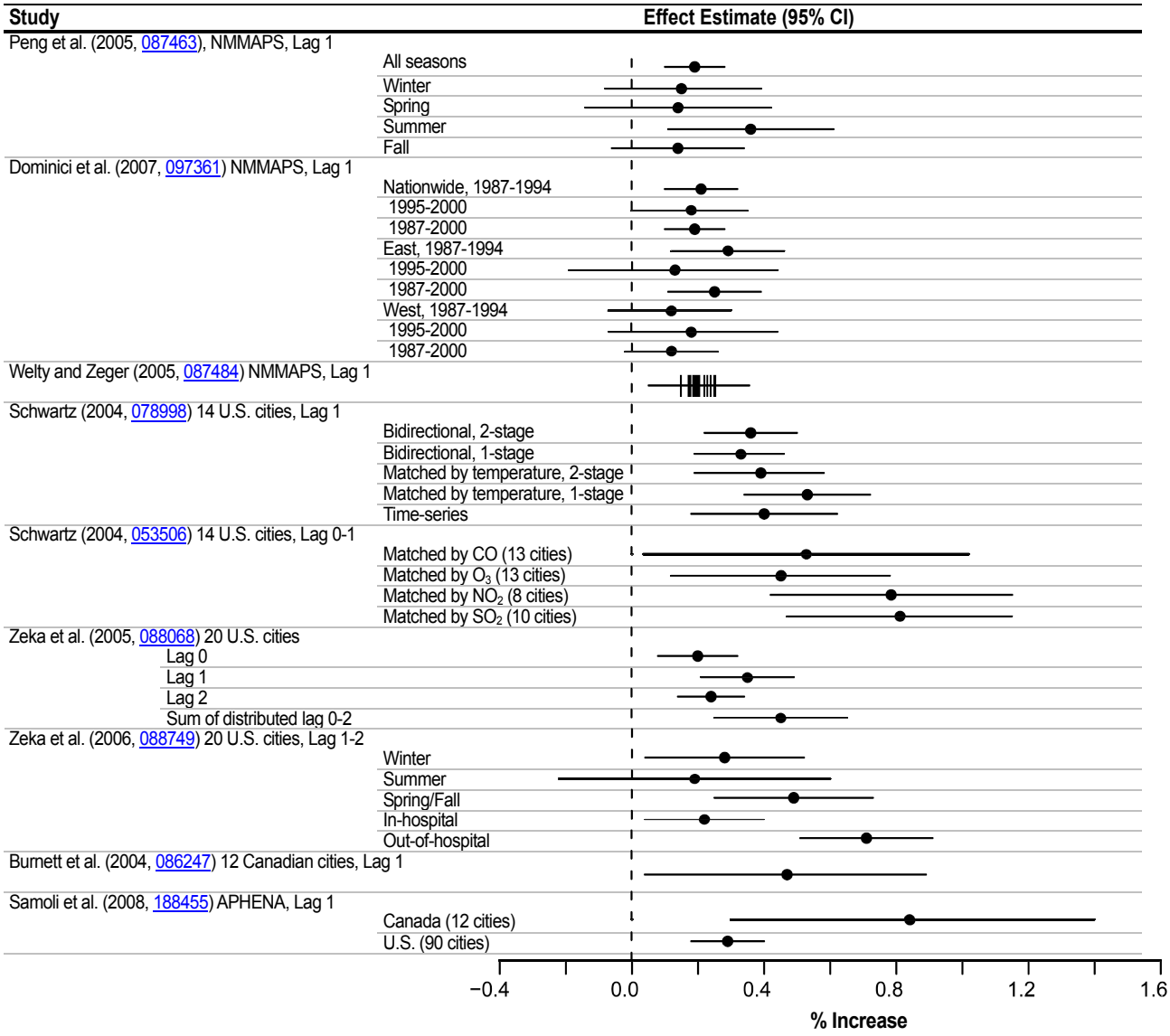


Figure 6-22. Summary of percent increase in all-cause (nonaccidental) mortality from recent multicity studies per 10 μg/m^3 increase in PM_{10}. The number after the study location indicates lag/average used for PM_{10} (e.g., "01" indicates the average of lag 0 and 1 days). For Welty and Zeger (2005, 087484), the vertical lines represent point estimates for 23 different weather models, and the horizontal band spans the 95% posterior intervals of these point estimates.

6.5.2.2. $PM_{2.5}$

A nationwide monitoring system for $PM_{2.5}$ was not established until 1999. This in conjunction with the unavailability of nationwide mortality data from the National Center of Health Statistics (NCHS) starting in 2001[1], has contributed to the relatively small literature base that has examined

[1] In 2008 the EPA facilitated the availability of the mortality data for EPA-funded researchers, which should eventually increase the literature base of studies that examine the association between short-term exposure to $PM_{2.5}$ and mortality.

the association between short-term exposure to $PM_{2.5}$ and mortality. To date, the studies that have been conducted examined national (i.e., in multiple cities across the country) or regional (i.e., in one location of the country) $PM_{2.5}$ associations with mortality.

$PM_{2.5}$ – Mortality Associations on a National Scale

The NMMAPS study conducted by Dominici et al. (2007, 097361) (described in Section 6.5.2.1), also conducted a national analysis of $PM_{2.5}$-mortality associations using the same methodology and data for 1999-2000. The $PM_{2.5}$ risk estimates at lag 1 day were 0.29% (95%PI: 0.01-0.57) and 0.38% (95%PI: -0.07 to 0.82) per 10 $\mu g/m^3$ increase for all-cause and cardio-respiratory mortality, respectively. The authors also conducted a sensitivity analysis of the risk estimates based on the extent of adjustment for temporal trends in the model, changing the degrees of freedom (df) of temporal adjustment from 1 to 20/yr (the main result used 7 df/yr). In comparison to the PM_{10} results, the $PM_{2.5}$ risk estimates appeared more sensitive to the extent of temporal adjustment between 5 and 10 df/yr, but this may be in part due to the much smaller sample size used for the $PM_{2.5}$ analysis (i.e., mortality counts from 1999-2000) compared to the PM_{10} analysis (i.e., mortality counts from 1987-2000).

Franklin et al. (2007, 091257) analyzed 27 cities across the U.S. that had $PM_{2.5}$ monitoring and daily mortality data for at least two years of a 6-yr period, 1997-2002. The mortality data up to year 2000 were obtained from the NCHS, while the 2001-2002 data were obtained from six states (CA, MI, MN, PA, TX, and WA), resulting in 12 out of the 27 cities having data up to 2002. The start year for each city included in the study was set at 1999, except for Milwaukee, WI (1997) and Boston, MA (1998), which is due to $PM_{2.5}$ data availability in these two cities. In the case-crossover analysis in each city, control days for each death were chosen to be every 3rd-day within the same month and year that death occurred in order to reduce autocorrelation. The first stage regression examined the interaction of effects with age and gender, while the second stage random effects model combined city-specific $PM_{2.5}$ risk estimates and examined possible effect modifiers using city-specific characteristics (e.g., prevalence of central AC and geographic region). For all of the mortality categories, the estimates for lag 1 day showed the largest estimates. The combined estimates at lag 1 day were: 1.2% (95%CI: 0.29-2.1), 0.94% (95%CI: -0.14 to 2.0), 1.8% (95%CI: 0.20-3.4), and 1.0% (95%CI: 0.02-2.0) for all-cause, cardiovascular, respiratory, and stroke deaths, respectively, per 10 $\mu g/m^3$. When examining the city-specific risk estimates most of the cities with negative estimates were also those with a high prevalence of central AC (Dallas, 89%; Houston, 84%; Las Vegas, 93%; Birmingham, 77%). It is unclear why these cities exhibit negative (and significant) risk estimates rather than null effects.

In the analysis of effect modifiers, Franklin et al. (2007, 091257) found that individuals $\geq$ 75 yr showed significantly higher $PM_{2.5}$ risk estimates than those individuals < 75 yr. The estimated effects were also found to vary by geographic location with larger estimates in the East than in the West, which are consistent with the regional pattern found in the NMMAPS PM_{10} risk estimates. In addition, a higher prevalence of central AC was associated with decreased $PM_{2.5}$ risk estimates when comparing the lower (25th percentile) versus the higher (75th percentile) AC use rates, especially in the cities where $PM_{2.5}$ concentrations peak in the summer. Finally, the risk estimates were not found to be different between communities with $PM_{2.5}$ concentrations $\leq$ 15 vs. >15 $\mu g/m^3$. The risk estimates for each effect modifier are presented in Figure 6-25. Note the wide confidence intervals associated with each of the risk estimates, specifically for Franklin et al. (2007, 091257) and Ostro et al. (2006, 087991), which suggests low statistical power for testing the differences between effect modifiers.

Franklin et al. (2008, 097426) analyzed 25 cities that had $PM_{2.5}$ monitoring and daily mortality data between the years 2000-2005 (with the study period varying from city to city). The choice of the 25 communities was based on the availability of $PM_{2.5}$ mass concentrations and daily mortality records for at least four years, along with $PM_{2.5}$ speciation data for at least 2 years between 2000 and 2005. Similar to Franklin et al. (2007, 091257), all-cause, cardiovascular, respiratory, and stroke deaths were examined; however, of the 25 cities included in the study, only 15 overlap with the 27 cities analyzed in Franklin et al. (2007, 091257). The authors obtained mortality data from the NCHS and various state health departments (CA, MA, MI, MN, MO, OH, PA, TX, and WA). Although the main objective of the study was to examine the role of $PM_{2.5}$ chemical species in the second stage analysis (Section 6.5.2.5), the first stage analysis conducted a time-series regression of

mortality on $PM_{2.5}$. In addition, the first stage regression performed a seasonal analysis in order to take advantage of seasonal variation in $PM_{2.5}$ chemical species across cities and to possibly explain the city-to-city variation in $PM_{2.5}$ mortality risk estimates. From this analysis a strong seasonal pattern was observed with the greatest effects occurring in the spring and summer seasons (Figure 6-25).

Overall, the risk estimates for all-cause, cardiovascular, and respiratory deaths reported by Franklin et al. (2008, 097426) are comparable to those presented in the 27 cities study (2007, 091257), as shown in Figure 6-26. When comparing the 2007 and 2008 studies conducted by Franklin et al. (2007, 091257; 2008, 097426), although only 15 cities overlap between the two studies and each study was designed differently (i.e., time-series vs. case-crossover), the magnitude of the $PM_{2.5}$ risk estimates reported were similar for the same averaging time, and both studies reported a regional pattern (East > West) similar to that found in the NMMAPS studies previously discussed.

Zanobetti and Schwartz (2009, 188462) conducted a multicity time-series study to examine associations between $PM_{2.5}$ and mortality in 112 U.S. cities. The cities included in this analysis encompass the majority of cities included in the Franklin et al. (2007, 091257; 2008, 097426) analyses. In this analysis a city represents a single county; however, 14 of the cities represent a composite of multiple counties. In addition to examining $PM_{2.5}$, the investigators also analyzed $PM_{10-2.5}$; these results are discussed in Section 6.5.2.3. Zanobetti and Schwartz (2009, 188462) analyzed $PM_{2.5}$ associations with all-cause, cardiovascular disease (CVD), MI, stroke, and respiratory mortality for the years 1999-2005. To be included in the analysis, each of the cities selected had to have at least 265 days of $PM_{2.5}$ data per year and at least 300 days of mortality data per year. The authors conducted a city- and season-specific Poisson regression to estimate excess risk for $PM_{2.5}$ lagged 0- and 1-days, adjusting for smooth functions (natural cubic splines) of days (1.5 df per season), the same-day and previous day temperature (3 df each), and day-of-week. The city specific estimates were then combined using a random effects model. Based on the assumption that climate affects PM exposures (e.g., ventilation and particle characteristics), the investigators combined city-specific estimates into six regions based on the Köppen climate classification scheme (e.g., "Mediterranean climates" for CA, OR, WA, etc.).

The overall combined excess risk estimates were: 0.98 % (95% CI: 0.75, 1.22) for all-cause; 0.85 % (95% CI: 0.46-1.24) for CVD, 1.18 % (95% CI: 0.48-1.89) for MI; 1.78 % (95% CI: 0.96-2.62) for stroke, and 1.68 % (95% CI: 1.04-2.33) for respiratory mortality for a 10 $\mu g/m^3$ increase in $PM_{2.5}$ at lag 0-1. When the risk estimates were combined by season, the spring estimates were the largest for all-cause and for all of the cause-specific mortality outcomes examined. For example, the risk estimate for all-cause mortality for the spring was 2.57% (95% CI: 1.96-3.19) with the estimates for the other seasons ranging from 0.25% to 0.95%. When examining cities that had both $PM_{2.5}$ and $PM_{10-2.5}$ data (i.e., 47 cities), the addition of $PM_{10-2.5}$ in the model did not alter the $PM_{2.5}$ estimates substantially, only decreasing slightly from 0.94% in a single pollutant model to 0.77% in a copollutant model with $PM_{10-2.5}$. When the risk estimates were combined by climatic regions, the estimated $PM_{2.5}$ risk for all-cause mortality were similar (all above 1% per 10 $\mu g/m^3$ increase) for all the regions except for the "Mediterranean" region (0.5%) which includes cities in CA, OR and WA, though the estimates in that region were significantly heterogeneous (Figure 6-24).

Source: Data from Zanobetti and Schwartz (2009, 188462).

Figure 6-23. Percent increase in all-cause (nonaccidental) and cause-specific mortality per 10 μg/m^3 increase in the average of 0- and 1-day lagged $PM_{2.5}$, combined by climatic regions.

The $PM_{2.5}$ risk estimate for all-cause mortality reported by Zanobetti and Schwartz (2009, 188462) for 112 cities (0.98% per 10 µg/m^3 increase in the average of 0- and 1-day lags) is generally consistent with that reported by Franklin et al. (2007, 091257) for 27 cities (0.82% [0.02-1.63]) and Franklin et al. (2008, 097426) for 25 cities (0.74% [95% CI: 0.41-1.07]) using the same 0- and 1-day avg exposure time. The seasonal pattern (i.e., higher risk estimates in the spring) found in this study is also consistent with the result from Franklin et al. (2008, 097426). Figure 6-23 highlights the risk estimates for all-cause, CVD, and respiratory morality combined by region. The regional division based on climatic types used in this study makes it difficult to directly compare the regional pattern of results from previous studies. However, an examination of empirical Bayes-adjusted effect estimates for each of the cities included in the analysis further confirms the heterogeneity observed between some cities and regions of the country (Figure 6-24). It is noteworthy that, unlike NMMAPS, which focused on PM_{10} and indicated larger risk estimates in the northeast, Zanobetti and Schwartz (2009, 188462) found that the all-cause mortality risk estimates were fairly uniform across the climatic regions, except for the "Mediterranean" region.

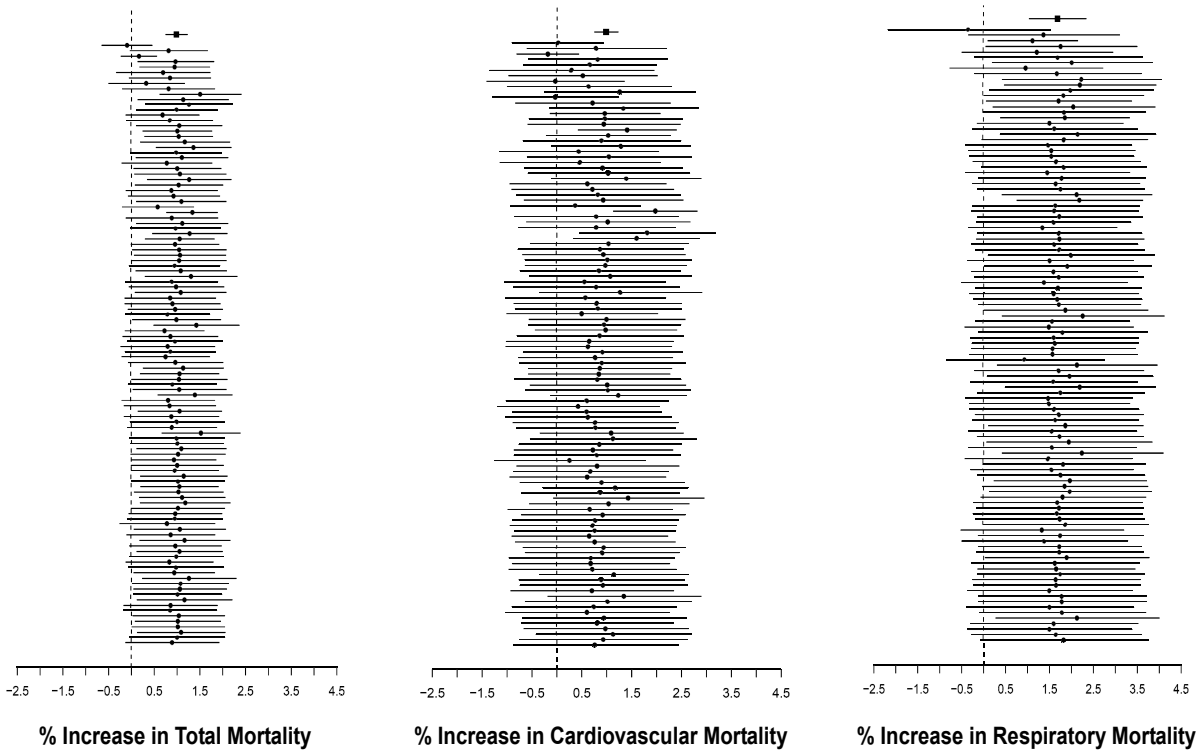


Figure 6-24. Empirical Bayes-adjusted city-specific percent increase in total (nonaccidental), cardiovascular, and respiratory mortality per 10 µg/m^3 increase in the average of 0- and 1-day lagged $PM_{2.5}$ by decreasing mean 24-h avg $PM_{2.5}$ concentrations. Based on estimates calculated from Zanobetti and Schwartz (2009, 188462) using the approach specified in Le Tertre et al. (2005, 087560).

Key to Figure 6-24

City	Mean	98th	City	Mean	98th	City	Mean	98th	City	Mean	98th
Rubidoux, CA	24.7	68.0	Taylors, SC	15.0	32.2	Waukesha, WI	13.4	35.3	Phoenix, AZ	11.4	30.7
Bakersfield, CA	21.7	80.3	Toledo, OH	14.9	36.6	Baton Rouge, LA	13.4	30.1	Tacoma, WA	11.4	38.1
Los Angeles, CA	19.7	51.1	Anaheim, CA	14.9	44.1	Memphis, TN	13.3	32.4	Port Arthur, TX	11.1	25.7
Fresno, CA	18.7	64.9	New York, NY	14.7	38.1	Erie, PA	12.9	36.1	Cedar Rapids, IA	11.0	31.0
Atlanta, GA	17.6	38.2	Washington, PA	14.7	37.0	Dallas, TX	12.8	28.7	Dodge, WI	10.9	32.9
Steubenville, OH	17.1	41.4	Winston, NC	14.7	34.1	Houston, TX	12.8	27.5	Oklahoma, OK	10.8	26.1
Cincinnati, OH	17.1	39.9	Elizabeth, NJ	14.6	38.2	Chesapeake, VA	12.8	29.8	Des Moines, IA	10.5	27.9
Birmingham, AL	16.5	38.8	Philadelphia, PA	14.6	36.6	Wilkes-Barre, PA	12.8	32.5	Jacksonville, FL	10.5	25.3
Middletown, OH	16.5	38.4	St. Louis, MO	14.5	33.7	Norfolk, VA	12.7	29.6	Omaha, NE	10.5	28.0
Indianapolis, IN	16.4	38.2	Allentown, PA	14.4	38.9	Sacramento, CA	12.6	45.0	Denver, CO	10.5	26.4
Cleveland, OH	16.3	40.5	Richmond, VA	14.3	33.0	Springfield, MA	12.5	35.1	Pinellas, FL	10.4	23.1
Dayton, OH	16.3	38.3	Spartanburg, SC	14.2	31.4	New Orleans, LA	12.5	29.0	Austin, TX	10.4	24.5
Columbus, OH	16.2	38.3	Durham, NC	14.2	32.9	Ft. Worth, TX	12.4	27.7	Orlando, FL	10.3	24.3
Detroit, MI	16.2	41.0	Little Rock, AR	14.2	31.8	Pensacola, FL	12.3	31.2	Klamath, OR	10.2	40.7
Akron, OH	16.0	39.0	Easton, PA	14.2	39.7	Davenport, IA	12.3	32.1	Seattle, WA	10.1	27.9
Louisville, KY	15.9	38.0	Raleigh, NC	14.1	31.8	Avondale, LA	12.3	28.6	Medford, OR	10.0	37.3
Chicago, IL	15.8	39.1	Greensboro, NC	14.1	31.0	Boston, MA	12.3	30.2	Bath, NY	9.6	29.3
Pittsburgh, PA	15.7	43.1	Mercer, PA	14.1	36.4	Holland, MI	12.1	35.0	Provo, UT	9.5	38.5
Harrisburg, PA	15.6	40.2	Annandale, VA	14.0	34.6	Charleston, SC	12.1	27.9	Miami, FL	9.4	20.5
Baltimore, MD	15.6	38.8	Nashville, TN	13.9	31.0	Tampa, FL	12.1	25.8	El Paso, TX	9.0	24.4
Youngstown, OH	15.6	38.1	Dumbarton, VA	13.8	31.9	Tulsa, OK	12.1	32.3	Spokane, WA	8.9	30.6
Knoxville, TN	15.5	32.9	Columbia, SC	13.7	30.7	Kansas, MO	12.0	28.6	San Antonio, TX	8.9	21.9
Gary, IN	15.5	37.5	Milwaukee, WI	13.7	36.3	Scranton, PA	11.9	33.0	Portland, OR	8.9	25.4
Charlotte, NC	15.3	32.7	New Haven, CT	13.6	36.8	Hartford, CT	11.8	33.5	Davie, FL	8.4	19.1
Warren, OH	15.2	37.4	Grand Rapids, MI	13.6	36.4	Minneapolis, MN	11.6	31.6	Eugene, OR	8.1	29.9
Washington, DC	15.2	37.2	El Cajon, CA	13.5	34.9	Worcester, MA	11.5	30.2	Palm Beach, FL	7.8	18.4
Wilmington, DE	15.1	37.6	Gettysburg, PA	13.4	36.5	Salt Lake, UT	11.5	52.4	Bend, OR	7.7	23.5
Carlisle, PA	15.1	40.0	State College, PA	13.4	38.5	Providence, RI	11.5	30.5	Albuquerque, NM	6.6	17.9

Note: The top effect estimate in the figures represents the overall effect estimate for that mortality outcome across all cities. The remaining effect estimates are ordered by the highest (i.e., Rubidoux, CA) to lowest (i.e., Albuquerque, NM) mean 24-h $PM_{2.5}$ concentrations across the cities examined. In the key the cities are reported in this order, which represents the policy relevant concentrations for the annual standard, but the policy relevant $PM_{2.5}$ concentrations for the daily standard (i.e., 98th percentile of the 24-h average) are also listed for each city (from Zanobetti and Schwartz (2009, 188462))

$PM_{2.5}$-Mortality Associations on a Regional Scale: California

Ostro et al. (2006, 087991) examined associations between $PM_{2.5}$ and daily mortality in nine heavily populated California counties (Contra Costa, Fresno, Kern, Los Angeles, Orange, Riverside, Sacramento, San Diego, and Santa Clara) using data from 1999 through 2002. The authors used a two-stage model to examine all-cause, respiratory, cardiovascular, ischemic heart disease, and diabetes mortality individually and by potential effect modifier (i.e., age, gender, race, ethnicity, and education level). The a priori exposure periods examined included the average of 0- and 1-day lags (lag 0-1) and the 2-day lag (lag 2). The authors selected these non-overlapping lags (i.e., rather than selecting lag 1 as the single-day lag) because previous studies have reported stronger associations at lags of 1 or 2 days or with cumulative exposure over three days. It is unclear why the investigators chose these non-overlapping lags (i.e., single-day lag of 2 instead of 1) even though they state they based the selection of their lag days on results presented in previous studies, which found the strongest association for PM lagged 1 or 2 days. Using the average of 0- and 1-day lags Ostro et al.

(2006, 087991) reported combined estimates of: 0.6% (95% CI: 0.2-1.0), 0.6% (95% CI: 0.0-1.1), 0.3% (95% CI: -0.5 to 1.0), 2.2% (95% CI: 0.6-3.9), and 2.4% (95% CI: 0.6-4.2) for all-cause, cardiovascular, ischemic heart disease, respiratory, and diabetes deaths, respectively, per 10 $\mu g/m^3$. The authors also conducted a sensitivity analysis of risk estimates based on the extent of temporal adjustment, which showed monotonic reductions for all of the death categories examined when 4, 8, and 12 degrees of freedom per year were used.

Five of the nine counties examined in the Ostro et al. (2006, 087991) analysis contain cities that are among the 27 cities examined in the Franklin et al. (2007, 091257) analysis for the same period, 1999-2002. While the lags used were different between these two studies, both presented $PM_{2.5}$ risk estimates in individual cities or counties (graphically in the Franklin et al. study (2007, 091257); in a table in the Ostro et al. study (2006, 087991)), which allowed for a cursory evaluation of consistency between the two analyses. In Franklin et al. (2007, 091257), $PM_{2.5}$ risk estimates at lag 1 day for the cities Los Angeles and Riverside were slightly negative, whereas Fresno, Sacramento, and San Diego showed positive values above 1% per 10 $\mu g/m^3$ increase in $PM_{2.5}$. The 2-day lag result presented in Ostro et al. (2006, 087991) is qualitatively consistent, with Los Angeles and Riverside, both of which show slightly negative estimates, while the other 3 locations all show positive, but somewhat smaller estimates, than those reported by Franklin et al. (2007, 091257). The estimates for the average of 0- and 1-day lags for these five counties in Ostro et al. (2006, 087991), which contain cities examined in Franklin et al. (2007, 091257), were all positive. Thus, these two $PM_{2.5}$ studies showed some consistencies in risk estimates even though they used different lag periods and a different definition for the study areas of interest (i.e., counties vs. cities). The risk estimates for Franklin et al. (2007, 091257) and Ostro et al. (2006, 087991), stratified by various effect modifiers (e.g., gender, race, etc.), are summarized in Figure 6-25. Of note is the contrast in the results presented for the effect modification analysis for "in-hospital" versus "out-of-hospital" deaths for Ostro et al. (2006, 087991), which differs from the results presented in the PM_{10} study conducted by Zeka et al. (2006, 088749). Ostro et al. (2006, 087991) observed comparable risk estimates for "in-hospital" vs. "out-of-hospital" deaths, whereas Zeka et al. (2006, 088749) observed a large difference between the two in the 20 cities study discussed earlier. This difference in effects observed between the two studies is more than likely due to the compositional differences in PM_{10} in the cities examined in Zeka et al. (2006, 088749) (i.e., PM_{10} more or less dominated by $PM_{2.5}$ and the subsequent composition of $PM_{2.5}$).

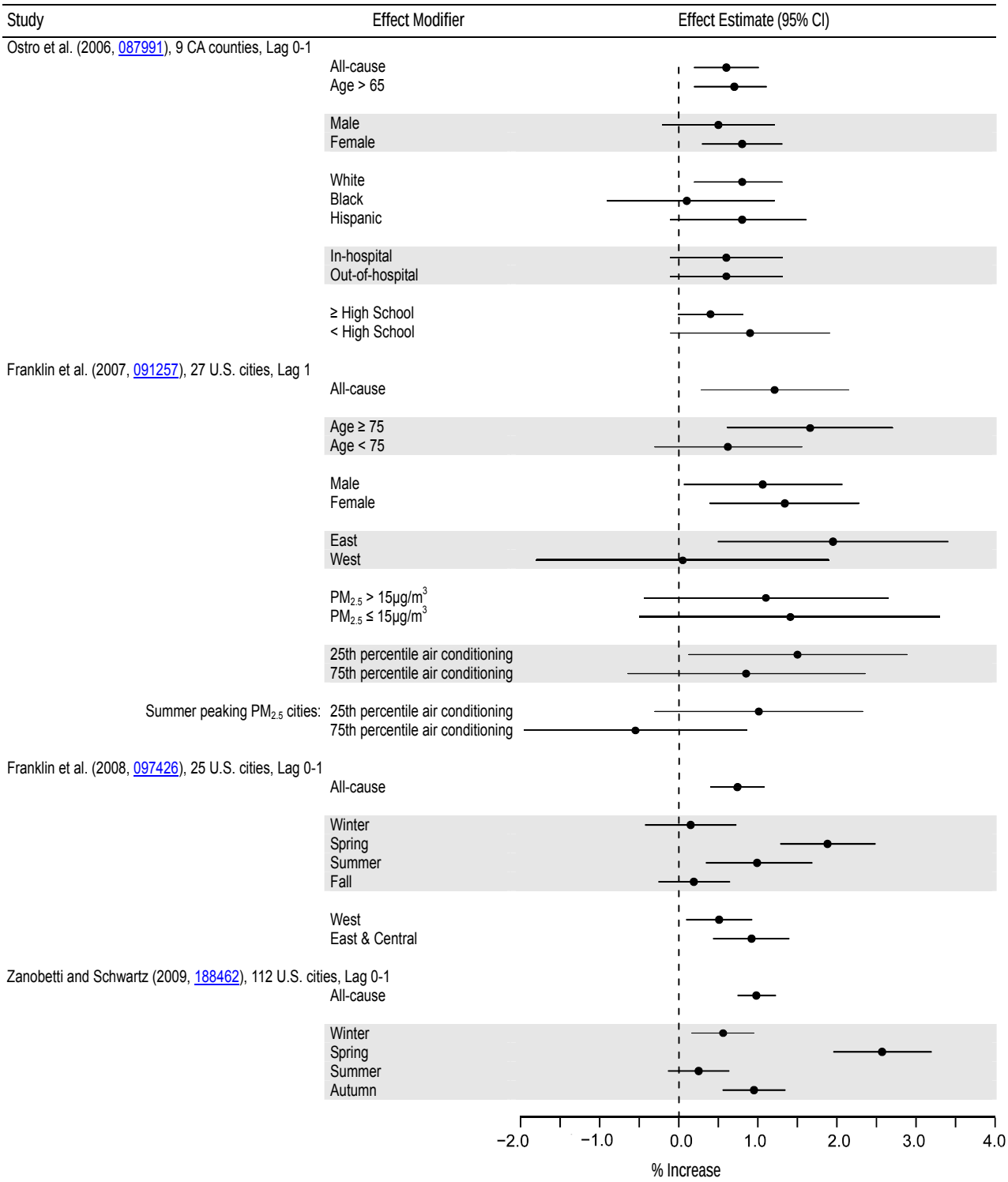


Figure 6-25. Summary of percent increase in all-cause (nonaccidental) mortality per 10 µg/m^3 increase in $PM_{2.5}$ by various effect modifiers.

$PM_{2.5}$-Mortality Associations in Canada

An analysis of multiple pollutants, including $PM_{2.5}$, in 12 Canadian cities found the most consistent associations for NO_2 (Burnett et al., 2004, 086247). In this analysis, $PM_{2.5}$ was only measured every 6th day in much of the study period, and the simultaneous inclusion of NO_2 and $PM_{2.5}$ in a model on the days when $PM_{2.5}$ data were available eliminated the $PM_{2.5}$ association (from 0.60% to -0.10% per 10 $\mu g/m^3$ increase in $PM_{2.5}$). However, the investigators noted that during the later study period of 1998-2000 when daily TEOM $PM_{2.5}$ data were available for 11 of the 12 cities, a simultaneous inclusion of NO_2 and $PM_{2.5}$ resulted in considerable reduction of the NO_2 risk estimate, while the $PM_{2.5}$ risk estimate was only slightly reduced from 1.1% to 0.98% (95% CI: -0.16 to 2.14). Thus, the relative importance of NO_2 and $PM_{2.5}$ on mortality effect estimates has not been resolved when using the Canadian data sets.

Summary of $PM_{2.5}$ Risk Estimates

The risk estimates for all-cause mortality for all ages ranged from 0.29% Dominici et al. (2007, 097361) to 1.21% Franklin et al. (2007, 091257) per 10 $\mu g/m^3$ increase in $PM_{2.5}$ (Figure 6-26). An examination of cause-specific risk estimates found that $PM_{2.5}$ risk estimates for cardiovascular deaths are similar to those for all-cause deaths (0.30-1.03%), while the effect estimates for respiratory deaths were consistently larger (1.01-2.2%), albeit with larger confidence intervals, than those for all-cause or cardiovascular deaths using the same lag/averaging indices. Figure 6-27 summarizes the $PM_{2.5}$ risk estimates for all U.S.- and Canadian-based studies by cause-specific mortality.

An examination of lag structure observed results similar to those reported for PM_{10} with most studies reporting either single day lags or two-day avg lags with the strongest effects observed on lag 1 or lag 0-1. In addition, seasonal patterns of $PM_{2.5}$ risk estimates were found to be similar to those reported for PM_{10}, with the warmer season showing the strongest association. An evaluation of regional associations found that in most cases the eastern U.S. had the highest $PM_{2.5}$ mortality risk estimates, but this was dependent on the geographic designations made in the study. When grouping cities by climatic regions, similar $PM_{2.5}$ mortality risk estimates were observed across the country except in the Mediterranean region, which included CA, OR, and WA.

Of the studies evaluated, only Burnett et al. (2004, 086247), a Canadian multicity study, analyzed gaseous pollutants and found mixed results, with possible confounding of $PM_{2.5}$ risk estimates by NO_2. Although the recently evaluated U.S.-based multicity studies did not analyze potential confounding of $PM_{2.5}$ risk estimates by gaseous pollutants, evidence from single-city studies evaluated in the 2004 PM AQCD (U.S. EPA, 2004, 056905) suggest that gaseous copollutants do not confound the $PM_{2.5}$-mortality association, which is further supported by studies that examined the PM_{10}-mortality relationship.

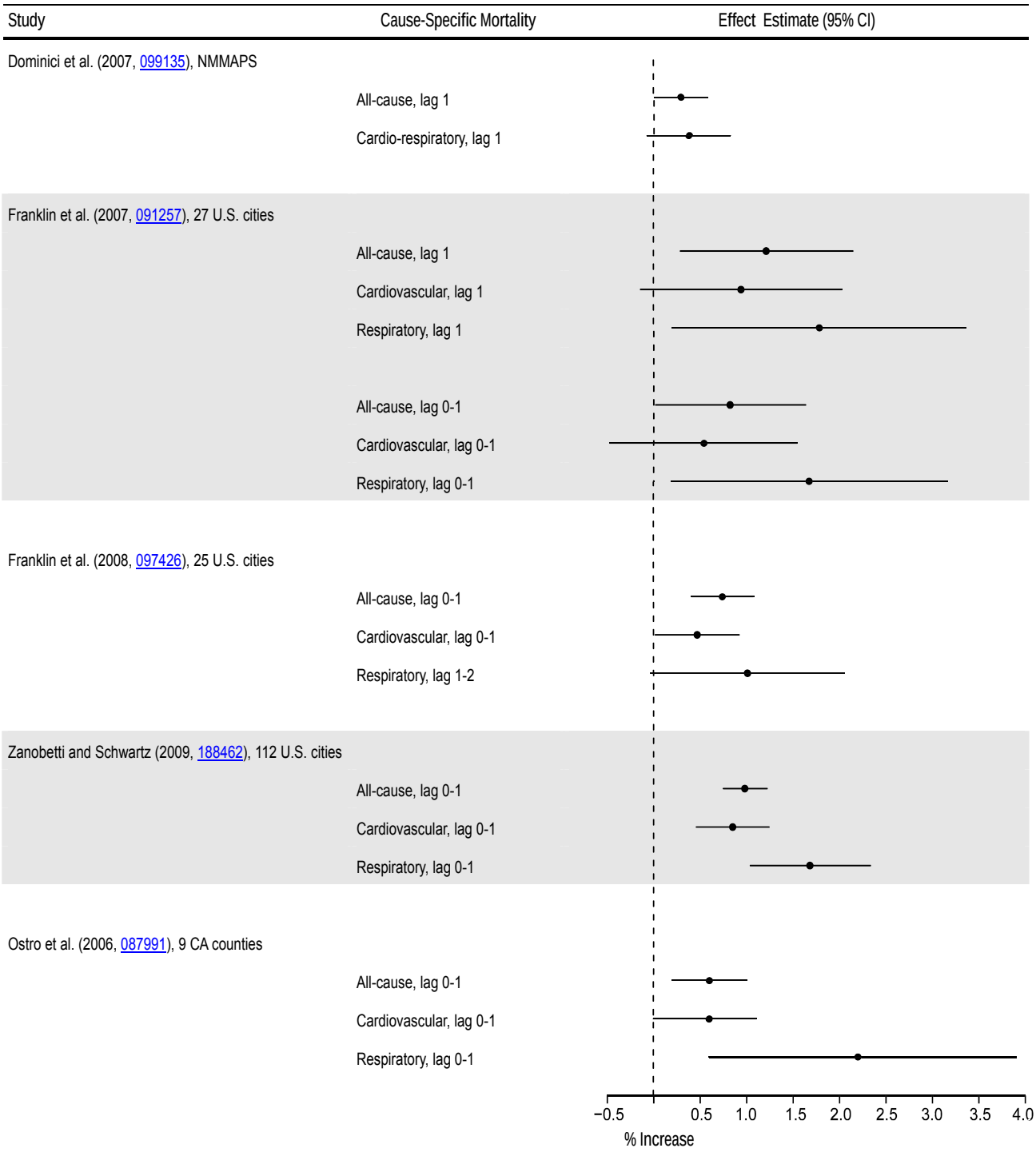


Figure 6-26. Summary of percent increase in all-cause (nonaccidental) and cause-specific mortality per 10 μg/m^3 increase in $PM_{2.5}$ from recent multicity studies.

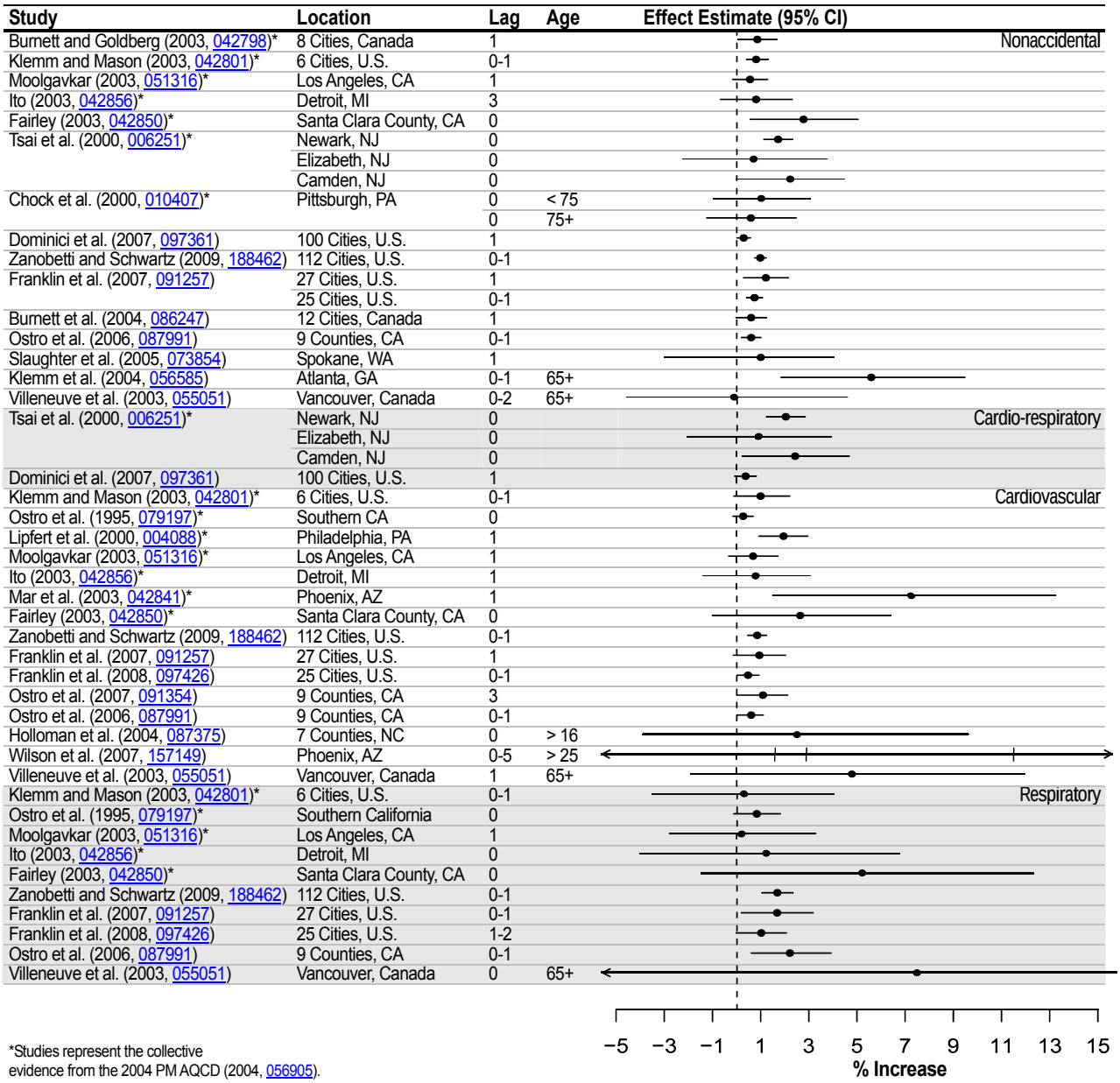


Figure 6-27. Summary of percent increase in all-cause (nonaccidental) and cause-specific mortality per 10 μg/m^3 increase in $PM_{2.5}$ for all U.S.- and Canadian-based studies. The three vertical lines for the Wilson et al. (2007, 157149) estimate represent the central, middle, and outer Phoenix estimates.

6.5.2.3. Thoracic Coarse Particles ($PM_{10-2.5}$)

In the 2004 PM AQCD (U.S. EPA, 2004, 056905), a limited number of studies, mostly single-city analyses, were evaluated that examined thoracic coarse ($PM_{10-2.5}$) PM for its association with mortality. Of these studies a small number examined both $PM_{2.5}$ and $PM_{10-2.5}$ effects, and found some evidence for $PM_{10-2.5}$ effects of the same magnitude as $PM_{2.5}$. However, multiple limitations in these studies were identified including measurement and exposure issues for $PM_{10-2.5}$ and the correlation between $PM_{2.5}$ and $PM_{10-2.5}$. These limitations increased the uncertainty surrounding the concentrations at which $PM_{10-2.5}$-mortality associations are observed.

A thorough analysis of $PM_{10-2.5}$ mortality associations requires information on the speciation of $PM_{10-2.5}$. This is because, while a large percent of the composition of coarse particles may consist of crustal materials by mass, depending on available sources, the surface chemical characteristics of $PM_{10-2.5}$ may also vary from city to city. Thus, without information on the chemical speciation of $PM_{10-2.5}$, the apparent variability in observed associations between $PM_{10-2.5}$ and mortality across cities is difficult to characterize. Although this type of information is not available in the current literature, the relative importance of the associations observed between $PM_{10-2.5}$ and mortality in the following studies is of interest.

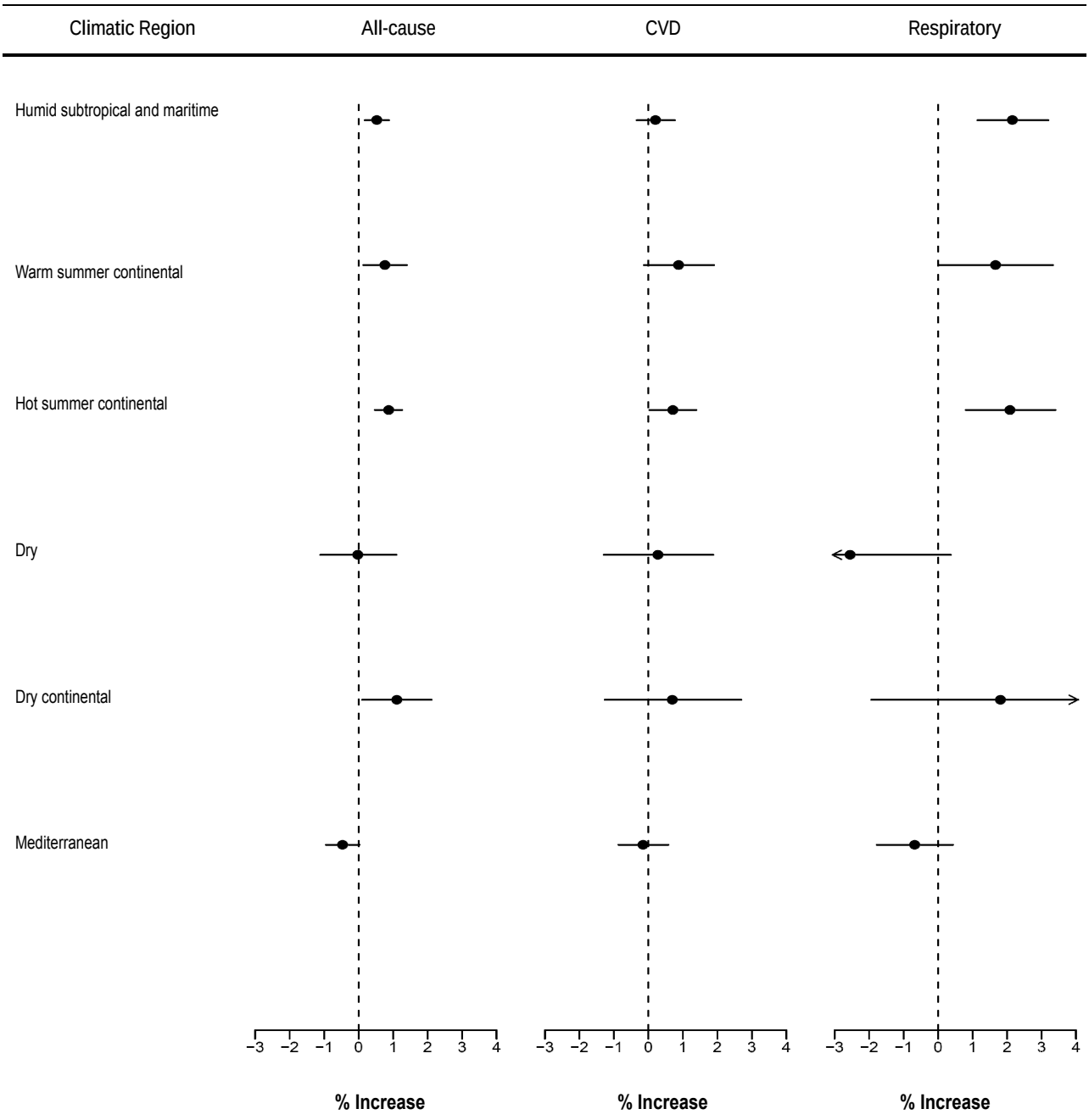
$PM_{10-2.5}$ Concentrations Estimated Using the Difference Method

The Zanobetti and Schwartz (2009, 188462) multicity analysis, described for $PM_{2.5}$ section (Section 6.5.2.2), also examined the association between computed $PM_{10-2.5}$ and all-causes, cardiovascular disease (CVD), MI, stroke, and respiratory mortality for the years 1999-2005. Of the 112 cities included in the $PM_{2.5}$ analysis only 47 cities had both $PM_{2.5}$ and PM_{10} data available. $PM_{10-2.5}$ was estimated in these cities by differencing the countywide averages of PM_{10} and $PM_{2.5}$. In addition to examining the association between $PM_{10-2.5}$ and mortality for the average of lags 0 and 1 day, the investigators also considered a distributed lag of 0-3 days. The risk estimates for $PM_{10-2.5}$ were presented for both a single pollutant model and a copollutant model with $PM_{2.5}$, and were also combined by season and climatic regions as was done in the $PM_{2.5}$ analysis.

The study found a significant association between the computed $PM_{10-2.5}$ and all-cause, CVD, stroke, and respiratory mortality. The combined estimate for the 47 cities using the average of 0- and 1-day lag $PM_{10-2.5}$ for all-cause mortality was 0.46% (95% CI: 0.21-0.71) per 10 $\mu g/m^3$ increase. The estimate obtained using the distributed lag model was smaller (0.31% [95% CI: 0.00-0.63]). The seasonal analysis showed larger risk estimates in the spring for all-cause (1.01%) and respiratory mortality (2.56%) (i.e., the same pattern observed in the $PM_{2.5}$ analysis); however, for CVD mortality, the estimates for spring (0.95%) and summer (1.00%) were comparable. When the risk estimates were combined by climatic region (Figure 6-28), for all-cause mortality, the "dry, continental" region (which included Salt Lake City, Provo, and Denver, all of which had relatively high estimated $PM_{10-2.5}$ concentrations) showed the largest risk estimate (1.11% [95% CI: 0.11-2.11]), but the "dry" region (which included Phoenix and Albuquerque, the two cities with high $PM_{10-2.5}$ concentrations) and the "Mediterranean" region (which included cities in CA, OR, and WA) did not show positive associations. The other three regions (i.e., "hot summer, continental," "warm summer, continental," and "humid, subtropical and maritime"), which included cities that correspond to the mid-west, southeast, and northeast geographic regions as defined in previous NMMAPS analyses, all showed significantly positive associations. Similar regional patterns of associations were found for CVD and respiratory mortality, which are further confirmed when examining the empirical Bayes-adjusted city-specific estimates in Figure 6-29. The regional pattern of associations for MI and stroke are less clear, because of the wider confidence intervals due to the smaller number of deaths in these specific categories. The lack of a $PM_{10-2.5}$-mortality association in the "dry" region reported in this study is in contrast to the results from three studies that analyzed Phoenix data and found associations, as reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905), and Wilson et al. (2007, 157149) (discussed below).

Although the results from this analysis are informative because it is the first multicity U.S.-based study that examined the association between short-term exposure to $PM_{10-2.5}$ and mortality on a large scale, some limitations do exist. Specifically, it is not clear how the computed $PM_{10-2.5}$ measurements used by Zanobetti and Schwartz (2009, 188462) compare with the $PM_{10-2.5}$ concentrations obtained by directly measuring $PM_{10-2.5}$ using a dichotomous sampler, or the $PM_{10-2.5}$ concentrations computed using the difference of PM_{10} and $PM_{2.5}$ measured at co-located samplers.

Additional studies evaluated the association between short-term exposure to $PM_{10-2.5}$ and mortality using $PM_{10-2.5}$ concentrations estimated by subtracting PM_{10} from $PM_{2.5}$ concentrations at co-located monitors. Although $PM_{10-2.5}$ concentrations estimated using this approach are not ideal, the results from these studies are informative in evaluating the $PM_{10-2.5}$ mortality association.



Source: Data from Zanobetti and Schwartz (2009, 188462).

Figure 6-28. Percent increase in all-cause (nonaccidental) and cause-specific mortality per 10 μg/m^3 increase in the average of 0- and 1-day lagged $PM_{10-2.5}$, combined by climatic regions.

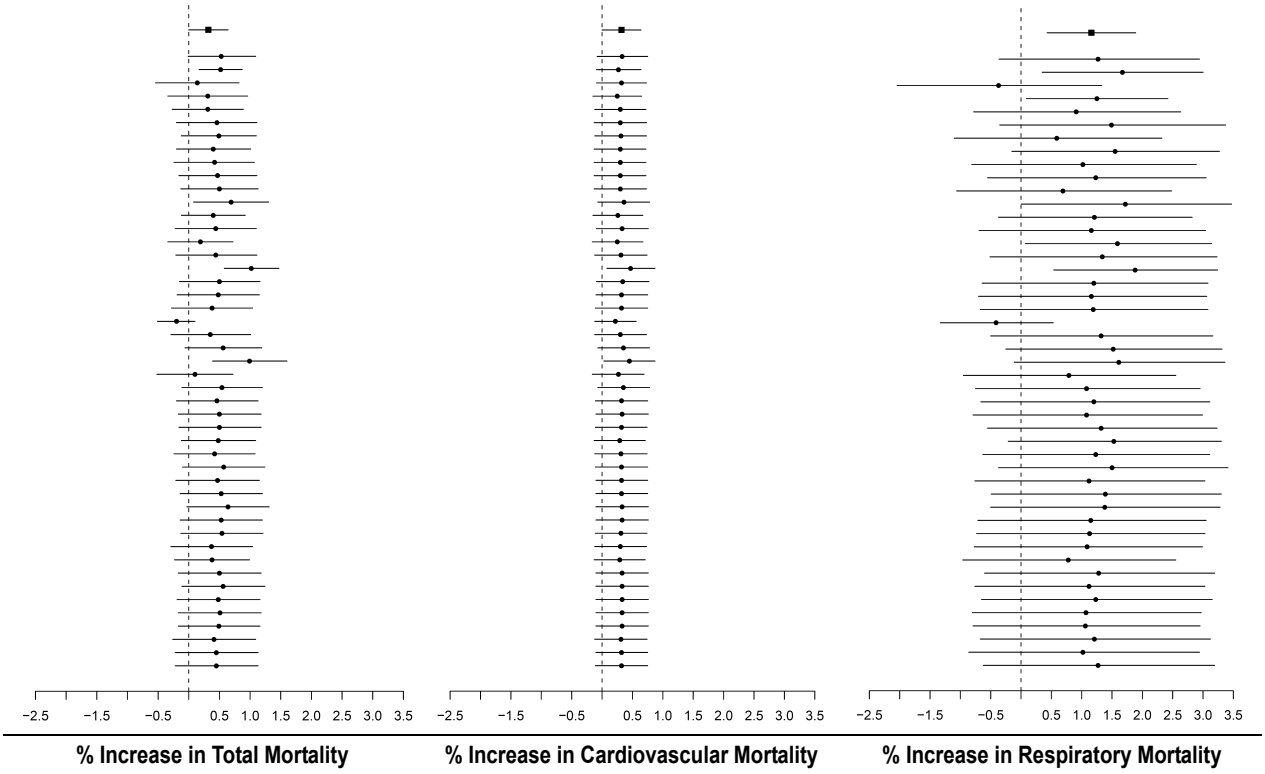


Figure 6-29. Empirical Bayes-adjusted city-specific percent increase in total (nonaccidental), cardiovascular, and respiratory mortality per 10 μg/m^3 increase in the average of 0- and 1-day lagged $PM_{10-2.5}$ by decreasing 98th percentile of mean 24-h avg $PM_{10-2.5}$ concentrations. Based on estimates calculated from Zanobetti and Schwartz (2009, 188462) using the approach specified in Le Tertre et al. (2005, 087560).

Key for Figure 6-29

City	98th	Mean	City	98th	Mean	City	98th	Mean	City	98th	Mean
El Paso, TX	105.1	25.4	Cleveland, OH	51.2	15.2	Sacramento, CA	31.5	10.2	Louisville, KY	23.3	8.3
St. Louis, MO	81.9	15.2	Davenport, IA	49.9	15.3	Tampa, FL	29.1	12.9	Wilkes-Barre, PA	22.2	6.2
Phoenix, AZ	80.1	33.3	Birmingham, AL	49.6	14.2	Toledo, OH	28.8	7.6	New York, NY	22.0	6.4
Detroit, MI	77.5	17.3	Provo, UT	49.3	18.2	Washington, PA	27.8	6.5	Wilmington, DE	21.8	7.0
Gary, IN	71.3	6.9	Chicago, IL	46.1	12.4	Allentown, PA	27.8	4.5	Raleigh, NC	20.9	6.9
Omaha, NE	65.6	24.7	Easton, PA	43.9	12.0	Atlanta, GA	27.4	8.6	Scranton, PA	19.2	6.1
Albuquerque, NM	64.3	22.9	Steubenville, OH	43.5	12.1	Davie, FL	25.5	9.4	Harrisburg, PA	18.6	5.4
New Haven, CT	58.4	11.9	Columbia, SC	42.9	8.4	Taylors, SC	25.4	8.0	Akron, OH	17.7	5.3
Bakersfield, CA	55.9	16.1	Los Angeles, CA	42.5	13.5	Memphis, TN	24.3	9.3	Charleston, SC	17.6	6.6
Des Moines, IA	55.0	16.2	Spokane, WA	41.8	13.8	Seattle, WA	23.7	9.0	Winston, NC	16.5	7.4
Denver, CO	53.8	18.1	Columbus, OH	40.0	11.2	Baltimore, MD	23.5	8.9	Erie, PA	14.9	3.1
Salt Lake, UT	52.6	19.2	Pittsburgh, PA	32.0	9.4	Cincinnati, OH	23.3	7.8			

Note: The top effect estimate in the figures represents the overall effect estimate for that mortality outcome across all cities. The remaining effect estimates are ordered by the highest (i.e., El Paso, TX) to lowest (i.e., Erie, PA) 98th percentile of the mean 24-h $PM_{10-2.5}$ concentrations across the cities examined, which is the policy relevant concentration for the daily standard [from Zanobetti and Schwartz (2009, 188462)].

Slaughter et al. (2005, 073854) examined the association of various PM size fractions (PM_1, $PM_{2.5}$, PM_{10}, $PM_{10-2.5}$) and CO with ED visits, HAs, and mortality in Spokane, WA for the period 1995-2001. Although the authors did not report mortality risk estimates for $PM_{10-2.5}$, they did not find an association between any PM size fraction (or CO) and mortality or cardiac HAs at lags of 0-3 days.

Wilson et al. (2007, 157149) examined the association between size-fractionated PM ($PM_{2.5}$ and $PM_{10-2.5}$) and cardiovascular mortality in Phoenix for the study period 1995-1997, using mortality data aggregated for three geographic regions: "Central Phoenix," "Middle Ring," and "Outer Phoenix," which were constructed as a composite of zip codes of residence in order to compare population size among the three areas. The authors reported apparently different patterns of associations between $PM_{2.5}$ and $PM_{10-2.5}$ in terms of the size of the risk estimate across the three areas and temporal patterns of associations. In the "Middle Ring" where $PM_{10-2.5}$ showed the strongest association, the estimated risk per 10 $\mu g/m^3$ increase for a 1 day lag was 3.4% (95% CI: 1.0-5.8). The estimated risk for $PM_{2.5}$ found for "Central Phoenix" was 6.6% (95% CI: 1.1-12.5) for lag 1. The authors speculated that the apparent difference in estimated risks across the areas might be due to the lower SES in "Central Phoenix" or the lower exposure error, but the relatively wide confidence bands of these estimates make it difficult to establish such relationships (Section 8.1.7 for a detailed discussion on SES and susceptibility to PM exposure).

Kettunen et al. (2007, 091242) analyzed UFPs, $PM_{2.5}$, PM_{10}, $PM_{10-2.5}$, and gaseous pollutants for their associations with stroke mortality in Helsinki during the study period of 1998-2004. The authors did not observe an association between air pollution and mortality for the whole year or cold season, but they did find associations for $PM_{2.5}$ (13.3% [95% CI: 2.3-25.5] per 10 $\mu g/m^3$), PM_{10}, and CO during the warm season, most strongly at lag 1 day. An association was also observed for $PM_{10-2.5}$ during the warm season (7.8% [95% CI: -7.4 to 25.5] per 10 $\mu g/m^3$ at lag 1 day); however, it was weaker than $PM_{2.5}$.

The Perez et al. (2008, 156020) analysis tested the hypothesis that outbreaks of Saharan dust exacerbate the effects of $PM_{2.5}$ and $PM_{10-2.5}$ on daily mortality. Changes of effects between Saharan and non-Saharan dust days were assessed using a time-stratified case-crossover design involving 24,850 deaths between March 2003 and December 2004 in Barcelona, Spain. Saharan dust days were identified from back-trajectory and satellite images. Chemical speciation, but not an analysis for microbes or fungi, was conducted approximately once a week during the study period. On Saharan dust days, mean concentrations were 1.2 times higher for $PM_{2.5}$ (29.9 $\mu g/m^3$) and 1.1 times higher for $PM_{10-2.5}$ (16.4 $\mu g/m^3$) than on non-Saharan dust days. During Saharan dust days (90 days out of 602), the $PM_{10-2.5}$ risk estimate was 8.4% (95% CI: 1.5-15.8) per 10 $\mu g/m^3$ increase at lag 1 day, compared with 1.4% (95% CI: -0.8 to 3.4) during non-Saharan dust days. In contrast, there was not an additional increased risk of daily mortality for $PM_{2.5}$ during Saharan dust days (5.0%

[95% CI: 0.5-9.7]) compared with non-Saharan dust days (3.5% [95% CI: 1.6-5.5]). However, differences in chemical composition (i.e., $PM_{2.5}$ was primarily composed of nonmineral carbon and secondary aerosols; whereas $PM_{10-2.5}$ was dominated by crustal elements) did not explain these observations. Note also when examining all days combined, both size fractions were associated with mortality, but the $PM_{2.5}$ association was found to be stronger.

$PM_{10-2.5}$ Concentrations Directly Measured

In Burnett et al. (2004, 086247), which analyzed the association of multiple pollutants with mortality in 12 Canadian cities, described previously; the authors also examined $PM_{10-2.5}$. In this study the authors collected $PM_{10-2.5}$ using dichotomous samplers with an every-6th-day schedule. When both NO_2 and $PM_{10-2.5}$ were included in the regression model, the $PM_{10-2.5}$ effect estimate was reduced from 0.65% (95% CI: -0.10 to 1.4) to 0.31% (95% CI: -0.49 to 1.1) per 10 $\mu g/m^3$ increase in 1-day lag $PM_{10-2.5}$. These risk estimates are similar to those reported for $PM_{2.5}$, which were also reduced upon the inclusion of NO_2 in the two-pollutant model, but to a greater extent, from 0.60% (95% CI: -0.03 to 1.2) to -0.1% (95% CI: -0.86 to 0.67).

Villeneuve et al. (2003, 055051) analyzed the association between $PM_{2.5}$, $PM_{10-2.5}$, TSP, PM_{10}, SO_4^{2-}, and gaseous copollutants in Vancouver, Canada, using a cohort of approximately 550,000 whose vital status was ascertained between 1986 and 1999. In this study $PM_{2.5}$ and $PM_{10-2.5}$ were directly measured using dichotomous samplers. The authors examined the association of each air pollutant with all-cause, cardiovascular, and respiratory mortality, but only observed significant results for cardiovascular mortality at lag 0 for both $PM_{10-2.5}$ and $PM_{2.5}$. They found that $PM_{10-2.5}$ (5.4% [95% CI: 1.1-9.8] per 10 $\mu g/m^{3)}$, was more strongly associated with cardiovascular mortality than $PM_{2.5}$ (4.8% [95% CI: -1.9 to 12.0] per 10 $\mu g/m^{3)}$.

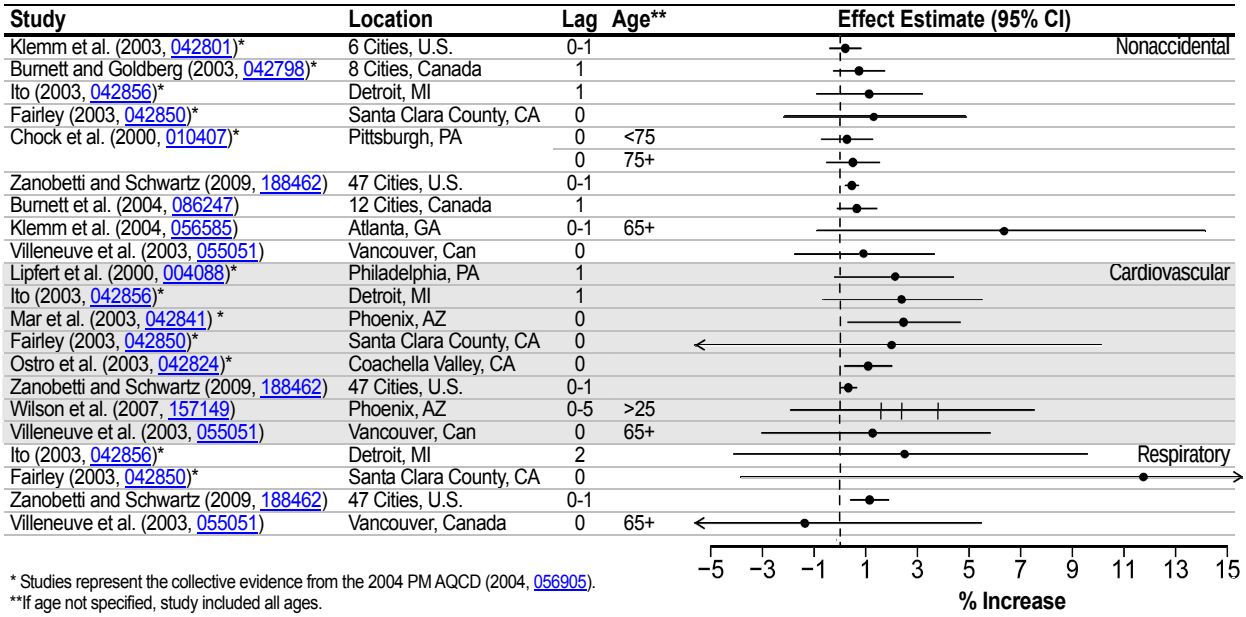
Klemm et al. (2004, 056585) analyzed various components of PM and gaseous pollutants for their associations with mortality in Fulton and DeKalb Counties, Georgia for the 2-yr period, 1998-2000. $PM_{10-2.5}$ concentrations were obtained from the ARIES database, which directly measured $PM_{10-2.5}$ using dichotomous samplers. In this analysis the authors adjusted for temporal trend using quarterly, monthly, and biweekly knots, and reported estimates for all-cause, circulatory, respiratory, cancer, and other causes mortality for each scenario. Overall, $PM_{2.5}$ was, more strongly associated with mortality than $PM_{10-2.5}$. For example, using the average of 0- and 1-day lags, the risk estimates for $PM_{2.5}$ and $PM_{10-2.5}$ in the monthly knots model for all-cause mortality, ages $\geq$ 65 yr were 5.6% (95% CI: 1.9-9.5) and 6.4% (95% CI: -0.5 to 14.1) per 10 $\mu g/m^3$ increase, respectively.[1]

Summary of $PM_{10-2.5}$ Risk Estimates

The results from newly available studies that examined the association between short-term exposure to $PM_{10-2.5}$ primarily consisted of single-city studies. Collectively these studies found consistent, positive associations, with the precision of each association varying by study location. The evidence from those single-city studies conducted in the U.S. and Canada in combination with the multicity studies evaluated (i.e., in the U.S. and Canada), provide evidence for $PM_{10-2.5}$ effects. However, the various methods used to estimate exposure to $PM_{10-2.5}$ (e.g., direct measurement of $PM_{10-2.5}$ using dichotomous samplers, calculating the difference between PM_{10} and $PM_{2.5}$ concentrations) in the studies evaluated add uncertainty to the associations observed. Specifically, a new U.S. multicity study (Zanobetti and Schwartz, 2009, 188462) estimated $PM_{10-2.5}$ by calculating the difference between the county-average PM_{10} and $PM_{2.5}$ concentrations. Although there are limitations in the method used by Zanobetti and Schwartz (2009, 188462) associations between $PM_{10-2.5}$ and mortality were observed throughout multiple regions of the country. However, some of the findings of this new multicity study (e.g., no associations in "dry" region where $PM_{10-2.5}$ levels are high) are not consistent with the findings of the $PM_{10-2.5}$ studies evaluated in the 2004 PM AQCD (U.S. EPA, 2004, 056905), and suggest that the coarse fraction is associated with mortality in areas of the U.S. where $PM_{10-2.5}$ levels are not high. Limitations also exist in the $PM_{10-2.5}$ associations reported due to the small number of $PM_{10-2.5}$ studies that have investigated confounding by gaseous

[1] The monthly knot model was selected for comparison because, overall, $PM_{2.5}$ showed the strongest association with all-cause mortality among the 15 air pollution indices examined when using this model.

copollutants or the influence of model specification on $PM_{10-2.5}$ risk estimates. Additionally, more data is needed to characterize the chemical and biological components that may modify the potential toxicity of $PM_{10-2.5}$. Figure 6-30 summarizes the $PM_{10-2.5}$ risk estimates for all U.S.-, Canadian-, and international-based studies by cause-specific mortality.



* Studies represent the collective evidence from the 2004 PM AQCD (2004, 056905).
**If age not specified, study included all ages.

Figure 6-30. Summary of percent increase in total (nonaccidental) and cause-specific mortality per 10 µg/m^3 increase in $PM_{10-2.5}$ for all U.S.-, Canadian-, and international-based studies. The three vertical lines for the Wilson et al. (2007, 157149) estimate represent the central, middle, and outer Phoenix estimates.

6.5.2.4. Ultrafine Particles

The 2004 PM AQCD (U.S. EPA, 2004, 056905) reviewed Wichmann et al.'s (reanalyzed by Stolzel et al., 2003, 042842; 2000, 013912) study of fine and ultrafine particles (UFPs) (diameter: 0.01-0.1 µm) in Erfurt, Germany, for the study period 1995-1998. Stölzel et al. (2007, 091374) extended the study period to include the years 1995-2001 and updated the analysis. Number concentrations (NC) for four size ranges of UFPs (0.01-0.1, 0.01-0.03, 0.03-0.05, and 0.05-0.1 µm) as well as mass concentration (MC) for three size ranges (0.01-2.5, 0.1-0.5, and 10 µm) were analyzed. The authors found associations with UFP NC and all-cause as well as cardio-respiratory mortality, each for a 4 day lag. The risk estimates associated with a 9,748/cm^3 increase in UFP NC was 2.9% (95% CI: 0.3-5.5) for all-cause mortality and 3.1% (95% CI: 0.3-6.0) for cardio-respiratory mortality. The UFP-mortality association, and the lag structure of association, is consistent with the results from their earlier analysis, but the $PM_{2.5}$ association found in the previous study was not observed in the updated analysis. Both UFP and $PM_{2.5}$ concentrations were higher during the cold season in this locale.

Breitner et al. (2009, 188439) analyzed UFP data from Erfurt, Germany, over a 10.5-yr period (October 1991-March 2002) after the German unification, when air quality improved. In this analysis associations between all-cause mortality and UFPs and $PM_{2.5}$ were analyzed from September 1995 to March 2002, while PM_{10}, NO_2 and CO was analyzed for the whole study duration. The exposure time window / averages used in this study were different from those used by Stölzel (2003, 042842) and Stölzel et al. (2007, 091374). Breitner et al. (2009, 188439) investigated the cumulative effect of air pollution on mortality at lags 0-5 and 0-14, using (a) a semiparametric Poisson regression model; and (b) a third degree polynomial distributed lag (PDL) model. The authors estimated the mortality risk for the entire study period as well as specific time periods to examine the effect of declining air pollution levels on the air pollution-mortality association. Of the air pollutants examined, UFPs were

found to be most consistently associated with mortality. NO_2 and CO were also found to be significantly associated with mortality using the 15-day PDL and 15-day avg models, respectively. $PM_{2.5}$ and PM_{10} also showed positive, but much weaker associations with mortality. In this data set, UFPs were only moderately correlated with $PM_{2.5}$ (r = 0.48) and PM_{10} (r = 0.57). Of the pollutants examined, NO_2 showed the strongest (but overall a moderate) correlation with UFPs (r = 0.62). When the risk estimates were compared between the two latter time periods of the study (September 1995-February 1998; and March 1998-March 2002), the estimates obtained using the 6-day avg for these pollutants generally declined. For example, the all-cause mortality risk estimates associated with a 8,439/cm^3 increase in UFP NC was 5.5% (95% CI: 1.1-10.5) for the earlier period and -1.1% (95% CI: -6.8 to 4.9) for the later period. However, such patterns were less clear when using 15-day avg pollutant concentrations. In summary, UFPs appear to be the pollutant most consistently associated with mortality in Erfurt, Germany, but combined with the results for NO_2 and CO, these associations may implicate the role of local combustion sources on the mortality association observed.

Kettunen et al.'s (2007, 091242) study in Helsinki also examined the relationship between UFPs and stroke mortality. As described earlier, $PM_{2.5}$, PM_{10}, and CO was associated with stroke mortality only during the warm season. The association with UFPs was borderline non-significant (8.5% [95% CI: -1.2 to19.1] per 4,979/cm^3 increase in UFPs at lag 1 day), but its lag structure of association and the magnitude of the effect estimate per interquartile-range are similar to those for $PM_{2.5}$. Note that the UFP NC levels in Helsinki (median equals 8,986/cm^3 during the cold season and 7,587/cm^3 during the warm season) are lower than those in Erfurt (mean = 13,549/cm^3), but clearly higher in the cold season.

Summary of UFP Risk Estimates

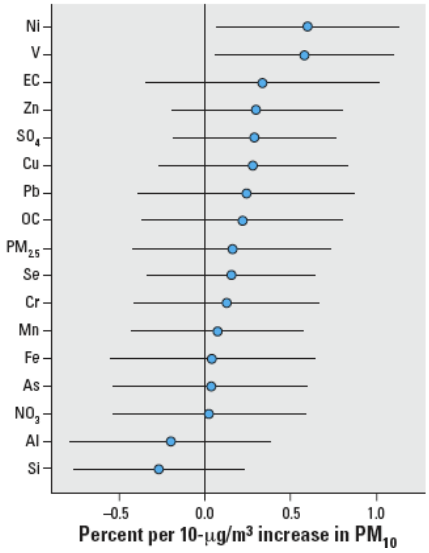
Only a few new studies, all of them conducted in Europe, examined and reported associations between UFPs and mortality. In Erfurt, UFPs showed the strongest associations with mortality among all of the PM indices, but its lag structure of association is either unique with the strongest association at lag 4 days in Stölzel et al. (2007, 091374), not consistent with the lag structure of associations found in other mortality studies, or the time-windows examined are longer (0-5 and 0-14 days) ((Breitner et al., 2009, 188439), making it difficult to compare whether the associations observed are consistent with those reported in other studies. In Helsinki, the association between UFPs and stroke mortality was weaker than that for $PM_{2.5}$, but its lag structure of association was similar to that for $PM_{2.5}$ (strongest at lag 1 day). However, Kettunen et al. (2007, 091242) only examined lags 0-3 days. Overall, the results of these studies should be viewed with caution because UFPs were consistently found to be correlated with gaseous pollutants derived from local combustion sources, and one or more of the gaseous pollutants were also found to be associated with mortality. Clearly, more research is needed to further investigate the role of UFPs on PM-mortality associations.

6.5.2.5. Chemical Components of PM

A few recent studies have examined the association between mortality and components of $PM_{2.5}$. This endeavor has been undertaken by some investigators through the use of the newly available $PM_{2.5}$ chemical speciation network data. The $PM_{2.5}$ chemical speciation network consists of more than 250 monitors that have been collecting over 40 chemical species since 2000; however, most sites started collecting data in 2001. One caveat to the new network is that because the sampling frequencies of the monitors are either every third day or every sixth day, there have not been, generally, a sufficient number of days to examine associations with mortality in single cities. To circumvent this issue, some investigators (Bell et al., 2009, 191997; Dominici et al., 2007, 099135; Franklin et al., 2008, 097426; Lippmann et al., 2006, 091165) have used the $PM_{2.5}$ chemical species data in a second stage regression to explain the heterogeneity in PM_{10} or $PM_{2.5}$ mortality risk estimates across cities. However, it should be noted these studies assume that the relative contributions of $PM_{2.5}$ have remained the same over time. There have also been some studies that directly analyzed speciated $PM_{2.5}$ data (e.g., Klemm et al., 2004, 056585; Ostro et al., 2007, 091354).

Explaining the Heterogeneity of PM_{10} Risk Estimates Using $PM_{2.5}$ Chemical Speciation Data

Lippmann et al. (2006, 091165), in addition to their primary analysis[1], investigated the consistency of the associations between specific elements and health outcomes by examining the heterogeneity of published 1-day lagged NMMAPS PM_{10} mortality risk estimates for 1987-1994 across cities as a function of the average $PM_{2.5}$ chemical components across cities. They matched $PM_{2.5}$ chemical species in 60 out of 90 cities. Lippmann et al. (2006, 091165) noted that the concentrations of the 16 chemical species examined averaged over the years 2000-2003 were highly skewed across cities. They therefore regressed PM_{10} risk estimates on each of the $PM_{2.5}$ components, raw and log-transformed, with weights based on the standard error of the PM_{10} risk estimates. The log-transformed values yielded better predictive power, and the authors subsequently presented the results with log-transformed values. As shown in Figure 6-31, the 16 $PM_{2.5}$ species showed varying extent of predictive power in explaining the PM_{10} risk estimates across 60 cities, with Ni and V being the best predictors.



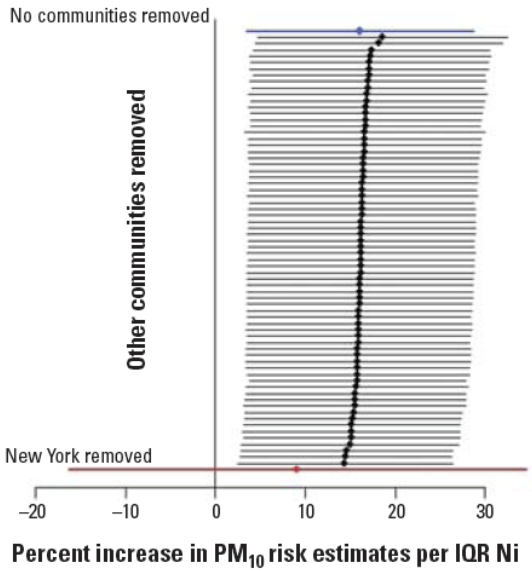
Source: Lippmann et al. (2006, 091165)

Figure 6-31. Percent increase in PM_{10} risk estimates (point estimates and 95% CIs) associated with a 5th-95th percentile increase in $PM_{2.5}$ and $PM_{2.5}$ chemical components. The $PM_{2.5}$ chemical components were log-transformed in the regression. The PM_{10} risk estimates were for 60 NMMAP cities for 1987-1994.

Dominici et al. (2007, 099135) examined the influence of Ni and V on the updated NMMAPS PM_{10} mortality risk estimates for 1987-2000, using 72 counties in which Ni and V data were collected. A Bayesian hierarchical model was used to estimate the role of Ni and V on the heterogeneity of PM_{10} risk estimates. While they found both Ni and V to be significant predictors of variation in PM_{10} mortality risk estimates across cities, they also noted that this result was sensitive to the inclusion of the New York City data. Lippmann et al. (2006, 091165) and Dominici et al. (2007, 099135) both reported that the Ni levels in New York City are particularly high (~10 times the national average). Figure 6-32 shows the result of the sensitivity analysis for Ni. Note that the Ni in this result was not log-transformed, as clearly reflected in the change in the width of confidence bands when the New York data were removed (i.e., a skewed distribution produces narrow bands).

[1] The main focus of the study was to examine the role of $PM_{2.5}$ chemical components in a mouse model of atherosclerosis ($ApoE^{-/-}$) exposed to concentrated fine PM (CAPs) in Tuxedo, NY.

Dominici et al. (2007, 099135) further noted that they reached "the same conclusion" when log-transformed data were used in the analysis, but the results were not presented.



Source: Reprinted with Permission of Oxford University Press from Dominici et al. (2007, 099135)

Figure 6-32. Sensitivity of the percent increase in PM_{10} risk estimates (point estimates and 95% CIs) associated with an interquartile increase in Ni. The Ni concentration was not log-transformed in this regression model. The PM_{10} risk estimates were for 72 NMMAP cities for 1987-2000. The top estimate is achieved by including data for all the 69 communities. The other estimates are calculated by excluding one of the 69 communities at a time.

Bell et al. (2009, 191997) presented a supplemental analysis similar to both Lippmann et al. (2006, 091165) and Dominici et al. (2007, 099135) in their examination of whether the variation in $PM_{2.5}$ risks for cardiovascular and respiratory hospital admissions is due to differences in $PM_{2.5}$ chemical composition. The authors used the 100 U.S. cities included in the Peng et al. (2005, 087463) analysis and PM_{10} data for the years 1987-2000 along with $PM_{2.5}$ chemical component data for 2000-2005. Using a Bayesian hierarchical model, Bell et al. (2009, 191997) found that PM_{10} relative risks for total mortality were greater in counties and during seasons with higher $PM_{2.5}$ Ni concentrations. However, in a sensitivity analysis when selectively removing cities from the overall estimate, the significant association between the PM_{10} mortality risk estimate and the $PM_{2.5}$ Ni fraction was diminished upon removing New York city from the analysis, which is consistent with the results presented by Dominici et al. (2007, 099135).

Explaining the Heterogeneity of $PM_{2.5}$ Risk Estimates Using $PM_{2.5}$ Chemical Speciation Data

The first stage of the Franklin et al. (2008, 097426) 25 cities study, described previously, focused on a time-series regression of mortality on $PM_{2.5}$ by season. In the second stage random effects meta regression, the $PM_{2.5}$ mortality risk estimates (25 cities×4 seasons = 100 estimates) were regressed on the ratio of mean seasonal $PM_{2.5}$ species to the total $PM_{2.5}$ mass. The authors included those species that had at least 25% of the reported concentrations above the minimum detection limit, which resulted in 18 species being included in the analysis. Their rationale for using species proportions as effect modifiers, according to the investigators, was that "in the first stage of the analysis the mortality risk was estimated per unit of the total $PM_{2.5}$ mass, which encompassed all

measured species, and therefore it would not be meaningful to use the species concentrations directly as the effect modifier" (Franklin et al., 2008, 097426). In the second stage regression model, Franklin et al. (2008, 097426) also included a quadratic function of seasonally averaged temperature to capture the inverted U-shape relationship between $PM_{2.5}$ penetration and temperature. They found that the fitted relationship between $PM_{2.5}$ risk estimates across cities and seasonally averaged temperature substantiates the use of temperature as a surrogate for ventilation (Franklin et al., 2008, 097426). Table 6-17 shows the resulting effect modification by $PM_{2.5}$ species. Al, As, Ni, Si, and SO_4^{2-} were found to be significant effect modifiers of $PM_{2.5}$ risk estimates, and simultaneously including Al, Ni, and SO_4^{2-} together, or Al, Ni, and As together further increased explanatory power. Of all the species examined, Al and Ni explained the most residual heterogeneity. Franklin et al. (2008, 097426) also examined the effect of demographic variables on $PM_{2.5}$ risk estimates and found that only median household income was significantly associated with mortality.

Table 6-17. Effect modification of composition on the estimated percent increase in mortality with a 10 μg/m^3 increase in $PM_{2.5}$.

Cause	Species	p-value for effect modification by species to $PM_{2.5}$ mass proportion	% increase in nonaccidental mortality per 10 μg/m^3 increase in $PM_{2.5}$ for an interquartile increase in species to $PM_{2.5}$ mass proportion*	Heterogeneity explained (%)†
Nonaccidental Univariate	Al	<0.001	0.58	45
	As	0.02	0.55	35
	Br	0.11	0.38	5
	Cr	0.12	0.33	16
	EC	0.79	0.06	0
	Fe	0.43	0.12	3
	K	0.10	0.41	28
	Mn	0.42	0.14	10
	Na+	0.22	0.20	14
	Ni	0.01	0.37	41
	NO_3	0.07	-0.49	28
	NH_4^+	0.84	0.04	3
	OC	0.59	-0.02	4
	Pb	0.31	0.17	11
	Si	0.03	0.41	25
	SO_4^{2-}	0.01	0.51	33
	V	0.28	0.30	3
	Zn	0.19	0.23	15
Nonaccidental Multivariate (1)	Al	<0.001	0.79	100
	Ni	0.01	0.34	
	SO_4^{2-}	<0.001	0.75	
Nonaccidental Multivariate (2)	Al	<0.001	0.61	100
	Ni	0.01	0.35	
	As	<0.001	0.58	

*Adjusted for temperature
†Includes heterogeneity explained by temperature

Source: Reprinted with Permission of Lippincott Williams & Wilkins from Franklin et al. (2008, 097426)

Although Lippmann et al. (2006, 091165) used NMMAPS PM_{10} risk estimates and Franklin et al. (2008, 097426) used $PM_{2.5}$ risk estimates to examine effect modification due to various PM

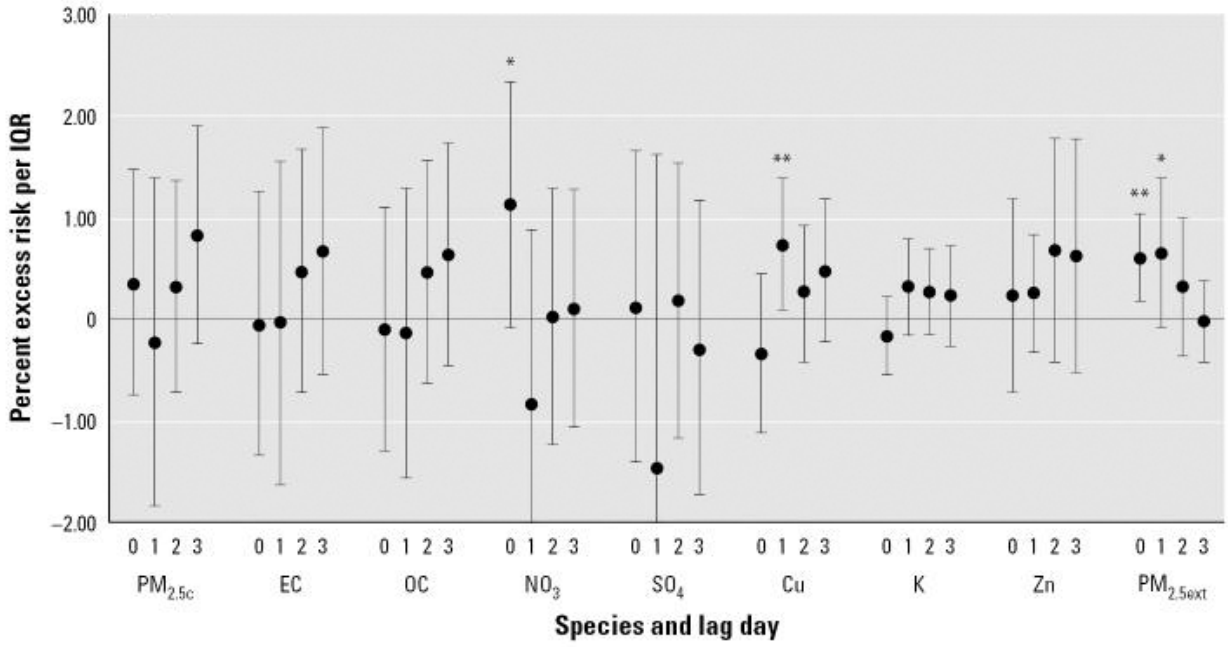
species, 14 out of the 18 species analyzed in these two studies overlap (Figure 6-31 and Table 6-17). Both studies found that Ni explained the heterogeneity in PM risk estimates. Note that New York City was not included in the 25 cities examined in Franklin et al. (2008, 097426) and, thus, could not influence the result. Sulfate positively, but not significantly, explained the PM_{10} risk estimates in the Lippmann et al. (2006, 091165) analysis. However, SO_4^{2-} was a significant predictor of $PM_{2.5}$ risk estimates in the Franklin et al. (2008, 097426) analysis. Al and Si were negative (i.e., less than the average PM_{10} risk estimates across cities), though not significant predictors in the Lippmann et al. (2006, 091165) analysis. Unlike the Franklin et al. (2008, 097426) analysis, arsenic (As) showed no association with mortality in the Lippmann et al. (2006, 091165) analysis. The source of these differences may be due to the difference in geographic coverage, PM size ($PM_{2.5}$ may represent more secondary aerosols than PM_{10}), or the difference in the analytical methods used in each study. Specifically, the analytical approach used by Franklin et al. (2008, 097426) does have an advantage of delineating seasonal variations in PM components and the associated potential seasonal mortality effects.

In light of the results presented in speciation studies it must be noted that second stage analyses that use PM chemical species as effect modifiers have some limitations. Unlike analyses that directly examine the associations between chemical species and mortality, if an effect modification is observed it may be confounded if the variations of the mean levels of the chemical species examined are correlated with other demographic factors that vary across cities. Thus, more concrete conclusions could be formulated if direct associations are found between mortality and PM chemical components in time-series analyses.

Association between $PM_{2.5}$ Chemical Components and Mortality

Ostro et al. (2007, 091354) examined associations between $PM_{2.5}$ chemical components and mortality in six California counties (Fresno, Kern, Riverside, Sacramento, San Diego, and Santa Clara), which had at least 180 days of speciation data for the years 2000-2003. The study examined all-cause, cardiovascular, and respiratory mortality for individual lags of 19 specific $PM_{2.5}$ chemical components. The second stage random-effects model combined risk estimates at each lag across cities. The number of available days for chemical species data ranged from 243 (San Diego County) to 395 (Sacramento County). The authors found an association between mortality, especially cardiovascular mortality, and several chemical components. For example, cardiovascular mortality was associated with EC, OC, nitrate, Fe, K, and Ti at various lags.

Even though this was a multicity study, the relatively small number of available days and the every-third-day (or every-sixth-day) sampling frequency for $PM_{2.5}$ chemical species made it difficult to interpret the results of the lag structure of associations observed for the chemical species. To evaluate the impact of non-daily sampling frequency, Ostro et al. (2007, 091354) examined both the $PM_{2.5}$ series that coincides with the speciation sampling days (for the initial six counties [i.e., $PM_{2.5c}$]) and $PM_{2.5}$ data that was available on all days for an extended set of counties (the initial six counties plus Contra Costa, Los Angeles, and Orange Counties [i.e., $PM_{2.5ext}$]). Figure 6-33 shows the association between all-cause mortality and selected $PM_{2.5}$ chemical species as well as for $PM_{2.5c}$ and $PM_{2.5ext}$. Note the wide confidence bands for the risk estimates for each $PM_{2.5}$ chemical species and $PM_{2.5c}$, apparently reflecting the low statistical power of the data. The lag structure of associations is more clearly defined for $PM_{2.5ext}$, and appears to be different from that for $PM_{2.5}$.



Source: Ostro et al. (2007, 091354)

Figure 6-33. Percent excess risk (CI) of total (nonaccidental) mortality per IQR of concentrations. Note: $PM_{2.5}$ has the same sampling days as chemical species. $PM_{2.5}$ has all available $PM_{2.5ext}$ data for nine counties. * p < 0.10; ** p < 0.05

Ostro et al. (2008, 097971) used the speciation data from the six counties analyzed in their 2007 analysis, described above, in an additional analysis to examine effect modification of cardiovascular mortality effects, which showed the strongest association in the 2007 analysis, attributed to $PM_{2.5}$ and 13 chemical components by socio-economic and demographic factors. The results of the analysis were combined using random effects meta-analysis. The investigators tested statistical differences in risk estimates between strata using a t-test, and reported that, for many of the $PM_{2.5}$ chemical species; there were significantly higher effect estimates among those with lower educational attainment and Hispanics. While these patterns were apparent in their results table, interpretation of the results is not straightforward because the table only presented the most significant (and positive) lags, and they were often different between the strata (e.g., the most frequent significant lag for the Hispanic group was 1 day, while it was 2 or 3 days for the White group). As the investigators pointed out, the every-third-day sampling frequency of the speciation data also complicates the interpretation of the results for different lags.

Overall, the two studies by Ostro et al. (2007, 091354) were the first attempt to directly analyze associations between the newly available chemical speciation data and mortality. While suggestive associations between several chemical species and mortality were reported, a longer length of observations is needed to more clearly determine the associations.

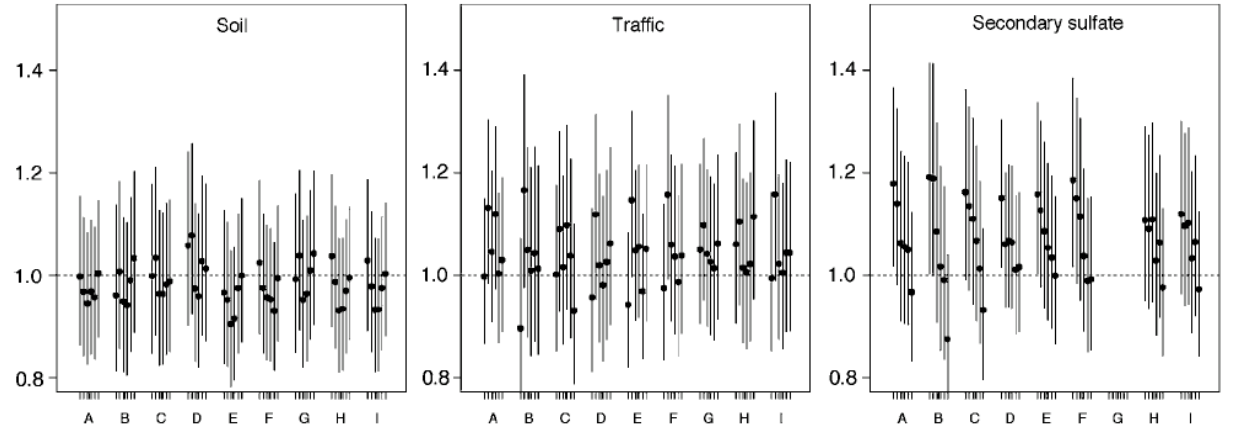
6.5.2.6. Source-Apportioned PM Analyses

Chemically speciated PM data allow for the source apportionment of PM. The idea of using source-apportioned PM for health effects analyses is appealing because, if such source-apportionment could be reliably conducted, it would allow for an evaluation of $PM_{2.5}$ mass concentrations by source types. However, the uncertainties associated with source-apportionment methods have not been well characterized.

To address this issue, in 2003, several groups of EPA-funded researchers organized a workshop and independently conducted source apportionment on two sets of data: Phoenix, AZ, and Washington, DC, compared the results (Hopke et al., 2006, 088390), and then conducted time-series

mortality regression analyses using each group's source-apportioned data (Ito et al., 2006, 088391; Mar et al., 2006, 086143; Thurston et al., 2005, 097949). The various research groups generally identified the same major source types, each with similar elemental compositions. Inter-group correlation analyses indicated that soil-, SO_4^{2-}-, residual oil-, and salt-associated mass concentrations were most unambiguously identified by various methods, whereas vegetative burning and traffic were less consistent. Aggregate source-specific mortality relative risk (RR) estimate confidence intervals overlapped each other, but the SO_4^{2-}-related $PM_{2.5}$ component was most consistently significant across analyses in these cities.

The results from the source-apportionment workshop quantitatively characterized the uncertainties associated with the factor analysis-based methods, but they also raised new issues. The mortality analyses conducted in Phoenix, AZ, and Washington, DC, both found that different source-types showed varying lag structure of associations with mortality. For example, Figure 6-34 shows cardiovascular mortality risk estimates for three of the $PM_{2.5}$ sources from the Phoenix, AZ, analysis (Mar et al., 2006, 086143). The strongest associations for "traffic" $PM_{2.5}$ was found for lag 1-day, while for "secondary SO_4^{2-}" $PM_{2.5}$, it was lag 0, with a monotonic decline towards longer lags. These results are consistent with those in the 2004 PM AQCD (U.S. EPA, 2004, 056905), in which associations were reported with combustion-related $PM_{2.5}$, but not crustal source $PM_{2.5}$. It is conceivable that PM from different source types produces different lagged effects, but it is also likely that different PM species have varying lagged correlations with the covariates in the health effects regression models (e.g., temperature, day-of-week) resulting in apparent differences in lagged associations with mortality. Thus, interpretation of these source-apportioned PM health effect estimates remains challenging.



Source: Reprinted with Permission of Nature Publishing Group from Mar et al. (2006, 086143)

Figure 6-34. Relative risk and CI of cardiovascular mortality associated with estimated $PM_{2.5}$ source contributions. Y-axis: relative risk per 5th-to-95th percentile increment of estimated $PM_{2.5}$ source contribution. X-axis: the alphabet denotes investigator/ method; lagged $PM_{2.5}$ source contribution for lag 0 through 5 days, left to right, are shown for each investigator/method.

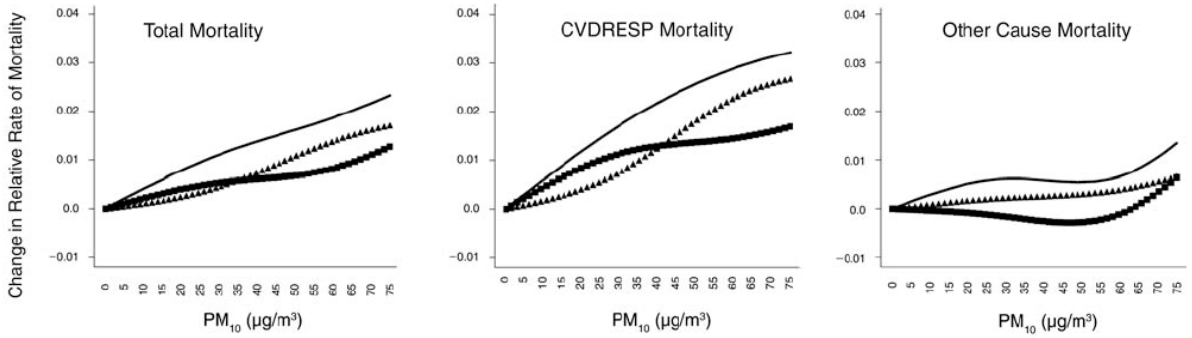
6.5.2.7. Investigation of Concentration-Response Relationship

The results from large multicity studies reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905) suggested that strong evidence did not exist for a clear threshold for PM mortality effects. However, as discussed in the 2004 PM AQCD (U.S. EPA, 2004, 056905), there are several challenges in determining and interpreting the shape of PM-mortality concentration-response functions and the presence of a threshold, including: (1) limited range of available concentration levels (i.e., sparse data at the low and high end); (2) heterogeneity of susceptible populations; and (3)

the influence of measurement error. Regardless of these limitations, studies have continued to investigate the PM-mortality concentration-response relationship.

Daniels et al. (2004, 087343) evaluated three concentration-response models: (1) log-linear models (i.e., the most commonly used approach, from which the majority of risk estimates are derived); (2) spline models that allow data to fit possibly non-linear relationship; and (3) threshold models, using PM_{10} data in 20 cities from the 1987-1994 NMMAPS data. They reported that the spline model, combined across the cities, showed a linear relation without indicating a threshold for the relative risks of death for all-causes and for cardiovascular-respiratory causes in relation to PM_{10}, but "the other cause" deaths (i.e., all cause minus cardiovascular-respiratory) showed an apparent threshold at around 50 $\mu g/m^3$ PM_{10}, as shown in Figure 6-35. For all-cause and cardio-respiratory deaths, based on the Akaike's Information Criterion (AIC), a log-linear model without threshold was preferred to the threshold model and to the spline model.

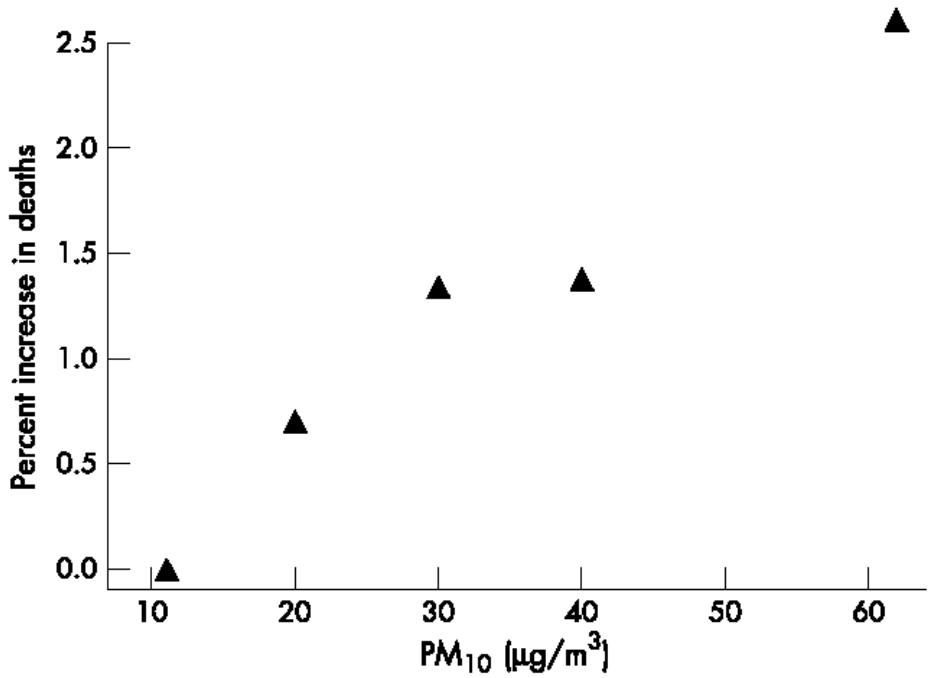
The HEI review committee commented that interpretation of these results required caution, because (1) the measurement error could obscure any threshold; (2) the city-specific concentration-response curves exhibited a variety of shapes; and (3) the use of AIC to choose among the models might not be appropriate due to the fact it was not designed to assess scientific theories of etiology. Note, however, that there has been no etiologically credible reason suggested thus far to choose one model over others for aggregate outcomes. Thus, at least statistically, the result of Daniels et al. (2004, 087343) suggests that the log-linear model is appropriate in describing the relationship between PM_{10} and mortality.



Source: Reprinted with Permission of HEI from Daniels et al. (2004, 087343)

Figure 6-35. Concentration-response curves (spline model) for all-cause, cardiovascular, respiratory and other cause mortality from the 20 NMMAPS cities. Estimates are posterior means under Bayesian random effects model. Solid line is mean lag, triangles are lag 0 (current day), and squares are lag 1 (previous day).

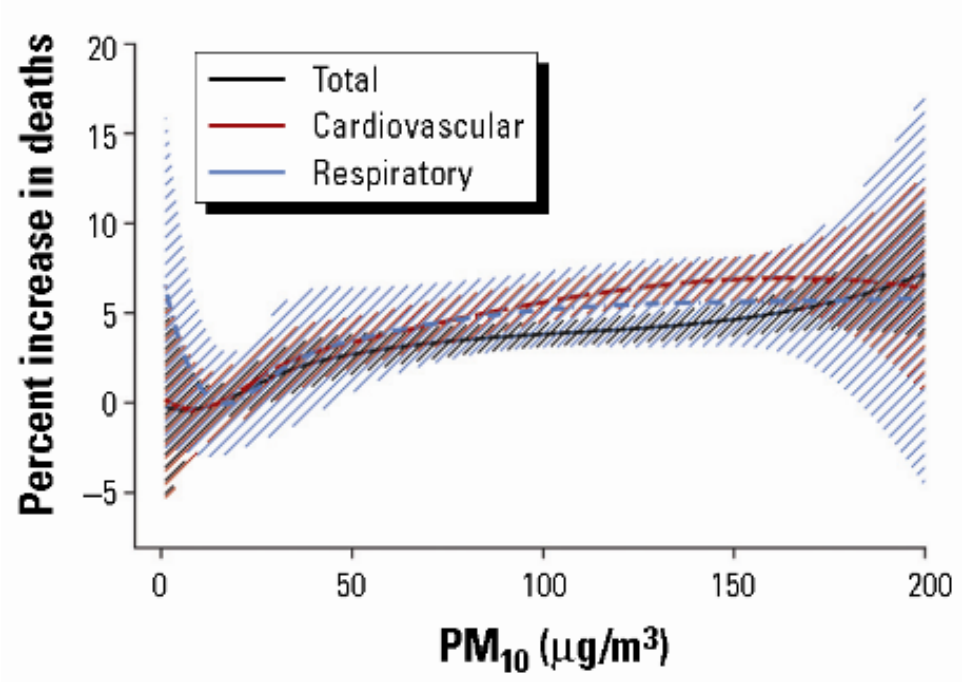
The Schwartz (2004, 078998) analysis of PM_{10} and mortality in 14 U.S. cities, described in Section 6.5.2.1, also examined the shape of the concentration-response relationship by including indicator variables for days when concentrations were between 15 and 25 $\mu g/m^3$, between 25 and 34 $\mu g/m^3$, between 35 and 44 $\mu g/m^3$, and 45 $\mu g/m^3$ and above. In the model, days with concentrations below 15 $\mu g/m^3$ served as the reference level. This model was fit using the single stage method, combining strata across all cities in the case-crossover design. Figure 6-36 shows the resulting relationship, which does not provide sufficient evidence to suggest that a threshold exists. The authors did not examine city-to-city variation in the concentration-response relationship in this study.



Source: Reprinted with Permission of BMJ Group from Schwartz (2004, 078998)

Figure 6-36. Percent increase in the risk of death on days with PM_{10} concentrations in the ranges of 15-24, 25-34, 35-44, and 45 µg/m^3 and greater, compared to a reference of days when concentrations were below 15 µg/m^3. Risk is plotted against the mean PM_{10} concentration within each category.

Samoli et al. (2005, 087436) investigated the concentration-response relationship between PM_{10} and mortality in 22 European cities (and BS in 15 of the cities) participating in the APHEA project. In nine of the 22 cities, PM_{10} levels were estimated using a regression model relating co-located PM_{10} to BS or TSP. They used regression spline models with two knots (30 and 50 µg/m^3) and then combined the individual city estimates of the splines across cities. The investigators concluded that the association between PM and mortality in these cities could be adequately estimated using the log-linear model. However, in an ancillary analysis of the concentration-response curves for the largest cities in each of the three distinct geographic areas (western, southern, and eastern European cities): London, England; Athens, Greece; and Cracow, Poland, Samoli et al. (2005, 087436) observed a difference in the shape of the concentration-response curve across cities. Thus, while the combined curves (Figure 6-37) appear to support no-threshold relationships between PM_{10} and mortality, the heterogeneity of the shapes across cities makes it difficult to interpret the biological relevance of the shape of the combined curves.



Source: Samoli et al. (2005, 087436)

Figure 6-37. Combined concentration-response curves (spline model) for all-cause, cardiovascular, and respiratory mortality from the 22 APHEA cities.

The results from the three multicity studies discussed above support no-threshold log-linear models, but issues such as the possible influence of exposure error and heterogeneity of shapes across cities remain to be resolved. Also, given the pattern of seasonal and regional differences in PM risk estimates depicted in recent multicity study results (e.g., Peng et al., 2005, 087463), the very concept of a concentration-response relationship estimated across cities and for all-year data may not be very informative.

6.5.3. Summary and Causal Determinations

6.5.3.1. $PM_{2.5}$

The 2004 PM AQCD (U.S. EPA, 2004, 056905) found that the strength of evidence from U.S.- and Canadian-based studies (both multi- and single-city) for $PM_{2.5}$ mortality associations varied across outcomes, with relatively stronger evidence for associations with cardiovascular compared to respiratory causes. The resulting effect estimates reported for these two endpoints ranged from 1.2 to 2.7% for cardiovascular-related mortality and 0.8 to 2.7% for respiratory-related mortality, per 10 µg/m^3 increase in $PM_{2.5}$ (U.S. EPA, 2004, 056905).

In the current review, $PM_{2.5}$ risk estimates were found to be consistently positive, and slightly larger than those reported for PM_{10} for all-cause, and respiratory- and cardiovascular-related mortality. The risk estimates for all-cause (nonaccidental) mortality ranged from 0.29% (Dominici et al., 2007, 097361) to 1.21% (Franklin et al., 2007, 091257) per 10 µg/m^3 increase in $PM_{2.5}$. These associations were consistently observed at lag 1 and lag 0-1, which have been confirmed through extensive analyses in PM_{10}-mortality studies. Cardiovascular-related mortality risk estimates were found to be similar to those for all-cause mortality; whereas, the risk estimates for respiratory-related mortality were consistently larger: 1.01% (Franklin et al., 2007, 091257) to 2.2% (Ostro et al., 2006, 087991) using the same lag (i.e., lag 1 and lag 0-1) and averaging indices. The studies evaluated that examined the relationship between short-term exposure to $PM_{2.5}$ and cardiovascular effects (section

6.2) provide coherence and biological plausibility for $PM_{2.5}$-induced cardiovascular mortality, which represents the largest component of total (nonaccidental) mortality (~ 35%) (American Heart Association, 2009, 198920). However, as noted in section 6.3, there is limited coherence between some of the respiratory morbidity findings from epidemiologic and controlled human exposure studies for the specific health outcomes reported and the subpopulations in which those health outcomes occur, complicating the interpretation of the $PM_{2.5}$ respiratory mortality effects observed.

Regional and seasonal patterns in $PM_{2.5}$ risk estimates were observed with results similar to those presented for PM_{10} (Dominici et al., 2007, 097361; Peng et al., 2005, 087463; Zeka et al., 2006, 088749), with the greatest effects occurring in the eastern U.S. (Franklin et al., 2007, 091257; Franklin et al., 2008, 097426) and during the spring (Franklin et al., 2007, 091257; Zanobetti and Schwartz, 2009, 188462). Of the studies evaluated only Burnett et al. (2004, 086247), a Canadian multicity study, analyzed gaseous pollutants and found mixed results, with possible confounding of $PM_{2.5}$ risk estimates by NO_2. Although the recently evaluated U.S.-based multicity studies did not analyze potential confounding of $PM_{2.5}$ risk estimates by gaseous pollutants, evidence from single-city studies evaluated in the 2004 PM AQCD (U.S. EPA, 2004, 056905) suggest that gaseous copollutants do not confound the $PM_{2.5}$-mortality association, which is further supported by studies that examined the PM_{10}-mortality relationship. An examination of effect modifiers (e.g., demographic and socioeconomic factors), specifically AC use which is sometimes used as a surrogate for decreased pollutant penetration indoors, has suggested that $PM_{2.5}$ risk estimates increase as the percent of the population with access to AC decreases (Franklin et al., 2007, 091257; 2008, 097426). Collectively, the epidemiologic evidence is sufficient to conclude that **a causal relationship exists between short-term exposure to $PM_{2.5}$ and mortality.**

6.5.3.2. $PM_{10-2.5}$

The 2004 PM AQCD (U.S. EPA, 2004, 056905) found a limited body of evidence that was suggestive of associations between short-term exposure to ambient $PM_{10-2.5}$ and various mortality outcomes (e.g., 0.08 to 2.4% increase in total [nonaccidental] mortality per 10 $\mu g/m^3$ increase in $PM_{10-2.5}$). As a result, the AQCD concluded that $PM_{10-2.5}$, or some constituent component(s) (including those on the surface) of $PM_{10-2.5}$, may contribute, in certain circumstances, to increased human health risks.

The majority of studies evaluated in this review that examined the relationship between $PM_{10-2.5}$ and mortality reported consistent positive associations in areas with mean 24-h avg concentrations ranging from 6.1-16.4 $\mu g/m^3$. However, uncertainty surrounds the $PM_{10-2.5}$ associations reported due to the different methods used to estimate $PM_{10-2.5}$ concentrations across studies (e.g., direct measurement of $PM_{10-2.5}$ using dichotomous samplers, calculating the difference between PM_{10} and $PM_{2.5}$ concentrations).

A new study of 47 U.S. cities (Zanobetti and Schwartz, 2009, 188462), which estimated $PM_{10-2.5}$ by calculating the difference between the county-average PM_{10} and $PM_{2.5}$, found associations between $PM_{10-2.5}$ and mortality across the U.S., including regions where $PM_{10-2.5}$ levels are not high. In addition, one well conducted multicity Canadian study (Burnett et al., 2004, 086247) provided evidence for an association between short-term exposure to $PM_{10-2.5}$ and mortality. However, unlike $PM_{2.5}$ very few of the $PM_{10-2.5}$ studies have investigated confounding by gaseous copollutants or the influence of model specification on $PM_{10-2.5}$ risk estimates. Zanobetti and Schwartz (2009, 188462) did provide preliminary evidence for greater effects occurring during the warmer months (i.e., spring and summer), which is consistent with the results from PM_{10}-mortality studies (Peng et al., 2005, 087463; Zeka et al., 2006, 088749). Overall, although more data is needed to: adequately characterize the chemical and biological components that may modify the potential toxicity of $PM_{10-2.5}$ and compare the different methods used to estimate exposure, consistent positive associations between short-term exposure to $PM_{10-2.5}$ and mortality were observed in the U.S. and Canadian-based multicity studies evaluated, as well as the single-city studies conducted in these locations. Therefore, the epidemiologic evidence **is suggestive of a causal relationship between short-term exposure to $PM_{10-2.5}$ and mortality.**

6.5.3.3. UFPs

Limited evidence was available during the review of the 2004 PM AQCD (U.S. EPA, 2004, 056905) regarding the potential association between UFPs and mortality. The lone study evaluated was conducted in Germany and provided some evidence for an association, but this association was reduced upon the inclusion of gaseous pollutants in a two-pollutant model.

Only a few new studies, all of them from Europe, were identified during this review, which examined the association between short-term exposure to UFPs and mortality. Inconsistencies were observed in the lag structure of association reported by each study in terms of both the lag day with the greatest association and the number of lag days considered in the study. Overall the studies consistently found that UFPs were correlated with gaseous pollutants derived from local combustion sources and that one or more of the gaseous pollutants were also associated with mortality. The limited number of studies available and the discrepancy in results between studies further confirms the need for additional data to examine the UFP-mortality relationship. In conclusion, the epidemiologic evidence **is inadequate to infer a causal association between short-term exposure to UFPs and mortality**.

6.6. Attribution of Ambient PM Health Effects to Specific Constituents or Sources

From a mechanistic perspective, it is highly plausible that the chemical composition of PM would be a better predictor of health effects than particle size. The observed geographical gradients in a number of $PM_{2.5}$ constituents (e.g., EC, OC, nitrate, and SO_4^{2-}) and regional heterogeneity in PM-related health effects reported in epidemiologic studies are consistent with this hypothesis. Recent studies in epidemiology, controlled human exposure, and toxicology have begun using information on ambient PM composition, and apportionment of constituents into sources, in an attempt to identify those with links to health outcomes and endpoints.

This section focuses on short-term exposure studies that (1) assessed health effects for ambient PM sources or components; and (2) used quantitative methods to relate those sources and components to health effects. Epidemiologic, controlled human exposure, and toxicological studies that took into consideration a large set of PM constituents (typically minerals, metals, EC, OC, and ions such as SO_4^{2-}) and aimed to segregate which constituents or groups of constituents may be responsible for the PM-related health effects observed are included. Most of these studies were reviewed earlier in this chapter and evaluated the relationship between specific chemical constituents derived from ambient PM and health effects. However, there were many studies presented earlier, as well as others only included in the Annexes, which only selected one or a small number of PM constituents *a priori*. Several controlled human exposure and toxicological studies likewise used a single compound found in PM rather than ambient PM. Additionally, studies that presented ambient PM composition and health data without systematically and explicitly investigating relationships are not included in this section. The few epidemiologic studies of long-term exposure that examined potential relationships between composition and sources of PM with mortality are discussed in Section 7.6.2.

Prior to the 2004 PM AQCD (U.S. EPA, 2004, 056905), only a handful of epidemiologic studies had attempted to relate specific constituents or sources of ambient PM to health outcomes without selecting constituents *a priori*. In this review, approximately 40 new epidemiologic, controlled human exposure, and toxicological studies explore the health effects attributed to chemical constituents and sources of ambient PM. The following summary (Section 6.6.3) provides a synthesis of the findings, including discussions on the coherence and consistency of the results.

6.6.1. Evaluation Approach

Relating a large number of ambient PM constituents with a large number of health outcomes presents difficulties that are related to both the nature of PM and methods of quantitative analysis. First, the number of constituents that comprise PM is not only large, but the correlations between them can be high. Reducing the correlation between constituents has been accomplished in most of

the recent studies through various forms of factor analysis, which limits the correlations between constituents by grouping the most highly correlated ambient PM constituents into less correlated groups or factors. Some studies identify the resulting groups or factors with named sources of ambient PM, but many do not draw explicit links between factors and actual sources. The methods used in estimating source contributions to ambient PM are reviewed in Section 3.6.1.

Most studies reviewed herein, regardless of discipline, were based on data for between 7 and 20 ambient PM constituents, with EC, OC, SO_4, and NO_3 most commonly measured. Most studies first reduced the number of ambient PM constituents by grouping them with various factorization or source apportionment techniques and the majority labeled the constituent groupings according to their presumed source. A separate analysis was then used to examine the relationship between the grouped PM constituents and various health effects. A few performed these two steps simultaneously using Partial Least Squares (PLS) procedures or Structural Equation Modeling (SEM). A small number of controlled human exposure and toxicological studies did not apply any kind of grouping to the ambient PM speciation data.

There are some differences in the type of PM constituent data used in epidemiologic, controlled human exposure and toxicological studies. In epidemiologic studies, ambient PM speciation data is obtained from atmospheric monitors; for controlled human exposure and toxicological studies, the technique used in the experimental exposure determines the type of PM data. Thus, all epidemiologic studies relied on monitor data, while all of the controlled human exposure and the majority of the toxicological studies used CAPs (and analyzed the concentrations of constituents therein). The remaining toxicological studies used ambient PM samples collected on filters at various U.S. sites. Further details on the studies included can be found in Appendix F.

Some important limitations in interpreting these studies together is that few, if any of the results are easily comparable, due to: (1) differences in the sets of ambient PM constituents that make up each of the factors; (2) the subjectivity involved in labeling factors as sources; (3) the numerous potential health effects examined in these studies, including definitive outcomes (e.g., HAs) as well as physiological alterations (e.g., increased inflammatory response); and (4) the various statistical methods and analytical approaches used in the studies. There are no well-established, objective methods for conducting the various forms of factor analysis and source apportionment, leaving much of the model operation and factor assignment open to judgment by the individual investigator. For example, the Al/Si factor identified in one study may differ from the Al/Ca/Fe/Si factor from another study, and the "Resuspended Soil" factor from a third study. After factorization or apportionment of the ambient PM data, the methods used for analyzing the potential association between ambient PM constituents or sources and health effects also varied. Except for the studies that used PLS or SEM, controlled human exposure and toxicological studies all used univariate mixed model regression for every identified PM factor or source. A number of toxicological studies followed the univariate step with multivariate regression for all factors. Epidemiologic studies generally related short-term exposure to sources with health outcomes through various forms of Poisson regression.

6.6.2. Findings

The results that follow are organized by discipline, with epidemiologic studies followed by controlled human exposure and toxicological studies. This section ends with a summary table, Table 6-18. Table 6-18 is broken out by $PM_{2.5}$ sources, and includes those epidemiologic, controlled human exposure, and in vivo toxicological studies that either grouped ambient $PM_{2.5}$ constituents or used tracers for each source. The table does not include all factors or sources examined in the studies listed: those factors or sources for which no association with effects was found not included.

6.6.2.1. Epidemiologic Studies

Results from the 2004 PM AQCD

Three epidemiologic studies that examined the association between PM constituents or sources and specific health effects were evaluated in the 2004 PM AQCD (U.S. EPA, 2004, 056905). Of

these studies, one study associated daily mortality with a mobile sources PM factor in Knoxville, TN and St. Louis, MO and coal in Boston, MA, while the crustal factor was not found to be significant for any of the six cities studied (Laden et al., 2000, 012102; Schwartz, 2003, 042811). Another study demonstrated an association between a regional SO_4^{2-} factor and total mortality at lag 0 in Phoenix and factors for regional SO_4^{2-}, motor vehicles, and vegetative burning with cardiovascular mortality at lags of 0, 1, and 3, respectively (Mar et al., 2000, 001760; 2003, 042841). Negative associations were observed between total mortality and regional SO_4^{2-} at lag 3, along with local SO_2 and soil factors (Mar et al., 2000, 001760; 2003, 042841). Finally, Tsai et al. (2000, 006251) identified significant associations between PM_{15}-derived industrial sources and total daily deaths in Newark and Camden, NJ; SO_4^{2-} was also linked to cardiopulmonary deaths in both locations. Total mortality and cardiopulmonary deaths were also significantly associated with PM from oil burning in Camden (2000, 006251).

Comparative Analyses of Source Apportionment Methods

Hopke et al. (2006, 088390) conducted a comparative analysis of source apportionment techniques used by investigators at multiple institutions, and subsequently used in epidemiologic analyses (Ito et al., 2006, 088391; Mar et al., 2006, 086143). An overarching conclusion of this set of analyses, reported in Thurston et al. (2005, 097949), is that variation in the source apportionment methods was not a major source of uncertainty in the epidemiologic effect estimates. In the primary analyses, mortality was associated with secondary SO_4^{2-} in both Phoenix and Washington D.C., although lag times differed (0 and 3, respectively). The SO_4^{2-} effect was stronger for total mortality in Washington D.C. and for cardiovascular mortality in Phoenix (Ito et al., 2006, 088391; Mar et al., 2006, 086143). In addition, Ito et al. (2006, 088391) found some evidence for associations with primary coal and traffic with total mortality in Washington D.C. (Ito et al., 2006, 088391) while copper smelter, traffic, and sea salt were associated with cardiovascular mortality in Phoenix at various lag times (Mar et al., 2006, 086143). In contrast to Phoenix, sea salt and traffic were not associated with mortality in Washington D.C. (Ito et al., 2006, 088391), but in both locations no associations were observed between biomass/wood combustion and mortality (Ito et al., 2006, 088391; Mar et al., 2006, 086143). In an additional study that compared three source apportionment methods in Atlanta–PMF, modified CMB, and a single-species tracer approach–found that the epidemiologic results were robust to the choice of analytic method (Sarnat et al., 2008, 097972). There were consistent associations between ED visits for cardiovascular diseases with $PM_{2.5}$ from mobile sources (gasoline and diesel) and biomass combustion (primarily prescribed forest burning and residential wood combustion), whereas $PM_{2.5}$ from secondary SO_4^{2-} was associated with respiratory disease ED visits (Sarnat et al., 2008, 097972). Sarnat et al. (2008, 097972) also found that the primary power plant $PM_{2.5}$ source identified by the CMB approach was negatively associated with respiratory ED visits while no association was found for $PM_{2.5}$ from soil and secondary nitrates/ammonium nitrate. In these studies, effect estimates based on the different source apportionment methods were generally in close agreement.

Source Apportionment Studies

A study that examined associations with mortality in Santiago, Chile, identified a motor vehicle source of $PM_{2.5}$ as having the greatest association with total and cardiac mortality at lag 1 (Cakmak et al., 2009, 191995). There was effect modification by age, with the total mortality relative risks associated with $PM_{2.5}$ from motor vehicles being greatest for those >85 yr. Soil and combustion sources were also associated with cardiac mortality. Risk estimates for respiratory mortality were the greatest for the motor vehicle source, with combustion and soil source factors also demonstrating positive associations for lag 1 (Cakmak et al., 2009, 191995).

An epidemiologic study that evaluated respiratory ED visits was conducted in Spokane, WA and used tracers as indicators of ambient $PM_{2.5}$ sources (Schreuder et al., 2006, 097959). In this study, only $PM_{2.5}$ from vegetative burning (total carbon) was associated with increased respiratory ED visits for lag 1, while $PM_{2.5}$ indicators for motor vehicles (Zn) and soil (Si) were not associated with cardiac hospital or respiratory ED visits. Andersen et al. (2007, 093201) conducted a source apportionment analysis to identify the sources of ambient PM_{10} associated with cardiovascular and

respiratory hospital admissions in older adults and children (ages 5-18) in Copenhagen, including two-pollutant models with various sources of PM_{10}. Andersen et al. (2007, 093201) found that secondary and crustal sources of PM_{10} were associated with cardiovascular hospital admissions; biomass sources were associated with respiratory hospital admissions; and vehicle sources were associated with asthma hospital admissions.

Several panel epidemiologic studies have examined the association between PM sources and physiological alterations in cardiovascular function. Lanki et al. (2006, 089788) reported positive associations between $PM_{2.5}$ from local traffic (measured as absorbance, which is correlated with EC content) and long-range transported $PM_{2.5}$ with ST-segment depression in elderly adults in a study conducted in Helsinki, Finland. Positive associations with ST-segment depression were also reported with $PM_{2.5}$ from crustal and salt sources, but these associations were not statistically significant. In an additional study, Yue et al. (2007, 097968) found that adult males with coronary artery disease in Erfurt, Germany, demonstrated changes in repolarization parameters associated with traffic-related $PM_{2.5}$, with increased vWF linked to traffic and combustion-generated particles, although the source apportionment was based solely on particle size distribution. In addition, elevated CRP levels were associated with all sources of $PM_{2.5}$ (soil, local traffic, secondary aerosols from local fuel combustion, diesel, and secondary aerosols from multiple sources) (Yue et al., 2007, 097968). Reidiker et al. (2004, 056992), in a study of young male highway patrol officers, found that the most significant effects (HRV, supraventricular ectopic beats, hematological markers, vWF) were associated with a speed-change factor for $PM_{2.5}$ (2004, 056992). In addition, the authors observed an association between crustal factor and cardiovascular effects, but no health-related associations with steel wear or gasoline $PM_{2.5}$ source factors.

Two recent studies have examined the associations between ambient $PM_{2.5}$ sources and respiratory symptoms and lung function. Positive associations with $PM_{2.5}$ motor vehicle and road dust sources were reported for respiratory symptoms and inhaler use in asthmatic children in New Haven, CT, and negative associations with wheeze or inhaler use for biomass burning at lag 0-2 (Gent et al., 2009, 180399). These positive effects for motor vehicle and road dust sources were robust to the inclusion of a gaseous copollutant (NO_2, CO, SO_2, or O_3) in the regression model. Penttinen et al. (2006, 087988) in a study consisting of asthmatic adults living in Helsinki, Finland, found that decrements in PEF were associated with ambient $PM_{2.5}$ soil, long-range transport, and local combustion sources at lags from 0-5 days. In addition, negative associations with asthma symptoms and medication use were reported for $PM_{2.5}$ from sea salt and long-range transport sources (Penttinen et al., 2006, 087988).

PM Constituent Studies

Some studies considered large sets of ambient PM constituents and attempted to identify which were associated with various health effects, but without grouping them into factors, or identifying sources. The majority of these studies focused on health effects associated with short-term exposure to $PM_{2.5}$. Peng et al. (2009, 191998) examined the association between $PM_{2.5}$ constituents (i.e., EC, OC, SO_4^{2-}, NO_3^-, Si, Na, NH_4^+) and cardiovascular and respiratory hospital admissions in 119 U.S. cities. When including each constituent in a multipollutant model, they found that EC and OC were robust to the inclusion of the other constituents at lag 0 for cardiovascular and respiratory hospital admissions, respectively. Although this study did not include analyses to identify sources of the constituents examined, EC and OC are often attributed to motor vehicle emissions, particularly diesel engines, and wood burning (Peng et al., 2009, 191998). Ostro et al. (2007, 091354; 2008, 097971) conducted two studies in six California counties to examine the association between ambient PM constituents and mortality. In the 2007 analysis, Ostro et al. (2006, 087991) found associations between Cu and all-cause mortality; EC, K, and Zn and CVD mortality; and Cu and Ti and respiratory mortality at lags ranging from 0 to 3 days. Associations during the summer were only observed between K for both CVD and respiratory mortality; and Al, Cl, Cu, Pb, Ti, and Zn and respiratory mortality. Overall, the most consistent associations were observed during the cool season. In a subsequent analysis, Ostro et al. (2008, 097971) examined the association between ambient PM constituents and cardiovascular mortality in potentially susceptible subpopulations. The authors found positive associations between EC, OC, NO_3^-, SO_4^{2-}, K, Cu, Fe, and Zn and cardiovascular mortality. These associations were higher in individuals with lower educational

attainment and of Hispanic ethnicity. In addition, similar to the 2007 analysis, associations were observed at lags ranging from 0 to 3 days.

Evaluation of Effect Modification by PM Constituents

Several studies have conducted secondary analyses to examine whether the variation in associations between $PM_{2.5}$ and morbidity and mortality or PM_{10} and mortality reflects differences in $PM_{2.5}$ constituents. An assumption in these types of analyses, especially when examining the effects on PM_{10} mortality risk estimates, is that the relative contributions of $PM_{2.5}$ have remained the same over time; these studies used PM_{10} data for years prior to 2000, while $PM_{2.5}$ speciation data has only been routinely collected since about 2000. Bell et al. (2009, 191997) found statistically significant associations between the county average concentrations of V, Ni, and EC (106 counties) and effect estimates for both cardiovascular and respiratory hospital admissions with short-term exposure to $PM_{2.5}$. In this analysis the ambient $PM_{2.5}$ constituents that comprised the majority of $PM_{2.5}$ total mass in the study locations were NH_4^+, EC, OC, NO_3^-, and SO_4^{2-}. Bell et al. (2009, 191997) also conducted a similar analysis for PM_{10}-mortality risk estimates and found that only Ni increased the risk estimate. However, in a sensitivity analysis, when selectively dropping out the communities examined one at a time, removing New York City diminished the Ni association. Both Lippmann et al. (2006, 091165) and Dominici et al. (2007, 099135) conducted similar analyses, albeit using a smaller subset of cities and/or different years of PM_{10} data. In both studies, Ni and V were found to modify the PM_{10}-mortality risk estimates. Similar to Bell et al. (2009, 191997), Dominici et al. (2007, 099135) also found that excluding New York City as part of a sensitivity analysis resulted in a diminished association with Ni and V. In an additional study, Franklin et al. (2008, 097426) examined the potential modification of the $PM_{2.5}$-mortality relationship by PM constituents in 25 U.S. cities. In a second-stage analysis using the species-to-$PM_{2.5}$ mass proportion of multiple constituents, the authors found that Al, As, Ni, Si, and SO_4^{2-} significantly modified the association between $PM_{2.5}$ and nonaccidental mortality.

6.6.2.2. Controlled Human Exposure Studies

A few controlled human exposure studies employed PCA, although not all linked groupings of PM constituents to the measured physiological parameters. Huang et al. (2003, 087377) demonstrated associations between increased fibrinogen and Cu/Zn/V and increased BALF neutrophils and Fe/Se/SO_4 in young, healthy adults exposed to RTP, NC CAPs; however, only water-soluble constituents were analyzed. In the other study that examined physiological cardiovascular effects, Fe and EC were associated with changes in ST-segment, while SO_4^{2-} was associated with decreased SBP in asthmatic and healthy human volunteers exposed to Los Angeles CAPs (2003, 087377). In Gong et al. (2003, 087365) the majority of the PM was in the thoracic coarse fraction. In the other study that used Los Angeles CAPs, the only observed association was between SO_4^{2-} content and decreased lung function (FEV_1 and FVC) in elderly volunteers with and without COPD (Gong et al., 2005, 087921). Two additional controlled human exposure studies that did not perform grouping and employed Toronto CAPs plus O_3 demonstrated increased DBP and increased brachial artery vasoconstriction associated with carbon content (Urch et al., 2004, 055629; 2005, 081080).

6.6.2.3. Toxicological Studies

The only toxicological in vivo study that characterized PM sources corresponding to identified sources was conducted in Tuxedo, NY, over a 5-mo period. This study reported that all sources (regional SO_4^{2-}, resuspended soil, residual oil, traffic and other unknown sources) were linked to HR or HRV changes in mice at one time or another during or after daily exposure (Lippmann et al., 2005, 087453). In a simultaneous in vitro study using CAPs from the same location, NF-κB in BEAS-2B cells were correlated with the oil combustion factor ($r = 0.289$ and 0.302 for V and Ni, respectively) (Maciejczyk and Chen, 2005, 087456). The other in vitro toxicological study (Duvall et al., 2008, 097969) that named sources employed samples from 5 U.S. cities and found a good fit for the regression model with increased IL-8 release in primary human airway epithelium cells and coal combustion ($R^2 = 0.79$), secondary nitrate ($R^2 = 0.63$), and mobile sources ($R^2 = 0.39$). In addition, soil ($R^2 = 0.48$), residual oil combustion ($R^2 = 0.38$), and wood combustion ($R^2 = 0.33$) were

associated with COX-2 effects; whereas, secondary SO_4^{2-} ($R^2 = 0.51$) was correlated with HO-1. Wood combustion and soil were negatively associated with HO-1.

Several toxicological studies employed Boston CAPs and identified at least four groupings of ambient $PM_{2.5}$ constituents (V/Ni, S, Al/Si, and Br/Pb), but they named sources only partially and tentatively (Batalha et al., 2002, 088109; Clarke et al., 2000, 011806; Godleski et al., 2002, 156478; Nikolov et al., 2008, 156808; Saldiva et al., 2002, 025988; Wellenius et al., 2003, 055691). When examining cardiovascular effects these studies reported that Si was associated with changes in the ST-segment of dogs (Wellenius et al., 2003, 055691) and decreased L/W ratio in rat pulmonary arteries (Batalha et al., 2002, 088109) in multivariate analyses. In addition, blood hematological results were associated with V/Ni, Al/Si, Na/Cl, and S in dogs (Clarke et al., 2000, 011806). An examination of respiratory effects in the latter study found that V/Ni and Br/Pb were associated with increased inflammation in BALF for only the third day of exposure (Clarke et al., 2000, 011806). Decreased respiratory rate and increased airway irritation (Penh) in dogs were associated with road dust (Al) and motor vehicles (OC), respectively (Nikolov et al., 2008, 156808). Individual $PM_{2.5}$ constituents associated with elevated neutrophils in BALF were Br, EC, OC, Pb, and SO_4^{2-} (Godleski et al., 2002, 156478), which is consistent with the findings (Br, EC, OC, Pb, V, and Cl) of Saldiva et al. (2002, 025988).

The two toxicological studies that used PLS methodologies identified $PM_{2.5}$ constituents linked to respiratory parameters. Seagrave et al. (2006, 091291) demonstrated associations between cytotoxic responses and a gasoline plus nitrates source factor (OC, Pb, hopanes/steranes, nitrate, and As) along with inflammatory responses and a gasoline plus diesel source factor (including major metal oxides) in rats exposed via IT instillation. In the other study, Veranth et al. (2006, 087479) collected loose surface soil from 28 sites in the Western U.S. and exposed BEAS-2B cells to $PM_{2.5}$. OC_1, OC_3, OC_2, EC_2, Br, EC_1, and Ni correlated with IL-8 release, decreased IL-6 release, and decreased viability at low and high doses (10 and 80 μg/cm^2, respectively).

Table 6-18. Study-specific $PM_{2.5}$ factor/source categories associated with health effects.

Source Category	Location	Health Effects	Time	Type of Study[1]	Species	Reference
CRUSTAL/SOIL/ROAD DUST						
Al, Si, Fe	Phoenix, AZ	negative association with total mortality	Lag 2	E	Human	Mar et al. (2000, 001760)
Not provided	Washington, D.C.	↑CV mortality	Lag 4	E	Human	Ito et al.(2006, 088391)
Al, Ca, Fe, Si	Santiago, Chile	↑CV mortality ↑ respiratory mortality	Lag 1	E	Human	Cakmak et al. (2009, 191995)
Al, Si, Ca, K, Fe	Helsinki, Finland	ST-segment depression	Lag 3	E	Human	Lanki et al. (2006, 089788)
Al, Si, Ca, K, Fe	Los Angeles, CA	↓ ST-segment voltage	2 days post-exposure	H	Human	Gong et al. (2003, 042106)
Al, Si	Boston, MA	ST-segment change	Following exposure	T	Dog	Wellenius et al. (2003, 055691)
Al, Si, Ca	Boston, MA	↓ lumen/wall ratio	24 h post-exposure	T	Rat	Batalha et al. (2002, 088109)
Al, Si, Ti, Fe	Wake County, NC	↑ uric acid ↑ mean cycle length	Lag 15 h	E	Human	Riediker et al. (2004, 056992)
Al, Si, Ca, Fe	Tuxedo, NY	↓ HR ↑ HR ↑ SDNN, ↑ RMSSD	During exposure Afternoon post-exposure. Night post-exposure	T	Mouse	Lippmann et al. (2005, 087453)
Al, Si	Boston, MA	↑ blood PMN % ↓ blood lymphocytes % ↑ WBC	Following exposure	T	Dog	Clarke et al.(2000, 011806)
Si, Fe, Al, Ca, Ba, Ti	New Haven, CT	↑ respiratory symptoms and inhaler use	Lag 0-2	E	Human	Gent et al. (2009, 180399)

Source Category	Location	Health Effects	Time	Type of Study[1]	Species	Reference
Si, Al, Ca, Fe, Mn	Helsinki, Finland	↓ mean PEF	Lag 3	E	Human	Penttinen et al. (2006, 087988)
Al	Boston, MA	↓ airway irritation (penh)	During exposure	T	Dog	Nikolov et al. (2008, 156808)
SALT						
Not provided	Phoenix, AZ	↑CV mortality ↑total mortality negative association with total mortality	Lag 5 Lag 0	E	Human	Mar et al. (2006, 086143)
Na, Cl	Helsinki, Finland	ST-segment depression	Lag 3	E	Human	Lanki et al. (2006, 089788)
Na, Cl	Boston, MA	↑ blood lymphocyte %	Following exposure	T	Dog	Clarke et al.(2000, 011806)
Na, Cl	Helsinki, Finland	Negatively associated with bronchodilator use and corticosteroid use	Lag 0-5 avg	E	Human	Penttinen et al. (2006, 087988)
Na, Cl	Boston, MA	↑ lung PMN density	24 h post-exposure	T	Rat	Saldiva et al. (2002, 025988)
SECONDARY SO_4^{2-} / LONG-RANGE TRANSPORT						
S	Phoenix, AZ	↑ total mortality negative association with total mortality	Lag 0 Lag 5	E	Human	Mar et al. (2000, 001760)
Not provided	Washington, D.C.	↑ total mortality	Lag 3	E	Human	Ito et al. (2006, 088391)
Not provided	Phoenix, AZ	↑CV mortality	Lag 0	E	Human	Mar et al. (2006, 086143)
S, K, Zn, Pb	Helsinki, Finland	ST-segment depression	Lag 2	E	Human	Lanki et al. (2006, 089788)
SO_4^{2-}	Los Angeles, CA	↓ SBP	4 h post-exposure	H	Human	Gong et al. (2003, 042106)
S, Si, OC	Tuxedo, NY	↓ HR ↓ SDNN, ↓ RMSSD	Afternoon post-exposure Night post-exposure	T	Mouse	Lippmann et al. (2005, 087453)
S	Boston, MA	↓ RBC ↑ hemoglobin	Following exposure	T	Dog	Clarke et al. (2000, 011806)
SO_4^{2-}, NH_4^+, OC	Atlanta, GA	↑ respiratory ED visits	Lag 0	E	Human	Sarnat et al. (2008, 097972)
S, K, Zn, PM mass	Helsinki, Finland	↓ mean PEF. Negative association with asthma symptom prevalence	Lag 1 Lag 3	E	Human	Penttinen et al. (2006, 087988)
SO_4^{2-} (+NO_2)	Los Angeles, CA	↓ FEV_1 ↓ FVC	Following exposure	H	Human	Gong et al. (2005, 087921)
TRAFFIC						
Pb, Br, Cu	Harvard Six Cities	↑ total mortality	Lag 0-1	E	Human	Laden et al. (2000, 012102)
Not provided	Phoenix, AZ	↑CV mortality	Lag 1	E	Human	Mar et al. (2006, 086143)
Mn, Fe, Zn, Pb, OC, EC, CO, NO_2	Phoenix, AZ	↑ CV mortality	Lag 1	E	Human	Mar et al. (2000, 001760)
CO, NO_2, EC, OC	Santiago, Chile	↑CV mortality ↑ respiratory mortality	Lag 1	E	Human	Cakmak et al. (2009, 191995)
Gasoline (OC, NO_3^-, NH_4^+)	Atlanta, GA	↑ CVD ED visits	Lag 0	E	Human	Sarnat et al. (2008, 097972)
Diesel (EC, OC, NO_3^-)	Atlanta, GA	↑ CVD ED visits	Lag 0	E	Human	Sarnat et al. (2008, 097972)
NO_X, EC, ultrafine count	Helsinki, Finland	ST-segment depression	Lag 2	E	Human	Lanki et al. (2006, 089788)

Source Category	Location	Health Effects	Time	Type of Study[1]	Species	Reference
Speed-change factor (Cu, S, aldehydes)	Wake County, NC	↑ blood urea nitrogen ↑ mean red cell volume ↑ blood PMN % ↓ blood lymphocytes % ↑ von Willebrand factor (vWF) ↓ protein C ↑ mean cycle length ↑ SDNN ↑ PNN50 ↑ supraventricular ectopic beats	Lag 15 h	E	Human	Riediker et al. (2004, 056992)
Motor vehicle/other (Br, Pb, Se, Zn, NO_3-)	Tuxedo, NY	↓ RMSSD	Afternoon post-exposure	T	Mouse	Lippmann et al. (2005, 087453)
EC, Zn, Pb, Cu, Se	New Haven, CT	↑ respiratory symptoms	Lag 0-2	E	Human	Gent et al. (2009, 180399)
Local combustion (NO_X, ultrafine PM, Cu, Zn, Mn, Fe)	Helsinki, Finland	↓ mean PEF	Lag 0-5 avg	E	Human	Penttinen et al. (2006, 087988)
Gasoline+secondary nitrate*	Birmingham, AL; Atlanta, GA; Pensacola, FL; Centreville, AL	cytotoxic responses (potency)	24 h post-exposure	T	Rat	Seagrave et al. (2006, 091291)
Gasoline+diesel*	Birmingham, AL; Atlanta, GA; Pensacola, FL; Centreville, AL	inflammatory responses (potency)	24 h post-exposure	T	Rat	Seagrave et al. (2006, 091291)
OIL COMBUSTION						
V, Ni	Boston, MA	↑ blood PMN % ↓ blood lymphocytes % ↑ BALF AM %	Following exposure Following exposure 24 h post-exposure	T	Dog	Clarke et al. (2000, 011806)
V, Ni, Se	Tuxedo, NY	↓ SDNN ↓ RMSSD	Afternoon post-exposure	T	Mouse	Lippmann et al. (2005, 087453)
Ni	Boston, MA	↓ respiratory rate	During exposure	T	Dog	Nikolov et al. (2008, 156808)
V, Ni	Boston, MA	↑ lung PMN density	24 h post-exposure	T	Rat	Saldiva et al. (2002, 025988)
COAL COMBUSTION						
Se, SO_4^{2-}	Harvard Six Cities	↑ total mortality	Lag 0-1	E	Human	Laden et al. (2000, 012102)
Not provided	Washington, D.C.	↑ total mortality	Lag 3	E	Human	Ito et al. (2006, 088391)
OTHER METALS						
Cu smelter (not provided)	Phoenix, AZ	↑CV mortality ↑total mortality	Lag 0	E	Human	Mar et al. (2006, 086143)
Incinerator	Washington, D.C.	Negative association with total and CV mortality	Lag 0	E	Human	Ito et al. (2006, 088391)
Metal processing (SO_4^{2-}, Fe, NH_4^+, EC, OC)	Atlanta, GA	↑ CVD ED visits	Lag 0	E	Human	Sarnat et al. (2008, 097972)

Source Category	Location	Health Effects	Time	Type of Study[1]	Species	Reference
Combustion (Cr, Cu, Fe, Mn, Zn)	Santiago, Chile	↑CV mortality ↑ respiratory mortality	Lag 1	E	Human	Cakmak et al. (2009, 191995)
WOODSMOKE / VEGETATIVE BURNING						
OC, K	Phoenix, AZ	↑ CV mortality	Lag 3	E	Human	Mar et al. (2000, 001760)
OC, EC, K, NH_4^+	Atlanta, GA	↑ CVD ED visits	Lag 0	E	Human	Sarnat et al. (2008, 097972)
Total C	Spokane, WA	↑ respiratory ED visits	Lag 1	E	Human	Schreuder et al. (2006, 097959)
UNNAMED FACTORS						
Zn-Cu-V	Chapel Hill, NC	↑ blood fibrinogen	18 h post-exposure	H	Human	Huang et al. (2003, 087377)
Fe-Se-SO_4^{2-}	Chapel Hill, NC	↑ BALF PMN	18 h post-exposure	H	Human	Huang et al. (2003, 087377)
Br, Cl, Pb	Santiago, Chile	↑CV mortality ↑ respiratory mortality	Lag 1	E	Human	Cakmak et al. (2009, 191995)
Br, Pb	Boston, MA	↑ BALF PMN %	24 h post-exposure	T	Dog	Clarke et al.(2000, 011806)
Br, Pb	Boston, MA	↑ lung PMN density	24 h post-exposure	T	Rat	Saldiva et al. (2002, 025988)

*Constituents not provided.
[1] E = Epidemiologic study; H = Controlled human exposure study; T = Toxicological study

An in vitro toxicological study that employed Chapel Hill PM_{10} used PCA but did not name specific PM sources (Becker et al., 2005, 088590). In this study, the release of IL-6 from human alveolar macrophages and IL-8 from normal human bronchial epithelial cells was associated with a PM_{10} factor comprised of Cr, Al, Si, Ti, Fe, and Cu. No statistically significant effects were observed for a second PM_{10} factor (Zn, As, V, Ni, Pb, and Se).

Those toxicological studies that did not apply groupings to the ambient $PM_{2.5}$ speciation data demonstrated a variety of results. Two Boston CAPs studies demonstrated lung oxidative stress correlated with a number of individual $PM_{2.5}$ constituents including, Mn, Zn, Fe, Cu, and Ca (Gurgueira et al., 2002, 036535) and Al, Si, Fe, K, Pb, and Cu (Rhoden et al., 2004, 087969) in rats using univariate regression.

The remaining toxicological study that did not use ambient PM constituent groupings reported a correlation between Zn and plasma fibrinogen in SH rats when constituents were normalized per unit mass of CAPs (Kodavanti et al., 2002, 035344).

6.6.3. Summary by Health Effects

Recent epidemiologic, toxicological, and controlled human exposure studies have evaluated the health effects associated with ambient PM constituents and sources, using a variety of quantitative methods applied to a broad set of PM constituents, rather than selecting a few constituents a priori. As shown in Table 6-18, numerous ambient $PM_{2.5}$ source categories have been associated with health effects, including factors for PM from crustal and soil, traffic, secondary SO_4^{2-}, power plants, and oil combustion sources. There is some evidence for trends and patterns that link particular ambient PM constituents or sources with specific health outcomes, but there is insufficient evidence to determine whether these patterns are consistent or robust.

For cardiovascular effects, multiple outcomes have been linked to a PM crustal/soil/road dust source, including cardiovascular mortality in Washington D.C. (Ito et al., 2006, 088391)and Santiago, Chile, (Cakmak et al., 2009, 191995) and ST-segment changes in Helsinki (Lanki et al., 2006, 089788), Los Angeles (Gong et al., 2003, 042106), and Boston (Wellenius et al., 2003, 055691). Interestingly, the ST-segment changes have been observed in an epidemiologic panel study, a controlled human exposure study, and a toxicological study, although the majority of the CAPs in the controlled human exposure study was $PM_{10-2.5}$. Further support for a crustal/soil/road dust source associated with cardiovascular health effects comes from a PM_{10} source apportionment study in Copenhagen that reported increased cardiovascular hospital admissions (Andersen et al., 2007, 093201).

$PM_{2.5}$ traffic and wood smoke/vegetative burning sources have also been linked to cardiovascular effects. Cardiovascular mortality in Phoenix (Mar et al., 2000, 001760; 2006, 086143) and Santiago, Chile, (Cakmak et al., 2009, 191995) was associated with traffic at lag 1. Gasoline and diesel sources were associated with ED visits in Atlanta for cardiovascular disease at lag 0 (Sarnat et al., 2008, 097972). Cardiovascular mortality in Phoenix (Mar et al., 2000, 001760) and ED visits in Atlanta (Sarnat et al., 2008, 097972) were associated with wood smoke/vegetative burning.

Studies that only examined the effects of individual $PM_{2.5}$ constituents linked EC to cardiovascular hospital admissions in a multicity analysis (Peng et al., 2009, 191998) and cardiovascular mortality in California (Ostro et al., 2007, 091354; 2008, 097971).

These studies suggest that cardiovascular effects may be associated with $PM_{2.5}$ from motor vehicle emissions, wood or biomass burning, and PM (both $PM_{2.5}$ and $PM_{10-2.5}$) from crustal or road dust sources. In addition, there are many studies that observed associations between other sources (i.e., salt, secondary SO_4^{2-}/long-range transport, other metals) and cardiovascular effects, but at this time, there does not appear to be a consistent trend or pattern of effects for those factors.

There is less consistency in observed associations between PM sources and respiratory health effects, which may be partially due to the fact that fewer studies have been conducted that evaluated respiratory-related outcomes and measures. However, there is some evidence for associations with secondary SO_4^{2-} $PM_{2.5}$. Sarnat et al. (2008, 097972) found an increase in respiratory ED visits in Atlanta that was associated with a $PM_{2.5}$ secondary SO_4^{2-} factor. Decrements in lung function in Helsinki (Lanki et al., 2006, 089788) and Los Angeles (Gong et al., 2005, 087921) in asthmatic and healthy adults, respectively, were also linked to this factor. Health effects relating to the crustal/soil/road dust and traffic sources of PM included increased respiratory symptoms in asthmatic children (Gent et al., 2009, 180399) and decreased PEF in asthmatic adults (Penttinen et al., 2006, 087988). Inconsistent results were also observed in those $PM_{2.5}$ studies that use individual constituents to examine associations with respiratory morbidity and mortality, although Cu, Pb, OC, and Zn were related to respiratory health effects in two or more studies.

A few studies have identified $PM_{2.5}$ sources associated with total mortality. These studies found an association between mortality and a $PM_{2.5}$ coal combustion factor (Laden et al., 2000, 012102), while others linked mortality to a secondary SO_4^{2-}/long-range transport $PM_{2.5}$ source (Ito et al., 2006, 088391; Mar et al., 2006, 086143).

Recent studies have evaluated whether the variation in associations between $PM_{2.5}$ and morbidity and mortality or PM_{10} and mortality reflects differences in $PM_{2.5}$ constituents (Bell et al., 2009, 191997; Dominici et al., 2007, 099135; Lippmann et al., 2006, 091165). In three studies (Bell et al., 2009, 191997; Dominici et al., 2007, 099135; Lippmann et al., 2006, 091165) PM_{10}-mortality effect estimates were greater in areas with a higher proportion of Ni in $PM_{2.5}$, but the overall PM_{10}-mortality association was diminished when New York City was excluded in a sensitivity analysis in two of the studies. V was also found to modify PM_{10}-mortality effect estimates as well as those for $PM_{2.5}$ with respiratory and cardiovascular hospital admissions (Bell et al., 2009, 191997). When examining the effect of species-to-$PM_{2.5}$ mass proportion on $PM_{2.5}$-mortality effect estimates Ni was found to modify the association along with Al, As, Si, and SO_4^{2-}, but not V (Franklin et al., 2008, 097426).

6.6.4. Conclusion

Recent studies show that source apportionment methods have the potential to add useful insights into which sources and/or PM constituents may contribute to different health effects. Of particular interest are several epidemiologic studies that compared source apportionment methods and the associated results. One set of studies compared epidemiologic associations with $PM_{2.5}$ source factors using several methods - PCA, PMF, and UNMIX - independently analyzed by separate research groups (Hopke et al., 2006, 088390; Ito et al., 2006, 088391; Mar et al., 2006, 086143; Thurston et al., 2005, 097949). Schreuder et al. (2006, 097959) compared UPM and two versions of UNMIX to derive tracers and Sarnat et al. (2008, 097972) compared PMF, modified CMB, and a single-species tracer approach. In all analyses, epidemiologic results based on the different methods were generally in close agreement. The variation in risk estimates for daily mortality between source categories was significantly larger than the variation between research groups (Ito et al., 2006, 088391; Mar et al., 2006, 086143; Thurston et al., 2005, 097949). Additionally, the variation in risk estimates based on the source apportionment model used had a much smaller effect than the

variation caused by the different source constituents. Further, the most strongly associated source types were consistent across all groups. This supports the general validity of such approaches, though greater integration of results would be possible if the methods employed for grouping PM constituents were more consistent across studies and disciplines. Further research would aid understanding of the contribution of different factors, sources, or source tracers of PM to health effects by increasing the number of locations where similar health endpoints or outcomes are examined.

Overall, the results displayed in Table 6-18 indicate that many constituents of PM can be linked with differing health effects and the evidence is not yet sufficient to allow differentiation of those constituents or sources that are more closely related to specific health outcomes. These findings are consistent with the conclusions of the 2004 PM AQCD (U.S. EPA, 2004, 056905), that a number of source types, including motor vehicle emissions, coal combustion, oil burning, and vegetative burning, are associated with health effects. Although the crustal factor of fine particles was not associated with mortality in the 2004 PM AQCD (U.S. EPA, 2004, 056905), recent studies have suggested that PM (both $PM_{2.5}$ and $PM_{10-2.5}$) from crustal, soil or road dust sources or PM tracers linked to these sources are associated with cardiovascular effects. In addition, secondary SO_4^{2-} $PM_{2.5}$ has been associated with both cardiovascular and respiratory effects.

Chapter 6 References

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▪Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISA) and the Integrated Risk Information System (IRIS).

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Chapter 7. Integrated Health Effects of Long-Term PM Exposure

7.1. Introduction

This chapter reviews, summarizes, and integrates the evidence on relationships between health effects and long-term exposures to various size fractions and sources of PM. Cardiopulmonary health effects of long-term exposure to PM have been examined in an extensive body of epidemiologic and toxicological studies. Both epidemiologic and toxicological studies provide a basis for examining reproductive and developmental and cancer health outcomes with regard to long-term exposure to PM. In addition, there is a large body of epidemiologic literature evaluating the relationship between mortality and long-term exposure to PM.

Conclusions from the 2004 PM AQCD are summarized briefly at the beginning of each section, and the evaluation of evidence from recent studies builds upon what was available during the previous review. For each health outcome (e.g., respiratory infections, lung function), results are summarized for studies from the specific scientific discipline, i.e., epidemiologic and toxicological studies. The major sections (i.e., cardiovascular, respiratory, reproductive/developmental, cancer) conclude with summaries of the evidence for the various health outcomes within that category and integration of the findings that lead to conclusions regarding causality based upon the framework described in Chapter 1. Determination of causality is made for the overall health effect category, such as cardiovascular effects, with coherence and plausibility being based upon the evidence from across disciplines and also across the suite of related health outcomes including cause-specific mortality. Section 7.6 provides detailed discussions on the epidemiologic literature for long-term exposure to PM and mortality. In each summary section (7.2.11, 7.3.9, 7.4.3, 7.5.4, and 7.6.5), the evidence is briefly reviewed and independent conclusions drawn for relationships with $PM_{2.5}$, $PM_{10-2.5}$, and UF particles (UFPs).

7.2. Cardiovascular and Systemic Effects

Studies examining associations between long-term exposure to ambient PM (over months to years) and CVD morbidity had not been conducted and thus were not included in the 1996 or 2004 PM Air Quality Criteria Documents (U.S. EPA, 1996, 079380; U.S. EPA, 2004, 056905). A number of studies were included in the 2004 PM AQCD that evaluated the effect of long-term $PM_{2.5}$ exposure on cardiovascular mortality and found consistent associations. No toxicological studies examined chronic atherosclerotic effects of PM exposure in animal models. However, a subchronic study that evaluated atherosclerosis progression in hyperlipidemic rabbits was discussed and this study provided the foundation for the subsequent work that has been conducted in this area (Suwa et al., 2002, 028588). No previous toxicological studies evaluated effects of subchronic or chronic PM exposure on diabetes measures, or HR or HRV changes, nor were there animal toxicological studies included in the 2004 PM AQCD that evaluated systemic inflammatory or blood coagulation markers following subchronic or chronic PM exposure.

Several new epidemiologic studies have examined the long-term PM-CVD association among U.S. and European populations. The studies investigate the association of both $PM_{2.5}$ and PM_{10} exposures with a variety of clinical and subclinical CVD outcomes. Epidemiologic and toxicological studies have provided evidence of the adverse effects of long-term exposure to $PM_{2.5}$ on

Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISA) and the Integrated Risk Information System (IRIS).

cardiovascular outcomes, including atherosclerosis, clinical and subclinical markers of cardiovascular morbidity, and cardiovascular mortality. The evidence of these effects from long-term exposure to $PM_{10-2.5}$ is weaker.

7.2.1. Atherosclerosis

Atherosclerosis is a progressive disease that contributes to several adverse outcomes, including acute coronary syndromes such as myocardial infarction, sudden cardiac death, stroke and vascular aneurysms. It is multifaceted, beginning with an early injury or inflammation that promotes the extravasation of inflammatory cells. Under conditions of oxidative or nitrosative stress and high lipid or cholesterol concentrations, the vessel wall undergoes a chronic remodeling that is characterized by the presence of foam cells, migrated and differentiated smooth muscle cells, and ultimately a fibrous cap. The advanced lesion that develops from this process can occlude perfusion to distal tissue, causing ischemia, and erode, degrade, or even rupture, revealing coagulant initiators (tissue factor) that promote thrombosis, stenosis, and infarction or stroke. Several detailed reviews of atherosclerosis pathology have been published elsewhere (Ross, 1999, 156926; Stocker and Keaney, 2004, 157013).

7.2.1.1. Epidemiologic Studies

Measures of Atherosclerosis

Although no study has examined the association between long-term PM exposure and longitudinal change in subclinical markers of atherosclerosis, several cross sectional studies have been conducted. Markers of atherosclerosis used in these studies include coronary artery calcium (CAC), carotid intima-media thickness (CIMT), ankle-brachial index (ABI), and abdominal aortic calcium (AAC). These measures are descried briefly below.

CAC represents the accumulation of calcium in coronary artery macrophages and represents an advanced stage of atherosclerosis. As such CAC is a measure of atherosclerosis assessed by non-contrast, cardiac-gated electron beam computed tomography (EBCT) or multidetector computed tomography (MDCT) of the coronary arteries in the heart (Greenland and Kizilbash, 2005, 156496; Hoffmann et al., 2005, 156556; Mollet et al., 2005, 155988). The prevalence of CAC is strongly related to age. Few people have detectable CAC in their second decade of life but the prevalence of CAC rises to approximately 100% by age 80 (Ardehali et al., 2007, 155662). Previous studies suggest that while the absence of CAC does not rule out atherosclerosis, it does imply a very low likelihood of significant arterial obstruction (Achenbach and Daniel, 2001, 156189; Arad et al., 1996, 155661; Shaw et al., 2003, 156083; Shemesh et al., 1996, 156085). Conversely, the presence of CAC confirms the existence of atherosclerotic plaque and the amount of calcification varies directly with the likelihood of obstructive disease (Ardehali et al., 2007, 155662). CAC is a quantified using the Agatston method (Agatston et al., 1990, 156197). Its repeatability depends on the laboratory and the method of calculation (O'Rourke et al., 2000, 192159). Agatston scores are frequently used to classify individuals into one of five groups (zero; mild; moderate; severe; extensive) or according to age- and sex-specific percentiles of the CAC distribution (Erbel et al., 2007, 155768).

CIMT is a measure of atherosclerosis assessed by high-resolution, B-mode ultrasonography of the carotid arteries in the neck, the walls of which have inner (intimal), middle (medial) and outer (adventitial) layers (Craven et al., 1990, 155740; O'Leary et al., 1999, 156826; Wendelhag et al., 1993, 157136). CIMT estimates the distance in mm or µm between the innermost (blood-intima) and outermost (media-adventitia) interfaces, often by averaging over three arterial segments in the common carotid, carotid bulb, and internal carotid artery (Amato et al., 2007, 155656). CIMT has been associated with atherosclerosis risk factors (Heiss et al., 1991, 156535; O'Leary et al., 1992, 156825; Salonen and Salonen, 1991, 156938), prevalent coronary heart disease (Chambless et al., 1997, 156329; Geroulakos et al., 1994, 155788), and incident coronary and cerebral events (O'Leary et al., 1999, 156826; van der Meer et al., 2004, 156129). Several studies have indicated that CIMT measurements are accurate (Girerd et al., 1994, 156474; Pignoli et al., 1986, 156026; Wendelhag et

al., 1991, 157135) and reproducible (Montauban et al., 1999, 156777; Smilde et al., 1997, 156988; Willekes et al., 1999, 157147), especially for the common carotid artery (Montauban et al., 1999, 156777).

ABI, which is also known as the ankle-arm or resting (blood) pressure index, is a measure of lower extremity arterial occlusive disease commonly caused by advanced atherosclerosis (Weitz et al., 1996, 156150). It is assessed by continuous wave Doppler and manual or automated oscillometric sphygmomanometry, the latter having been shown to have higher repeatability and validity (Weitz et al., 1996, 156150). ABI is defined as the unitless ratio of ankle to brachial systolic blood pressures measured in mmHg. As ankle pressure is normally equal to or slightly higher than arm pressure (resulting in an ABI $\geq$ 1.0), epidemiologic studies typically define the normal ABI range as 0.90 to 1.50 (Resnick et al., 2004, 156048). Low ABI has been associated with all-cause and CVD mortality (Newman et al., 1993, 156805; Vogt et al., 1993, 157100), as well as myocardial infarction and stroke (Karthikeyan and Lip, 2007, 156626).

AAC is a measure of atherosclerosis assessed by non-contrast, EBCT or MDCT of the abdominal aorta. It is scored much like CAC (Agatston et al., 1990, 156197), but the age-specific prevalence and extent of AAC is greater, particularly among women and at ages >50 yr. Although AAC has not been studied as extensively as CAC, it is associated with carotid and coronary atherosclerosis as well as cardiovascular morbidity and mortality (Allison et al., 2004, 156210; Allison et al., 2006, 155653; Hollander et al., 2003, 156562; Khoury et al., 1997, 156636; Oei et al., 2002, 156820; Walsh et al., 2002, 157103; Wilson et al., 2001, 156159; Witteman et al., 1986, 156161) and measurements are sufficiently reproducible to allow serial investigations over time (Budoff et al., 2005, 192105).

Study Findings

Diez Roux et al. (2008, 156401) conducted cross-sectional analyses of the association of three of these subclinical markers of atherosclerosis (CAC, CIMT and ABI), collected from 2000 to 2003 during baseline examinations of participants enrolled in the Multi-Ethnic Study of Atherosclerosis (MESA), with long-term exposure to $PM_{2.5}$ and PM_{10}. The study population included 5,172 ethnically diverse people (53% female) residing in Baltimore, MD; Chicago, IL; Forsyth County, NC; Los Angeles, CA; New York, NY; and St. Paul, MN ranging in age from 45 to 84 yr old. Authors used spatio-temporal modeling of pollutant concentrations, weather and demographic data to impute 20-yr avg exposures to $PM_{2.5}$ and PM_{10}. They reported small increases in CIMT of 1% (95% CI: 0-1.4) and 0.5% (95% CI: 0-1), which correspond to absolute changes of 8 (95% CI: 0-12) and 7 (95% CI: 0-14) µm, per 10 µg/m^3 increase in 20-yr avg PM_{10} and $PM_{2.5}$ concentration, respectively. Evidence of age-, gender-, lipid- and smoking-related susceptibility was lacking. They also reported weak, non-significant increases in the relative prevalence of CAC of 1% (95% CI: -2 to 4) and 0.5% (95% CI: -2 to 3) per 10 µg/m^3 increase in PM_{10} and $PM_{2.5}$, respectively. Among the subset of 2,586 participants with EBCT-identified calcification, similarly weak associations were observed. There was little evidence of modification of the CAC associations by demographic, socioeconomic or clinical characteristics. Finally, the authors report no differences in mean ABI with PM_{10} or $PM_{2.5}$ concentrations. The null findings for ABI exhibited little heterogeneity among participant subgroups and were similarly null when ABI was modeled as a dichotomous outcome using a cutpoint of 0.9 units.

MESA investigators also examined the chronic $PM_{2.5}$-AAC association in a residentially stable subset of 1,147 participants (mean age = 66 yr; 50% female) randomly selected from all MESA centers, except Baltimore, MD for enrollment in its Aortic Calcium Ancillary Study(Allen et al., 2009, 156209). The authors used kriging and inverse residence-to-monitor distance-weighted averaging of EPA AQS data to estimate 2-yr mean exposures to $PM_{2.5}$. In cross-sectional analyses, the authors found a 6% (95% CI: -4 to 16) excess risk of a non-zero Agatston score and an 8% (95% CI: -30 to 46) increase in AAC, i.e., approximately 50 (95% CI: -251 to 385) Agatston units, per 10 µg/m^3 increase in $PM_{2.5}$ concentration. These associations were stronger among users than non-users of lipid lowering drugs.

Kunzli et al. (2005, 087387) used baseline data collected between 1998-2003 from two randomized placebo-controlled clinical trials, the Vitamin E Atherosclerosis Progression Study (VEAPS) and the B-Vitamin Atherosclerosis Intervention Trial (BVAIT), for their ancillary cross-sectional analyses of the effect of long-term $PM_{2.5}$ exposure on CIMT. The study population included 798 residents of the greater Los Angeles, CA area who were more than 40 yr old at baseline and 44% were female. The authors used universal kriging of $PM_{2.5}$ data from 23 state and local monitors

operating in 2000 to estimate 1-yr avg exposure to $PM_{2.5}$ at each participant's geocoded U.S. Postal Service ZIP code. They found a 4.2% (95% CI: -0.2 to 8.9) or approximately 32 (95% CI: -2 to 68) μm increase in CIMT per 10 $\mu g/m^3$ increase in $PM_{2.5}$ concentration. In contrast to findings from the relatively large, ethnically diverse, yet geographically overlapping MESA ancillary study described above, PM-related increases in CIMT were two- to three-fold larger among older and female participants taking lipid lowering drugs in this study. PM-related increases in CIMT were also higher in never smokers when compared with current or former smokers.

Hoffmann et al. (2007, 091163) conducted a cross-sectional analysis of data collected at baseline (2000-2003) for 4,494 residents of Essen, Mülheim and Bochum, Germany enrolled in the Heinz Nixdorf Recall Study from 2000 to 2003. The age of participants ranged from 45-74 yr and 51% were female. In this cross-sectional study the authors used dispersion and chemistry transport modeling of emissions, climate and topography data to estimate 1-yr avg exposure to $PM_{2.5}$ in 2002 (the midpoint of the baseline exam.) They reported an imprecise 43% (95% CI: -15 to 115) or 102 (95% CI: -77 to 273) Agatston unit increase in CAC per 10 $\mu g/m^3$ increase in $PM_{2.5}$. Differences in strength of association between subgroups defined by demographic and clinical characteristics were small. The authors reported a more consistent association of CAC with traffic exposure (distance from a major roadway) than with $PM_{2.5}$ in this study.

In a subsequent analysis of these data, Hoffmann et al. (2009, 190376) examined the PM-ABI association in this population. In this cross-sectional study, no changes in ABI were observed in association with $PM_{2.5}$ concentration nor was evidence of effect modification by demographic and clinical characteristics apparent. As in the previous study (Hoffmann et al., 2007, 091163), residing near a major roadway was a stronger predictor of atherosclerotic changes. Absolute changes in ABI of -0.024 (95% CI: -0.047 to -0.001) were associated with living within 50 m of a major roadway compared to living more than 200 m away.

Each of the studies described above relied on cross-sectional analyses examining differences in long-term average $PM_{2.5}$ concentrations across space (as well as time to the extent baseline examinations were conducted over time). Such associations may reflect the effect of compositional differences in $PM_{2.5}$ as well as the effect of higher $PM_{2.5}$ concentrations. Most associations of $PM_{2.5}$ with CAC (Diez et al., 2008, 156401; Hoffmann et al., 2007, 091163), CIMT (Diez et al., 2008, 156401; Kunzli et al., 2005, 087387), ABI (Diez et al., 2008, 156401; Hoffmann et al., 2009, 190376) and AAC (Allen et al., 2009, 156209) reviewed in this section were weak and/or imprecise. However, several factors including exposure measurement error, variation in baseline measures atherosclerosis, as well as limited power may contribute to the insensitivity of these cross-sectional studies to detect small differences in CAC, CIMT, ABI and AAC. The study by Hoffmann et al. (2007, 091163), which reported large, imprecise and non-significant increases in CAC in association with $PM_{2.5}$, is not distinguished from the other studies reviewed by a superior study design or larger sample size. The several fold difference in the magnitude of CIMT associations reported by Kunzli et al. (2005, 087387) and Diez Roux et al. (2008, 156401) may be related to differences between the study populations. The ambient PM concentrations from these studies are characterized in Table 7-1.

7.2.1.2. Toxicological Studies

In the only study of this kind described in the 2004 PM AQCD, Suwa et al. (2002, 028588) demonstrated more advanced atherosclerotic lesions based on phenotype and volume fraction in the left main and right coronary arteries of rabbits exposed to PM_{10} (5 mg/kg, 2 times/wk×4 wk). Although this study was conducted using IT exposure methodology at a relatively high dose, it provided the first experimental evidence that PM exposure may result in progression of atherosclerosis. Recent toxicological studies conducted using inhalation exposures have replicated these findings at relevant concentrations and are discussed below.

CAPs

New studies have demonstrated increased atherosclerotic plaque area in aortas of $ApoE^{-/-}$ mice exposed to $PM_{2.5}$ CAPs for 4-6 mo (6 h/day×5 days/wk). Average CAPs concentrations ranged from 85 to 138 $\mu g/m^3$ and all of the studies were conducted in Tuxedo or Manhattan, NY. Chen and Nadziejko (2005, 087219) reported that the percentage of aortic intimal surface covered by atherosclerotic lesions in $ApoE^{-/-}$ mice was increased. In male $ApoE^{-/-}/LDLR^{-/-}$ mice, both lesion area

and cellularity in the aortic root were enhanced by Tuxedo, NY CAPs exposure, although there was no change in lipid content. Genetic profiles within plaques recovered from $ApoE^{-/-}$ mice included many of the molecular pathways known to contribute to atherosclerosis, including inflammation (Floyd et al., 2009, 190350). Sun (2005, 087952) similarly demonstrated an enhancement of atherosclerosis in $ApoE^{-/-}$ mice exposed Tuxedo, NY CAPs. Plaque area in the aortic arch and abdominal aorta was significantly increased in the PM-exposed, high fat-chow group compared to air-exposed, high fat-chow group. Macrophage infiltration in the abdominal aorta was also observed in the groups exposed to CAPs. A study conducted in Manhattan for 4 mo (May- September 2007) showed that $PM_{2.5}$ CAPs exposure increased atherosclerotic plaque area and led to higher levels of macrophage infiltration, collagen deposition, and lipid composition in thoracic aortas of $ApoE^{-/-}$ mice (Ying et al., 2009, 190111), which is consistent with the previous two studies described that were conducted in Tuxedo, NY.

Alteration of vasomotor function has been observed in aortic rings of $ApoE^{-/-}$ mice on a high fat diet with long-term exposure to CAPs (Sun et al., 2005, 087952; Ying et al., 2009, 190111). Sun (2005, 087952) reported that. $PM_{2.5}$-exposed animals exhibited increased vasoconstrictor responsiveness to serotonin and PE. Increased ROS and elevated iNOS protein expression in aortic sections of CAPs-exposed mice may have resulted alterations in the NO pathway and generation of peroxynitrite that could have affected vascular reactivity. In contrast, Ying, et al. (2009, 190111) demonstrated decreased maximum constriction induced by PE following Manhattan CAPs exposure. Pretreatment with the soluble guanylate cyclase (sGC) inhibitor ODQ attenuated the response, indicating that CAPs exposure resulted in abnormal NO/sGC signaling. Expression of iNOS mRNA and protein was increased in aortas of CAPs-exposed mice, further supporting a role for NO production. In conjunction with increased NO, aortic superoxide production was demonstrated that appeared to be partially driven by increased NADPH oxidase activity. The difference in vasoconstrictor responses between these two studies may be attributable to varying durations (6 versus 4 mo, respectively) or CAPs compositions.

Sun (2005, 087952) and Ying et al. (2009, 190111) reported similar relaxation responses to ACh for air- and CAPs-exposed mice. However, Manhattan CAPs-exposed mice had a markedly decreased response to A23187, indicating that NO release occurred via Ca^{2+}-dependent mechanisms (Ying et al., 2009, 190111). Abnormal eNOS function is likely responsible for the decreased relaxation response, as activation of eNOS (but not iNOS) is Ca^{2+}-dependent.

A recent study (Sun et al., 2008, 157033) that was part of the research described above (Sun et al., 2005, 087952) investigated tissue factor (TF) expression in aortas, which is a major regulator of hemostasis and thrombosis following vascular injury or plaque erosion. In $PM_{2.5}$-exposed $ApoE^{-/-}$ mice on a high-fat diet, TF was significantly elevated in the plaques of aortic sections compared to air-exposed mice on the high-fat diet. TF expression was generally detected in (1) the extracellular matrix surrounding macrophages and foam cell-rich areas; and (2) around smooth muscle cells.

One new study of CAPs $PM_{2.5}$ or UFPs derived from traffic was conducted. Araujo et al. (2008, 156222) compared the relative impact of UF (0.01-0.18 μm) and fine (0.01-2.5 μm) PM inhalation on aortic lesion development in $ApoE^{-/-}$ mice following a 40-day exposure (5 h/day×3 days/wk for 75 total h). Animals were on a normal chow diet and exposed to CAPs in a mobile inhalation laboratory parked 300 m from a freeway in downtown Los Angeles. Exposure concentrations were ~440 $\mu g/m^3$ for $PM_{2.5}$ and ~110 $\mu g/m^3$ for UFPs, and the number concentrations were roughly equivalent (4.56×10^5 and 5.59×10^5 particles/cm^3 for $PM_{2.5}$ and UFPs, respectively). Significant increases in plaque size (estimated by lesions at the aortic root) were reported for mice exposed to UFPs only. The lesions were largely comprised of macrophages with intracellular lipid accumulation. Increased total cholesterol measured at the end of the exposure protocol was observed only in the $PM_{2.5}$ group. HDL isolated from the UF PM-exposed mice demonstrated decreased anti-inflammatory protective capacity against LDL-induced monocyte chemotactic activity in an in vitro assay. The livers from the UFP-exposed mice demonstrated significant increases in lipid peroxidation and several stress-related gene products (catalase, glutathione S-transferase Y_a, NADPH-quinone oxidoreductase1, superoxide dismutase 2). Thus, UFPs in these exposures had a substantially greater impact on the systemic response than did $PM_{2.5}$.

Ambient Air

A study employing young BALB/c mice examined the effects of a 4-month exposure (24 h/day×7 days/wk) to ambient air on arterial histopathology (Lemos et al., 2006, 088594). Outdoor exposure chambers were located in downtown Sao Paulo, Brazil next to streets of high traffic density. In the control chamber, PM_{10} and NO_2 were filtered with 50% and 75% efficiency, respectively. The average pollutant concentrations were 2.06 ppm for CO (8-h mean), 104.75 $\mu g/m^3$ for NO_2 (24-h mean), 11.07 $\mu g/m^3$ for SO_2 (24-h mean), and 35.52 $\mu g/m^3$ for PM_{10} (24-h mean) at a monitoring site within 100 m of the inhalation chambers. The pulmonary and coronary arteries demonstrated significant decreases in L/W ratio for animals exposed to the entire ambient mixture compared to controls, indicating thicker walls in these vessels. There was no difference reported for the L/W ratio in renal arteries. Morphologic examination suggested that the increases in L/W ratio were due to muscular hypertrophy rather than fibrosis. The results of this study indicate vascular remodeling of the pulmonary and coronary arteries, as opposed to changes in tone.

To examine the role of systemic inflammation and recruitment of monocytes into plaque tissue as a possible pathway for accelerated atherosclerosis, Yatera et al. (2008, 157162) exposed female Watanabe heritable hyperlipidemic rabbits (42 week old) to Ottawa PM_{10} (EHC-93) via IT instillation (5 mg/rabbit; approximately 1.56 mg/kg) twice a week for 4 wk. Transfusion of whole blood harvested to from exposed and non-exposed animals to donor rabbits supplied labeled monocytes for assessment of monocyte recruitment from the blood to the aortic wall. The fraction of aortic surface and volume of aortic wall taken up by atherosclerotic plaque was increased and the number of labeled monocytes in the atherosclerotic plaques was elevated in rabbits exposed to PM_{10}. In addition, labeled monocytes were attached onto the endothelium overlying atherosclerotic plaques and the number that migrated into the smooth muscle underneath plaques in aortic vessel walls was greater with PM_{10} exposure compared to control. These responses were not observed in normal vessel walls. ICAM-1 and VCAM-1 expression was elevated in atherosclerotic lesions, likely indicating enhanced monocyte adhesion to endothelium and migration into plaques. Monocytes in plaque tissue stained with immunogold demonstrated foam cell characteristics, which were more numerous in the rabbits exposed to PM_{10}.

Gasoline Exhaust

Lund and colleagues (2007, 125741) used whole emissions from gasoline exhaust to investigate changes in the transcriptional regulation of several gene products with known roles in both the chronic promotion and acute degradation/destabilization of atheromatous plaques. These 50-day exposures (6 h/day×7 days/wk) employed $ApoE^{-/-}$ mice on high-fat chow and the concentrations of the high exposure group were 61 $\mu g/m^3$ for PM, 19 ppm for NO_X, 80 ppm for CO, and 12.0 ppm for total hydrocarbons. The average particle number median diameter was approximately 15 nm (McDonald et al., 2007, 156746). Dilutions of gasoline engine emissions induced a concentration-dependent increase in transcription of matrix metalloproteinase (MMP) isoform 9, ET-1, and HO-1 in aortas; MMP-3 and -9 mRNA levels were only increased in animals in the highest exposure group. Strong increases in oxidative stress markers (nitrotyrosine and TBARS) in the aortas were also observed. However, using a high-efficiency particle trap, they established that most of the effects were caused by the gaseous portion of the emissions and not the particles. This study did not directly address lesion area.

7.2.2. Venous Thromboembolism

One epidemiologic study examined the relationship between long term PM_{10} concentration, venous thromboembolism, and laboratory measures of hemostasis (prothrombin and activated partial thomboplastin times [PT; PTT]). PT and PTT measure the extrinsic and intrinsic blood coagulation pathways, the former activated in response to blood vessel injury, the latter, key to subsequent amplification of the coagulation cascade and propagation of thrombus (Mackman et al., 2007, 156723). Decreases in PT and PTT are consistent with a hypercoagulable, prothrombotic state.

7.2.2.1. Epidemiologic Studies

Baccarelli et al. (2008, 157984) studied 2,081 residents (56% female) of the Lombardy region of Italy whose ages ranged from 18 to 84 yr old. In this case-control study of 871 patients with ultrasonographically or venographically diagnosed lower extremity deep vein thrombosis (DVT) and 1,210 of their healthy friends or relatives (1995-2005), the authors used arithmetic averaging of PM_{10} data available at 53 monitors in nine geographic areas to estimate 1-yr avg residence-specific exposures. They found -0.06 (95% CI: -0.11 to 0) and -0.12 (95% CI: -0.23 to 0) decreases in standardized correlation coefficients for PT as well as 0.01 (95% CI: -0.03 to 0.04) and -0.09 (95% CI: -0.19 to 0.01) decreases in standardized correlation coefficients for PTT among cases and controls, respectively, per 10 $\mu g/m^3$ increase in PM_{10}. Patients with DVT who were taking heparin or coumarin anticoagulants were not asked to stop taking them before measurement of PT and aPTT. Of additional note, PT was neither adjusted for differences in reagents used to determine it nor conventionally reported as the International Normalized Ratio (INR). The ambient PM concentrations from this study are characterized in Table 7-1.

7.2.3. Metabolic Syndromes

7.2.3.1. Epidemiologic Studies

Chen and Schwartz (2008, 190106) studied 2,978 residentially stable participants in 33 U.S. communities (age range = 20-89 yr; 49% female) who were examined during phase 1 of the National Health and Nutrition Examination Survey III (1989-1991). In this cross-sectional study, the authors used inverse-distance weighted averaging of U.S. EPA AQS monitored data from participant and adjacent counties of residence to estimate 1-yr avg exposures to PM_{10}. They found that after adjustment, residents of communities with lower PM_{10} concentrations had fewer white blood cells than residents of communities with higher PM_{10} concentrations. This difference increased with increasing number of metabolic abnormalities (insulin resistance; hypertension; hypertriglyceridemia; low high-density lipoprotein cholesterol; abdominal obesity) reported by the participant. This observed difference across individuals with different degrees of metabolic abnormalities supports the concept that the presence of a metabolic syndrome may impart greater susceptibility to PM-associated long-term CVD effects.

7.2.3.2. Toxicological Studies

Diabetics as a potentially susceptible subpopulation have only recently been evaluated. A toxicological study of a diet-induced obesity mouse model (C57BL/6 fed high-fat chow for 10 wk) examined the effects of a 128-day $PM_{2.5}$ CAPs exposure (mean mass concentration 72.7 $\mu g/m^3$; Tuxedo, NY) on insulin resistance, adipose inflammation, and visceral adiposity (Sun et al., 2009, 190487). Elevated fasting glucose and insulin levels were observed in CAPs-exposed mice compared to air-exposed during the glucose tolerance test. Aortic rings of mice exposed to CAPs demonstrated decreased peak relaxation to ACh or insulin, which was associated with reduced NO bioavailability. Additionally, insulin signaling was impaired in aortic tissue via lowered endothelial Akt phosphorylation. Increases in adipokines and systemic inflammatory markers (i.e., TNF-α, IL-6, E-selectin, ICAM-1, PAI-1, resistin, leptin) were reported for CAPs-exposed mice. CAPs resulted in increased visceral and mesenteric fat mass, as well as greater adipose tissue macrophages in epididymal fat pads and larger adipocyte size compared to mice in the filtered air group. The results of this study demonstrate that $PM_{2.5}$ exposure can exaggerate insulin resistance, visceral adiposity, and inflammation in mice fed high-fat chow.

7.2.4. Systemic Inflammation, Immune Function, and Blood Coagulation

7.2.4.1. Epidemiologic Studies

As discussed in Section 7.2.3.1, Chen and Schwartz (2008, 190106) conducted a cross-sectional study in 33 U.S. communities and used inverse-distance weighted averaging of U.S. EPA AQS monitored data from participant and adjacent counties of residence to estimate 1-yr avg exposures to PM_{10} (median concentration within quartiles = 23.1, 31.2, 38.8 and 53.7 $\mu g/m^3$). They found that after adjustment, residents of communities in quartile 1 had 138 (95% CI: 2-273) fewer white blood cells ($\times 10^6$/L) than residents of communities in quartiles 2-4. This difference increased with increasing number of metabolic abnormalities.

Forbes et al. (2009, 190351) studied approximately 25,000 adults (age ≥ 16 yr; 53% female) who were representatively sampled from 720 English postcode sectors and participated in the Health Survey for England (1994, 1998 and 2003). In this fixed-effects meta-analysis of year-specific cross-sectional findings, the authors used dispersion modeling of emissions and weather data to estimate 2-yr avg exposures to PM_{10} at participant postcode sector centroids (median in 1994, 1998 and 2003 = 19.5, 17.9 and 16.2 $\mu g/m^3$, respectively). They found little evidence of a PM_{10}-inflammatory marker association, i.e., only a -0.08% (95% CI: -0.25 to 0.10) decrease in fibrinogen concentration and a 0.14% (95% CI: -1.00 to 1.30) increase in CRP concentration per 1 $\mu g/m^3$ increase in PM_{10}.

Calderon-Garciduenas et al. (2007, 091252) compared residentially stable, non-smoking healthy children (age range: 6-13 yr) living and attending school between 2003-2004 in Mexico City (historically high PM; altitude 2,250 m) and Polotitlán (historically low PM; altitude 2,380 m). In this ecologic study, residents of Mexico City (n = 59; 93% female) had fewer white blood cells and neutrophils ($\times 10^9$/L) than residents of Polotitlán (n = 22; 69% female): unadjusted mean 6.2 (95% CI: 5.7-6.6) versus 6.9 (95% CI: 6.3-7.5) and 2.9 (95% CI: 2.3-3.5) versus 3.8 (95% CI: 3.2-4.4), respectively.

Calderon-Garciduenas et al. (2009, 192107) subsequently compared 37 unadjusted mean measures of immune function and inflammation among an expanded number of these participants. They found that under a two-sided type I error rate (α) = 0.05, 16 (43%) of the measures were significantly different in residents of southwest Mexico City (n = 66; 48% female) than those in Polotitlán (n = 93; 57% female). However, only 8 measures were significantly different after Bon Ferroni-correction (α = 0.05 / 37 = 0.001) and even fewer would be after adjustment for reported correlation between the measures of immune function and inflammation, e.g., CRP and lipopolysaccharide binding protein (Pearson's r = 0.71).

Two cross-sectional analyses of PM_{10} concentration and markers of immune function or inflammation have been conducted with significant changes observed in the NHANES population (stronger effects among those with metabolic disorders) (Chen and Schwartz, 2008, 190106) but not in a relative large survey of adults, which was conducted in England (Forbes et al., 2009, 190351). Ecological analyses comparing children in high versus low pollution regions in Mexico show differences in unadjusted blood markers that may be related to PM concentration or other unmeasured risk factors that differs across the communities studied (Calderon-Garciduenas et al., 2007, 091252; Calderón-Garcidueñas et al., 2009, 192107).

7.2.4.2. Toxicological Studies

In addition to the $PM_{2.5}$ study mentioned previously that showed increased TF expression (an important initiator of thrombosis) in aortas of $ApoE^{-/-}$ mice following subchronic CAPs exposure (Sun et al., 2008, 157033), three recent studies examined hematology and clotting parameters in rats and mice exposed to DE, gasoline exhaust, or hardwood smoke for 1 week or 6 mo (Reed et al., 2004, 055625; Reed et al., 2006, 156043; Reed et al., 2008, 156903). In all studies, male and female F344 rats were exposed to the mixtures by whole-body inhalation for 6 h/day, 7 day/wk. Respiratory effects for these studies are presented in Section 7.3.3.

Diesel Exhaust

The target PM concentrations in the DE study was 30, 100, 300, and 1,000 μg/m^3 and the MMAD was 0.10-0.15 μm (Reed et al., 2004, 055625). Male and female rats exposed to DE at the highest concentration (NO concentration 45.3 ppm; NO_2 concentration 4.0 ppm; CO concentration 29.8 ppm; SO_2 concentration 365 ppb) for 6 mo demonstrated decreased serum Factor VII, but no change in plasma fibrinogen or thrombin anti-thrombin complex (TAT) (Reed et al., 2004, 055625). White blood cells were decreased only in female rats in the highest exposure group. Another DE study of shorter duration (4 wk, 4 h/day, 5day/wk; PM mass concentration 507 or 2201 μg/m^3, CO 1.3 and 4.8 ppm, NO <2.5 and 5.9 ppm, NO_2 <0.25 and 1.2 ppm, SO_2 0.2 and 0.3 ppm for low and high PM exposures, respectively) did not demonstrate changes in hematologic parameters or those related to coagulation (i.e., PT, PPT, plasma fibrinogen, D-dimer) or inflammation (i.e., CRP) in SH or WKY rats (Gottipolu et al., 2009, 190360). Together, these findings do not support a DE-related stimulation of blood coagulation following 1 or 6 mo of exposure.

Hardwood Smoke

The target PM concentrations in the hardwood smoke study was 30, 100, 300, and 1,000 μg/m^3 and the MMAD was 0.25-0.36 μm (Reed et al., 2006, 156043). In male rats exposed to hardwood smoke, the mid-low group (PM concentration 113 μg/m^3; NO, NO_2, SO_2 concentrations 0 ppm; CO concentration 1,832.3 ppm) had the greatest responses in hematology parameters, including increased hematocrit, hemoglobin, lymphocytes, and decreased segmented neutrophils (Reed et al., 2006, 156043). Platelets were elevated in male and female rats after 1 week of exposure, but this response returned to control values following the 6-month exposure. No changes were observed for any coagulation markers at 6 mo.

Gasoline Exhaust

PM mass in the gasoline exhaust study ranged from 6.6 to 59.1 μg/m^3, with the corresponding number concentration between 2.6×10^4 and 5.0×10^5 particles/cm^3; the dilutions for the gasoline exhaust were 1:10, 1:15 or 1:90 and filtered PM at the 1:10 dilution (Reed et al., 2008, 156903). Similar to the responses observed with hardwood smoke, male and female rats in the mid- and high-gasoline exhaust exposure groups (NO concentrations 11.9 and 18.4 ppm; NO_2 concentrations 0.5 and 0.9 ppm; CO concentration 73.2 and 107.3 ppm; SO_2 concentration 0.38 and 0.62 ppm, respectively) demonstrated elevated hematocrit and hemoglobin; RBC count was also elevated in these groups (Reed et al., 2008, 156903). The only response that appeared somewhat dependent on the presence of particles was increased RBC in female rats at 6 mo, although the authors attributed the observed increases to the high concentration of CO.

Collectively, these studies do not indicate robust systemic inflammation or coagulation responses in F344 rats following 6-month exposures to diesel, hardwood smoke, or gasoline exhaust. The limited effects that were observed could possibly be due to the varying gas concentrations in the exposure mixtures.

7.2.5. Renal and Vascular Function

Two recent epidemiologic studies have tested associations between PM exposure and indicators of renal and vascular function (urinary albumin to creatinine ratio [UACR] and blood pressure). UACR is a measure of urinary albumin excretion (National Kidney Foundation, 2008, 156796). When calculated as the ratio of albumin to creatinine concentrations in untimed ("spot") urine samples, UACR approximates 24-h urinary albumin excretion and can be used to identify albuminuria, a marker of generalized vascular endothelial damage (Xu et al., 2008, 157157). Values ≥ 30 mg/g (3.5 mg/mmol) and ≥ 300 mg/g (34 mg/mmol) usually define micro- and macroalbuminuria, both of which are associated with increases in CVD incidence and mortality (Bigazzi et al., 1998, 156272; Deckert et al., 1996, 156389; Dinneen and Gerstein, 1997, 156403; Gerstein et al., 2001, 156466; Mogensen, 1984, 156769). Several researchers have called the

dichotomization of albuminuria into question, observing that there is no threshold below which risk of cardiovascular and end-stage kidney disease disappears (Forman and Brenner, 2006, 156439; Knight and Curhan, 2003, 179900; Ruggenenti and Remuzzi, 2006, 156933).

Systolic, diastolic, pulse, and mean arterial blood pressures (SBP; DBP; PP; MAP) in mmHg have also been used as measures of cardiovascular disease. Franklin et al. (1997, 156446) suggested that SBP and PP were the only two measures predictive of carotid stenosis in a multivariable analysis considering all 4 measures, whereas Khattar et al. (2001, 155896) suggested that their prognostic significance in hypertensive populations may differ by age, with SBP and PP being most predictive among those ≥ 60 yr and DBP among those <60 yr old (Khattar et al., 2001, 155896).

7.2.5.1. Epidemiologic Studies

O'Neill et al. (2007, 156006) examined the association of UACR with $PM_{2.5}$ and PM_{10} among members of the MESA population described previously (Diez et al., 2008, 156401). For this study of UACR, which included cross-sectional and longitudinal analyses, the study population was restricted to a subset of 3,901 participants (mean age = 63 yr; 52% female) with complete covariate, outcome and exposure data at their first through third exams (2000-2004). In cross-sectional analyses, the authors found that after adjustment for demographic and clinical characteristics, 10 $\mu g/m^3$ increases in 20-yr imputed exposures to $PM_{2.5}$ and PM_{10} were associated with negligible 0.002 (95% CI: -0.048 to 0.052) and -0.002 (95% CI: -0.038 to 0.035) mean differences in baseline log UACR, respectively. Similarly, small statistically non-significant decreases in the prevalence of microalbuminuria (defined in this setting as ≥ 25 mg/g) provided little evidence of an effect on renal function. These largely null cross-sectional findings mirrored those based on the study's shorter-term (30- and 60-day) $PM_{2.5}$ and PM_{10} exposures. Moreover, longitudinal analyses revealed only a weak association between 3-yr change in log UACR and 20-yr PM_{10} exposure. Evidence of effect modification by demographic and geographic characteristics was not apparent in either the cross-sectional or longitudinal analyses.

Auchincloss et al. (2008, 156234) focused on automated, oscillometric, sphygmomanometric measures of blood pressures in mmHg (SBP; DBP; PP; MAP). Like O'Neill (2007, 156006), Diez et al. (2008, 156401) and Allen et al. (2007, 156006), Auchincloss et al. (2008, 156234) based their examination on the previously described MESA population. The authors included 5,112 study participants (age range = 45-84 yr; 52% female) who were free of clinically manifested CVD at their baseline exam in one of six primarily urban U.S. locations (2000-2002). In this cross-sectional study, they used arithmetic averaging of EPA AQS $PM_{2.5}$ data available at the monitor nearest to each participant's geocoded U.S. Postal Service ZIP code centroid to estimate 30- and 60-day avg exposures to $PM_{2.5}$. They found small nonsignificant increases of 1.5 (95% CI: -0.2 to 3.2), 0.2 (95% CI: -0.7 to 1.0), 1.3 (95% CI: 0.1 to 2.6), and 0.6 (95% CI: -0.4 to 1.7) mmHg increases in SBP, DBP, PP and MAP, respectively, per 10 $\mu g/m^3$ increase in 30-day avg $PM_{2.5}$ exposure, Associations were slightly weaker for 60-day avg $PM_{2.5}$ exposure and among participants without hypertension, during cooler weather, in the presence of low NO_2, residing >300 m from a highway, or surrounded by lower road density.

Finally, the Calderon-Garciduenas et al. (2007, 091252) ecologic study introduced in Section 7.2.3.1 also found that children residing in Mexico City had higher mean pulmonary artery pressure as assessed by Doppler echocardiography and fasting plasma endothelin-1 (ET-1) than residents in Polotitlán: unadjusted mean 17.5 (95% CI: 15.7-19.4) versus 14.6 (95% CI: 13.8-15.4) mmHg and 2.23 (95% CI: 1.93-2.53) versus 1.23 (95% CI: 1.11-1.35) pg/mL, respectively. Within Mexico City, ET-1 was higher in residents of the Northeast (historically higher $PM_{2.5}$) than those of the Southwest (historically lower $PM_{2.5}$).

The MESA analyses of UACR (O'Neill et al., 2007, 156006) and the ecologic study of children living in a highly polluted area of Mexico (Calderon-Garciduenas et al., 2007, 091252) provide little evidence that long-term exposure to $PM_{2.5}$ had an effect on renal and vascular function, respectively. Auchincloss et al. (2008, 156234) reports small nonsignificant associations of blood pressure with 30- and 60-day avg $PM_{2.5}$ concentrations. PM concentrations from the analyses are characterized in Table 7-1.

Table 7-1. Characterization of ambient PM concentrations from studies of subclinical measures of cardiovascular diseases and long-term exposure.

Study	Location	Mean Concentration (μg/m^3)	Upper Percentile Concentrations (μg/m^3)
PM_{10}			
Diez Roux et al. (2008, 156401)	MESA: 6 Cities U.S.	20 yr imputed mean: 34	NR
O'Neill et al. (2007, 156006)	MESA: 6 Cities U.S.	Long-Term Exposure: 1982-2002: 34.7 1982-1987: 40.5 1988-1992: 38 1993-1997: 30.6 1998-2002: 29.7 Previous Month: 27.5	NR
Baccarelli et al. (2008, 157984)	Lombardy Region Italy	NR	NR
Rosenlund et al. (2006, 089796)	Stockholm, Sweden	30-y avg PM_{10} (traffic) Cases: 2.6 Controls: 2.4	5th-95th %: 0.5-6 0.6-5.9
Chen and Swartz (2008, 190106)	US Population (NHANES)	Annual avg: 36.8	NR
Forbes et al. (2009, 190351)	British Population	1994: 19.5 (median) 1998: 17.9 (median) 2003: 16.2 (median)	1994, Min-Max: 12.5-36.1 1998, Min-Max: 12.6-27.0 2003, Min-Max: 11.0-22.7
$PM_{2.5}$			
Hoffmann et al.(2007, 091163)	HNRS, 3 Cities Germany	Annual avg: 22.8	NR
Allen et al. (2009, 156209)	MESA: 5 Cities	Annual avg: 15.8	Min-Max: 10.6-24.7
Kunzli et al. (2005, 087387)	VEAPS BVAIT	Annual avg: 20.3	Min-Max: 5.2-26.9
Auchincloss et al. (2008, 156234)	MESA: 6 Cities	Prior 30 days: 16.8 Prior 60 days: 16.7	NR
O'Neill (2007, 156006)	MESA: 6 Cities U.S.	Previous Month: 16.5	NR
Diez Roux et al. (2008, 156401)	MESA: 6 Cities U.S.	20-y imputed mean: 21.7	NR
Hoffmann et al. (2009, 190376)	HNRS: 3 Cities Germany	Annual avg: 22.8	Min-max: 19.8-26.8
Calderon-Garciduenas et al. (2009, 192107)	Southwest Mexico (high pollution)	Annual avg: 25	NR
	Potitlan (low pollution)	Annual avg: <15	NR
Calderon-Garciduenas et al. (2007, 091252)	Southwest Mexico (high pollution)	NR	NR
	Potitlan (low pollution)	NR	NR

MESA: Multi-Ethnic Study of Atherosclerosis
HNRS: Heinz Nixdorf Recall Study
VEAPS: Vitamin E Atherosclerosis Progression Study
BVAIT: B-Vitamin Atherosclerosis Intervention Trial

7.2.5.2. Toxicological Studies

In a $PM_{2.5}$ CAPs study of 10 wk (6 h/day×5 days/wk) in Tuxedo, NY (mean mass concentration 79.1 μg/m^3), there was no difference in mean arterial pressure (MAP) in SD rats between groups (Sun et al., 2008, 157032). When angiotensin II (Ang II) was infused during the last week of exposure to induce systemic hypertension, the MAP slope was consistently greater in the CAPs-exposed rats compared to the filtered air group. Furthermore, thoracic aortic rings were more responsive to phenylephrine-induced constriction and less responsive to ACh-induced relaxation in the PM+Ang II vessels. In contrast to the latter findings, the relaxation response was exaggerated in the PM+Ang II aortic segments with a Rho-kinase (ROCK) inhibitor. Superoxide production in aortic rings increased in the PM+Ang II group compared to the filtered air group and the addition of

NAD(P)H oxidase inhibitor (apocynin) or a NOS inhibitor (L-NAME) attenuated the superoxide generation. The levels of tetrahydrobiopterin (BH_4) were decreased in mesenteric vasculature and the heart by 46% and 41% in the PM+Ang II group compared to controls, respectively; furthermore, levels of BH_4 in the liver were similarly reduced, which is consistent with a systemic effect of CAPs. Together, these findings indicate that CAPs potentiate Ang II-induced hypertension and alter vascular reactivity, perhaps through activated NADPH oxidase and eNOS uncoupling that result in oxidative stress generation and triggering of the Rho/ROCK signaling pathway.

7.2.6. Autonomic Function

7.2.6.1. Toxicological Studies

Hwang et al. (2005, 087957) and Chen and Hwang (2005, 087218) used radiotelemetry to examine the chronic changes in HR and HRV resulting from the same CAPs exposures described previously (Chen and Nadziejko, 2005, 087219). The overall average CAPs exposure concentration was 133 μg/m^3 and results indicate differing responses to CAPs between $ApoE^{-/-}$ mice and their genetic background strain, C57BL/6J mice (Hwang et al., 2005, 087957). Using the time period of 1:30-4:30 a.m., C57BL/6J mice showed a HR increase only over the last month of exposure. In contrast, $ApoE^{-/-}$ mice had chronic decreases of 33.8 beat/min for HR. Changes in HRV (SDNN and rMSSD) were somewhat more complicated, with biphasic responses in $ApoE^{-/-}$ mice over the 5-month period (initial increase over first 6 wk, decrease over next 12 wk, and slight upward turn for remainder of the study)(Chen and Hwang, 2005, 087218). Increasing linear trends were observed in C57BL/6J mice for SDNN and rMSSD. The average CAPs concentration for the HRV study was 110 μg/m^3. However, only three C57BL/6J mice in the exposure group were included in the analysis compared to ten $ApoE^{-/-}$ animals, thus making it difficult to interpret the C57BL/6J mice responses (Chen and Hwang, 2005, 087218; Hwang et al., 2005, 087957).

7.2.7. Cardiac changes

7.2.7.1. Toxicological studies

Two recent toxicological studies have evaluated the effects of PM on cardiac effects including pathology and gene expression. Cardiac mitochondrial function has also been evaluated following PM exposure in rats.

Diesel Exhaust

A recent study of DE exposure (PM mass concentration 507 or 2,201 μg/m^3, CO 1.3 or 4.8 ppm, NO <2.5 or 5.9 ppm, NO_2 <0.25 or 1.2 ppm, SO_2 0.2 or 0.3 ppm for low and high PM exposures, respectively; geometric median number diameter 85 nm) indicated a hypertensive-like cardiac gene expression in WKY rats that mimicked baseline patterns in air-exposed SH rats (Gottipolu et al., 2009, 190360). Exposure to the high concentration of DE for 4 wk (4 h/day, 5 day/wk) led to downregulation of genes involved in stress, antioxidant compensatory response, growth and extracellular matrix regulation, membrane transport of molecules, mitochondrial function, thrombosis regulation, and immune function. No genes were affected by DE in SH rats. A dose-dependent inhibition of mitochondrial aconitase activity in both rat strains was observed, indicating a DE effect on oxidative stress. It should be noted that while DE-related cardiovascular effects were found in WKY rats only, pulmonary inflammation and injury were observed in both strains (Sections 7.3.3.2 and 7.3.5.1).

Model Particles

Wallenborn et al. (2008, 191171) examined the subchronic (5 h/day, 3 day/wk, 16 wk) pulmonary, cardiac, and systemic effects of nose-only exposure to particulate $ZnSO_4$ (9, 35, or 120 μg/m^3) in WKY rats. Particle size was reported to be 31-44 nm measured as number median diameter. Although changes in pulmonary inflammation or injury and cardiac pathology were not observed, effects on cardiac mitochondrial protein and enzyme levels were noted (i.e., increased ferritin levels, decrease in succinate dehydrogenase activity), possibly indicating a small degree of mitochondrial dysfunction. Glutathione peroxidase, an antioxidant enzyme, was also decreased in the cardiac cytosol. Gene expression analysis identified alterations in cardiac genes involved in cell signaling events, ion channels regulation, and coagulation in animals exposed to the highest $ZnSO_4$ concentration only. This study demonstrates a possible direct effect of $ZnSO_4$ on extrapulmonary systems, as suggested by the lack of pulmonary effects (Section 7.3.3.2).

7.2.8. Left Ventricular Mass and Function

Van Hee et al. (2009, 192110) studied 3,827 participants (age range = 45-84 yr; 53% female) who underwent magnetic resonance imaging (MRI) of the heart at the baseline examination of the MESA cohort (2000-2002). This cross-sectional study focused on two MRI-based outcome measures: left ventricular mass index (LVMI, g/m^2) and ejection fraction (EF, %), the former estimated using the DuBois formula for body surface area, the latter as the ratio of stroke volume to end diastolic volume. The study also estimated annual mean exposures to $PM_{2.5}$ at participants' geocoded residential addresses in 2000 using ordinary kriging of U.S. EPA AQS concentration data. In fully adjusted models, it found 3.8 (95% CI: -6.1 to 13.7) g/m^2 and -3.0% (-8.0 to 2.0) differences in LVMI and EF per 10 μg/m^3 increment in $PM_{2.5}$. The findings were small and imprecise, albeit suggestive of a slight, PM-associated increase in the mass and decrease in the function of the left ventricle. The effect of living within 50 m of a major roadway on LVMI was greater than the effect of $PM_{2.5}$ (i.e., 1.4 g/m^2 [95% CI: 0.3-2.5] per 10 μg/m^3.)

7.2.9. Clinical Outcomes in Epidemiologic Studies

Several epidemiologic studies of U.S. and European populations have examined associations between long-term PM exposures and clinical CVD events (Baccarelli et al., 2008, 157984; Hoffmann et al., 2006, 091162; Hoffmann et al., 2009, 190376; Maheswaran et al., 2005, 088683; Maheswaran et al., 2005, 090769; Miller et al., 2007, 090130; Rosenlund et al., 2006, 089796; Solomon et al., 2003, 156994; Zanobetti and Schwartz, 2007, 091247). Results from these studies are summarized in Figure 7-1. The ambient PM concentrations from these studies are characterized in Table 7-2.

Coronary Heart Disease

Epidemiologic studies examining the association of coronary heart disease (CHD) with long-term PM exposure are discussed below (Hoffmann et al., 2006, 091162; Maheswaran et al., 2005, 090769; Miller et al., 2007, 090130; Puett et al., 2008, 156891; Rosenlund et al., 2006, 089796; Rosenlund et al., 2009, 190309; Zanobetti and Schwartz, 2007, 091247). Cases of CHD were variably defined in these studies to include history of angina pectoris, MI, coronary artery revascularization (bypass graft; angioplasty; stent; atherectomy), and congestive heart failure (CHF). Results pertaining to death from CHD are described in Section 7.6.

Miller et al. (2007, 090130) studied incident, validated MI, revascularization, and CHD death, both separately and collectively, among 58,610 post-menopausal female residents of 36 U.S. metropolitan areas (age range = 50-79 yr) enrolled in the Women's Health Initiative Observational Study (WHI OS, 1994-1998). In this prospective cohort study of participants free of CVD at baseline (median duration of follow-up = 6 yr), the authors used arithmetic averaging of year 2000 EPA AQS $PM_{2.5}$ data available at the monitor nearest to each participant's geocoded U.S. Postal Service five-digit ZIP code centroid to estimate 1-yr avg exposures. They found 6% (95% CI: -15 to 34), 20% (95% CI: 0-43) and 21% (95% CI: 4-42) increases in the overall risk of MI, revascularization, and

their combination with CHD death per 10 μg/m^3 increase in $PM_{2.5}$, respectively. Hazards were higher within than between cities and in the obese. For the combined CVD outcome (MI, revascularization, stroke, CHD death, cerebrovascular disease), authors reported a 24% (95% CI: 9-41) increase in risk that was higher among participants at higher than lower quintiles of body mass index, waist-to-hip ratio, and waist circumference. The $PM_{2.5}$-CVD association was stronger among non-diabetic than diabetic participants.

Table 7-2. Characterization of ambient PM concentrations from studies of clinical cardiovascular diseases and long-term exposure.

Study	Location	Mean Annual Concentration (μg/m^3)	Upper Percentile Concentrations (μg/m^3)
PM_{10}			
Puett et al. (2008, 156891)	13 U.S. States	21.6	
Zanobetti and Schwartz (2007, 091247)	21 U.S. Cities	28.8	Overall range NR
Rosenlund et al. (2006, 089796)	Stockholm, Sweden	30 y avg PM_{10} (traffic) Cases: 2.6 Controls: 2.4	5th-95th Percentile 0.5-6.0 0.6-5.9
Rosenlund et al. (2009, 190309)	Stockholm, Sweden	5-yr avg PM_{10} from traffic: Cases: 2.4 (median) Controls: 2.2 (median)	
Maheswaran et al. (2005, 090769)	Sheffield, U.K.	Range of means in each quintile: 16-23.3	NR
Baccarelli et al. (2008, 157984)	Lombardia Region, Italy	NR	NR
$PM_{2.5}$			
Miller et al. (2007, 090130)	WHI: 36 Metropolitan areas	Citywide avg (yr 2000): 13.5	Min-max: 4-19.3
Hoffmann et al. (2006, 091162)	HNRS: 2 Cities Germany	23.3	NR
Hoffman et al. (2009, 190376)	HRNS: 2 Cities German	22.8	NR

WHI: Womens Health Initiative
HNRS: Hans Nixdorf Recall Study

Puett et al. (2008, 156891) studied incident, validated CHD, CHD death, and non-fatal MI among 66,250 female residents (mean age = 62 yr) of metropolitan statistical areas in thirteen northeastern U.S. states who were enrolled in the Nurses' Health Study (NHS, 1992-2002). In this prospective cohort study of women without a history of non-fatal MI at baseline (maximum duration of follow-up = 4 yr), the authors used two-stage, spatially smoothed, land use regression to estimate residence-specific, 1-yr ma PM_{10} exposures from U.S. EPA AQS and emissions, IMPROVE, and Harvard University monitor data. They found a 10% (95% CI: -6 to 29) increase in risk of first CHD event per 10 μ/m^3 increase in 1-yr avg PM_{10} exposure, while the association with MI was close to the null value. The association with fatal CHD event of 30% (95% CI: 0-71) was stronger. Furthermore, associations with CHD death were higher in the obese and in the never smokers.

Rosenlund et al. (2006, 089796) studied 2,938 residents of Stockholm County, Sweden (age range = 45-70 yr; 34% female). In this case-control study of 1,085 patients with their first, validated non-fatal MI and an age-, gender- and catchment-stratified random sample of 1,853 controls without MI (1992-1994), the authors used street canyon-adjusted dispersion modeling of emissions data to estimate 30-yr avg exposure to PM_{10} (median = 2.4 μg/m^3). They found that the OR for prevalent MI per 10 μg/m^3 increase in PM_{10} was 0.85 (95% CI: 0.50-1.42). The OR for fatal MI was elevated, but not statistically significant.

In a more recent study, Rosenlund et al. (2009, 190309) evaluated 554,340 residents (age range = 15-79 yr; 49% female) of Stockholm County, Sweden (1984-1996). In this population-based, case-control study of 43,275 cases of incident, validated MI, the authors used dispersion modeling of traffic emissions and land use data to estimate 5-yr avg exposure to PM_{10}. They found that after

adjustment for demographic, temporal, and socioeconomic characteristics, the OR for MI per 5 μg/m^3 increase in PM_{10} was 1.04 (95% CI: 1.00-1.09). ORs were higher after restriction to fatal cases, in- or out-of-hospital deaths, and participants who did not move between population censuses. Authors state that control for confounding was superior in their previous study (Rosenlund et al., 2006, 089796) although the size of the population was larger in this recent study (Rosenlund et al., 2009, 190309).

Zanobetti and Schwartz (2007, 091247) studied ICD-coded recurrent MI (ICD 9 410) and post-infarction CHF (ICD 9 428) among 196,131 Medicare recipients (age ≥ 65 yr; 50% female) discharged alive following MI hospitalization in 21 cities from 12 U.S. states (1985-1999). In this ecologic, open cohort study of re-hospitalization among MI survivors (mean duration of follow-up = 3.6 and 3.7 yr for MI and CHF, respectively), the authors used arithmetic averaging of EPA AQS PM_{10} data available in the county of hospitalization to estimate 1-yr avg exposures. They found 17% (95% CI: 5-31) and 11% (95% CI: 3-21) increases in the risk of recurrent MI and post-infarction CHF, respectively, per 10 μg/m^3 increase in PM_{10} exposure. Hazards were somewhat higher among persons aged >75 yr.

Hoffmann et al. (2006, 091162) studied self-reported CHD (MI or revascularization) among 3,399 residents of Essen and Mülheim, Germany (age range = 45-75 yr; 51% female) at the baseline exam of the Heinz Nixdorf Recall Study (2000-2003) introduced previously. In this cross-sectional ancillary study, the authors used dispersion modeling of emissions, climate and topography data to estimate 1-yr avg exposure to $PM_{2.5}$ (mean = 23.3 μg/m^3). They found little evidence of an association between $PM_{2.5}$ and CHD in these data. After adjustment for geographic, demographic and clinical characteristics, the OR for prevalent CHD per 10 μg/m^3 increase in exposure was 0.55 (95% CI: 0.14-2.11).

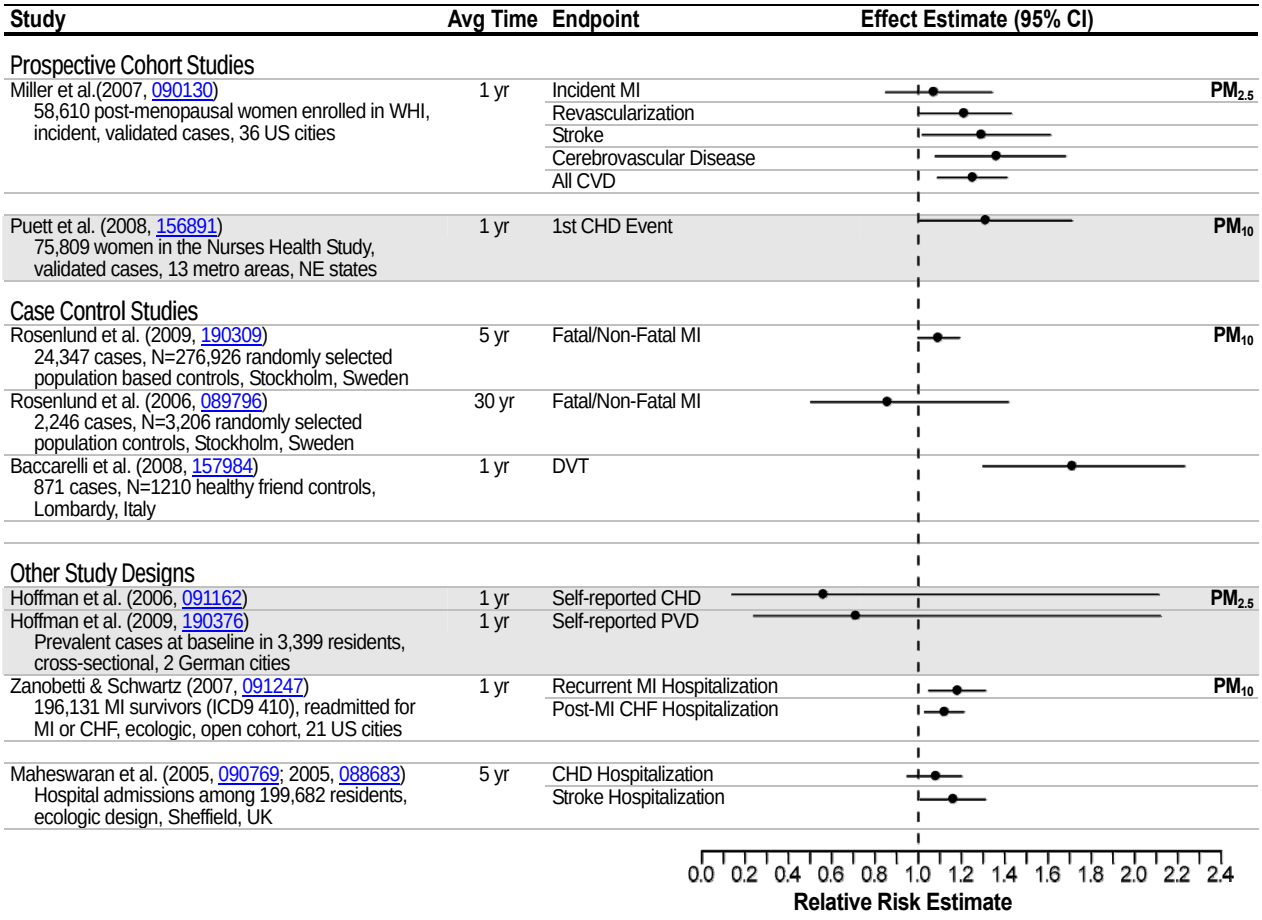


Figure 7-1. Risk estimates for the associations of clinical outcomes with long-term exposure to ambient $PM_{2.5}$ and PM_{10}.

In the study of 1,030 census enumeration districts in Sheffield, U.K. described previously, Maheswaran et al. (2005, 090769) studied 11,407 ICD-10-coded emergency hospitalizations for CHD (ICD10 I20-25) among 199,682 residents (age ≥ 45 yr; 45% female). In this ecologic study, the authors used dispersion modeling of emissions and climate data to estimate 5-yr avg exposure to PM_{10}. They found that after adjusting for smoking prevalence, controlling for socioeconomic factors, and smoothing, the age- and gender-standardized rate ratios for CHD admission were 1.01 (95% CI: 0.92-1.11), 1.04 (95% CI: 0.93-1.15), 0.97 (95% CI: 0.87-1.08), and 1.07 (95% CI: 0.95-1.20) across PM_{10} quintiles. The linear trend was somewhat stronger for CHD mortality (Section 7.3).

The study of post-menopausal women enrolled in the WHI OS by Miller et al. (2007, 090130) was the only U.S. study to examine the effect of $PM_{2.5}$ rather than PM_{10}. This study, which provides strong evidence of an association, was distinguished by its prospective cohort design, validation of incident cases and large population. Puett et al. (2008, 156891), the other U.S. study with comparable design features, provides evidence of an association of incident CHD with long- term PM_{10} exposure. Findings from Swedish case control studies of incident validated cases of MI were not consistent. A cross-sectional study of self-reported CHD did not provide evidence of an association with $PM_{2.5,}$ while findings from two ecologic studies of PM_{10} indicated positive associations of CHD hospitalizations with PM_{10} (Maheswaran et al., 2005, 088683; Zanobetti and Schwartz, 2007, 091247).

Stroke

Miller et al. (2007, 090130) found 28% (95% CI: 2-61) and 35% (95% CI: 8-68) increases in the overall risk of validated stroke and cerebrovascular disease, respectively, per 10 $\mu g/m^3$ increase in 1-yr avg $PM_{2.5}$ exposure. Risks were higher within than between cities. In the study of 1030 Census of enumeration districts in Sheffield, U.K. described previously, Maheswaran et al. (2005, 088683) studied 5,122 ICD-10-coded emergency hospital admissions for stroke (I60-69) among 199,682 residents (age ≥ 45 yr; 45% female) of 1,030 census enumeration districts in Sheffield, U.K. (1994-1999). In this ecologic study, the authors used dispersion modeling of emissions and climate data to estimate 5-yr avg exposure to PM_{10}. They found that the age- and gender-standardized rate ratios for stroke admission were 1.05 (95% CI: 0.94-1.17), 1.07 (95% CI: 0.95-1.20), 1.06 (95% CI: 0.94-1.20), and 1.15 (95% CI: 1.01-1.31) across PM_{10} quintiles. Linear trend was somewhat stronger for stroke mortality (Section 7.6).

These studies examining the long-term PM-stroke relationship provide evidence of association. Maheswaran et al. (2005, 088683) examined emergency room hospital admissions in Sheffield, U.K. using an ecologic design while results reported by Miller et al. (2007, 090130) are based on the prospective cohort study of the WHI OS population (both introduced previously).

Peripheral Arterial Disease

The German Heinz Nixdorf Recall cross-sectional study described in Section 7.2.1.1 (Hoffmann et al., 2009, 190376) also evaluated the association between 1-yr avg exposure to $PM_{2.5}$ and peripheral arterial disease (self-reported history of a surgical or procedural intervention or an ABI <0.9 in one or both legs). The authors found no evidence of an increase in risk. The OR for peripheral arterial disease was 0.87 (95% CI: 0.57-1.34) per 3.9 $\mu g/m^3$ increase in $PM_{2.5}$. However, evidence of an association with traffic exposure was present in these data. ORs of 1.77 (95% CI: 1.01-3.10), 1.02 (95% CI: 0.58-1.80), and 1.07 (95% CI: 0.68-1.68) for residing ≤ 50, 50-100, and 100-200 m of a major road (reference category: >200 m), respectively were observed. ORs were higher among participants with CAC scores ≤ 75th percentile, women, and smokers.

Deep Vein Thrombosis

The Italian case-control study (introduced in Section 7.2.1.2) also examined the chronic PM_{10}-DVT association (Baccarelli et al., 2008, 157984). The authors found a 70% (95% CI: 30-223) increase in the odds of DVT per 10 $\mu g/m^3$ increase in 1-yr avg PM_{10} exposure. This finding was consistent with the decreases in PT and PTT also observed among controls in this context as well as

the 47% (95% CI: 11-96) increase in the odds of DVT per inter-decile range (242 m) increase in the residence-to-major-roadway distance observed among a subset of cases and controls (Baccarelli et al., 2009, 188183). The PM_{10}-DVT and distance-DVT associations were both weaker among women and among users of oral contraceptives or hormone therapy.

7.2.10. Cardiovascular Mortality

New epidemiologic evidence reports a consistent association between long-term exposure to $PM_{2.5}$ and increased risk of cardiovascular mortality. There is little evidence for the long-term effects of $PM_{10-2.5}$ on cardiovascular mortality. This section focuses on cardiovascular mortality outcomes in response to long-term exposure to PM. The studies that investigate long-term exposure and mortality due to any specific or all (nonaccidental) causes are evaluated in Section 7.6. A summary of the mean PM concentrations reported for the studies characterized in this section is presented in Table 7-8, and the effect estimates are presented in Figure 7-7 and Figure 7-8.

A number of large, U.S. cohort studies have found consistent associations between long-term exposure to $PM_{2.5}$ and cardiovascular mortality. The American Cancer Society (ACS) (Pope et al. (2004, 055880) reported positive associations with deaths from specific cardiovascular diseases, particularly ischemic heart disease, and a group of cardiac conditions including dysrhythmia, heart failure and cardiac arrest (RR for cardiovascular mortality = 1.12 [95% CI: 1.08-1.15] per 10 $\mu g/m^3$ $PM_{2.5}$). In an additional reanalysis that extended the follow-up period for the ACS cohort to 18 yr (1982-2000) (Krewski et al., 2009, 191193), investigators found effect estimates that were similar, though generally higher, than those reported in previous ACS analyses.

A follow-up to the Harvard Six Cities study (Laden et al., 2006, 087605) used updated air pollution and mortality data and found positive associations between long-term exposure to $PM_{2.5}$ and mortality. Of special note is a statistically significant reduction in mortality risk reported with reduced long-term fine particle concentrations. This reduced mortality risk was observed for deaths due to cardiovascular and respiratory causes, but not for lung cancer deaths.

The WHI cohort study (Miller et al., 2007, 090130) (described previously) found that each 10 $\mu g/m^3$ increase of $PM_{2.5}$ was associated with a 76% increase in the risk of death from cardiovascular disease (hazard ratio, 1.76 [95% CI: 1.25-2.47]). The WHI study not only confirms the ACS and Six City Study associations with cardiovascular mortality in yet another well characterized cohort with detailed individual-level information, it also has been able to consider the individual medical records of the thousands of WHI subjects over the period of the study. This has allowed the researchers to examine not only mortality, but also related morbidity in the form of heart problems (cardiovascular events) experienced by the subjects during the study. These morbidity co-associations with $PM_{2.5}$ in the same population lend even greater support to the biological plausibility of the air pollution-mortality associations found in this study.

In an analysis for the Seventh-Day Adventist cohort in California (AHSMOG), a positive association with coronary heart disease mortality was reported among females (92 deaths; RR = 1.42 [95% CI: 1.06-1.90] per 10 $\mu g/m^3$ $PM_{2.5}$), but not among males (53 deaths; RR = 0.90 [95% CI: 0.76-1.05] per 10 $\mu g/m^3$ $PM_{2.5}$) (Chen et al., 2005, 087942). Associations were strongest in the subset of postmenopausal women (80 deaths; RR = 1.49 [95% CI: 1.17-1.89] per 10 $\mu g/m^3$ $PM_{2.5}$). The authors speculated that females may be more sensitive to air pollution-related effects, based on differences between males and females in dosimetry and exposure. As was found with $PM_{2.5}$, a positive association with coronary heart disease mortality was reported for $PM_{10-2.5}$ and PM_{10} among females (RR = 1.38 [95% CI: 0.97-1.95] per 10 $\mu g/m^3$ $PM_{10-2.5}$; RR = 1.22 [95% CI: 1.01-1.47] per 10 $\mu g/m^3$ PM_{10}), but not for males (RR = 0.92 [95% CI: 0.66-1.29] per 10 $\mu g/m^3$ $PM_{10-2.5}$; RR = 0.94 [95% CI: 0.82-1.08] per 10 $\mu g/m^3$ PM_{10}); associations were strongest in the subset of postmenopausal women (80 deaths) (Chen et al., 2005, 087942).

Two additional studies explored the effects of PM_{10} on cardiovascular mortality. The Nurses' Health Study (Puett et al., 2008, 156891) is an ongoing prospective cohort study examining the relation of chronic PM_{10} exposures with all-cause mortality and incident and fatal coronary heart disease consisting of 66,250 female nurses in MSAs in the northeastern region of the U.S. The association with fatal CHD occurred with the greatest magnitude when compared with other specified causes of death (hazard ratio 1.42 [95% CI: 1.11-1.81]). The North Rhine-Westphalia State Environment Agency (LUA NRW) initiated a cohort of approximately 4,800 women, and assessed whether long-term exposure to air pollution originating from motorized traffic and industrial sources was associated with total and cause-specific mortality (Gehring et al., 2006, 089797). They found

that cardiopulmonary mortality was associated with PM_{10} (RR = 1.52 [95% CI: 1.09-2.15] per 10 $\mu g/m^3$ PM_{10}).

In summary, the 2004 PM AQCD concluded that there was strong evidence that long-term exposure to $PM_{2.5}$ was associated with increased cardiopulmonary mortality. Recent studies investigating cardiovascular mortality provide some of the strongest evidence for a cardiovascular effect of PM. A number of large cohort studies have been conducted throughout the U.S. and reported consistent increases in cardiovascular mortality related to $PM_{2.5}$ concentrations. The results of two of these studies have been replicated in independent reanalyses. These effects are coherent with short-term epidemiologic studies of CVD morbidity and mortality and with long-term epidemiologic studies of CVD morbidity. In addition, biological plausibility and coherence are provided by toxicological studies demonstrating short-term cardiovascular effects as well as $PM_{2.5}$-related plaque progression in chronically exposed mice.

7.2.11.Summary and Causal Determinations

7.2.11.1. $PM_{2.5}$

Epidemiologic studies examining associations between long-term exposure to ambient PM (over months to years) and CVD morbidity had not been conducted and thus were not included in the 1996 or 2004 PM AQCDs (U.S. EPA, 1996, 079380; U.S. EPA, 2006, 157071). A number of studies were included in the 2004 AQCD that evaluated the effect of long-term $PM_{2.5}$ exposure on cardiovascular mortality and found strong and consistent associations. No toxicological studies had evaluated the effects of subchronic or chronic PM exposure on CVD effects in the 2004 PM AQCD. Recently, epidemiologic and toxicological studies have provided evidence of the adverse effects of long-term exposure to $PM_{2.5}$ on cardiovascular outcomes and endpoints, including atherosclerosis and clinical and subclinical markers of cardiovascular morbidity.

The strongest evidence for a CVD health effect related to long-term $PM_{2.5}$ exposure comes from epidemiologic studies of cardiovascular mortality. A number of large, multicity U.S. studies (the ACS, Six Cities Study, WHI, and AHSMOG) provide consistent evidence of an effect between long-term exposure to $PM_{2.5}$ and cardiovascular mortality (Section 7.2.10). These studies were conducted in urban areas across the U.S. where mean concentrations ranged from 10.2-29.0 $\mu g/m^3$ (Table 7-8). An epidemiologic study investigating the relationship between $PM_{2.5}$ and clinical CVD morbidity among post-menopausal women (Miller et al., 2007, 090130) provides evidence of an effect that is coherent with the cardiovascular mortality studies. This large, prospective cohort study of incident, validated cases found large increases in the adjusted risk of MI, revascularization, and stroke using a 1-yr avg $PM_{2.5}$ concentration (mean = 13.5 $\mu g/m^3$). A cross-sectional analyses of self-reported prevalence of CHD and peripheral arterial disease found no such increase in the odds of CVD morbidity (Hoffmann et al., 2006, 091162); the inconsistency of these findings with Miller et al. (2007, 090130) may be explained by differences in study design or location.

The effect of long-term $PM_{2.5}$ exposure on pre-clinical measures of atherosclerosis (CIMT, CAC, AAC or ABI) has been studied in several populations using a cross-sectional study design. The magnitude of the $PM_{2.5}$ effects and their consistency across different measures of atherosclerosis in these studies varies widely, and they may be limited in their ability to discern small changes in these measures. Kunzli et al. (2005, 087387) observed a non-significant 4.2% increase in CIMT associated with long-term $PM_{2.5}$ exposure among participants of a clinical trial in greater Los Angeles, which was several fold higher than the 0.5% increase observed by Diez-Roux et al. (2008, 156401) in their analyses of MESA baseline data. The associations in MESA of CAC and ABI with long-term $PM_{2.5}$ exposure were largely null (Diez et al., 2008, 156401), while an increase in AAC with long-term $PM_{2.5}$ exposure was reported (Chang et al., 2008, 180393). By contrast, a 43% increase in CAC was associated with long-term $PM_{2.5}$ exposure in a German study, but no similar association with ABI was observed (Hoffmann et al., 2009, 190376). Although the number of studies examining these relationships is limited, effect modification by use of lipid lowering drugs and smoking status was reported in more than one study of long-term $PM_{2.5}$ and PM_{10} exposure.

Evidence of enhanced atherosclerosis development was demonstrated in new toxicological studies that report increased plaque and lesion areas, lipid deposition, and TF in aortas of $ApoE^{-/-}$ mice exposed to CAPs (Section7.2.1.2). In addition, alterations in vasoreactivity were observed,

suggesting an impaired NO pathway. Additional toxicological studies of PM_{10} are consistent with these results. Further support is provided by a study that reported decreased L/W ratio in the pulmonary and coronary arteries of mice exposed to ambient air. However, $PM_{2.5}$ CAPs derived from traffic in Los Angeles did not affect plaque size (Araujo et al., 2008, 156222). Collectively, these toxicological studies provide biological plausibility for the associations reported in epidemiologic studies.

There is limited evidence for the effects of $PM_{2.5}$ on renal or vascular function. Cross-sectional and longitudinal epidemiologic analyses of $PM_{2.5}$ and UACR revealed no evidence of an effect (O'Neill et al., 2007, 156006), while small non-statistically significant increases in BP with 30- and 60-day avg $PM_{2.5}$ concentrations were reported (Auchincloss et al., 2008, 156234). A toxicological study did not show changes in MAP with CAPs, but indicated a CAPs-related potentiation of experimentally-induced hypertension (Sun et al., 2008, 157032). In addition, CAPs has induced changes in insulin resistance, visceral adiposity, and inflammation in a diet-induced obesity mouse model (Sun et al., 2009, 190487), indicating that diabetics may be a potentially susceptible population to PM exposure.

In summary, a number of large U.S. cohort studies report associations of long-term $PM_{2.5}$ concentration with cardiovascular mortality. These studies provide the strongest evidence for an effect of long-term $PM_{2.5}$ exposure on CVD effects. Additional evidence comes from a methodologically rigorous epidemiology study that demonstrates coherent associations between long-term $PM_{2.5}$ exposure and CVD morbidity among post-menopausal women. Toxicological studies demonstrate that this effect is biologically plausible and the effect is coherent with studies of short-term $PM_{2.5}$ exposure and CVD morbidity and mortality, and with long-term exposure to $PM_{2.5}$ and CVD mortality. Associations between $PM_{2.5}$ and subclinical measures of atherosclerosis are inconsistent, but cross-sectional studies may be limited in their ability to discern small changes in these measures. In addition, potential modification of the $PM_{2.5}$-CVD association by smoking status and the use of lipid lowering drugs has been demonstrated in epidemiologic studies that used individual-level data. Toxicological studies provide evidence for accelerated development of atherosclerosis in $ApoE^{-/-}$ mice exposed to CAPs and show effects on coagulation factors, experimentally-induced hypertension, and vascular reactivity. Available studies of clinical cardiovascular disease outcomes report inconsistent results. Based on the above findings, the epidemiologic and toxicological evidence is **sufficient to infer a causal relationship between long-term $PM_{2.5}$ exposures and cardiovascular effects.**

7.2.11.2. $PM_{10-2.5}$

One epidemiologic study evaluated the relationship between long-term exposure to $PM_{10-2.5}$ and cardiovascular mortality and found a positive association with coronary heart disease mortality among females, but not for males; associations were strongest in the subset of post-menopausal women (Chen et al., 2005, 087942). No toxicological studies of long-term exposure to ambient $PM_{10-2.5}$ and cardiovascular effects have been conducted to date. Evidence is **inadequate to infer the presence or absence of a causal relationship.**

7.2.11.3. UFPs

A few toxicological studies of long-term exposure to UFPs have been conducted. Increased plaque size was reported in mice exposed to UF CAPs derived from traffic (Araujo et al., 2008, 156222). Studies of diesel and gasoline exhaust reported relatively few changes in hematologic or coagulation parameters (Section 7.2.4.2) and one DE study demonstrated altered cardiac gene expression in normotensive rats that reflected the development of hypertension (Gottipolu et al., 2009, 190360). Whole and filtered gasoline exhaust induced increases in gene products involved in atheromatous plaque formation and/or degradation, but these effects were largely due to the gaseous emissions (Lund et al., 2007, 125741). Evidence from these studies alone is **inadequate to infer the presence or absence of a causal relationship**.

7.3. Respiratory Effects

Several cohort studies reviewed in the 2004 PM AQCD provided evidence for relationships between long-term PM exposure and effects on the respiratory system, though it did not rule out the possibility that the observed respiratory effects may have been confounded by other pollutants. In 12 southern California communities in the Children's Health Study (CHS), Gauderman et al. (2000, 012531; 2002, 026013) found that decreases in lung function growth among schoolchildren were associated with long-term exposure to PM. Declines in pulmonary function were reported with all three major PM size classes – PM_{10}, $PM_{10-2.5}$ and $PM_{2.5}$ – though the three PM measures were highly correlated. In another analysis of data from the CHS cohort, McConnell et al. (1999, 007028), reported an increased risk of bronchitis symptoms in children living in communities with higher PM_{10} and $PM_{2.5}$ concentrations. These results were found to be consistent with results of cross-sectional analyses of the 24-city study by Dockery et al. (1996, 046219) and Raizenne et al. (1996, 077268), that were assessed in the 1996 PM AQCD. These studies reported associations between increased bronchitis rates and decreased peak flow with fine particle sulfate and fine particle acidity. However, the high correlation of PM_{10}, acid vapor and NO_2 precluded clear attribution of the bronchitis effects reported by McConnell et al. (1999, 007028) to PM alone. In a prospective cohort study among a subset of children in the CHS (n = 110) who moved to other locations during the study period, Avol et al. (2001, 020552) reported that those subjects who moved to areas of lower PM_{10} showed increased growth in lung function compared with subjects who moved to communities with higher PM_{10} concentrations. Finally, the 2004 PM AQCD concluded that there was strong epidemiologic evidence for associations between long-term exposures to $PM_{2.5}$ and cardiopulmonary mortality, though the respiratory effects were not separated from the cardiovascular effects in this conclusion.

The 2004 PM AQCD (U.S. EPA, 2004, 056905) concluded that the evidence for an association between long-term exposure to PM and respiratory effects may be confounded by other pollutants. Gauderman et al. (2002, 026013) reported declines for FEV_1 and McConnell et al. (1999, 007028) reported increased ORs for bronchitic symptoms in asthmatics for PM_{10} and $PM_{2.5}$. Recent epidemiologic literature includes results from several prospective cohort studies, which found consistent, positive associations between long-term exposure to PM and respiratory morbidity. Associations were reported with $PM_{2.5}$ and PM_{10}, and the studies showing associations only with PM_{10} were conducted in locations where the PM consisted predominantly of fine particles, providing support for associations with long-term exposure to fine particles. These results are summarized below; further details of these studies are summarized in Annex E.

Very few subchronic and chronic toxicological studies investigating respiratory effects were available in the 2004 PM AQCD. However, the 2002 EPA Health Assessment Document for DE reported that chronic exposure to DE was associated with histopathology including alveolar histiocytosis, aggregation of alveolar macrophages, tissue inflammation, increased polymorphonuclear leukocytes, hyperplasia of bronchiolar and Type 2 epithelial cells, thickened alveolar septa, edema, fibrosis, emphysema and lesions of the trachea and bronchi. Since then a number of animal toxicological studies have been conducted involving inhalation exposure to CAPs, urban air, DE, gasoline exhaust, and wood smoke. These subchronic and chronic studies provide evidence of altered pulmonary function, inflammation, histopathological changes and oxidative and allergic responses following $PM_{2.5}$ exposures. These results are summarized below; further details of these studies are summarized in Annex D.

7.3.1. Respiratory Symptoms and Disease Incidence

7.3.1.1. Epidemiologic Studies

New longitudinal cohort studies provide the best evidence to evaluate the relationship between long-term exposure to ambient PM and increased incidence of respiratory symptoms or disease. A summary of the mean PM concentrations reported for the long-term exposure studies characterized in this section is presented in Table 7-3.

Bayer-Oglesby et al. (2005, 086245) examined the decline of ambient pollution levels and improved respiratory health demonstrated by a reduction in respiratory symptoms and diseases in school children (n = 9,591) in Switzerland. Reduced air pollution exposure resulted in improved respiratory health of children. Further, the average reduction of symptom prevalence was more pronounced in areas with stronger reduction of air pollution levels. The average decline of PM_{10} between 1993 and 2000 across the nine study regions was 9.8 $\mu g/m^3$ (29%). Declining levels of PM_{10} were associated with declining prevalence of chronic cough, bronchitis, common cold, nocturnal dry cough, and conjunctivitis symptoms, but no significant associations were reported for wheezing, sneezing, asthma, and hay fever, as shown in Figure 7-2. In Figure 7-2, Panel (B) illustrates that on an aggregate level across regions, the mean change in adjusted prevalence of chronic cough is associated with the mean change in PM_{10} levels ($r = 0.78$; $p = 0.02$). Similar associations were seen for nocturnal dry cough and conjunctivitis symptoms and PM_{10} levels. Röösli et al. (2000, 010296; 2001, 108738; 2005, 156923) have demonstrated that PM_{10} levels are homogeneously distributed within regions of Basel, Switzerland and are not substantially affected by local traffic, justifying the single-monitor approach for assignment of PM_{10} exposures. Based on parallel measurements of $PM_{2.5}$ and PM_{10} at seven sites in Switzerland, $PM_{2.5}$ and PM_{10} at all sites are generally highly correlated (r^2 ranging from 0.85 to 0.98) (Gehrig and Buchmann, 2003, 139678), indicating that PM_{10} consists predominantly of fine particles in these locations.

Schindler et al. (2009, 191950) reported that sustained reduction in ambient PM_{10} concentrations can lead to decreases in respiratory symptoms among Swiss adults in the SAPALDIA study. They compared baseline data in 1991 to a follow-up interview in 2002 after a substantial decline in PM_{10} concentrations served as a natural experiment. Each subject was assigned model-based estimates of PM_{10} concentrations averaged over the 12 mo preceding each health assessment with mean decline in PM_{10} levels of 6.2 $\mu g/m^3$ (SD = 3.9 $\mu g/m^3$). When the authors tested the joint hypothesis of no association between the PM_{10} difference and symptom incidence or persistence, positive results were obtained for regular cough, chronic cough or phlegm and wheezing but not regular phlegm or wheezing without a cold.

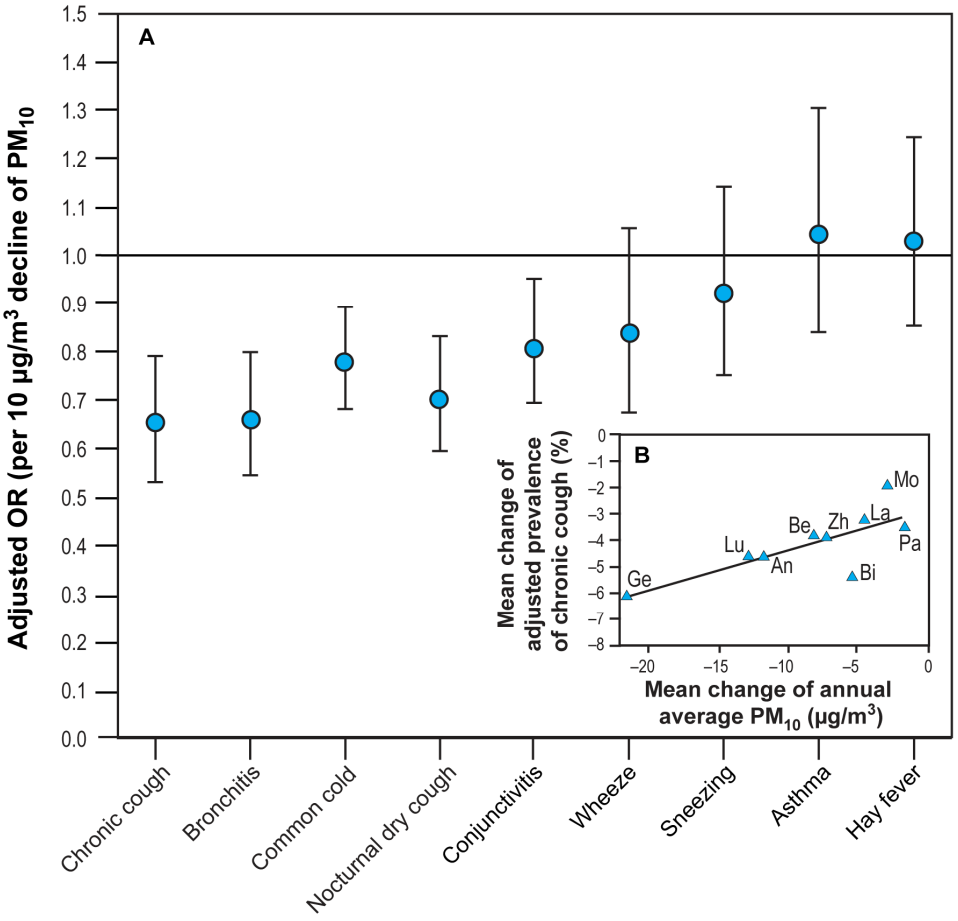
Pierse et al. (2006, 088757) studied the association between primary PM_{10} (particles directly emitted from local sources/traffic) and the prevalence and incidence of respiratory symptoms in a randomly sampled cohort of 4,400 children (aged 1-5 yr) in Leicestershire, England surveyed in 1998 and again in 2001. Annual exposure to primary PM_{10} was calculated for the home address using the Airviro statistical dispersion model. After adjusting for confounders, mean annual exposure to locally generated PM_{10} was associated with an increased prevalence of cough without a cold in both the 1998 (OR 1.21 [95% CI: 1.07-1.38], n = 2,164) and 2001 surveys (OR 1.56 [95% CI: 1.32-1.84], n = 1,756).

Nordling et al. (2008, 097998) examined the relationship between estimated PM exposure levels and respiratory health effects in a Swedish birth cohort of preschool children (n = 4,089). The spatial distributions of PM from traffic in the study area were estimated with emission databases and statistical dispersion modeling. Children were examined at 2 mo and 1, 2, and 4 yr of age. Using GIS methods, the average contribution of traffic-generated PM_{10} above regional background to the children's residential outdoor air pollution levels was determined. To evaluate the exposure assessment, the authors compared the estimated levels of traffic-generated PM_{10} with $PM_{2.5}$ measurements from 42 locations (Hoek et al., 2002, 042364) and reported modeled traffic-generated PM_{10} correlated reasonably well with measured $PM_{2.5}$ ($r = 0.61$). Persistent wheezing (cumulative incidence up to age 4 yr) was associated with exposure to traffic-generated PM_{10} (OR 2.28 [95% CI: 0.84-6.24] per 10 $\mu g/m^3$ increase) while transient and late onset wheezing was not associated. This study demonstrates that respiratory effects may be present in preschool children.

Table 7-3. Characterization of ambient PM concentrations from studies of respiratory symptoms/disease and long-term exposures.

Study	Location	Mean Annual Concentration (μg/m^3)	Upper Percentile Concentrations (μg/m^3)
$PM_{2.5}$			
Annesi-Maesano et al. (2007, 093180)	6 French Cities	Range of means across sites: 8.7-23.0 Avg of means across sites: 15.5	
Brauer et al. (2007, 090691)	The Netherlands	16.9	75th: 18.1 90th: 19.0 Max: 25.2
Goss et al. (2004, 055624)	U.S.	13.7	75th: 15.9
Islam et al. (2007, 090697)	12 CHS/CA communities		Max: 29.5
Janssen et al. (2003, 133555)	The Netherlands	20.5	75th: 22.1 Max: 24.4
Kim et al. (2004, 087383)	San Francisco, CA	Range of means across sites: 11-15 Avg of means across sites: 12	
McConnell et al. (2003, 049490)	12 CHS/CA communities	13.8	Max: 28.5
Morgenstern et al. (2008, 156782)	Munich, Germany	11.1	
PM_{10}			
Bayer-Oglesby et al. (2005, 086245)	Nine study regions in Switzerland		Max: 46
Kunzli et al. (2009, 191949)	Switzerland	21.5	
Nordling et al. (2008, 097998)	Sweden	4*	
Schindler et al. (2009, 191950)	Switzerland	**	
McConnell et al. (2003, 049490)	12 CHS/CA communities	30.8	Max: 63.5
Pierse et al. (2006, 088757)	Leicestershire, U.K.	1.33	75th: 1.84

*Source specific; PM_{10} from traffic
**Only reported change in PM concentration



Source: Bayer-Oglesby et al. (2005, 086245)

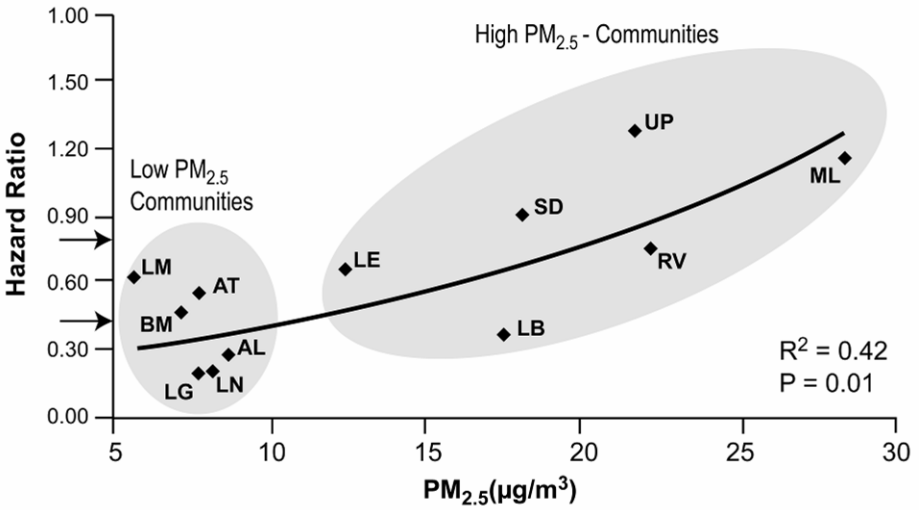
Figure 7-2. Adjusted ORs and 95% CIs of symptoms and respiratory diseases associated with a decline of 10 µg/m^3 PM_{10} levels in Swiss Surveillance Program of Childhood Allergy and Respiratory Symptoms[1]. Inset: Mean change in adjusted prevalence (1998-2001 to 1992-1993) versus mean change in regional annual averages of PM_{10} (1997-2000 to 1993) for chronic cough, across nine SCARPOL regions (An: Anières. Be: Bern. Bi: Biel. Ge: Geneva. La:, Langnau. Lu: Lugano. Mo: Montana. Pa: Payerne. Zh: Zürich).

McConnell et al. (2003, 049490) conducted a prospective study examining the association between air pollution and bronchitic symptoms in 475 school children with asthma in 12 Southern California communities as part of the CHS from 1996 to 1999. They investigated both the differences between- communities with 4-yr avg and within-communities yearly variation in PM (i.e., PM_{10}, $PM_{2.5}$, $PM_{10-2.5}$, EC, and OC). Based on a 10 µg/m^3 change in $PM_{2.5}$, within-communities effects were larger (OR 1.90 [95% CI: 1.10-2.70]) than those for between-communities (OR 1.30 [95% CI: 1.10-1.50]). The OR for the 10 µg/m^3 range in 4-yr avg $PM_{2.5}$ concentrations across the 12 communities was 1.29 (95% CI: 1.06-1.58). Similar results were reported for PM_{10} and $PM_{10-2.5}$ but the effect estimates were smaller in magnitude and generally not statistically significant. Within-community associations were not confounded by any time-fixed personal covariates. In two-

[1] Adjusted for age, sex, nationality, parental education, number of siblings; farming status, low birth weight, breastfeeding, child who smokes, family history of asthma, bronchitis, and/or atopy, mother who smokes, indoor humidity, mode of heating and cooking, carpeting, pets allowed in bedroom, removal of carpet and/or pets for health reasons, person who completed questionnaire, month when questionnaire was completed, number of days with the maximum temperature <0°C, and belief of mother that there is an association between environmental exposures and children's respiratory health

pollutant models, the within-community effect estimates for $PM_{2.5}$ and OC were significant in the presence of several other pollutants. While the within-community single-pollutant effect of $PM_{2.5}$ (ß = 0.085/μg/m^3) was only modestly attenuated after adjusting for some pollutants, it was markedly reduced after adjusting for NO_2 or OC. The between-community effect estimates generally were not significant in the presence of other pollutants in copollutant models.

In the CHS, Islam et al. (2007, 090697) examined the hypothesis that ambient air pollution attenuates the reduced risk for childhood asthma that is associated with higher lung function (n = 2,057). At each age a distribution of pulmonary functions exists. Haland et al. (2006, 156511) found evidence that children with high lung function have a reduced risk for asthma. Islam et al. (2007, 090697) used the CHS data to study how the association of asthma incidence with lung function is modified by long-term PM exposure. The incidence rate (IR) of newly diagnosed asthma increased from 9.5/1,000 person-years for children with percent-predicted FEF_{25-75} values ≥ 120% to 20.4/1,000 person-years for children with FEF_{25-75} value ≤ 100%. Over the 10th-90th percentile range for FEF_{25-75} (57.1%), the hazard ratio of new onset asthma was 0.50 (95% CI: 0.35-0.71). The IR of asthma for FEF_{25-75} ≥ 120% in the "high" $PM_{2.5}$ (13.7-29.5 μg/m^3) communities was 15.9/1,000 person-years compared to 6.4/1,000 person-years in "low" $PM_{2.5}$ (5.7-8.5 μg/m^3) communities. Loss of protection by high lung function against new onset asthma in the "high" $PM_{2.5}$ communities was observed for all the lung function measures. Figure 7-3 shows the effect of $PM_{2.5}$ on the association of lung function with asthma. Of all the pollutants examined (NO_2, PM_{10}, $PM_{2.5}$, acid vapor, O_3, EC, and OC), $PM_{2.5}$ appeared to have the strongest modifying effect on the association between lung function with asthma as it had the highest R^2 value (0.42). Over the 10th-90th percentile range of FEF_{25-75}, the hazard ratio of new onset asthma was 0.34 (95% CI: 0.21-0.56) in a community with low $PM_{2.5}$ (<13.7 μg/m^3) and 0.76 (95% CI: 0.45-1.26) in a community with high $PM_{2.5}$ (≥ 13.7 μg/m^3). The data do not indicate that PM exposure increased rates of incident asthma among children with poor lung function at study entry because rates among those with poor lung function were similar in both low and high pollution communities.



Source: Reprinted with Permission of BMJ Publishing Group Ltd & British Thoracic Society from Islam et al. (2007, 090697)

Figure 7-3. Effect of $PM_{2.5}$ on the association of lung function with asthma. Community-specific hazard ratio of newly diagnosed asthma over 10-90th percentile range (57.1%) of $FEF_{25-75\%}$ by level of ambient $PM_{2.5}$ (μg/m^3). The 12 CHS communities are shown.

In a prospective birth cohort study (n = 4,000) in The Netherlands, Brauer et al. (2007, 090691) assessed the development of asthma, allergic symptoms, and respiratory infection during the first 4 yr of life in relation to long-term $PM_{2.5}$ concentration at the home address with a validated model using GIS. $PM_{2.5}$ was associated with doctor-diagnosed asthma (OR = 1.32 [95% CI:

1.04-1.69]) for a cumulative lifetime indicator. These findings extend observations made at 2 yr of age in the same cohort (Brauer et al., 2002, 035192) providing greater confidence in the association. No associations were observed for bronchitis.

Kunzli et al. (2009, 191949) used the SAPALDIA cohort study discussed previously in this section to evaluate the relationship between the 11-yr change (1991-2002) in traffic-related PM_{10} and asthma incidence-adult onset asthma. In a cohort of 2,725 never-smokers without asthma at baseline (age: 18-60 yr in 1991), subjects reporting doctor-diagnosed asthma at follow-up were considered incident cases. Modeled traffic-related PM_{10} levels were used. Cox proportional hazard models for time to asthma onset were used with adjustments for cofounders. The study findings suggest that PM contributes to asthma development and that reductions in PM decrease asthma risk. A strong feature of SAPALDIA is the ability to assign space, time, and source-specific pollution to each subject. Further, Kunzli et al. (2008, 129258) discusses the impact of attributable health risk models for exposures that are assumed to cause both chronic disease and its exacerbations. The added impact of causing disease increases the risk compared to only exacerbations.

A matched case-control study of infant bronchiolitis (ICD 9 code 466.1) hospitalization and two measures of long-term exposure – the month prior to hospitalization (subchronic) and the lifetime average (chronic) – to $PM_{2.5}$ and gaseous air pollutants in the South Coast Air Basin of southern California was conducted by Karr et al. (2007, 090719) among 18,595 infants born between 1995-2000. For each case, 10 controls matched on date were randomly selected from birth records. Exposure was based on $PM_{2.5}$ measurements collected every third day. The mean distance between the subjects' residential ZIP code and the assigned monitor was generally 4-6 mi with a maximum distance of 30 mi. For 10 $\mu g/m^3$ increases in both sub-chronic and chronic $PM_{2.5}$ exposure, an adjusted OR of 1.09 (95% CI: 1.04-1.14) was observed. In multipollutant model analyses, the association with $PM_{2.5}$ was robust to the inclusion of gaseous pollutants. Also, in a cohort of children in Germany, Morgenstern et al. (2008, 156782) modeled $PM_{2.5}$ data at birth addresses found statistically significant effects for asthmatic bronchitis, hay fever, and allergic sensitization to pollen.

Goss et al. (2004, 055624) conducted a national study examining the relationship between air pollutants and health effects in a cohort of cystic fibrosis (CF) patients (n = 11,484) over the age of 6 yr (mean age = 18.4, SD = 10) enrolled in the Cystic Fibrosis Foundation National Patient Registry in 1999 and 2000. Exposure was assessed by linking air pollution values from the closest population monitor from the Air Quality System (AQS) with the centroid of the patient's home ZIP code that was within 30 mi. The mean distance from the patient's ZIP code to monitors for $PM_{2.5}$ and PM_{10} was 10.8 mi (SD 7.8) and 11.5 mi (SD 7.9), respectively. $PM_{2.5}$ and PM_{10} 24-h avg were collected every 1 to 12 days. CF diagnosis involves genetic screening panels and a common severe mutation used is the loss of phenylalanine at the 508th position. Genotyping was available in 74% of the population and of those genotyped, 66% carried one or more delta F508 deletions. After adjusting for confounders, a 10 $\mu g/m^3$ increase in $PM_{2.5}$ or PM_{10} was associated with a 21% (95% CI: 7-33) or 8% (95% CI: 2-15) increase in the odds of two or more exacerbations, respectively. The exacerbations were defined as a CF-related pulmonary condition requiring admission to the hospital or use of home intravenous antibiotics. The estimate for the associations between pulmonary exacerbations and $PM_{2.5}$ and PM_{10} were attenuated when the models were adjusted for lung function. Brown et al. (2001, 012307) found that particle deposition was increased in CF and that particle distribution in the lungs was enhanced in poorly ventilated tracheobronchial regions in CF patients. Such focal deposition may partially explain the association of PM and CF exacerbation.

Annesi-Maesano (2007, 093180) relate individual data on asthma and allergy from 5,338 school children (10.4 ± 0.7 yr) attending 108 randomly chosen schools in 6 French cities to the concentration of $PM_{2.5}$ monitored in school yards. Atopic asthma was related to $PM_{2.5}$ (OR 1.43 [95% CI: 1.07-1.91]) when high $PM_{2.5}$ concentrations (20.7 $\mu g/m^3$) were compared to low $PM_{2.5}$ concentrations (8.7 $\mu g/m^3$). The report is consistent with the results in an earlier paper (Penard-Morand et al., 2005, 087951) in the same sample of children that related the findings to PM_{10}.

Kim et al. (2004, 087383) conducted a school-based cross-sectional study in the San Francisco metropolitan area in 2001 comprised of 10 neighborhoods to examine the relationship between traffic-related pollutants and current bronchitic symptoms and asthma obtained by parental questionnaire (n = 1,109). They related traffic-related pollutants (PM) and bronchitic and asthma symptoms in the past 12 mo. No multipollutant models were evaluated because of the high interpollutant correlations. $PM_{2.5}$ levels ranged across the school sites from 11 to 15 $\mu g/m^3$.

Schikowski et al. (2005, 088637) examined the relationship between both long-term air pollution exposure and living close to busy roads and COPD in the Rhine-Ruhr Basin of Germany

from 1985 to 1994 using consecutive cross-sectional studies. Seven monitoring stations that were <8 km to a woman's home address provided TSP data that PM_{10} was estimated from using a conversion factor (obtained from parallel measurement of TSP and PM_{10} conducted at 7 sites in the Ruhr area). Distance to a major road was determined using GIS. The results of the study suggest that long-term exposure to air pollution from PM_{10} and living near a major road might increase the risk of developing COPD and can have a detrimental effect on lung function. All ORs for 5-yr exposures were stronger than those for 1-yr exposures.

In summary, the 2004 PM AQCD evaluated the available studies which primarily related effects to bronchitic symptoms in school-age children. New studies are using several different methods to include individual estimates of exposure to ambient PM that may reduce the impact of exposure error. The strength and consistency of the outcomes is enhanced by results being reported by several different researchers in different countries using different designs. Most recent studies have focused on children, but a few studies have also reported associations in adults.

The CHS (McConnell et al., 2003, 049490) provides evidence in a prospective longitudinal cohort study that relates $PM_{2.5}$ and bronchitic symptoms and reports larger associations for within-community effects that are less subject to confounding than between-community effects. Several new studies report similar findings with long-term exposure to PM_{10} in areas where fine particles are the predominant fraction of PM_{10}. In England, in a cohort of 4,400 children (aged 1-5 yr), an association is seen with an increased prevalence of cough without a cold. Further evidence includes a reduction of respiratory symptoms corresponding to decreasing PM levels in "natural experiments" in both a cohort of Swiss school children (Bayer-Oglesby et al., 2005, 086245) and adults (Schindler et al., 2009, 191950).

In a separate analysis of the CHS, Islam et al. (2007, 090697) showed that $PM_{2.5}$ had the strongest modifying effect on the association between lung function with asthma such that loss of protection by high lung function against new onset asthma in high $PM_{2.5}$ communities was observed for all the lung function measures from 10 to 18 yr of age. This relates new onset asthma to long-term PM exposure. In the Netherlands, Brauer et al. (2007, 090691) augments the literature with data examining the first 4 yr of life in a birth cohort showing an association with doctor-diagnosed asthma. Further, in an adult cohort in the SALPALDIA study, Kunzli et al. (2009, 191949) relate PM to asthma incidence.

7.3.2. Pulmonary Function

Several cohort studies reviewed in the 2004 PM AQCD provided evidence for relationships between long-term PM exposure and effects on the respiratory system. In 12 southern California communities in the Children's Health Study (CHS), Gauderman et al. (2000, 012531; 2002, 026013) found that decreases in lung function growth among school children were associated with long-term exposure to PM. Declines in pulmonary function were reported with all three major PM size classes – PM_{10}, $PM_{10-2.5}$ and $PM_{2.5}$ – though the three PM measures were highly correlated. These results were found to be consistent with results of cross-sectional analyses of Raizenne et al. (1996, 077268), that was assessed in the 1996 PM AQCD. That study reported associations between decreased peak flow with fine particle sulfate and fine particle acidity. Finally, in a prospective cohort study among a subset of children in the CHS (n = 110) who moved to other locations during the study period, Avol et al. (2001, 020552) reported that those subjects who moved to areas of lower PM_{10} showed increased growth in lung function compared with subjects who moved to communities with higher PM_{10} concentrations who showed decrease growth in lung function.

7.3.2.1. Epidemiologic Studies

New longitudinal cohort studies have evaluated the relationship between long-term exposure to PM and changes in measures of pulmonary function (FVC, FEV_1, and measures of expiratory flow). Cross-sectional studies also offer supportive information (Annex E) and may provide insights derived from within community analysis. Lung function increases continue through early adulthood with growth and development, then declines with aging (Stanojevic et al., 2008, 157007; Thurlbeck, 1982, 093260; Zeman and Bennett, 2006, 157178). A summary of the mean PM concentrations reported for the long-term exposure studies characterized in this section is presented in Table 7-4.

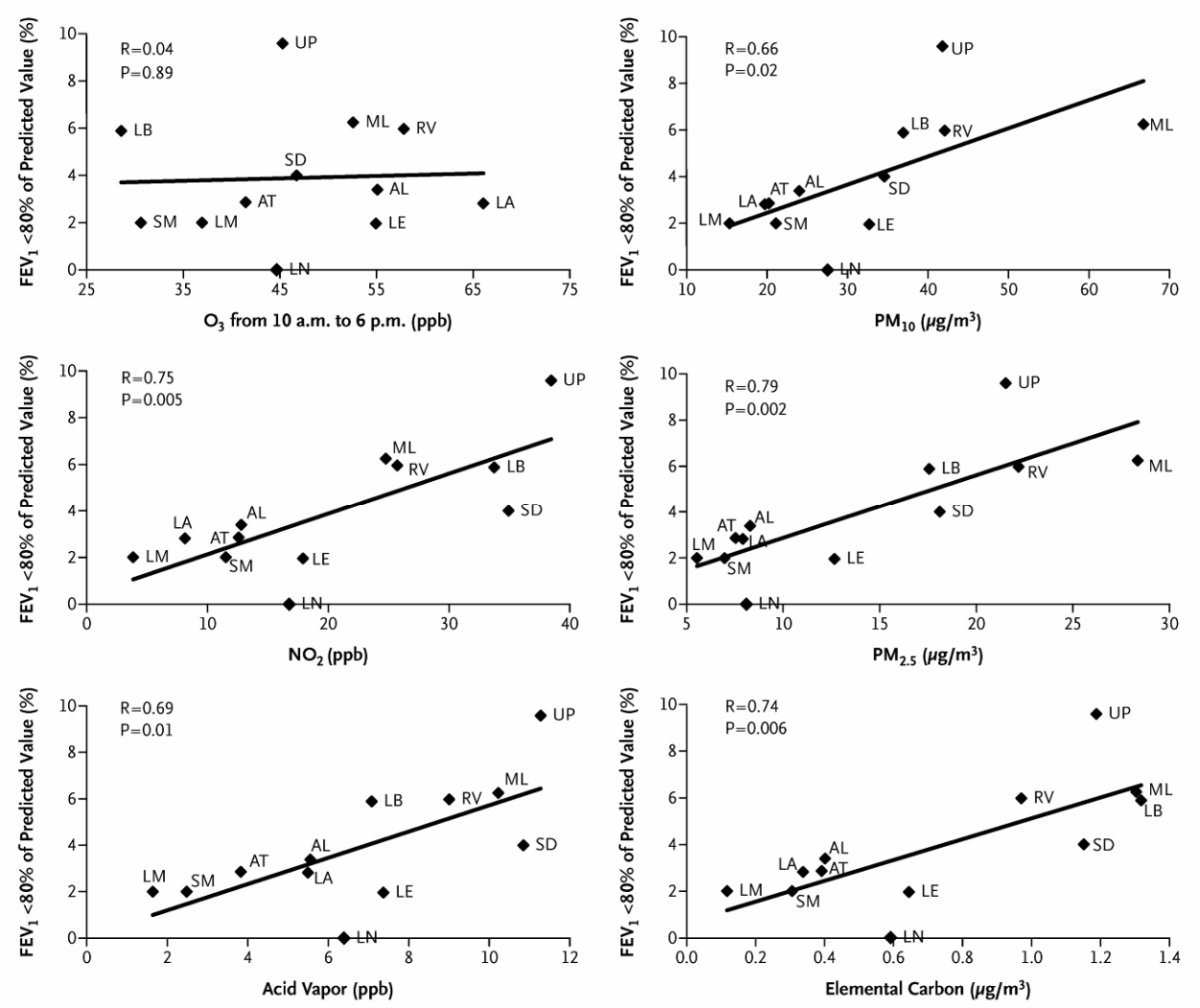
Table 7-4. Characterization of ambient PM concentrations from studies of FEV_1 and long-term exposures.

Study	Location	Mean Annual Concentration ($\mu g/m^3$)	Upper Percentile Concentrations ($\mu g/m^3$)
$PM_{2.5}$			
Gauderman et al. (2002, 026013)	12 CHS/CA communities	5-30	
Gauderman et al. (2004, 056569)	12 CHS/CA communities	6-27	
Goss et al. (2004, 055624)	U.S.	13.7	75th: 15.9
Gotschi et al. (2008, 180364)	21 European cities	Range of means across sites: 3.7-44.7 Avg of mean across sites: 16.8	
PM_{10}			
Downs et al. (2007, 092853)	8 cities in Switzerland	Range of means across sites: 9-46 Avg of mean across sites: 21.6	
Gauderman et al. (2002, 026013)	12 CHS/CA communities	Range of means across sites: 13-78 Avg of mean across sites: NR	
Gauderman et al. (2004, 056569)	12 CHS/CA communities	Range of means across sites: 18-68 Avg of mean across sites: NR	
Nordling et al. (2008, 097998)	Sweden	Modeled exposure	
Avol et al. (2001, 020552)	Southern CA/CHS	Range of means across sites: 15.0-66.2	
Rojas-Martinez et al. (2007, 091064)	Mexico City, Mexico	75.6	75th: 92.2 90th: 112.7

The CHS prospectively examined the relationship between air pollutants and lung function (FVC, FEV_1, MMEF) in a cohort (n = 1,759) of children between the ages of 10 and 18 yr, a period of rapid lung development (Gauderman et al., 2004, 056569). Air pollution monitoring stations provided data in each of the 12 study communities from 1994-2000. The results for O_3, PM_{10}, NO_2, $PM_{2.5}$, acid vapor, and EC are depicted in Figure 7-4. In general, copollutant models for any pair of pollutants did not provide a substantially better fit to the data than the corresponding single-pollutant models due to the strong correlation between most pollutants. The pollution-related deficits in the average growth in lung function over the 8-yr period resulted in clinically important deficits in attained lung function at the age of 18.

Downs et al. (2007, 092853) prospectively examined 9,651 randomly selected adults (18-60 yr of age) in eight cities in Switzerland (see alsoAckermann-Liebrich et al., 1997, 077537) to ascertain the relationship between reduced exposure to PM_{10} and age-related decline in lung function (FVC, FEV_1, and FEF_{25-50}). An evaluated statistical dispersion model (Liu et al., 2007, 093093) provided spatially resolved concentrations of PM_{10} that enabled assignment to residential addresses for the participant examinations in 1991 and 2002 that yielded a median decline of 5.3 $\mu g/m^3$ (IQR 4.1-7.5). Decreasing PM_{10} concentrations attenuated the decline in lung function. Effects were greater in tests reflecting small airway function. No other pollutant relationships were evaluated, though a related study indicated that levels of NO_2 also declined over the same period (Ackermann-Liebrich et al., 2005, 087826). Generalized cross-validation essentially chose a linear fit for the concentration-response curve for age-related decline in lung function.

These data show that improvement in air quality may slow the annual rate of decline in lung function in adulthood indicating positive consequences for public health. Further evidence on improvement in respiratory health with reduction in air pollution levels is provided from studies conducted in East Germany related to dramatic emissions reductions after the reunification in 1990 (Fryer and Collins, 2003, 156454; Heinrich et al., 2002, 034825; Sugiri et al., 2006, 088760). This type of "natural experiment" provides additional support for epidemiologic findings that relatively low levels of airborne particles have respiratory effects.



Source: Adapted from Gauderman et al. (2004, 056569)

Figure 7-4. Proportion of 18-yr olds with an FEV_1 below 80% of the predicted value plotted against the average levels of pollutants from 1994 through 2000 in the 12 southern California communities of the Children's Health Study. AL = Alpine; AT = Atascadero; LA = Lake Arrowhead; LB = Long Beach; LE = Lake Elsinore; LM = Lompoc; LN = Lancaster; ML = Mira Loma; RV = Riverside; SD = San Dimas; SM = Santa Maria; UP = Upland.

In a prospective cohort study consisting of school-age children (n = 3,170) who were 8 yr of age at the beginning of the study, had not been diagnosed with asthma, and were located in Mexico City, Rojas-Martinez et al. (2007, 091064) evaluated the association between long-term exposure to PM_{10}, O_3 and NO_2 and lung function growth every 6 mo from April 1996 through May 1999. Exposure data were provided by 10 air quality monitor stations located within 2 km of each child's school. The multipollutant model effect of PM_{10} over the age of 8-10 yr of life in this cohort on FVC, FEV_1, and FEF_{25-75} showed an association. Single pollutant models showed an association between ambient pollutants (O_3, PM_{10} and NO_2) and deficits in lung function growth. The association between PM_{10} and FEF_{25-75} was not statistically significant. While the estimates from copollutant models were not substantially different than single pollutant models, independent effects for pollutants could not be estimated accurately because the traffic-related pollutants were correlated.

Although no $PM_{2.5}$ data were presented in this study, in a separate study Chow et al. (2002) report that during the winter of 1997 approximately 50% of PM_{10} was in the $PM_{2.5}$ fraction in Mexico City.

Gotschi et al. (2008, 156485) examined the relationship between air pollution and lung function in adults in the European Community Respiratory Health Survey (ECRHS). FEV_1 and FVC were assessed at baseline and after 9 yr of follow-up from 21 European centers (followed-up sample n = 5,610). No statistically significant associations were found between city-specific annual mean $PM_{2.5}$ and average lung function levels which is in contrast to the results seen by Ackermann-Liebrich (1997, 077537) (SAPALDIA) and Schikowski et al. (2005, 088637) (SALIA) which compared across far more homogenous populations than for the population assessed in the ECRHS. Misclassification and confounding may partially explain the discrepancy in findings.

In a birth cohort (n = 2,170) in Oslo, Norway, Oftedal et al. (2008, 093202) examined effects of exposure to $PM_{2.5}$ and PM_{10} on lung function (FVC, FEV_1, $FEF_{50\%}$). Spirometry was performed in 2,307 children aged 9-10 yr in 2001-2002. Residential air pollution levels over the time period 1992-2002 were calculated using EPISODE dispersion models to provide three time scales of exposure: (1) first year of life; (2) lifetime exposure; and (3) just before the lung function test. Only single pollutant models were evaluated because air pollutants were highly correlated (r = 0.83-0.95). PM exposure was associated with changes in adjusted peak respiratory flow, especially in girls. No effect was found for forced volumes. Adjusting for contextual socioeconomic factors diminished associations. Results for PM_{10} were similar to those for $PM_{2.5}$.

In an exploratory study, Mortimer et al. (2008, 187280) examined the association of prenatal and lifetime exposure to air pollutants using geocoded monthly average PM_{10} levels with pulmonary function in a San Joaquin Valley, California cohort of 232 children (ages 6-11 yr) with asthma. First and second trimester PM_{10} exposures (based on monthly average concentrations) had a negative effect on pulmonary function and may relate to prenatal exposures affecting the lungs as they begin to develop at 6-wk gestation.

Dales et al. (2008, 156378) in a cross-sectional prevalence study examined the relationship of pulmonary function and PM measures, other pollutants, and indicators of motor vehicle emissions in Windsor, Ontario, in a cohort of 2,402 school children. $PM_{2.5}$ and PM_{10} concentrations were estimated for each child's residence at the postal code level. Each 10 $\mu g/m^3$ increase in $PM_{2.5}$ was associated with a 7.0% decrease in FVC expressed in a percentage of predicted.

In Leicester, England, investigators examined the carbon content of airway macrophages in induced sputum in 64 of 114 healthy 8-15 year-old children (Grigg et al., 2008, 156499; Kulkarni et al., 2006, 089257). The carbon content of airway macrophages (Finch et al., 2002, 054603; Strom et al., 1990, 157020) was used as a marker of individual exposure to PM_{10}. Near each child's home, exposure to PM_{10} was estimated using a statistical dispersion model (Pierse et al., 2006, 088757). The authors reported a dose-dependent inverse association between the carbon content of airway macrophages and lung function in children and found no evidence that reduced lung function itself causes an increase in carbon content. Consistent results were obtained for both FVC and FEF_{25-75}. Caution should be used when interpreting these results as the accuracy of the estimates on individual PM_{10} exposures were not validated; there is potential for confounding by ethnic origin; and there is concern that the magnitude of the changes in pulmonary function associated with increased particle area appear large (Boushey et al., 2008, 192162).

Nordling et al. (2008, 097998) discussed above in the respiratory symptoms section, also reported that lower PEF at age 4 was associated with exposure to traffic-related PM_{10} (-8.93 L/min [95% CI: -17.78 to -0.088]). Goss et al. (2004, 055624), discussed in Section 7.3.1.1, found strong inverse relationships between FEV_1 and $PM_{2.5}$ concentrations in both cross-sectional and longitudinal analyses.

In summary, recent studies have greatly expanded the evidence available for the 2004 PM AQCD. The earlier CHS studies followed young children for 2-4 yr. New analyses have been conducted that include longer follow-up periods of this cohort through 18 yr of age (considered early adulthood for lung development (Stanojevic et al., 2008, 157007) and provide evidence that effects from exposure to $PM_{2.5}$ persist into early adulthood. Longitudinal studies follow effects over time and are considered to provide the best evidence as opposed to studies across communities as in cross-sectional studies. The longitudinal cohort studies in the 2004 PM AQCD provided data for children in one location in one study and new longitudinal studies have been conducted in other locations.

Gauderman et al. (2004, 056569) reported that $PM_{2.5}$ exposure was associated with clinically and statistically significant deficits in FEV_1 attained at the age of 18 yr. Clinical significance was

defined as a FEV_1 below 80% of the predicted value, a criterion commonly used in clinical settings to identify persons at increased risk for adverse respiratory conditions. This clinical aspect is an important enhancement over the earlier results reported in the 2004 PM AQCD. Further, the association reported in this study that evaluated the 8-yr time period into early adulthood not only provided evidence for the persistence of the effect, but in addition the strength and robustness of the outcomes were more positive, larger, and more certain than previous CHS studies of shorter follow-up.

Supporting this result are new longitudinal cohort studies conducted by other researchers in other locations with different methods. Though these studies report results for PM_{10}, available data discussed above indicate that the majority of PM_{10} is composed of $PM_{2.5}$ in these areas. New studies provide positive results from Mexico City, Sweden, and a national cystic fibrosis cohort in the U.S. One study reported null results in a European cohort described as having potential misclassification and confounding concerns as well as lacking a homogenous population potentially rendering the outcome as non-informative. A natural experiment in Switzerland, where PM levels had decreased, reported that improvement in air quality may slow the annual rate of decline in lung function in adulthood, indicating positive consequences for public health. These natural experiments are considered especially supportive.

The relationship between long-term PM exposure and decreased lung function is thus seen during lung growth and lung development in school-age children into adulthood. At adult ages studies continue to show a relationship between decreased lung function and long-term PM exposure. Some newer studies attempting to study the relationship of long-term PM exposure from birth through preschool are reporting a relationship. Thus, the impact of long-term PM exposure is seen over the time period of lung function growth and development and the decline of lung function with aging.

Overall, effect estimates from these studies are negative (i.e., indicating decreasing lung function) and the pattern of effects are similar between the studies for FVC and FEV_1. Thus, the data are consistent and coherent across several designs, locations, and researchers. With cautions noted, the results relating carbon content of airway macrophages to decreased measures of pulmonary function add plausibility to the epidemiologic findings. Some new studies are using individual estimates of exposure to ambient PM to reduce the impact of exposure error (Downs et al., 2007, 092853; Jerrett et al., 2005, 087381).

As was found in the 2004 PM AQCD, the studies report associations with $PM_{2.5}$ and PM_{10}, while most did not evaluate $PM_{10-2.5}$. Associations have been reported with fine particle components, particularly EC and OC. Source apportionment methods generally have not been used in these long-term exposure studies. However, numerous studies have evaluated exposures to PM related to traffic or motor vehicle sources. For example, Meng et al. (2007, 093275) investigated the associations between traffic and outdoor pollution levels and poorly controlled asthma among adults who were respondents to the California Health Interview Survey and found associations for traffic density and PM_{10}, but not $PM_{2.5}$.

7.3.2.2. Toxicological Studies

Urban Air

One new study evaluated the effects of chronic exposure to ambient levels of urban particles on lung development in the mouse (Mauad et al., 2008, 156743). Both functional and anatomical indices of lung development were measured. Male and female BALB/c mice were continuously exposed to ambient or filtered Sao Paolo air for 8 mo. Concentrations in the "polluted chamber" versus "clean chamber" were 16.8 versus 2.9 $\mu g/m^3$ $PM_{2.5}$. Thus PM levels were reduced by filtration but not entirely eliminated. Ambient concentrations of CO, NO_2 and SO_2 were 1.7 ppm, 89.4 $\mu g/m^3$ and 8.1 $\mu g/m^3$, respectively. Concentrations of gaseous pollutants were assumed to be similar to ambient levels in both chambers. After 4 mo, the animals were mated and the offspring were divided into 4 groups to provide for a prenatal exposure group, a postnatal exposure group, a pre and postnatal exposure group and a control group. Animals were sacrificed at 15 and 90 days of age for histological analysis of lungs. Pulmonary pressure-volume measurements were also conducted in the 90-day-old offspring. Statistically significant reductions in inspiratory and

expiratory volumes were found in the group receiving both prenatal and postnatal exposure, but not in the groups receiving only prenatal exposure or only postnatal exposure, compared with controls. These changes in pulmonary function correlated with anatomical changes which are discussed in Section 7.3.5.1.

Diesel Exhaust

Li et al. (2007, 155929) exposed BALB/c and C56BL/6 mice to clean air or to low-dose DE (at a PM concentration of 100 $\mu g/m^3$) for 7 h/day and 5 days/week for 1, 4 and 8 wk. Average gas concentrations were reported to be 3.5 ppm CO, 2.2 ppm NO_2, and less than 0.01 ppm SO_2. Airway hyperresponsiveness (AHR) was evaluated by whole-body plethysmography at Day 0 and after 1, 4 and 8 wk of exposure. Short-term exposure responses are discussed in Section 6.3.2.3, 6.3.3.3 and 6.3.4.2. The increased sensitivity of airways to methacholine (measured as Penh) seen in C57BL/6 but not BALB/c mice at 1 week was also seen at 4 wk but not at 8 wk. This study suggests that adaptation occurs during prolonged DE exposure. Influx of inflammatory cells, markers of oxidative stress and effects of antioxidant intervention were also evaluated (Sections 7.3.3.2 and 7.3.4.1). Although no attempt was made in this study to determine the effects of gaseous components of DE on the measured responses, concentrations of gases were very low suggesting that PM may have been responsible for the observed effects.

In many animal studies changes in ventilatory patterns are assessed using whole-body plethysmography, for which measurements are reported as enhanced pause (Penh). Some investigators report increased Penh as an indicator of AHR, but these are inconsistently correlated and many investigators consider Penh solely an indicator of altered ventilatory timing in the absence of other measurements to confirm AHR. Therefore use of the terms AHR or airway responsiveness has been limited to instances in which the terminology has been similarly applied by the study investigators.

Gottipolu et al. (2009, 190360) exposed WKY and SH rats to filtered air or DE (particulate concentration 500 and 2,000 $\mu g/m^3$) for 4 h/day and 5 days/wk over a 4-wk period. Concentrations of gases were 1.3 and 4.8 ppm CO, NO <2.5 and 5.9 ppm NO, <0.25 and 1.2 ppm NO_2, 0.2 and 0.3 ppm SO_2 for low and high PM exposures, respectively. Particle size, measured as geometric median number and volume diameters, was 85 and 220 nm, respectively. No DE-related effects were found for breathing parameters measured by whole-body plethysmography. Other pulmonary effects are described in Sections 7.3.3.2 and 7.3.5.1.

Woodsmoke

One study evaluated the effects of subchronic woodsmoke exposure on pulmonary function in Brown Norway rats. Rats were exposed 3 h/day and 5 days/week for 4 and 12 wk to air or to concentrated wood smoke from the pinyon pine which is native to the U.S. Southwest (Tesfaigzi et al., 2002, 025575). PM concentrations in the woodsmoke were 1,000 and 10,000 $\mu g/m^3$. The particles in this woodsmoke had a bimodal size distribution with the smaller size fraction (74%) characterized by a MMAD of 0.405 µm and the larger size fraction (26%) characterized by a MMAD of 6.7-11.7 µm. Many of these larger particles would not be inhalable by the rat since 8 µm MMAD particles are about 50% inhalable (Ménache et al., 1995, 006533). Concentrations of gases were reported to be 15-106.4 ppm CO, 2.2-18.9 ppm NO, 2.4-19.7 ppm NO_X and 3.5-13.8 ppm total hydrocarbon in these exposures. Respiratory function measured by whole-body plethysmography demonstrated a statistically significant increase in total pulmonary resistance in rats exposed to 1000 $\mu g/m^3$ woodsmoke. Additional effects were found at 10,000 $\mu g/m^3$. Inflammatory and histopathological responses were also evaluated (Sections 7.3.3.2 and 7.3.5.1).

7.3.3. Pulmonary Inflammation

7.3.3.1. Epidemiologic Studies

One epidemiologic study examined the relationship of airway inflammation (eNO) and PM measures, other pollutants, and indicators of motor vehicle emissions in Windsor, Ontario (Dales et al., 2008, 156378). This cohort of 2,402 school children estimated $PM_{2.5}$ and $PM_{10-2.5}$ for each child's residence at the postal code level with an evaluated statistical model (Wheeler et al., 2006, 103905). Each 10 μg/m^3 increase in 1-yr $PM_{2.5}$ was associated with a 39% increase in eNO ($p = 0.058$). Associations between eNO and $PM_{10-2.5}$ were positive but not statistically significant.

7.3.3.2. Toxicological Studies

CAPs Studies

A set of subchronic studies involved exposure of normal (C57BL1/6) mice, ApoE$^{-/-}$ and the double-knockout ApoE$^{-/-}$/LDLR$^{-/-}$ mice to Tuxedo, NY CAPs for 5-6 month (March, April or May through September 2003 (Lippmann et al., 2005, 087452). The average $PM_{2.5}$ exposure concentration was 110 μg/m^3. Animals were fed a normal chow diet during the CAPs exposure period. No pulmonary inflammation was observed in response to CAPs exposure as measured by BALF cell counts and histology. The lack of a persistent pulmonary response may have been due to adaptation of the lung following repeated exposures. In fact, a parallel study examined CAPs-related gene expression in the double-knockout animals and found upregulation of numerous genes in lung tissue (Gunnison and Chen, 2005, 087956). An in vitro study conducted simultaneously found daily variations in CAPs-mediated NF-κB activation in cultured human bronchial epithelial cells, suggesting that transcription factor-mediated gene upregulation could occur in response to CAPs (Maciejczyk and Chen, 2005, 087456). It should be noted that significant cardiovascular effects were observed in these subchronic studies which are discussed in Section 7.2.1.2.

Araujo et al. (2008, 156222) compared the relative impact of UF (0.01-0.18 μm) versus fine (0.01-2.5 μm) PM inhalation in ApoE$^{-/-}$ mice following a 40 day exposure (5 h/day×3 days/wk for 75 total hours). Animals were fed a normal chow diet and exposed to PM from November 3 -December 12, 2005 in a mobile inhalation laboratory that was parked 300 m from the 110 Freeway in downtown Los Angeles. Particles were concentrated to ~440 μg/m^3 for $PM_{2.5}$ exposures and ~110 μg/m^3 for the UF exposures, representing a roughly 15-fold increase in concentration from ambient levels; the number concentration of PM in the fine and UF chambers were roughly equivalent (4.56×10^5 and 5.59×10^5 particles/cm^3, respectively). Over 50% of the UFPs were comprised of OC compared to only 25% for $PM_{2.5}$. No major increase in BALF inflammatory cells was found in response to PM. However UFP exposure resulted in significant cardiovascular and systemic effects (Section 7.2.1.2).

Diesel Exhaust

Gottipolu et al. (2009, 190360) exposed WKY and SH rats to filtered air or DE for 4 wk as described in Section 7.3.2.2. Previous studies from this laboratory have shown enhanced effects of PM in SH compared with WKY rats. Although the main focus of this recent study was on DE-induced mitochondrial oxidative stress and hypertensive gene expression in the heart (Section 7.2.7.1), some pulmonary effects were also found. Subchronic exposure to DE resulted in a dose-dependent increase in BALF neutrophils in both rat strains although levels of measured cytokines were not altered. Histological analysis of lung tissue from rats exposed to the higher concentration of DE demonstrated accumulation of particle-laden macrophages as well as focal alveolar hyperplasia and inflammation. Effect on indices of injury are discussed in Section 7.3.5.1.

Ishihara and Kagawa (2003, 096404) exposed Wistar rats to filtered air and DE containing 200, 1,000 and 3,000 μg/m^3 PM for 16 h/day and 6 days/wk for 6, 12, 18 or 24 mo. The mass median particle diameter was reported to be between 0.3 and 0.5 μm. Concentrations of gases ranged from

2.93-35.67 ppm NO_X, 0.23-4.57 ppm SO_2, 1.8-21.9 ppm CO in the DE exposures. Statistically significant increases in total numbers of inflammatory cells and neutrophils in BALF were observed beginning at 6-12 mo of exposure to DE containing 1,000 and 3,000 µg/m^3 PM. When rats were exposed to DE containing 1,000 µg/m^3 PM, which was filtered to remove PM, the inflammatory cell response was significantly diminished. These results implicate the PM fraction of DE as a key determinant of the inflammation. The PM fraction was also found to mediate the increase in protein levels, the decrease in PGE_2 levels and alterations in mucus and surfactant components observed in BALF (Section 7.3.5.1).

Li et al. (2007, 155929) exposed BALB/c and C56BL/6 mice to low dose DE as described in Section 7.3.2.2. for 1, 4 and 8 wk. Increases in numbers of BALF macrophages and total inflammatory cells were observed in BALB/c mice at 8 wk but not 4 wk of DE exposure. Persistent increases in numbers of BALF neutrophils and lymphocytes were observed in both strains at 4 and 8 wk of DE exposure. Corresponding increases in BALF cytokines differed between the two strains. These results should be interpreted with caution since comparisons were made with Day 0 controls rather than age-matched controls. No histopathological changes in the lungs were seen at any time point after DE exposure. This study demonstrated differences in pulmonary responses to low dose DE between two mouse strains. AHR, pulmonary inflammation, markers of oxidative stress and effects of antioxidant intervention were also evaluated (Sections 7.3.2.2 and 7.3.4.1). Although no attempt was made in this study to determine the effects of gaseous components of DE on the measured responses, concentrations of gases were very low suggesting that PM may have been responsible for the observed effects.

In a study by Hiramatsu et al. (2003, 155846), BALB/c and C57BL/6 mice were exposed to DE (PM concentrations 100 and 3,000 µg/m^3) for 1 or 3 mo. Concentrations of gases were reported to be 3.5-9.5 ppm CO, 2.2-14.8 ppm NO_X, and less than 0.01 ppm SO_2. Modest increases in BALF neutrophils and lymphocytes were observed in response to DE in both mouse strains at 1 and 3 mo. Histological analysis demonstrated diesel exposure particle-laden alveolar macrophages in alveoli and peribronchial tissues at both time points. Bronchus-associated lymphoid tissue developed after 3-month exposure to the higher concentration of DE in both mouse strains. Mac-1 positive cells (a marker of phagocytic activation of alveolar macrophages) were also increased in BALF of BALB/c mice exposed to the higher concentration of DE for 1 and 3 mo. Increased expression of several cytokines and decreased expression of iNOS mRNA was observed in DE-exposed mice at 1 and 3 mo. NF-κB activation was also noted following 1-month exposure to the lower concentration of DE. No attempt was made in this study to determine the responses to gaseous components of the DE.

In a study by Reed et al. (2004, 055625), healthy Fisher 344 rats and A/J mice were exposed to DE (PM concentration = 30, 100, 300 and 1,000 µg/m^3) by whole body inhalation for 6 h/day, 7 days/wk for either 1 week or 6 mo. Concentrations of gases were reported to be 2.0-45.3 ppm NO, 0.2-4.0 ppm NO_2, 1.5-29.8 ppm CO and 8-365 ppb SO_2. Short-term responses are discussed in Section 6.3.3.3 and 6.3.7.2, and sub-chronic systemic effects are presented in Section 7.2.4.1. Six months of exposure resulted in no measurable effects on pulmonary inflammation. However numerous black particles were observed within alveolar macrophages after 6 mo of exposure.

Seagrave et al. (2005, 088000) evaluated pulmonary responses in male and female CDF (F-344)/CrlBR rats exposed 6 h/day for 6 mo to filtered air or DE at concentrations ranging from 30-1000 µg/m^3 PM. Concentrations of gases were reported for the highest exposure as 45.3 ppm NO, 4.0 ppm NO_2, 29.8 ppm CO and 2.2 ppm total vapor hydrocarbon. No changes in BALF cells were noted. A small decrease in TNF-α was seen in BALF of female rats exposed to the highest concentration of DE for 6 mo. Pulmonary injury also was evaluated (Section 7.3.5.1). Thus changes in BALF markers were modest and gender-specific.

Woodsmoke

Seagrave et al. (2005, 088000) also evaluated pulmonary responses in male and female CDF (F344)/CrlBR rats exposed 6 h/day for 6 mo to filtered air or hardwood smoke concentrations ranging from 30-1,000 µg/m^3 PM. Concentrations of gases were reported for the highest exposure as 3.0 ppm CO and 3.1 ppm total vapor hydrocarbon. A small increase in BALF neutrophils was observed in male rats exposed to the lowest concentration of hardwood smoke. Female rats exhibited a decrease in BALF macrophage inflammatory protein-2 (MIP-2) at the highest concentration of hardwood smoke. Pulmonary injury also was evaluated (Section 7.3.5.1). In general, responses to

hardwood smoke were more remarkable than responses to DE seen in a parallel study. However these gender-specific responses were modest and difficult to interpret.

In a study by Reed et al. (2006, 156043), Fisher 344 rats, SHR rats, A/J mice and C57BL/6 mice were exposed to clean air or hardwood smoke (PM concentrations 30, 100, 300 and 1,000 $\mu g/m^3$) by whole body inhalation for 6 h/day, 7 days/wk for either 1 week or 6 mo. Concentrations of gases ranged from 229.0-14887.6 mg/m^3 for CO, 54.9-139.3 $\mu g/m^3$ for ammonia, and 177.6- 3455.0 $\mu g/m^3$ nonmethane VOC in these exposures. Short-term responses are discussed in Section 6.3.7.2 and sub-chronic effects are presented in Section 7.2.4.1. Histological analysis of lung tissue showed minimal increases in alveolar macrophages. The effects of hardwood smoke on bacterial clearance are discussed below (Section 7.3.7.2).

Another study evaluated the effects of subchronic woodsmoke exposure in Brown Norway rats and is described in detail in Section 7.3.2.2 (Tesfaigzi et al., 2002, 025575). Numbers of alveolar macrophages in BALF were significantly increased in rats exposed to 1,000 $\mu g/m^3$ woodsmoke for 12 wk, but no changes were seen in numbers of other inflammatory cells. A large percent of BALF macrophages contained carbonaceous material. Histological analysis of lung tissue showed minimal to mild inflammation in the epiglottis of the larynx in rats exposed to both concentrations of woodsmoke.

Ramos et al. (2009, 190116) examined the effects of subchronic woodsmoke exposure on the development of emphysema in guinea pigs. Inflammation is thought to be involved in the pathogenesis of this form of COPD. Statistically significant increases in total numbers of BALF cells were observed in guinea pigs exposed to smoke for 1-7 mo, with numbers of macrophages increased at 1-4 mo and numbers of neutrophils increased at 4-7 mo. At 4 mo, alveolar mononuclear phagocytic and lymphocytic peribronchiolar inflammation were observed by histological analysis of lung tissue. This study is discussed in depth in Section 7.2.5.1.

Model Particles

Wallenborn et al. (2008, 191171) examined the pulmonary, cardiac and systemic effects of subchronic exposure to particulate $ZnSO_4$. WKY rats were exposed nose-only to 10, 30, or 100 $\mu g/m^3$ UFP of $ZnSO_4$ for 5 h/day and 3 day/wk over a 16-wk period. Particle size was reported to be 31-44 nm measured as number median diameter. No changes in pulmonary inflammation or injury were observed although cardiac effects were noted (Section 7.2.7.1). This study possibly demonstrates a direct effect of $ZnSO_4$ on extrapulmonary systems, as suggested by the lack of pulmonary effects.

7.3.4. Pulmonary Oxidative Response

7.3.4.1. Toxicological Studies

Urban Air

One new study evaluated the effects of subchronic exposure to ambient levels of urban particles on the development of emphysema in papain-treated mice (Lopes et al., 2009, 190430). Since oxidative stress is thought to contribute to the development of emphysema, 8-isoprostane levels were measured in lung tissue from the four groups of mice used in this study. A statistically significant increase in 8-isoprostane, a marker of oxidative stress, was observed in lungs from mice treated with papain and exposed to ambient air compared with the other groups of mice. This study is described in greater depth in Section 7.3.5.1.

Diesel Exhaust

Li et al. (2007, 155929) exposed mice to low dose DE for 1, 4 and 8 wk as described in Section 7.3.2.2. Markers of oxidative stress and effects of antioxidant intervention were evaluated in this model. While HO-1 mRNA and protein were increased in lung tissues of both mouse strains after 1 week of DE exposure (Section 6.3.4.2), at 8 wk of DE exposure, HO-1 protein levels remained high in C57BL/6 mice but returned to control values in BALB/c mice. This study demonstrates differences in pulmonary responses to low dose DE between two mouse strains. Furthermore, this study suggests that adaptation occurs in BALB/c mice during prolonged DE exposure since the increase in HO-1 protein seen in both strains at 1 week of exposure was only seen in C57BL/6 mice at 8 wk. AHR (Section 7.3.2.2) and pulmonary inflammation (Section 7.3.3.2) were also evaluated. Although no attempt was made in this study to determine the effects of gaseous components of DE on the measured responses, concentrations of gases were very low. This suggests that PM may have been responsible for the observed effects.

7.3.5. Pulmonary Injury

7.3.5.1. Toxicological Studies

Urban Air

One new study evaluated the effects of chronic exposure to ambient levels of urban particles on lung development in the mouse (Mauad et al., 2008, 156743). Both functional and anatomical indices of lung development were measured in mice exposed prenatally and/or postnatally as described in Section 7.3.2.2. Animals were sacrificed at 15 and 90 days of age for histological analysis of lungs. Histological analysis demonstrated the presence of mild foci of macrophages containing black dots of carbon pigment in the prenatal and postnatal exposure group at 90 days. In addition, the alveolar spaces of 15-day old mice in the prenatal and postnatal exposure group were enlarged compared with controls. Morphometric analysis demonstrated statistically significant decreases in surface to volume ratio at 15 and 90 days in the prenatal and postnatal exposure group compared with controls. Since alveolarization is normally complete by 15 days of age, these results suggest incomplete alveolarization in the 15-day-old group and an enlargement of air spaces in the 90-day-old group. These anatomical changes correlated with decrements in pulmonary function which are discussed in Section 7.3.2.2.

Prolonged exposure to low levels of ambient air pollution beginning in early life has been linked to secretory changes in the nasal cavity of mice, specifically increased production of acidic mucosubstances (Pires-Neto et al., 2006, 096734). Six-day-old Swiss mice were continuously chamber exposed to ambient or filtered São Paulo air for 5 mo. Concentrations in the "polluted chamber" versus "clean chamber" were (in $\mu g/m^3$) 59.52 versus 37.08 for NO_2, 12.52 versus 0 for BC, and 46.49 versus 18.62 for $PM_{2.5}$. Thus, pollutant levels were reduced by filtration but not entirely eliminated. Compared to filtered air, exposure to ambient air resulted in increased total mucus and acidic mucus in the epithelium lining the nasal septum, but no statistically significant differences in other parameters (amount of neutral mucus, volume proportions of neutral mucus, total mucus, or nonsecretory epithelium, epithelial thickness, or ratio between neutral and acidic mucus). The physicochemical properties of mucus glycoproteins are critical to the protective function of the airway mucus layer. Acidified mucus is more viscous, and is associated with a decrease in mucociliary transport. Thus acidic mucosubstances may represent impaired defense mechanisms in the respiratory tract.

One new study evaluated the effects of subchronic exposure to ambient levels of urban particles on the development of emphysema in papain-treated mice (Lopes et al., 2009, 190430). Emphysema is a form of COPD caused by the destruction of extracellular matrix in the alveolar region of the lung which results in airspace enlargement, airflow limitation and a reduction of the gas-exchange area of the lung. Inflammation, oxidative stress, protease imbalance and apoptosis are thought to contribute to the development of emphysema. In this study, male BALB/c mice were

continuously exposed to ambient or filtered Sao Paulo air for 2 mo. Concentrations of $PM_{2.5}$ in the "polluted chamber" versus "clean chamber" were 33.86 ± 2.09 versus 2.68 ± 0.38 μg/m^3. Thus filtration reduced PM levels considerably. Ambient concentrations of CO and SO_2 were 1.7 ppm and 16.2 μg/m^3 respectively. No significant difference was observed in the concentrations of NO_2 in the "polluted chamber" versus "clean chamber" (60-80 μg/m^3). Half of the mice were pre-treated with papain by intranasal instillation in order to induce emphysema. Morphometric analysis of lung tissue demonstrated a statistically significant increase in mean linear intercept, a measure of airspace enlargement, in papain-treated mice compared with saline-treated controls exposed to filtered air. While exposure to ambient air failed to increase mean linear intercept values in saline-treated mice, mean linear intercept values were significantly increased in papain-treated mice exposed to ambient air compared with papain-treated mice exposed to filtered air. A similar pattern of responses was observed for the volume proportion of collagen and elastin fibers in alveolar tissue, which are markers of alveolar wall remodeling. Lung immunohistochemical analysis demonstrated an effect of papain, but not ambient air, on macrophage cell density and matrix metalloproteinase 12-positive cell density. No differences in caspase-3 positive cells, a marker of apoptosis, were observed between the four groups of mice. Oxidative stress was evaluated in this model as described in Section 7.3.4.1. Taken together, results of this study demonstrate that urban levels of PM, mainly from traffic sources, worsen protease-induced emphysema in an animal model.

Pulmonary vascular remodeling, measured by a decrease in the lumen to wall ratio, was observed in mice exposed to ambient São Paulo air for 4 mo (Lemos et al., 2006, 088594). This study is described in greater detail in Section 7.2.1.2.

Kato and Kagawa (2003, 089563) exposed Wistar rats to roadside air contaminated mainly with automobile emissions (55.7-65.2 ppb NO_2 and 63-65 μg/m^3 suspended PM [SPM]) and examined the effects on respiratory tissue after 24, 48, or 60 wk of exposure. The surface of the lungs was light gray in color after all durations of exposure, and BC particle deposits accumulated with prolonged exposure. These characteristics were not evident in filtered air-exposed control animals, although filtered air contained low levels of air pollutants (≤ 6.2 ppb NO_2 and 15 μg/m^3 SPM). The most common change observed using transmission electron microscopy was the presence of particle laden (anthracotic) alveolar macrophages, or anthracosis, in a wide range of pulmonary tissues, including the submucosa, tracheal- and bronchiole-associated lymph nodes, alveolar wall and space, pleura, and perivascular connective tissue. These changes were evident after 24 wk and increased with duration of exposure. Other changes included increases in the number of mucus granules in goblet cells, mast cell infiltration (but no degranulation) after 24 wk, increased lysosomes in ciliated cells, some altered morphology of Clara cells, and hypertrophy of the alveolar walls after 48 wk. No goblet cell proliferation was observed, but slight, variable acidification of mucus granules appeared after 24 and 48 wk and disappeared after 60 wk. Anthracotic macrophages were seen in contact with plasma cells and lymphocytes in the lymphoid tissue, suggesting immune cell interaction in the immediate vicinity of particles. Even after 60 wk, no lymph node anthracosis was observed in the filtered air group.

In a post-mortem study of lung tissues from 20 female lifelong residents of Mexico City, a high PM locale, histology demonstrated significantly greater amounts of fibrous tissue and muscle in the airway walls compared to subjects from Vancouver (Churg et al., 2003, 087899), a city with relatively low PM levels. Electron microscopy showed carbonaceous aggregates of UFPs, which the authors conclude penetrate into and are retained in the walls of small airways. The study shows an association between retained particles and airway remodeling in the form of excess muscle and fibrotic walls. The subjects were deemed suitable for examination based on never-smoker status, no use of biomass fuels for cooking, no known occupational particle/dust exposure, death by cause other than respiratory disease, and extended residence in each locale (lifelong for Mexico City and >20 yr for Vancouver). However, subjects from the two locales were not matched with respect to ethnicity, sex (20 females from Mexico City versus 13 females and 7 males from Vancouver), or mean age at death (66 ± 9 versus 76 ± 11), and other possibly influential factors such as exercise or diet were not considered.

Diesel Exhaust

Gottipolu et al. (2009, 190360) exposed WKY and SH rats to filtered air or DE as described in Section 7.3.2.2. Previous studies from this laboratory have shown enhanced effects of PM in SH

compared with WKY rats. Although the main focus of this recent study was on DE-induced mitochondrial oxidative stress and hypertensive gene expression in the heart (Section 7.2.7.1), some pulmonary effects were found. Inflammatory effects are described in Section 7.3.3.2. GGT activity in BALF was increased in both strains in response to the higher concentration of DE. No DE-related changes were observed in BALF protein or albumin. Histological analysis of lung tissue from rats exposed to the higher concentration of DE demonstrated accumulation of particle-laden macrophages as well as focal alveolar hyperplasia and inflammation. No effects on indices of pulmonary function were observed (Section 7.3.2.2.)

Ishihara and Kagawa (2003, 096404) exposed rats to DE for up to 24 mo as described in Section 7.3.3.2. A statistically significant increase in BALF protein was observed at 12 mo of exposure to DE containing 1,000 $\mu g/m^3$ PM. This response was attenuated when the DE was filtered to remove PM. Pulmonary inflammation was noted and is described in Section 7.3.3.2.

Seagrave et al. (2005, 088000) evaluated pulmonary responses in rats exposed to DE for up to 6 mo as described in Section 7.3.3.2. A small increase in LDH was seen in BALF of female rats exposed to the highest concentration of DE for 6 mo. Pulmonary inflammation was also evaluated (Section 7.3.3.2). The changes in BALF markers in this study were modest and gender-specific.

Gasoline Exhaust

Reed et al. (2008, 156903) examined a variety of health effects following subchronic inhalation exposure to gasoline engine exhaust. Male and female CDF (F344)/CrlBR rats, SHR rats and male C57BL/6 mice were exposed for 6 h/day and 7 days/wk for a period of 3 days-6 mo. The dilutions for the gasoline exhaust were 1:10, 1:15 and 1:90; filtered PM was at the 1:10 dilution. PM mass ranged from 6.6 to 59.1 $\mu g/m^3$, with the corresponding number concentration between 2.6×10^4 and 5.0×10^5 particles/cm^3. Concentrations of gases ranged from 12.8-107.3 ppm CO, 2.0-17.9 ppm NO, 0.1-0.9 ppm NO_2, 0.09-0.62 ppm SO_2 and 0.38-3.37 ppm NH_3. Other effects are described in Sections 7.2.4.1 and 7.3.6.1. No pulmonary inflammation or histopathological changes were noted in the F344 rats and A/J mice, except for a time-dependent increase in the number of macrophages containing PM. However statistically significant increases of 47% and 29% in BALF LDH were observed in female and male F344 rats, respectively, after 6 mo of exposure to the highest concentration of engine exhaust. This response was absent when gasoline exhaust was filtered, implicating PM as a key determinant of this response. In addition, exposure to the highest concentration of gasoline exhaust resulted in statistically significant decreases in hydrogen peroxide and superoxide production in unstimulated and stimulated BALF macrophages. Hypermethylation of lung DNA was observed in male F344 rats following 6 mo of exposure to gasoline exhaust containing 30 $\mu g/m^3$ PM. This response was PM-dependent since it was absent in mice exposed to filtered gasoline exhaust. The significance of this epigenetic change in terms of respiratory health effects is not known. However, altered patterns of DNA methylation can affect gene expression and are sometimes associated with altered immune responses and/or the development of cancer.

Woodsmoke

Seagrave et al. (2005, 088000) also evaluated pulmonary responses in rats exposed to hardwood smoke for 6 mo as described in Section 7.3.3.2. Increases in BALF LDH and protein were seen in male but not female rats. Female rats exhibited a decrease in BALF glutathione at the highest concentration of hardwood smoke. Decreases in BALF alkaline phosphatase were found in both males and females exposed to 1,000 $\mu g/m^3$ hardwood smoke. Male rats exposed to 100 and 300 $\mu g/m^3$ hardwood smoke exhibited a decrease in BALF β-glucuronidase activity. Pulmonary inflammation was also evaluated (Section 7.3.3.2). These changes in BALF markers in this study were modest and gender-specific.

Another study evaluated the effects of subchronic woodsmoke exposure in Brown Norway rats as described in Section 7.3.2.2. (Tesfaigzi et al., 2002, 025575). Exposure to 1,000 $\mu g/m^3$ woodsmoke for12 wk resulted in a statistically significant increase in Alcian Blue- (AB) and Periodic Acid Schiff- (PAS) positive airway epithelial cells compared to controls, indicating an increase in mucous secretory cells containing neutral and acid mucus, respectively. More significant histopathological responses were found following exposure to 10,000 $\mu g/m^3$ of DE. Pulmonary

function and inflammation were evaluated also but are not discussed here due to the extremely high exposure level (Sections 7.3.2.2. and 7.3.3.2).

Ramos et al. (2009, 190116) examined the effects of subchronic woodsmoke exposure on the development of emphysema in guinea pigs. In particular, the involvement of macrophages and macrophage-derived MMP in woodsmoke-related responses was investigated. Guinea pigs were exposed to ambient air or to whole smoke from pine wood for 3 h/day and 5 days/wk over a 7-month period. PM_{10} and $PM_{2.5}$ concentrations in the exposure chambers were reported to be 502 ± 34 and 363 ± 23 $\mu g/m^3$, respectively, while the concentration of CO was less than 80 ppm. COHb levels were reported to be 6% in controls and 15-20% in smoke-exposed guinea pigs. Statistically significant decreases in body weight were observed in guinea pigs exposed to smoke for 4 or more months compared with controls. Statistically significant increases in total numbers of BALF cells were observed in guinea pigs exposed to smoke for 1-7 mo, with numbers of macrophages increased at 1-4 month and numbers of neutrophils increased at 4-7 mo. At 4 mo, alveolar mononuclear phagocytic and lymphocytic peribronchiolar inflammation, as well as bronchiolar epithelial and smooth muscle hyperplasia, were observed by histological analysis of lung tissue. Emphysematous lesions, smooth muscle hyperplasia and pulmonary arterial hypertension were noted at 7 mo. Morphometric analysis of lung tissue demonstrated statistically significant increases in mean linear intercept values, a measure of airspace enlargement, in guinea pigs at 6 and 7 mo of exposure. Statistically significant increases in elastolytic activity was observed in BALF macrophages and lung tissue homogenates at 1-7 mo of exposure. Lung collagenolytic activity was also increased at 4-7 mo of exposure and corresponded in time with the presence of active forms of MMP-2 and MMP-9 in lung tissue homogenates and BALF. Furthermore, MMP-1 and MMP-9 immunoreactivity was detected in macrophages, epithelial and interstitial cells in smoke-exposed animals at 7 mo. Increased levels of MMP-2 and MMP-9 mRNA were also found in smoke-exposed guinea pigs after 3-7 mo. Apoptosis was found in BALF macrophages (TUNEL assay) from guinea pigs exposed to smoke for 3-7 mo and in alveolar epithelial cells (caspase-3 immunoreactivity) after 7 mo. Taken together, these results provide evidence that subchronic exposure to woodsmoke leads to the development of emphysematous lesions accompanied by the accumulation of alveolar macrophages, increased levels and activation of MMPs, connective tissue remodeling and apoptosis. However, the high levels of CO and COHb reported in this study make it difficult to conclude that woodsmoke PM alone is responsible for these dramatic effects.

7.3.6. Allergic Responses

7.3.6.1. Epidemiologic Studies

A number of epidemiologic studies have found associations between PM and allergic (or atopic) indicators. Allergy is a major driver of asthma, which has been associated with PM in studies discussed in previous sections. In a study by Annesi-Maesano (2007, 093180) (described in Section 7.3.1.1) atopic asthma was related to $PM_{2.5}$ (OR 1.43 [95% CI: 1.07-1.91]) and positive skin prick test to common allergens was also increased with higher PM levels. This report is consistent with the results from an earlier study (Penard-Morand et al., 2005, 087951) in the same sample of children that associated allergic rhinitis and atopic dermatitis with PM_{10}. Also, Morgenstern et al. (2008, 156782) found statistically significant effects for asthmatic bronchitis, hay fever, and allergic sensitization to pollen in a cohort of children in Germany examining modeled $PM_{2.5}$ data at birth addresses. Distance to a main road had a dose-response relationship with sensitization to outdoor allergens. Nordling et al. (2008, 097998) (discussed above in Section 7.3.2.1) reported a positive association of PM_{10} exposure during the first year of life with allergenic sensitization (IgE antibodies) to inhaled allergens, especially pollen. In a study by Brauer et al. (2007, 090691) (discussed above in Section 7.3.1.1) an interquartile range increase in $PM_{2.5}$ was associated with an increased risk of sensitization to food allergens (OR 1.75 [95% CI 1.23-2.47]). A significant association was found for sensitization to any allergen, but none was found for sensitization to specific indoor or outdoor aeroallergens or atopic dermatitis (eczema). In a study by Janssen et al. (2003, 133555), $PM_{2.5}$ was associated with allergic indicators such as hay fever (ever), skin prick test reactivity to outdoor allergens, current itchy rash, and conjunctivitis in Dutch children. These same outcomes were also associated with proximity of the school to truck traffic but not car traffic,

suggesting a role for diesel-related pollution. Consistent with the aforementioned Dutch study by Brauer et al. (2007, 090691), $PM_{2.5}$ was not associated with eczema.

Mortimer et al. (2008, 187280) examined the association between prenatal and early-life exposures to air pollutants with allergic sensitization in a cohort of 170 children with asthma, ages 6-11 yr, living in central California. Sensitization to at least one allergen was associated with higher levels of PM_{10} and CO during the entire pregnancy and 2nd trimester and higher PM_{10} during the first 2 yr of life. Sensitization to at least one indoor allergen was associated with higher exposures to PM_{10} and CO in during the entire pregnancy and during the 2nd trimester. However, no significant associations remained for PM_{10} after adjustment for copollutants, effect modifiers, or potential cofounders in addition to year of birth. The authors advise that the large number of comparisons may be of concern and this study should be viewed as an exploratory, hypothesis-generating undertaking. In examining the National Health Interview Survey for the years 1997-2006, Bhattacharyya et al. (2009, 180154) found relationships between air quality and the prevalence of hay fever and sinusitis. However, the air quality data were not clearly defined and as such caution is required in interpretation of these results. In contrast, Bayer-Oglesby et al. (2005, 086245) found no significant association between declining levels of PM_{10} and hay fever in Switzerland. In a study by Oftedal et al. (2007, 191948) conducted in Oslo, Norway, early-life exposure to PM_{10} or $PM_{2.5}$ was generally not associated with sensitization to allergens in 9- to 10-yr-old children; lifetime exposures to PM_{10} and $PM_{2.5}$ were associated with dust mite allergy, but the association was diminished by adjustment for socioeconomic factors . In Norway, wood burning in the wintertime is thought to account for about half of the $PM_{2.5}$ levels. Although associations between PM and reactivity to specific allergens have been reported in long-term studies, there is a consistent lack of correlation between PM and total IgE levels, indicating a selective enhancement of allergic responses.

7.3.6.2. Toxicological Studies

Diesel Exhaust

Exposure to relatively low doses of DE has been shown to exacerbate asthmatic responses in ovalbumin (OVA) sensitized and challenged BALB/c mice (Matsumoto et al., 2006, 098017). Mice were intraperitoneally sensitized and intranasally challenged 1 day prior to inhalation exposure to DE (PM concentration 100 $\mu g/m^3$; CO, 3.5 ppm; NO_2, 2.2 ppm; SO_2 <0.01 ppm) for 1 day or 1, 4, or 8 wk (7/h/day, 5 days/wk, endpoints 12 h post DE exposure). Results from the 1- and 4-wk exposures are described in Section 6.3.6.3. It should be noted that control mice were left in a clean room as opposed to undergoing chamber exposure to filtered air. The significant increases in AHR and airway sensitivity observed following shorter exposure periods did not persist at 8 wk. BALF cytokines were altered by DE exposure with only RANTES significantly elevated after 8 wk. DE had no effect on OVA challenge-induced peribronchial inflammatory or mucin positive cells. These results suggest that adaptive processes may have occurred during prolonged exposure to DE.

Gasoline Exhaust

In a study by Reed et al. (2008, 156903), BALB/c mice were exposed to whole gasoline exhaust diluted 1:10 (H), 1:15 (M), or 1:90 (L), filtered exhaust at the 1:10 (HF), or clean air for 6 h/day (atmospheric characterization described in Section 6.3.6.3). GEE exposure from conception through 4 wk of age induced slight but non-significant increases in OVA-specific IgG1 in offspring but had no significant effect on airway reactivity, BALF cytokine or cell concentrations, although there were non-significant increases in lung neutrophils and eosinophils. Significant increases in total serum IgE were observed, but this effect persisted after filtration of particles and was thus attributed to gas phase components.

Woodsmoke

In a study by Tesfaigzi et al. (2005, 156116), Brown Norway rats were sensitized and challenged with OVA. Rats were exposed for 70 days to filtered air or to 1,000 µg/m^3 hardwood smoke. Particles were characterized by a MMAD of 0.36 µm. Concentrations of gases were reported to be 13.0 ppm CO and 3.1 ppm total vapor hydrocarbon with negligible NO_X. Respiratory function was measured in anesthetized animals by whole-body plethysmography and demonstrated a significant increase in functional residual capacity as well as a significant increase in dynamic lung compliance in hardwood smoke-exposed animals compared to controls. No change in total pulmonary resistance or airway responsiveness to methacholine was observed. BALF inflammatory cells were not increased, although histological analysis demonstrated focal inflammation including granulomatous lesion and eosinophilic infiltrations in hardwood smoke-exposed rats. Alterations of several cytokines in BALF and plasma were noted. Changes in airway epithelial mucus cells and intraepithelial stored mucosubstances were modest and did not achieve statistical significance. Results of this study demonstrate that subchronic exposure to hardwood smoke had minimal effects on pulmonary responses in a rat model of allergen sensitization and challenge.

7.3.7. Host Defense

7.3.7.1. Epidemiologic Studies

Epidemiologic studies of respiratory infections indicate an association with PM. This is more evident when considering short-term exposures (Chapter 6), but studies of long-term exposures have observed associations with general respiratory symptoms often caused by infection, such as bronchitis. In a birth cohort study of approximately 4,000 Dutch children, Brauer et al. (2007, 090691)(described in Section 7.3.1.1) found significant positive associations for $PM_{2.5}$ with ear/nose/throat infections and doctor-diagnosed flu/serious cold in the first 4 yr of life. These results are consistent with an earlier study by Brauer et al. (2006, 090757), which found that an increase of 10 µg/m^3 $PM_{2.5}$ was associated with increased risk for ear infections in the Netherlands [OR 1.50 (95% CI, 1.00-2.22)]. A Swiss study by Bayer-Oglesby et al. (2005, 086245), discussed in Section 7.3.1.1 above, demonstrated that declining levels of PM_{10} were associated with declining prevalence of common cold and conjunctivitis. Because traffic-related pollutants such as UFPs are high near major roadways and then decay exponentially over a short distance, Williams, et al. (2009, 191945) assessed exposure according to residential proximity to major roads in a Seattle area study of postmenopausal women. Proximity to major roads was associated with a 21% decrease in natural killer cell function, which is an important defense against viral infection and tumors. This finding was limited to women who reported exercising near traffic; other markers of inflammation and lymphocyte proliferation did not consistently differ according to proximity to major roads. In the Puget Sound region of Washington, Karr et al. (2009, 191946) reported that there may be a modest increased risk of bronchiolitis related to $PM_{2.5}$ exposure for infants born just before the peak respiratory syncytial virus (RSV) season. Risk estimates were stronger when restricted to cases specifically attributed to RSV and for infants residing closer to highways. Emerging evidence suggests that respiratory infections, particularly infection by viruses such as RSV, can cause asthma or trigger asthma attacks.

7.3.7.2. Toxicological Studies

Diesel Exhaust

DE may affect systemic immunity. The proliferative response of A/J mouse spleen cells following stimulation with T cell mitogens was suppressed by 6 mo of daily exposure to DE at concentrations at or above 300 µg/m^3 PM (Burchiel et al., 2004, 055557). B cell proliferation was increased at 300 µg/m^3 but unaffected at higher concentrations (up to 1,000 µg/m^3). Concentrations of gases and were reported in the parallel study by Reed et al. (2004, 055625), described in

Section 7.3.3.2. The Reed study reported a decrease in spleen weight in male mice (27% reduction in the 300 μg/m^3 exposure group). The immunosuppressive effects of DE were not due to PAHs or benzo(a)pyrene (BaP)-quinones (BPQs) since there were little, if any, of these compounds present in the chamber atmosphere. It should be noted that sentinel animals were negative for mouse parvovirus at the start of the study, but seroconverted by the end of the study, indicating possible infection. Parvovirus can interfere with the modulation of lymphocyte mitogenic responses (Baker, 1998, 156245). A 6-month exposure (6h/day, 7d/wk) to 30, 100, 300 or 1,000 μg/m^3 of PM in DE did not significantly affect bacterial clearance in C57BL/6 mice infected with *Pseudomonas aeruginosa*, although all levels reduced bacterial clearance when the exposure only lasted a week (Harrod et al., 2005, 088144). Characterization of the exposure atmosphere was given by Reed et al. (2004, 055625) (Section 7.3.3.2.).

Gasoline Exhaust

In a study by Reed et al. (2008, 156903) (described in Section 6.3.7.2) long-term exposure to fresh gasoline exhaust (6h/day, 7d/wk for 6 mo) did not affect clearance of *P. aeruginosa* from the lungs of C57BL/6 mice.

Hardwood Smoke

One study demonstrated immunosuppressive effects of hardwood smoke (Burchiel et al., 2005, 088090). Exposure to hardwood smoke increased proliferation of T cells from A/J mice exposed daily to 100 μg/m^3 PM for 6 mo, but produced a concentration-dependent suppression of proliferation at PM concentrations >300 μg/m^3. No effects on B cell proliferation were observed. Concentrations of NO and NO_2 were not detectable or <40 ppb for all exposure levels. CO was reported to be 2, 4, and 13 ppm for the 100, 300 and 1,000 μg/m^3 PM concentrations, respectively. Exposure atmospheres contained significant levels of naphthalene and methylated napthalenes, fluorene, phenanthrene, and anthracene, as well as low concentrations of several metals (K, Ca, and Fe) (Burchiel et al., 2005, 088090). It should be noted that serologic analysis of study sentinel animals indicated infection with parvovirus , which can interfere with the modulation of lymphocyte mitogenic responses (Baker, 1998, 156245). In another study by Reed et al. (2006, 156043) C57BL/6 mice were exposed to 30-1,000 μg/m^3 hardwood smoke by whole-body inhalation for 6 mo prior to instillation of *P. aeruginosa*. Exposure characterizations are described in Section 7.3.3.2. Although there was a trend toward increased clearance with increasing exposure concentrations, there was no statistically significant effect of hardwood smoke exposure on bacterial clearance.

7.3.8. Respiratory Mortality

Two large U.S. cohort studies examined the effect of long-term exposure to $PM_{2.5}$ on respiratory mortality with mixed results. In the ACS study, Pope et al. (2004, 055880) reported positive associations with deaths from specific cardiovascular diseases, but no $PM_{2.5}$ associations were found with respiratory mortality. A follow-up to the Harvard Six Cities study (Laden et al., 2006, 087605) used updated air pollution and mortality data and found positive associations between long-term exposure to $PM_{2.5}$ and mortality. Of special note is a statistically significant reduction in mortality risk reported with reduced long-term fine particle concentrations observed for deaths due to cardiovascular and respiratory causes, but not for lung cancer deaths. There is some evidence for an association between $PM_{2.5}$ and respiratory mortality among post-neonatal infants (ages 1 month-1 year) (Section 7.4.1). In summary, when deaths due to respiratory causes are separated from all-cause (nonaccidental) and cardiopulmonary deaths, there is limited and inconsistent evidence for an effect of $PM_{2.5}$ on respiratory mortality, with one large cohort study finding a reduction in deaths due to respiratory causes associated with reduced $PM_{2.5}$ concentrations, and another large cohort study finding no $PM_{2.5}$ associations with respiratory mortality.

7.3.9. Summary and Causal Determinations

7.3.9.1. $PM_{2.5}$

The epidemiologic studies reviewed in the 2004 PM AQCD suggested relationships between long-term PM_{10} and $PM_{2.5}$ (or $PM_{2.1}$) exposures and increased incidence of respiratory symptoms and disease. One of these studies indicated associations with bronchitis in the 24-city cohort (Dockery et al., 1996, 046219). They also suggested relationships between long-term exposure to $PM_{2.5}$ and pulmonary function decrements in the CHS (Gauderman et al., 2000, 012531; Gauderman et al., 2002, 026013). These findings added to the database of the earlier 22-city study of $PM_{2.1}$ (Raizenne et al., 1996, 077268) that found an association between exposure to ambient particle strong acidity and impairment of lung function in children. No long-term exposure toxicological studies were reported in the 2004 PM AQCD.

Recent studies have greatly expanded the evidence available since the 2004 PM AQCD. New analyses have been conducted that include longer follow-up periods of the CHS cohort through 18 yr of age and provide evidence that effects from exposure to $PM_{2.5}$ persist into early adulthood. Gauderman et al. (2004, 056569) reported that $PM_{2.5}$ exposure was associated with clinically and statistically significant deficits in FEV_1 attained at the age of 18 yr. In addition, the strength and robustness of the outcomes were larger in magnitude, and more precise than previous CHS studies with shorter follow-up periods. Supporting this result are new longitudinal cohort studies conducted by other researchers in other locations with different methods. These studies report results for PM_{10} that is dominated by $PM_{2.5}$. New studies provide positive associations from Mexico City, Sweden, and a national cystic fibrosis cohort in the U.S. A natural experiment in Switzerland, where PM levels had decreased, reported that improvement in air quality may slow the annual rate of decline in lung function in adulthood, indicating positive consequences for public health. Thus, the data are consistent and coherent across several study designs, locations and researchers. As was found in the 2004 PM AQCD, the studies report associations with $PM_{2.5}$ and PM_{10}, while most did not evaluate $PM_{10-2.5}$. Associations have been reported with fine particle components, particularly EC and OC. Source apportionment methods generally have not been used in these long-term exposure studies.

Coherence and biological plausibility for the observed associations with lung function decrements is provided by toxicological studies (Section7.3.2.2). A recent study demonstrated that pre- and postnatal exposure to ambient levels of urban particles affected mouse lung development, as measured by anatomical and functional indices (Mauad et al., 2008, 156743). Another study suggested that the developing lung may be susceptible to PM since acute exposure to UF iron-soot decreased cell proliferation in the proximal alveolar region of neonatal rats (Pinkerton et al., 2004, 087465) (Section 6.3.5.3). Impaired lung development is a viable mechanism by which PM may reduce lung function growth in children. Other animal toxicological studies have demonstrated alterations in pulmonary function following exposure to DE and wood smoke (Section 7.3.2.2).

An expanded body of epidemiologic evidence for the effect of $PM_{2.5}$ on respiratory symptoms and asthma incidence now includes prospective cohort studies conducted by different researchers in different locations, both within and outside the U.S. with different methods. The CHS provides evidence in a prospective longitudinal cohort study that relates $PM_{2.5}$ and bronchitic symptoms and reports larger associations for within-community effects that are less subject to confounding than between-community effects (McConnell et al., 2003, 049490). Several new studies report similar findings with long-term exposure to PM_{10} in areas where fine particles predominate. In England, an association was seen with an increased prevalence of cough without a cold. Further evidence includes a reduction of respiratory symptoms corresponding to decreasing PM levels in natural experiments in cohorts of Swiss school children (Bayer-Oglesby et al., 2005, 086245) and adults (Schindler et al., 2009, 191950).

New studies examined the relationship between long-term $PM_{2.5}$ exposure and asthma incidence. $PM_{2.5}$ had the strongest modifying effect on the association between lung function with asthma in an analysis of the CHS (Islam et al., 2007, 090697). The loss of protection by high lung function against new onset asthma in high $PM_{2.5}$ communities was observed for all the lung function measures. In the Netherlands, an association with doctor-diagnosed asthma was found in a birth cohort examining the first 4 yr of life (Brauer et al., 2007, 090691) Further, findings from an adult cohort suggest that traffic-related PM_{10} contributes to asthma development and that reductions in PM decrease asthma risk (Kunzli et al., 2009, 191949).

A large proportion of asthma is driven by allergy, and the majority of recent epidemiologic studies examining allergic (or atopic) indicators found positive associations with $PM_{2.5}$ or PM_{10} (Section 7.3.6.1) . Limited evidence for PM-mediated allergic responses is provided by toxicological studies of DE and woodsmoke, while effects of gasoline exhaust were attributed to gaseous components (Section 7.3.6.2).

Long-term $PM_{2.5}$ exposure is associated with pulmonary inflammation and oxidative responses. An epidemiologic study found a relationship between $PM_{2.5}$ and increased inflammatory marker eNO among school children (Dales et al., 2008, 156378). Toxicological studies of pulmonary inflammation have demonstrated mixed results, with subchronic DE exposures generating increases and CAPs and wood smoke inducing little or no response (Section 7.3.3.2). The pulmonary inflammation observed with DE was attributable to the particle fraction. Toxicological studies also reported evidence of oxidative responses (Section 7.3.4.1). Adaptation to prolonged DE was observed for some oxidative responses in addition to some allergic and pulmonary function responses (Section 7.3.2.2 and 7.3.6.2).

Additional support for the relationship between long-term $PM_{2.5}$ exposures and respiratory outcomes is provided by pulmonary injury responses observed in toxicological studies (Section 7.3.5.1). Markers of pulmonary injury were increased in rats exposed to DE and gasoline exhaust; and these changes were attributable to PM. Further, lung DNA methylation was observed in the gasoline exhaust study. Histopathological changes have also been reported following exposure to heavily-trafficked urban air and woodsmoke. Findings include nasal and airway mucous cell hyperplasia accompanied by alterations in mucus production which can lead to a loss of mucus–mediated protective functions; exacerbation of protease-induced emphysema; and mast cell infiltration and hypertrophy of alveolar walls. These results provide biological plausibility for adverse respiratory outcomes following long-term PM exposure.

Limited information is available on host defense responses (Section 7.3.7) and respiratory mortality (Section 7.3.8) resulting from $PM_{2.5}$ exposure. Several recent epidemiologic studies suggest a relationship between long-term exposure to $PM_{2.5}$ or PM_{10} and infection in children and infants (Section 7.3.7.1). A few toxicological studies suggest that DE exposure affects systemic immunity, and although impaired bacterial clearance is associated with short-term exposures to DE, neither DE or gasoline exhaust seems to have this effect after longer exposures (Section 7.3.7.2).

In summary, the strongest evidence for a relationship between long-term exposure to $PM_{2.5}$ and respiratory morbidity is provided by epidemiologic studies demonstrating associations with decrements in lung function growth in children and with respiratory symptoms and disease incidence in adults. Mean $PM_{2.5}$ concentrations in these study locations ranged from 13.8 to 30 $\mu g/m^3$ during the study periods. These studies provide evidence for associations in areas where PM is predominantly fine particles. A major challenge to interpreting the results of these studies is that the PM size fractions and concentrations of other air pollutants are often correlated; however, the consistency of findings across different locations supports an independent effect of $PM_{2.5}$. Recent toxicological studies provide support for the associations with $PM_{2.5}$ and decreases in lung function growth in children. Pre- and postnatal exposure to ambient levels of urban particles was found to affect mouse lung development, which provides biological plausibility for the epidemiologic findings. Recent subchronic and chronic toxicological studies also demonstrate altered pulmonary function, mild inflammation, oxidative responses, histopathological changes including mucus cell hyperplasia and enhanced allergic responses in response to CAPs, DE, urban air and woodsmoke and provide further coherence and biological plausibility. Exacerbation of emphysematous lesions was noted in one study involving exposure to urban air in a heavily-trafficked area. **Collectively, the evidence is sufficient to conclude that the relationship between long-term $PM_{2.5}$ exposure and respiratory effects is likely to be causal.**

7.3.9.2. $PM_{10-2.5}$

The 2004 PM AQCD did not report long-term exposure studies for $PM_{10-2.5}$. The only recent study to evaluate long-term exposure to $PM_{10-2.5}$ found positive, but not statistically significant associations with eNO (Dales et al., 2008, 156378). The evidence is **inadequate to determine if a causal relationship exists between long-term $PM_{10-2.5}$ exposures and respiratory effects**.

7.3.9.3. UFPs

The 2004 PM AQCD did not report long-term exposure studies for UFPs. The current evidence for long-term UFP effects is limited to toxicological studies. Generally, subchronic exposure to DE induced pulmonary inflammation, which was in contrast to UF CAPs exposure (Section 7.3.3.2) It appeared that the PM fraction was responsible for the inflammatory response with DE exposure. Long-term exposure to DE also resulted in oxidative and allergic responses, although lung injury was not remarkable (Sections 7.3.4.1 and 7.3.6.2). The evidence is **inadequate to determine if a causal relationship exists between long-term UFP exposures and respiratory effects**.

7.4. Reproductive, Developmental, Prenatal and Neonatal Outcomes

7.4.1. Epidemiologic Studies

This section evaluates and summarizes the scientific evidence on PM and developmental and pregnancy outcomes and infant mortality. Infants and fetal development processes may be particularly vulnerable to PM exposure, and although the physical mechanisms are not fully understood, several hypotheses have been proposed involving direct effects on fetal health, altered placenta function, or indirect effects on the mother's health (Bracken et al., 2003, 156288; Clifton et al., 2001, 156360; Maisonet et al., 2004, 156725; Schatz et al., 1990, 156073; Sram et al., 2005, 087442). Study of these outcomes can be difficult given the need for detailed data and potential residential movement of mothers during pregnancy. Two recent articles have reviewed methodological issues relating to the study of outdoor air pollution and adverse birth outcomes (Ritz and Wilhelm, 2008, 156914; Slama et al., 2008, 156985). Some of the key challenges to interpretation of these study results include the difficulty in assessing exposure as most studies use existing monitoring networks to estimate individual exposure to ambient PM; the inability to control for potential confounders such as other risk factors that affect birth outcomes (e.g., smoking); evaluating the exposure window (e.g., trimester) of importance; and limited evidence on the physiological mechanism of these effects (Ritz and Wilhelm, 2008, 156914; Slama et al., 2008, 156985). Another uncertainty is whether PM effects differ by the child's sex. A review of preterm birth and low birth weight studies found limited indication that effects may differ by gender, however sample size was limited (Ghosh et al., 2007, 091233).

Previous summaries of the association between PM concentrations and pregnancy outcomes and infant mortality were presented in previous PM AQCDs. The 1996 PM AQCD concluded that although few studies had been conducted on the link between PM and infant mortality, the research "suggested an association," particularly for post-neonates (U.S. EPA, 1996, 079380). In the 2004 PM AQCD, additional evidence was available on PM's effect on fetal and early postnatal development and mortality (U.S. EPA, 2004, 056905) and although some studies indicated a relationship between PM and pregnancy outcomes, others did not. Studies identifying associations found that exposure to PM_{10} early during pregnancy (first month of pregnancy) or late in the pregnancy (6 wk prior to birth) were linked with higher risk of preterm birth, including models adjusted for other pollutants, and that $PM_{2.5}$ during the first month of pregnancy was associated with intrauterine growth restriction. However, other work did not identify relationships between PM_{10} exposure and low birth weight. The state of the science at that time, as indicated in the 2004 PM AQCD, was that the research provided mixed results based on studies from multiple countries, and that additional research was required to better understand the impact of PM on pregnancy outcomes and infant mortality. Considering evidence from recent studies discussed below, along with previous AQCD conclusions, epidemiologic studies consistently report associations between PM_{10} and $PM_{2.5}$ exposure and low birth weight and infant mortality, especially during the post-neonatal period. Animal toxicological evidence supports these associations with $PM_{2.5}$, but provides little mechanistic information or biological plausibility. Information on the ambient concentrations of PM_{10} and $PM_{2.5}$ in these study locations can be found in Table 7-5.

7.4.1.1. Low Birth Weight

A large number of studies have investigated exposure to ambient PM and low birth weight at term, including a U.S. national study, as well as two studies in the northeast U.S., and four in California. Parker and Woodruff (2008, 156846) linked U.S. birth records for singletons delivered at 40-wk gestation in 2001-2003 during the months of March, June, September and December to quarterly estimates of PM exposure by county of residence and month of birth. They found an association between $PM_{10-2.5}$ and birthweight (-13 g [95% CI: -18.3 to -7.6]) per 10 $\mu g/m^3$ increase), but no such association for $PM_{2.5}$.

Maisonet et al. (2001, 016624) analyzed 89,557 births (1994-96) in six northeastern cities (Boston and Springfield MA; Hartford CT; Philadelphia and Pittsburgh PA; and Washington DC). Each city had three PM_{10} monitors measuring every sixth day. Results from multiple monitors were averaged in each city. Exposure was determined for each trimester of pregnancy and categorized by quartiles (<25, 25-30, 31-35, 36-43 $\mu g/m^3$) and 95th percentile (>43$\mu g/m^3$). There was no increased risk for low birth weight at term associated with PM_{10} exposure during any trimester of pregnancy. When birth weight was considered as a continuous outcome, exposure to PM_{10} was not associated with a reduction in mean birth weight.

In contrast, Bell et al. (2007, 093256) reported positive associations for both $PM_{2.5}$ and PM_{10} with birth weight in a study of births (n = 358,504) in Connecticut and Massachusetts (1999-2002). Birth data indicated county, not street address or ZIP code, so women were assigned exposure based on county residence at delivery. The difference in birth weight per 10 $\mu g/m^3$ associated with $PM_{2.5}$ was -66.8 (95% CI: -77.7 to -55.9) g. For PM_{10} it was -11.1 (95% CI: -15.0 to -7.2) g. The increased risk for low birth weight was OR = 1.054 (95% CI: 1.022-1.087) for $PM_{2.5}$ and OR = 1.027 (95% CI: 0.991-1.064) for PM_{10}, based on average exposure during pregnancy. Reductions in birth weight were also associated with third trimester exposure to PM_{10} and second and third trimester exposure to $PM_{2.5}$. Comparing this study to Maisonet et al. (2001, 016624), a larger sample size was able to detect a small increase in risk. In addition, birth weight was reduced more by exposure to $PM_{2.5}$ than by exposure to PM_{10}. Measured $PM_{2.5}$ concentrations were not available in the earlier study.

The Children's Health Study is a population based cohort of children living in 12 southern California communities, selected on the basis of differing levels of air pollution (Salam et al., 2005, 087885), as previously discussed in Section 7.3. The children in grades 4, 7 and 10 were recruited through schools. A subset of this cohort (n = 6,259) were born in California from 1975-1987. Of these, birth certificates were located for 4,842, including 3,901 infants born at term and 72 cases of low birth weight at term. Using the mother's ZIP code at the time of birth, exposure was determined by inverse distance weighting of up to three PM_{10} monitors within 50 km of the ZIP code centroid. If there was a PM_{10} monitor within 5 km of the ZIP code centroid (40% of data), exposure from that monitor was used. Exposure was calculated for the entire pregnancy, and for each trimester of pregnancy. A 10 $\mu g/m^3$ increase in PM_{10} during the third trimester reduced mean birth weight -10.9 g (95% CI: -21.1 to -0.6) in single pollutant models, but became non-significant in copollutant models controlling for the effects of O_3. Increased risks of low birth weight (<2,500 g) were not statistically significant (OR = 1.3 [95% CI: 0.9-1.9]). A strength of this study was the cohort data available included information on SES and smoking during pregnancy. A limitation is the assignment of exposure based on monitoring stations up to 50 km distant; this may have introduced substantial exposure misclassification obscuring some associations.

Table 7-5. Characterization of ambient PM concentrations from studies of reproductive, developmental, prenatal and neonatal outcomes and long-term exposure.

Study	Location	Mean Annual Concentration (µg/m^3)	Upper Percentile Concentrations (µg/m^3)
$PM_{2.5}$			
Basu et al. (2004, 087896)	CA	Range of means across sites: 14.5-18.2 Avg of means across sites: 16.2	Max: 26.3-34.1
Bell et al. (2007, 091059)	CT & MA	22.3	
Brauer et al. (2008, 156292)	Vancouver, Canada	5.3	Max: 37.0
Huynh et al. (2006, 091240)	CA	Range of means across trimesters: 17.5-18.8 Avg of means across trimesters: 18.2	
Jalaludin et al. (2007, 156601)	Sydney, Australia	9.0	
Liu (2007, 090429)	Multicity, Canada	12.2	75th: 15
Loomis et al. (1999, 087288)	Mexico City	27.4	Max: 85
Mannes et al. (2005, 087895)	Sydney, Australia	9.4	75th: 11.2; Max: 82.1
Parker et al. (2005, 087462)	CA	15.4	
Ritz et al. (2007, 096146)	Los Angeles, CA	20.0	
Wilhelm and Ritz (2005, 088668)	Los Angeles, CA	21.0	Max: 38.9-48.5
Woodruff et al. (2006, 088758)	CA	19.2[a]	75th: 22.7
Woodruff et al. (2008, 098386)	U.S.	Range of means across effects: 14.5-14.9[a] Avg of means across effects: 14.8[a]	75th: 18.5-18.7
$PM_{10-2.5}$			
Parker et al. (2008, 156013)	U.S.	13.2	75th: 17.5
PM_{10}			
Bell et al. (2007, 093256)	CT & MA	22.3	
Brauer et al. (2008, 156292)	Vancouver, Canada	12.7	Max: 35.4
Chen et al. (2002, 024945)`	Washoe County, NV	31.53	75th: 39.35; Max: 157.32
Gilboa et al. (2005, 087892)	TX	23.8[a]	75th: 29
Ha et al. (2003, 042552)	Seoul, South Korea	69.2	75th: 87.7; Max: 245.4
Hansen et al. (2006, 089818)	Brisbane, Australia	19.6	Max: 171.7
Hansen et al. (2007, 090703)	Brisbane, Australia	19.6	75th: 22.7; Max: 171.7
Jalaludin et al. (2007, 156601)	Sydney, Australia	16.3	
Kim et al. (2007, 156642)	Seoul, Korea	Range of means across time: 88.7-89.7 Avg of means across time: 89.2	
Lee et al. (2003, 043202)	Seoul, Korea	71.1	75th: 89.3; Max: 236.9
Leem et al. (2006, 089828)	Incheon, Korea	53.8[a]	75th: 64.6; Max: 106.39
Lipfert et al. (2000, 004103)	U.S.	33.1	Max: 59
Maisonet et al. (2001, 016624)	NE U.S.	31.0[a]	75th: 36.1; Max: 46.5
Mannes et al. (2005, 087895)	Sydney, Australia	16.8	75th: 19.9; Max: 104.0
Pereira et al. (1998, 007264)	Sao Paulo, Brazil	65.04	Max: 192.8
Ritz et al. (2000, 012068)	CA	49.3	Max: 178.8
Ritz et al. (2006, 089819)	CA	46.3	Max: 83.5

Study	Location	Mean Annual Concentration (μg/m^3)	Upper Percentile Concentrations (μg/m^3)
Rogers and Dunlop (2006, 091232)	GA	3.75	75th: 15.07
Romieu et al. (2004, 093074)	Ciudad Juarez, Mexico	33.0-45.9	
Sagiv et al. (2005, 087468)	PA	Range of means across time: 25.3-27.1 Avg of means across time: 26.2	Max: 68.9-156.3
Salam et al. (2005, 087885)	CA	Range of means across trimesters: 45.4-46.6 Avg of means across trimesters: 45.8	
Suh et al. (2008, 192077)	Seoul, Korea	Range of means across trimesters: 54.6-61.1 Avg of means across trimesters: 58.27	75th: 62.8-67.8 Max: 85.1-107.36
Tsai et al. (2006, 090709)	Kaohsiung, Taiwan	81.5	75th: 111.5; Max: 232.0
Wilhelm and Ritz (2005, 088668)	Los Angeles, CA	38.1	Max: 74.6-103.7
Woodruff et al. (2008, 098386)	U.S.	Range of means across effects: 28.6-29.8[a] Avg of means across effects: 29.1[a]	75th: 33.8-36.5
Yang et al. (2006, 090760)	Taipei, Taiwan	53.2	75th: 64.9; Max: 234.9

[a]Median concentration

Parker et al. (2005, 087462) examined births in California within 5 miles of a monitoring station (n = 18,247). Only infants born at 40 wk gestation were included. Thus all infants were the same gestational age, and had been exposed in the same year. Exposure to $PM_{2.5}$ in quartiles (<11.9, 11.9-13.9, 14.0-18.4, >18.4) was associated with decrements in birth weight. Infants exposed to >13.9 μg/m^3 experienced reductions in birth weight (third quartile -13.7 g (95% CI: -34.2 to 6.9), fourth quartile -36.1 g (95% CI: -55.8 to -16.5). These are larger reductions than have been seen in some other studies. However, this study reduced misclassification by including only women living within 5 miles of a monitoring station, and only included births at 40 wk gestation. Reducing misclassification should lead to a stronger association, if the association is causal.

The effects of spatial variation in exposure were also investigated by Wilhelm and Ritz (2005, 088668). Their study included all women living in ZIP codes where 60% of the ZIP code was within two miles of a monitoring station in the Southern California Basin, and women with known addresses in Los Angeles County within 4 miles of a monitoring station. Exposure to average PM_{10} in the third trimester was analyzed for increased risk of low birth weight at term (≥ 37-wk gestation). Analysis at the ZIP code level did not detect increased risk (per 10 μg/m^3 PM_{10}, OR = 1.03 [95% CI: 0.97-1.09]). However the analysis based on geocoded addresses indicated that increasing exposure to PM_{10} was associated with increased risk of low birth weight for women living within 1 mile of the station where PM_{10} was measured. For these women (n = 247 cases, 10,981 non-cases), each 10 μg/m^3 increase in PM_{10} was associated with a 22% increase in risk of term low birth weight (OR = 1.22 [95% CI: 1.05-1.41]). In the categorical analysis, exposure to PM_{10} >44.4 μg/m^3 was associated with a 48% increase in risk (OR = 1.48 [95% CI: 1.00-2.19]). Increased risk of low birth weight also was associated with exposure to CO in single pollutant models. However, when multipollutant models were considered, the effects of CO were attenuated but the effects of PM_{10} increased. Controlling for CO, NO_2, and O_3, each 10 μg/m^3 increase in exposure to PM_{10} increased risk of low birth weight 36% (OR = 1.36 [95% CI: 1.12-1.65]).

Spatial variation in $PM_{2.5}$ exposure was investigated by Basu et al. (2004, 087896). They included only mothers who lived within 5 miles of a $PM_{2.5}$ monitor and within a California county with at least 1 monitor. To minimize potential confounding, they included only white (n = 8,597) or Hispanic (n = 8,114) women, who were married, between 20 and 30 yr of age, completed at least high school and were having their first child. Consistently, $PM_{2.5}$ exposure measured by the county monitor was more strongly associated with reductions in birth weight than exposure measured by the neighborhood monitor. The results were replicated in both the white and the Hispanic samples. Reductions in birth weight ranged from 15.2 to 43.5 g per 10 μg/m^3 increase in $PM_{2.5}$.

In the remaining U.S. study, Chen et al. (2002, 024945) analyzed 33,859 birth certificates of residents of Washoe County in northern Nevada (1991-1999). There were four sites monitoring PM_{10} during the study period, it appears (not stated) that exposure was averaged over the county. A

10 μg/m^3 increase in exposure to PM_{10} during the third trimester of pregnancy was associated with an 11 g reduction in birth weight (95% CI: -2.3 to -19.8). Effects on risk of low birth weight were not statistically significant. For exposure in the third trimester of 19.77 to 44.74 μg/m^3 compared to <19.74 μg/m^3 the odds ratio for low birth weight was 1.05 (95% CI: 0.81-1.36). Comparing exposure >44.74 to the same reference category, the odds ratio was 1.10 (95% CI: 0.71-1.71). Misclassification of exposure may have occurred when exposure was averaged over a large geographic area (16,968 km^2).

Recent international studies investigating effects of particles on low birth weight include one in Munich (Slama et al., 2007, 093216), two in Canada (Brauer et al., 2008, 156292; Dugandzic et al., 2006, 088681), two in Australia (Hansen et al., 2007, 090703; Mannes et al., 2005, 087895), two in Taiwan (Lin et al., 2004, 089827; Yang et al., 2003, 087886) one in Korea (Ha et al., 2003, 042552) and two in Sao Paulo, Brazil (Gouveia et al., 2004, 055613; Medeiros and Gouveia, 2005, 089824). The majority of these studies found that PM concentrations were associated with low birth weight, though two studies (Hansen et al., 2007, 090703; Lin et al., 2004, 089827) found no associations. The effect estimates were similar in magnitude to those reported in the U.S. studies.

Considerations in Interpreting Results of Low Birth Weight Studies

Studies included subjects at distances from monitoring stations varying from as close as 1 mile or 2 km, to as far as 50 km or the size of the county. Studies that only included subjects living within a short distance (1 mile, 2 km) of the monitoring station (thus likely reducing exposure measurement error) were more likely to find that PM exposure was associated with increased risk of low birth weight. However, Basu et al. (2004, 087896) reported a stronger association between $PM_{2.5}$ exposure and birth weight when exposure was estimated based on the county monitor, rather than the monitor within 5 miles of the residence. They suggest that county level exposure may be more representative of where women spend their time, including not only home, but also other time spent away from home. Other pollutants also appeared to influence the risk associated with particle exposure. In one study, exposure to PM_{10} in a single pollutant model reduced birth weight by 11 g, but became non-significant in copollutant models with O_3 (Salam et al., 2005, 087885). In another study the risk associated with PM_{10} exposure increased from 22% to 36% when other pollutants were included in the model (Wilhelm and Ritz, 2005, 088668). All but one study in the U.S. found some association between particle exposure and reduced birth weight (Maisonet et al., 2001, 016624). The results of international studies were inconsistent. This might be related to the chemical composition of particles in the U.S., or to differences in the pollutant mixture. Studies with null results must be interpreted with caution when the comparison groups have significant exposure. This was certainly the situation in studies in Taiwan and Korea (Lee et al., 2003, 043202; Lin et al., 2004, 089827; Yang et al., 2003, 087886). Differences in geographical locations, study samples and linkage decisions may contribute to the diverse findings in the literature on the association between PM and birthweight, even within the U.S. (Parker and Woodruff, 2008, 156846).

7.4.1.2. Preterm Birth

A potential association of exposure to airborne particles and preterm birth has been investigated in numerous epidemiologic studies, including some conducted in the U.S. and others in foreign countries. Three U.S. studies have been carried out by the same group of investigators in California.

A natural experiment occurred when an open-hearth steel mill in Utah Valley was closed from August 1986 through September 1987. Parker et al. (2008, 156013) compared birth outcomes for Utah mothers within and outside of the Utah Valley, before, during, and after the mill closure. They report that mothers who were pregnant around the time of the closure of the mill were less likely to deliver prematurely than mothers who were pregnant before or after. The strongest effect estimates were observed for exposure during the second trimester (14% decrease in risk of preterm birth during mill closure). Preterm birth outside of the Utah Valley did not change during the time of the mill closure.

In 2000, Ritz et al. (2000, 012068) published the first study investigating the association of preterm birth with PM in the U.S. The study population was women living in the southern California Basin. There were eight monitoring stations measuring PM_{10} every 6th day during the study period.

Birth certificates (1989-1993) were analyzed for women living in ZIP codes within 2 miles of a monitoring station. Women with multiple gestations, chronic disease prior to pregnancy and women who delivered by cesarean section were excluded resulting in a study population of 48,904 women. The risk of preterm birth increased by 4% (RR = 1.04 [95% CI: 1.02-1.6]) per 10 μg/m^3 increase in PM_{10} averaged in the 6 wk before birth. Exposure to PM_{10} in the first month of pregnancy resulted in a 3% increase in risk (RR = 1.03 [95% CI: 1.01-1.05]). These results were robust in multipollutant models.

Wilhelm and Ritz (2005, 088668) reinvestigated this association among women in the same area in 2005, when air pollution had declined from a mean level near 50 μg/m^3 to a mean level near 40 μg/m^3. Birth certificate data from 1994-2000 was analyzed for women living in ZIP codes within 2 miles of a monitoring station, or with addresses within 5 miles of a monitoring station. No significant effects of exposure to PM_{10} were reported. Exposure to $PM_{2.5}$ 6 wk before birth resulted in an increase in preterm birth (RR = 1.19 [95% CI: 1.02-1.40]) for the highest quartile of exposure ($PM_{2.5}$ >24.3 μg/m^3). Using a continuous measure of $PM_{2.5}$, there was a 10% increase in risk for each 10 μg/m^3 increase in $PM_{2.5}$ (RR = 1.10 [95% CI: 1.00-1.21]).

There have been two major criticisms of air pollution studies using birth certificate data. First, that birth certificates only indicate the address at birth and the exposure of women who moved during pregnancy may be misclassified; second, that information about some important confounders may not be available (e.g., smoking). To obtain more precise information about these variables, Ritz et al. (2007, 096146) conducted a case-control study nested within a cohort of birth certificates (Jan 2003-Dec 2003) in Los Angeles County. Births to women residing in ZIP codes (n = 24) close to monitoring stations or major population centers or roadways (n = 87) were eligible (n = 58,316 births). All cases of low birth weight or preterm birth and an equal number of randomly sampled controls in the 24 ZIP codes close to monitors were selected. In the other 87 ZIP codes, 30% of cases and an equal number of controls were randomly sampled. Of 6,374 women selected for the case control study, 2,543 (40%) were interviewed. The association of preterm birth with exposure to $PM_{2.5}$ differed between women responding to the survey and women who did not respond. Among responders, exposure to each 10 μg/m^3 increase in $PM_{2.5}$ concentration in the first trimester increased risk to preterm birth by 23% (RR = 1.23 [95% CI: 1.02-1.48]). There was no increase in risk among non-responders (RR = 0.95 [95% CI: 0.82-1.10]), or in the entire birth cohort (RR = 1.00 [95% CI: 0.94-1.07]).

An additional case control study of preterm birth and $PM_{2.5}$ exposure (Huynh et al., 2006, 091240) used California birth certificate data. Singleton preterm infants (24-36-wk gestation) born in California (1999-2000) whose mothers lived within 5 miles of a $PM_{2.5}$ monitor were eligible. Each of these 10,673 preterm infants were matched to three term (39- to 44-wk gestation) controls (having a last menstrual period within 2 wk of the case infant), resulting in a study population of 42,692. Controlling for maternal race/ethnicity, education, marital status, parity and CO exposure, exposure to $PM_{2.5}$ >17.7 μg/m^3 increased the risk of preterm birth by 14% (OR = 1.14 [95% CI: 1.07-1.23]). Averaging $PM_{2.5}$ exposure over the first month of pregnancy, the last 2 wk before birth, or the entire pregnancy did not substantially change the risk estimate.

Two additional studies of preterm birth and exposure to particulate air pollution have been conducted in the U.S. Each has used a unique methodology. Sagiv et al. (2005, 087468) used time series to analyze births in four Pennsylvania counties between January 1997 and December 2001. In this analysis, exposure to PM_{10} is compared to the rate of preterm births each day. Both acute exposure (on the day of birth) and longer term exposure (average exposure for the preceding 6 wk) were considered in the analysis. An advantage of this analysis is that days, rather than individuals are compared, so confounding by individual risk factors is minimized. For exposure averaged over the 6 wk prior to birth, there was an increase in risk (RR = 1.07 [95% CI: 0.98-1.18]), which persisted for acute exposure with a 2-day lag (RR = 1.10 [95% CI: 1.00-1.21]) and 5-day lag (RR = 1.07 95% CI: 0.98-1.18]).

Rogers and Dunlop (2006, 091232) examined exposure to particles and risk of delivery of an infant weighing less than 1,500 g (all of which were preterm) from 24 counties in Georgia. The study included 69 preterm, small for gestational age (SGA) infants, 59 preterm appropriate for gestational age (AGA) infants and 197 term AGA controls. Exposure was estimated using an environmental transport model that considered PM_{10} emissions from 32 geographically located industrial point sources, meteorological factors, and geographic location of the birth home. Exposure was categorized by quartiles. Comparing women who delivered a preterm AGA infant to those who

delivered a term AGA infant, exposure to PM_{10}>15.07 μg/m^3 tripled the risk (OR = 3.68 [95% CI: 1.44-9.44]).

Brauer et al. (2008, 156292) evaluated the impacts of $PM_{2.5}$ on preterm birth using spatiotemporal exposure metrics in Vancouver, Canada. The authors found similar results when they used a land-use regression model or inverse distance weighting as the exposure metric. For preterm births <37 wk, they reported an OR of 1.06 (95% CI: 1.01-1.11), and for preterm births <35 wk the OR increased to 1.12 (95% CI: 1.02-1.24). There were no consistent trends for early or late gestational period to be more strongly associated with preterm births.

Suh et al. (2008, 192077) conducted a study to determine if the effects of exposure to PM_{10} during pregnancy on preterm delivery are modified by maternal polymorphisms in metabolic genes. They analyzed the effects of the gene-environment interaction between the GSTM1, GSTT1, CYP1a1-T6235C and -1462V polymorphisms and exposure to PM_{10} during pregnancy on preterm birth in a case-control study in Seoul, Korea. PM_{10} concentration ≥ 75th percentile alone was significant in the third trimester of pregnancy (OR = 2.33 [95% CI: 1.33-4.80]), but not in the first or second trimester. The risk of preterm delivery conferred by the GSTM1 null genotype was increased, and the highest risk was found during the third trimester of pregnancy (OR = 2.58 [95% CI: 1.34-4.97]). There were no statistical associations with the GSTT1 or CYP1A1 genotypes. When the gene-environment interaction was analyzed, the risk for preterm birth was substantially higher for women who carried the GSTM1 null genotype and were exposed to high levels of PM_{10} (≥ 75th percentile) than for those who carried the GSTM1 positive genotype but were only exposed to low levels of PM_{10} (<75th percentile) during the third trimester of pregnancy (OR = 6.22, 95% CI: 2.14-18.08).

In Incheon, Korea, Leem et al. (2006, 089828) estimated PM_{10} exposure spatially as well as temporally. Exposure was based on 26 monitors and kriging was used to determine exposure for 120 dongs (administrative districts, mean area 7.82 km^2, median area 1.42 km^3). The sample included 52,113 births, from 2001-2002. PM_{10} was very weakly correlated with other pollutants. Exposure was compared in quartiles for the first and third trimester of pregnancy. In the first trimester, relative risks for the second, third and fourth quartiles were RR = 1.14 (95% CI: 0.97-1.34), RR = 1.07 (95% CI: 0.94-1.37), and RR = 1.24 (95% CI: 1.09-1.41), respectively. Exposure to PM_{10} in quartile one (reference group) was 26.9-45.9 μg/m^3; fourth quartile exposure equaled 64.6-106.4 μg/m^3. The p-value for trend was 0.02. Exposure in the third trimester was not related to preterm birth, however no information was provided to determine how exposure in the third trimester was adjusted for women who delivered preterm.

Two studies investigating risks of preterm birth related to particle exposure have been reported from Australia. In Brisbane, Hansen et al. (2006, 089818) studied 28,200 births (2000-2003) in an area of low PM_{10} concentrations. Exposure to an interquartile range increase in PM_{10} exposure in the first trimester resulted in a 15% increased risk of preterm birth (OR = 1.15 [95% CI: 1.06-1.25]). This result was strongly influenced by the effect of PM_{10} exposure in the first month of pregnancy (OR = 1.19 [95% CI: 1.13-1.26]). PM_{10} was correlated with O_3 (r = 0.77) in this study and O_3 also increased risk in the first trimester. No effects were associated with exposure to PM_{10} in the third trimester.

In Sydney, associations between exposure to particles and preterm birth varied by season. Jalaludin et al. (2007, 156601) obtained information on all births in metropolitan Sydney (1998-2000). Exposure to $PM_{2.5}$ in the 3 mo preceding birth was associated with an increased risk of preterm birth (OR = 1.11 [95% CI: 1.04-1.19]). Additional effects were dependent on season of conception. Both PM_{10} (OR = 1.3 [95% CI: 1.2-1.5]) and $PM_{2.5}$ (OR = 1.4 [95% CI: 1.3-1.6]) were associated with increased risk for conceptions in the winter. Conceptions in summer were associated with reductions in risk (PM_{10} OR = 0.91 [95% CI: 0.88-0.93]) ($PM_{2.5}$ OR = 0.87 [95% CI: 0.84-0.92]). Due to both positive and negative findings, the authors recommend caution in interpreting their results.

Considerations in Analyzing Environmental Exposures and Preterm Birth

A major issue in studying environmental exposures and preterm birth is selecting the relevant exposure period, since the biological mechanisms leading to preterm birth and the critical periods of vulnerability are poorly understood (Bobak, 2000, 011448). Exposures proximate to the birth may be most relevant if exposure causes an acute effect. However, exposure occurring in early gestation

might affect placentation, with results observable later in pregnancy, or cumulative exposure during pregnancy may be the most important determinant. The studies reviewed have dealt with this issue in different ways. Many have considered several exposure metrics based on different periods of exposure.

Often the time periods used are the first month (or first trimester) of pregnancy and the last month (or 6 wk) prior to delivery. Using a time interval prior to delivery introduces an additional problem since cases and controls are not in the same stage of development when they are compared. For example, a preterm infant delivered at 36 wk is a 32-week fetus 4 wk prior to birth, while an infant born at term (40 wk) is a 36-week fetus 4 wk prior to birth. Only one study (Huynh et al., 2006, 091240) adjusted for this in the design.

Many of these studies compare exposure in quartiles, using the lowest quartile as the reference (or control) group. No studies use a truly unexposed control group. If exposure in the lowest quartile confers risk, than it may be difficult to demonstrate additional risk associated with a higher quartile. Thus negative studies must be interpreted with caution.

Preterm birth occurs both naturally (*idiopathic preterm*), and as a result of medical intervention (*iatrogenic preterm*). Ritz et al. (2000, 012068; 2007, 096146) excluded all births by Cesarean section, to limit their studies to idiopathic preterm. No other studies attempted to distinguish the type of preterm birth, although PM exposure maybe associated with only one type. This is a source of potential effect misclassification.

7.4.1.3. Growth Restriction

Low birth weight has often been used as an outcome measure because it is easily available and accurately recorded on birth certificates. However, low birth weight may result from either short gestation, or inadequate growth in utero. Most of the studies investigating air pollution exposure and low birth weight, limited their analysis to term infants to focus on inadequate growth. A number of studies were identified that specifically addressed growth restriction in utero by identifying infants who failed to meet specific growth standards. Usually these infants had birth weights less than the 10th percentile for gestational age, using an external standard. Many of these studies have been previously discussed, since they also examined other reproductive outcomes (low birth weight or preterm delivery).

Three studies in the U.S. examined intrauterine growth. A recent study (Rich et al., 2009, 180122) investigated very small for gestational age (defined as a fetal growth ratio <0.75), small for gestational age (defined as ≥ 75 and <85) and "reference" births (≥ 85) to women residing in New Jersey and mean air pollutant concentrations during the first, second and third trimesters. They reported an increased risk of SGA associated with first and third trimester $PM_{2.5}$ concentrations (1.116 [95% CI: 1.012, 1.232], and 1.106 [1.008-1.212], per 10 μg/m^3 $PM_{2.5}$, respectively). Parker et al. (2005, 087462) reported a positive association between exposure to $PM_{2.5}$. Since this study only included singleton live births at 40-wk gestation, birth weights less than 2,872 g for girls and 2,986 g for boys were designated SGA, based on births in California. Infants exposed to the highest quartile $PM_{2.5}$ (>18.4 μg/m^3) compared to the lowest quartile $PM_{2.5}$ (<11.9 μg/m^3) were 23% more likely to be small for gestational age (OR = 1.23 [95% CI: 1.03-1.50]). Very similar results were found for exposure in each of the three trimesters respectively (OR = 1.26 [95% CI: 1.04-1.51], OR = 1.24 [95% CI: 1.04-1.49], OR = 1.21 [95% CI: 1.02-1.43]). These results controlled for exposure to CO, which did not increase risk for SGA.

In contrast, Salam et al. (2005, 087885) found no association between exposure to PM_{10} and intrauterine growth retardation (IUGR) in the California Children's Health Study. IUGR was defined as less than the 15th percentile of predicted birth weight based on gestational age and sex in term infants. Apparently no external standard was used since 15% of infants in the study were designated as IUGR. An IQR increase in PM_{10} exposure was not significantly associated with IUGR for the whole pregnancy (OR = 1.1 [95% CI: 0.9-1.3]) or for any specific trimester. Differences between this study and the study by Parker et al. (2005, 087462) include measurement of PM_{10} versus $PM_{2.5}$, a less stringent definition of IUGR, and exposures determined by monitors located much farther away from the subjects' residences (up to 50 km versus within 5 mi). All of these factors could lead to misclassification.

Two studies investigating particle exposure and SGA were conducted in Australia, with differing results (Hansen et al., 2007, 090703; Mannes et al., 2005, 087895). Mannes et al. (2005, 087895) defined SGA as birth weight less than two standard deviations below the national mean

birth weight for gestational age. In this study there was a statistically significant effect of exposure to both PM_{10} (OR = 1.10 [95% CI: 1.00-1.48], per 10 μg/m^3 increase) and $PM_{2.5}$ (OR = 1.34 [95% CI: 1.10-1.63], per 10 μg/m^3 increase) for exposure during the second trimester. When analysis was restricted to births within 5 km of the monitoring station, the association for PM_{10} became slightly stronger (OR = 1.22 [95% CI: 1.10-1.34]). Exposure during other trimesters of pregnancy was not associated with IUGR.

In Brisbane, Hansen et al. (2007, 090703) examined head circumference (HC), crown heel length (CHL) and risk of SGA, defined as less than the tenth percentile of weight for gestational age and gender based on an Australian national standard. There was no consistent relationship between PM_{10} exposure and SGA, HC or CHL in any trimester of pregnancy. PM_{10} exposure was determined by averaging values from the five monitoring stations. Due to the sample size and limited number of monitoring stations, it was not possible to analyze the data for women living within 5 km of a monitoring station, as was done in Sydney.

In Canada, Liu et al. (2007, 090429) investigated the effect of $PM_{2.5}$ exposure on fetal growth in three cities, Calgary, Edmonton and Montreal. IUGR was defined as birth weight below the tenth percentile, by sex and gestational week (37-42) for all singleton live births in Canada between 1986 and 2000. Models were adjusted for maternal age, parity, infant sex, season of birth, city of residence, and year of birth. A 10 μg/m^3 increase in $PM_{2.5}$ was associated with an increased risk for IUGR (OR = 1.07 [95% CI: 1.03-1.10]) in the first trimester, and similar risks were associated with exposure in the second or third trimesters. The effect of $PM_{2.5}$ was reduced in multipollutant models including CO and NO_2.

Brauer et al. (2008, 156292) observed consistent increased risks of SGA for $PM_{2.5}$, PM_{10}, NO_2, NO and CO in Vancouver, Canada (20% increase in risk in $PM_{2.5}$ and PM_{10} per 10 μg/m^3 increase). The effects were similar for exposure estimates based on nearest monitor, inverse distance weighting, and land-use regression modeling. ORs for early or late pregnancy exposure windows were remarkably similar to those for the full duration of pregnancy.

7.4.1.4. Birth Defects

Four recent studies examined PM and birth defects. The Seoul, Korea study discussed above also considered congenital anomalies, defined as a defect in the child's body structure (Kim et al., 2007, 156642). PM_{10} levels were associated with higher risk of birth defects for the second trimester, with a 16% (95% CI: 0-34) increase in risk per 10 μg/m^3 in PM_{10}.

Two U.S. studies examined air pollution and risk of birth defects. Data were collected from the California Birth Defects Monitoring Program for four counties in Southern California (Los Angeles, Riverside, San Bernardino, and Orange) for the period 1987-1993, although each county included a subset of this period (Ritz et al., 2002, 023227). Cases (i.e., infants with birth defects) were identified as live birth infants and fetal deaths from 20-wk gestation to 1 yr post-birth, with isolated, multiple, syndrome, or chromosomal cardiac or orofacial cleft defects. Cases were restricted to those with registry data for gestational age and residence ZIP code, and those with residences <10 miles from an air pollution monitor. Six types of categories were included: aortic defects; atrium and atrium septum defects; endocrinal and mitral value defects; pulmonary artery and valve defects; conotruncal defects; and ventricular septal defects not part of the conotruncal category. PM_{10} measurements were available every 6 days. While results indicated increased risk of birth defects for higher levels of CO or O_3, the authors determined that results for PM_{10} were inconclusive, finding no consistent trend of effect after adjustment for CO and O_3.

The other U.S. study examined birth defects through a case-control design in seven Texas counties for the period 1997-2000 (Gilboa et al., 2005, 087892). Births were excluded for parents <18 yr and several non-air pollution risk factors known to be associated with birth defects (e.g., maternal diabetes, holoprosencephaly in addition to oral clef). Comparison of the highest (≥ 29.0 μg/m^3) and lowest (<19.521 μg/m^3) quartiles of PM_{10} for exposure defined as the third to eighth week of pregnancy generated an OR of 2.27 (95% CI: 1.43-3.60) for risk of isolated atrial septal defects and 1.26 (95% CI: 1.03-1.55) for individual atrial septal defects. Including other pollutants (CO, NO_2, O_3, SO_2) in the model did not greatly alter results; numerical results for copollutant analysis were not provided. Strong evidence was not observed for a relationship between PM_{10} and the other birth defect categories. Review articles have concluded that the scientific literature is not sufficient to conclude a relationship between air pollution and birth defects (Sram et al., 2005, 087442).

A recent study of oral clefts conducted in Taiwan found no association between this birth defect and concentrations of PM_{10} during the first or second gestational month (Hwang and Jaakkola, 2008, 193794). This population-based case-control study included 653 cases and a random sample of 6,530 controls born in Taiwan between 2001 and 2003.

7.4.1.5. Infant Mortality

Many studies have identified strong associations between exposure to particles and increased risk of mortality in adults or the general population, including for short- and long-term exposure (Sections 6.5 and 7.6). Less evidence is available for the potential impact on infant mortality, although studies have been conducted in several countries. The results of these infant mortality studies are presented here with the other reproductive and developmental outcomes because it is likely that in vitro exposures contribute to this outcome. Both long-term and short-term exposure studies of infant mortality are included in this section. Results on PM and infant mortality includes a range of findings, with some studies finding associations and many statistically non-significant or null effects. Yet, more consistency is observed when results are divided into the type of health outcome based on the age of infant and cause of death.

An important question regarding the association between PM and infant mortality is the critical window of exposure during development for which infants are susceptible. Several age intervals have been explored: neonatal (<1 mo); infants (<1 yr); and postneonatal (1 mo-1 yr). Within these various age categories, multiple causes of deaths have been investigated, particularly total deaths and respiratory-related deaths. The studies reflect a variety of study designs, particle size ranges, exposure periods, regions, and adjustment for confounders.

Stillbirth

Only one study of stillbirths and PM was identified. A prospective cohort of pregnant women in Seoul, Korea from 2001 to 2004 was examined with respect to exposure to PM_{10} (Kim et al., 2007, 156642). Gestational age was estimated by the last menstrual period or by ultrasound. Whereas many of the previously discussed studies of PM and pregnancy outcomes were based on national registries, this study examined medical records and gathered individual information through interviews on socioeconomic condition, medical history, pregnancy complications, smoking, second-hand smoke exposure, and alcohol use. Mother's exposure to PM_{10} was based on residence for each month of pregnancy, each trimester defined as a three month period, and the 6 wk prior to death. Exposure was assigned by the nearest monitor. A 10 $\mu g/m^3$ increase in PM_{10} in the third trimester was associated with an 8% (95% CI: 2-14) increase in risk of stillbirth.

In São Paulo, Brazil, Poisson regression of stillbirth counts for the period 1991-1992 found that a 10 $\mu g/m^3$ increase in PM_{10} was associated with a 0.8% increase in stillbirth rates (Pereira et al., 1998, 007264). When other pollutants (NO_2, SO_2, CO, O_3) were included simultaneously in the model, the association did not remain. Stillbirths were defined as fetal loss at >28 wk of pregnancy age, weight >1,000 g, or length of fetus >35 cm.

Neonatal Mortality and Neonatal Respiratory Mortality, <1 Month

Studies on PM and neonatal mortality (<1 month) included a time-series analysis of PM_{10} for 4 yr of data (1998-2000) for São Paulo, Brazil (Lin et al., 2004, 095787). The analysis used daily counts of deaths from government registries and adjusted for temporal trend, day of the week, weather, and holidays. Findings indicated that a 10 $\mu g/m^3$ increase in PM_{10} was associated with a 1.71% (95% CI: 0.31-3.32) increase in risk of neonatal death.

A case-crossover study of 11 yr (1989-2000) in Southern California did not find an association between PM_{10} and neonatal deaths (Ritz et al., 2006, 089819). Quantitative results were not provided. The authors considered adjustment for season, county, parity, gender, prenatal care, and maternal age, education, and race/ethnicity.

These results add to previous work on PM and neonatal death, including studies identifying higher risk of neonatal mortality with higher TSP in the Czech Republic in an ecological analysis (Bobak and Leon, 1992, 044415) and case-crossover study (Bobak and Leon, 1999, 007678), and a

Poisson model study in Kagoshima City, Japan (Shinkura et al., 1999, 090050). An ecological study evaluated U.S. PM_{10} data for the year 1990 using long-term pollution levels in 180 U.S. counties (Lipfert et al., 2000, 004103). Analysis considered birth weight, sex, month of birth, location by state and county, prenatal care, and mother's race, age, educational level, marital status, and smoking status. County-level variables were included for socioeconomic status, altitude, and climate. Results indicate a 13.1% increase in neonatal mortality (95% CI: 4.4-22.6) per 10 $\mu g/m^3$ PM_{10} for non-low birth weight infants. Statistically significant associations were also observed considering all infants or low birth weight infants. However, higher levels of SO_2 were associated with lower risk of infant mortality. When sulfate and an estimate of non-sulfate particles were included in the regression simultaneously, associations were observed with non-sulfate particles and an inverse relationship with sulfate particles. Respiratory neonatal mortality was not associated with higher TSP in the Czech Republic case-control study (Bobak and Leon, 1999, 007678).

Infant Mortality and Infant Respiratory Mortality, <1Year

A literature search did not reveal new studies on PM and infant mortality (<1 year) since the previous PM AQCD. Previously conducted studies include a case-control study that reported associations between infant mortality and TSP levels over the period between birth and death for infants in the Czech Republic (Bobak and Leon, 1999, 007678). An ecological study evaluated U.S. PM_{10} data for the year 1990 using long-term pollution levels in 180 U.S. counties (Lipfert et al., 2000, 004103). The authors found a 9.64% (95% CI: 4.60-14.9) increase in risk of infant mortality for non-low birth weight infants per 10 $\mu g/m^3$ increase in PM_{10}, a 13.4% (95% CI: -10.3 to 43.5) increase in non-low birth weight respiratory-disease related deaths (ICD 9 460-519) and a 19.5% (95% CI: 0.07-42.8) increase in all non-low birth weight respiratory-related infant deaths (ICD 9 460-519, 769, 770).

Postneonatal Mortality and Postneonatal Respiratory Mortality, 1 Month–1 Year

Several studies have been conducted on PM and postneonatal mortality since the previous PM AQCD, including three from the U.S., one from Mexico, and three from Asia. Two case-control studies examined the risk of PM to postneonatal death in California. Research focused on Southern California for the period 1989-2000 linked birth and death certificates and considered PM_{10} 2 mo prior to death with adjustment for prenatal care, gender, parity, county, season, and mother's age, race/ethnicity, and education (Ritz et al., 2006, 089819). As previously noted, this study did not find an association between PM_{10} and neonatal mortality (<1 month), however an association was observed for post-neonatal mortality, with a 10 $\mu g/m^3$ increase in PM_{10} associated with a 4% (95% CI: 1-6) increase in risk. The exposure period of 2 wk before death was also considered, producing effect estimates of 5% (95% CI: 1-10) for the same PM_{10} increment. Even larger effect estimates were observed for those who died at ages 4-12 mo. When CO, NO_2, and O_3 were simultaneously included with PM_{10} in the model, the central estimate reduced to 2% for the 2-wk exposure period and 4% for the 2-mo exposure period, and both estimates lost statistical significance. The other case-control study of California considered $PM_{2.5}$ from 1999 to 2000 for infants born to mothers within five miles of a $PM_{2.5}$ monitoring station (Woodruff et al., 2006, 088758). Infants who died during the postneonatal period were matched to infants with date of birth within 2 wk and birth weight category. Exposure was estimated from the time of birth to death. Models considered parity and maternal race, education, age, and martial status. A 10 $\mu g/m^3$ increase in $PM_{2.5}$ was associated with a 7% (95% CI: -7 to 24) increase in postneonatal death

County-level PM_{10} and $PM_{2.5}$ for the first 2 mo of life for births in urban U.S. counties ($\geq$ 250,000 residents) from 1999 to 2002 were evaluated in relation to postneonatal mortality with GEE models (Woodruff et al., 2008, 098386). Births were restricted to singleton births with gestational age $\leq$ 44 wk, same county of residence at birth and death, and non-missing data on birth order, birth weight, and maternal race, education, and martial status. Higher levels of either PM metric were associated with higher risk of postneonatal mortality, with 4% (95% CI: -1 to 10) increase in mortality risk per 10 $\mu g/m^3$ in PM_{10} and 4% (95% CI: -2 to 11) increase in mortality risk for the same increment of $PM_{2.5}$. This work builds on a previous study of 86 U.S. urban areas from

1989 to 1991, finding a 4% (95% CI: 2-7) increase in postneonatal mortality per 10 μg/m^3 county-level PM_{10} over the first 2 mo of life (Woodruff et al., 1997, 084271).

In Ciudad Juarez, Mexico, a case-crossover approach was applied to data from 1997 to 2001 based on death certificates and the cumulative PM_{10} for the day of death and previous two days (Romieu et al., 2004, 093074). A case-crossover study of Kaohsiung, Taiwan from 1994 to 2000 compared the average of PM_{10} on the day of death and two previous days to PM_{10} in control periods a week before and week after death (Tsai et al., 2006, 090709). A similar approach was also applied to 1994-2000 data from Taipei, Taiwan, also using case-crossover methods for the lag 0-2 PM_{10} with referent periods the week before and after death (Yang et al., 2006, 090760). In these case-crossover studies, season was addressed through matching in the study design. A 10 μg/m^3 increase in PM_{10} was associated with a 2.0% (95% CI: -2.8 to 7.0) increase in the Mexico study, a 0.59 (95% CI: -15.0 to 18.8) increase in postneonatal death in the Kaohsiung study, and a 1.02% (95% CI: -13.2 to 17.6) increase in the Taipei study. A study in Seoul, South Korea from 1995 to 1999 used time-series approaches adjusted for temporal trend and weather, based on national death registries excluding accidental deaths (Ha et al., 2003, 042552). A 10 μg/m^3 increase in PM_{10} was associated with a 3.14% (95% CI: 2.16-4.14) increase in risk of death for postneonates.

A subset of the studies examining postneonatal mortality also considered the subset of postneonatal deaths from respiratory causes. These include the time-series study in South Korea, finding a 17.8% (95% CI: 14.4-21.2) increase in respiratory-mortality per 10 μg/m^3 increase in PM_{10} (Ha et al., 2003, 042552) and the case-crossover study in Mexico, for which the same increment in PM_{10} was associated with a 1.5% (95% CI: -14.1 to 13.0) decrease in risk (Romieu et al., 2004, 093074). Both California case-control studies identified associations, with a 5% (95% CI: 1-10) increase in risk in Southern California (Ritz et al., 2006, 089819) and 57.4% (95% CI: 7.0-132) increase in California per 10 μg/m^3 PM_{10} (Woodruff et al., 2006, 088758). The U.S. study found this increment in PM_{10} to be linked with a 16% (95% CI: 6.0-28.0) increase in respiratory postneonatal mortality, although effect estimates for $PM_{2.5}$ were not statistically significant (Woodruff et al., 2008, 098386). Earlier studies on respiratory-related postneonatal mortality include the study of 86 U.S. urban areas, finding statistically significant effects (Woodruff et al., 1997, 084271).

Sudden Infant Death Syndrome

Three studies examining the relationship between PM and sudden infant death syndrome (SIDS) have been published from 2002 onward. These studies examined infant mortality and were thereby discussed in this section previously. A case-control study over a 12-year period (1989 to 2000) matched 10 controls to deaths (cases) in Southern California (Ritz et al., 2006, 089819). A 10 μg/m^3 increase in PM_{10} the 2 mo prior to death was associated with a 3% (95% CI: -1 to 8) increase in SIDS. Adjusted for other pollutants (CO, NO_2, and O_3), the effect estimate reduced to 1% (95% CI: -5 to 7).

A case-control study, also based in California, found an OR of 1.008 (95% CI: 1.006-1.012) per 10 μg/m^3 increase in $PM_{2.5}$, considering a SIDS definition of ICD 10 R95 (Woodruff et al., 2006, 088758). Due to changes in SIDS diagnosis, another SIDS definition was explored for ICD 10 R99 in addition to ICD 10 R95. Under this SIDS definition, the effect estimate changed to 1.03 (95% CI: 0.79-1.35). The authors also examined whether the relationship between $PM_{2.5}$ and SIDS differed by season, finding no significant difference. PM_{10} and $PM_{10-2.5}$ were not associated with risk of SIDS; numerical results were not provided for these PM metrics. The third recent study of PM and SIDS examined U.S. urban counties from 1999 to 2002 (Woodruff et al., 2008, 098386). Statistically non-significant relationships were observed between SIDS and PM_{10} or $PM_{2.5}$ in the first 2 mo of life.

These studies add to earlier work, such as a U.S. study that found higher risk of SIDS with higher annual $PM_{2.5}$ levels, including in a separate analysis of normal birth weight infants (Lipfert et al., 2000, 004103), and a U.S. study identifying a 12% (95% CI: 7-17) increase in SIDS risk per 10 μg/m^3 in PM_{10} for the first 2 mo of life for normal weight births (Woodruff et al., 1997, 084271). A study based on Taiwan found higher SIDS risk with lower visibility (Knöbel et al., 1995, 155905), whereas a 12-city Canadian time-series study identified no significant associations (Dales et al., 2004, 087342).

Deaths by SIDS were identified by different methods in the studies, partly due to transition from ICD 9 to ICD 10 codes, but also due to different choices within the research design. Two studies examined multiple approaches (ICD 10 R95, ICD 10 R95 and R99) (Woodruff et al., 2006,

088758; Woodruff et al., 2008, 098386), and other studies investigated ICD 9 798.0 and ICD 10 R95 (Ritz and Wilhelm, 2008, 156914), ICD 9 798.0 (Woodruff et al., 1997, 084271), ICD 9 798.0 and 799.0 (Knöbel et al., 1995, 155905), as well as a sudden unexplained death of infant <1 year for which an autopsy did not identify a specific cause of death (Dales et al., 2004, 087342). These variations in the definition of health outcomes add to differences in populations and study designs.

Although some findings indicate a potential effect of PM on risk of SIDS, with the strongest evidence perhaps from the case-control study in California (Woodruff et al., 2006, 088758), others do not find an effect or observe an uncertain association. For the relationship between PM and SIDS, a 2004 review article concluded consistent evidence exists compared to evidence for other infant mortality effects (Glinianaia et al., 2004, 087898), whereas other reviews found weaker or insufficient evidence (Heinrich and Slama, 2007, 156534). Another review concluded that the scientific literature on air pollution and SIDS suggests an effect, but that further research is needed to draw a conclusion (Tong and Colditz, 2004, 087883).

Considerations for Comparisons across Studies

Comparison of results across studies can be challenging due to several issues, including differences in methodologies, populations and study areas, pollution levels, and the exposure timeframes used. Given the large variation in study designs, the methods to address potential confounders vary. For example, weather and season were addressed in the case-control studies by matching, in the time-series study through non-linear functions of temperature and temporal trend, and in the ecological study through county-level variables. All studies included consideration of seasonality and weather. Researchers used different definitions of respiratory-related deaths, including ICD 9 460-519 (Bobak and Leon, 1999, 007678; Lipfert et al., 2000, 004103); ICD 9 460-519, 769-770 (Lipfert et al., 2000, 004103); ICD 9 460-519, 769, 770.4, 770.7, 770.8, 770.9, and ICD 10 J00-J98, P22.0, P22.9, P27.1, P27.9, P28.0, P28.4, P28.5, and P28.9 (Ritz et al., 2006, 089819); and ICD 9 460-519 and ICD 10 J00-J99 for any cause on death certificate (Romieu et al., 2004, 093074); ICD 10 J00-99 and P27.1 excluding J69.0 (Woodruff et al., 2006, 088758; Woodruff et al., 2008, 098386); and ICD 9 460-519 (Woodruff et al., 1997, 084271).

Socioeconomic conditions were included at the individual level, typically maternal education, in many studies (e.g., Bobak and Leon, 1999, 007678; Ritz and Wilhelm, 2008, 156914; Ritz et al., 2006, 089819; Woodruff et al., 1997, 084271; Woodruff et al., 2006, 088758) and at the community-level in others (e.g., Bobak and Leon, 1992, 044415; Penna and Duchiade, 1991, 073325) or for both individual and community-level data (e.g., Lipfert et al., 2000, 004103). The time-series approach is unlikely to be confounded by socioeconomic and other variables that do not exhibit day-to-day variation. Similarly, case-crossover methods use each case as his/her own control, thereby negating the need for individual-level confounders such as socioeconomic status (e.g., Romieu et al., 2004, 093074; Tsai et al., 2006, 090709; Yang et al., 2006, 090760). All studies published after 2001 incorporated individual-level socioeconomic data or were of case-crossover or time-series design. One study specifically examined whether socioeconomic status modified the PM and mortality relationship, dividing subjects into three socioeconomic strata based on the ZIP code of residence at death (Romieu et al., 2004, 093074). This work, based in Mexico, found that at lower socio-economic levels the association between PM_{10} and postneonatal mortality increased. Although the overall association showed higher risk of death with higher PM_{10} with statistical uncertainty, for the lowest socio-economic group, a 10 $\mu g/m^3$ increment in cumulative PM_{10} over the 2 days before death was associated with a 60% (95% CI: 3-149) increase in postneonatal death. A trend of higher effect for lower socio-economic condition is observed in all 3 lag structures.

Studies differ in terms of the time frame of pregnancy that was used to estimate exposure. Exposure to PM for infant mortality (<1 yr) was estimated as the levels between birth and death (Bobak and Leon, 1999, 007678), annual community levels (Lipfert et al., 2000, 004103; Penna and Duchiade, 1991, 073325) and the 3-5 days prior to death (Loomis et al., 1999, 087288). For neonatal deaths, exposure timeframes considered were the time between birth and death (Bobak and Leon, 1992, 044415; Bobak and Leon, 1999, 007678), annual levels (Bobak and Leon, 1999, 007678; Lipfert et al., 2000, 004103), monthly levels (Shinkura et al., 1999, 090050), the same day concentrations (Lin et al., 2004, 095787), and the 2 mo or 2 wk prior to death (Ritz et al., 2006, 089819). Postneonatal mortality was associated with PM concentrations based on annual levels (Bobak and Leon, 1992, 044415; Lipfert et al., 2000, 004103), between birth and death (Bobak and

Leon, 1999, 007678; Woodruff et al., 2006, 088758), 2 mo before death (Ritz et al., 2006, 089819), the first 2 mo of life (Woodruff et al., 1997, 084271; Woodruff et al., 2006, 088758), the day of death (Ha et al., 2003, 042552), and the average of the same day as death and previous 2 days (Romieu et al., 2004, 093074; Tsai et al., 2006, 090709; Yang et al., 2006, 090760). Thus, no consistent window of exposure was identified across the studies.

PM_{10} concentrations were highest in South Korea (69.2 $\mu g/m^3$) (Ha et al., 2003, 042552) and Taiwan (81.45 $\mu g/m^3$) (Tsai et al., 2006, 090709), and lowest in the U.S. (29.1 $\mu g/m^3$) (Woodruff et al., 2008, 098386) and Japan (21.6 $\mu g/m^3$) (Shinkura et al., 1999, 090050). All studies used community-level exposure information based on ambient monitors, as opposed to exposure measured at the individual level (e.g., subject's home) or personal monitoring.

Given similar sources for multiple pollutants (e.g., traffic), disentangling the health responses of copollutants is a challenge in the study of ambient air pollution. Several studies examined multiple pollutants, most by estimating the effect of different pollutants through several univariate models. Some studies noted the difficulty of separating PM effects from those of other pollutants, but noted stronger evidence for particles than other pollutants (Bobak and Leon, 1999, 007678). A few studies applied copollutant models by including multiple pollutants simultaneously in the same model. Effect estimates for the relationship between PM_{10} and neonatal deaths in São Paulo were reduced to a null effect when SO_2 was incorporated (Lin et al., 2004, 095787). Associations between PM_{10} and postneonatal mortality or respiratory postneonatal mortality remained but lost statistical significance in a multiple pollutant model with CO, NO_2, and O_3 (Ritz et al., 2006, 089819).

Several review articles in recent years have examined whether exposure to PM affects risk of infant mortality, generally concluding that more consistent evidence has been observed for postneonatal mortality, particularly from respiratory causes (Bobak and Leon, 1999, 007678; Heinrich and Slama, 2007, 156534; Lacasaña et al., 2005, 155914; Sram et al., 2005, 087442). In one review authors identified 14 studies on infant mortality and air pollution and determined that studies on PM and infant mortality do not provide consistent results, although more evidence was present for an association for some subsets of infant mortality such as postneonatal respiratory-related mortality (Bobak and Leon, 1999, 007678). The relationship between PM and postneonatal respiratory mortality was concluded to be causal in one review (Sram et al., 2005, 087442), and strong and consistent in another (Heinrich and Slama, 2007, 156534). Meta-analysis using inverse-variance weighting of PM_{10} studies found that a 10 $\mu g/m^3$ increase in acute PM_{10} exposure was associated with 3.3% (95% CI: 2.4-4.3) increase in risk of postneonatal mortality, whereas the same increment of chronic PM_{10} exposure was linked with a 4.8% (95% CI: 2.2-7.2) increase in postneonatal mortality and a 21.6% (95% CI: 10.2-34.2) increase for respiratory postneonatal mortality (Lacasaña et al., 2005, 155914).

Studies that examined multiple outcomes and ages of death allow a direct comparison based on the same study population and methodologies, thereby negating the concern that inconsistent results are due to underlying variation in population, approaches, etc. In this review, one study, based in Southern California identified no association for neonatal effects (numerical results not provided) but statistically significant results for postneonatal mortality (Ritz et al., 2006, 089819). Figure 7-5compares risk for the postneonatal period for respiratory and total mortality. In six of the seven studies, higher effect estimates were observed for respiratory-related mortality. Results from the neonatal period found higher effects for total mortality compared to respiratory mortality (Bobak and Leon, 1999, 007678) and the reverse for a study examining infant mortality (Lipfert et al., 2000, 004103). Thus, there exists evidence for a stronger effect at the postneonatal period and for respiratory-related mortality, although this trend is not consistent across all studies.

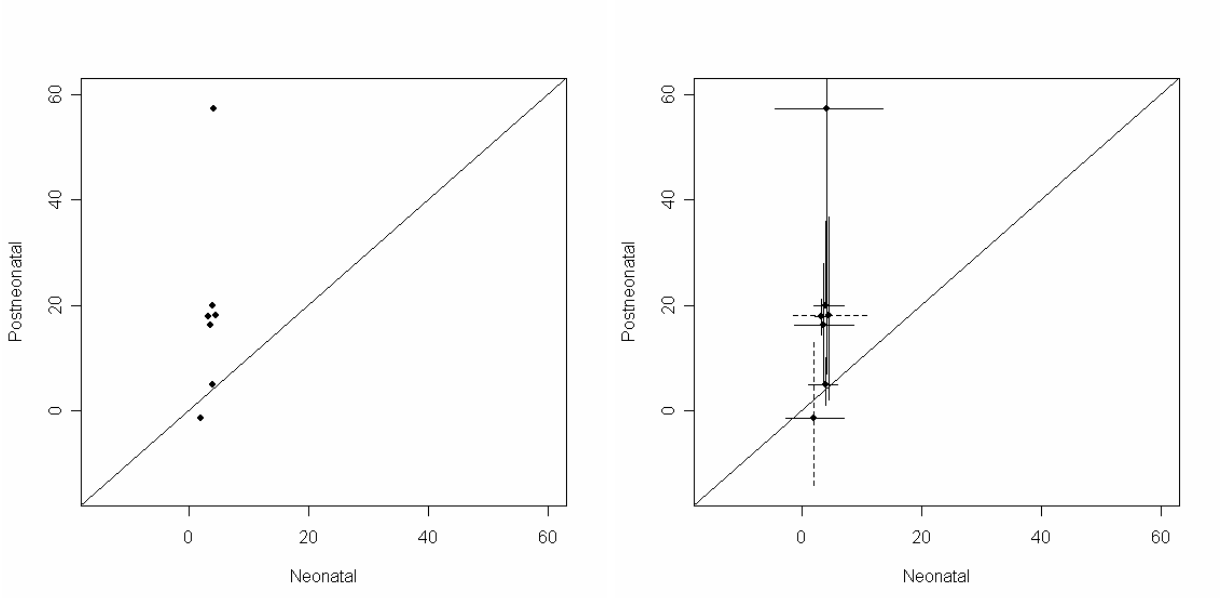


Figure 7-5. Percent increase in postneonatal mortality per 10 µg/m^3 in PM_{10}, comparing risk for total and respiratory mortality. Panel a (left) provides central estimates; panel b (right) also adds the 95% intervals. The points reflect central estimates and the lines the 95% intervals. Solid lines represent statistically significant effect estimates; dashed lines represent non-statistically significant estimates.[1]

7.4.1.6. Decrements in Sperm Quality

Limited research conducted in the Czech Republic on the effect of ambient air pollution on sperm production has found associations between elevated air pollution and decrements in proportionately fewer motile sperm, proportionately fewer sperm with normal morphology or normal head shape, proportionately more sperm with abnormal chromatin (Selevan et al., 2000, 012578), and an increase in the percentage of sperm with DNA fragmentation (Rubes et al., 2005, 078091). These results were not specific to PM, but for exposure to a high-, medium- or low-polluted air mixture. Similarly, in Salt Lake City, Utah, $PM_{2.5}$ was associated with decreased sperm motility and morphology (Hammoud et al., 2009, 192156). Research in Los Angeles, California examined 5,134 semen samples from 48 donors in relation to ambient air pollution measured 0-9, 10-14, 70-90 days before semen collection over a 2-yr period (1996-1998). Ambient O_3 during all exposure periods had a significant negative correlation with average sperm concentration, and no other pollutant measures were significantly associated with sperm quality parameters, or presented quantitatively (Sokol et al., 2006, 098539).

7.4.2. Toxicological Studies

This section summarizes recent evidence on reproductive health effects reported with exposure to ambient PM; no evidence was presented in this area in the 2004 PM AQCD. Studies from different toxicological rodent models allow for investigation of specific mechanisms and modes of

[1] Studies included are Bobak and Leon (1999, 007678), Ha et al. (2003, 042552), Ritz et al. (2006, 089819), Romieu et al. (2004, 093074), Romieu et al. (2008, 156922), Woodruff et al. (1997, 084271), Woodruff et al. (2006, 088758). Findings from Bobak and Leon (1999, 007678) were based on TSP and were converted to PM_{10} estimates assuming $PM_{10}/TSP = 0.8$ as per summary data in the original article (Bobak and Leon, 1999, 007678). Findings from Woodruff et al. (1997, 084271) for respiratory-related mortality were based on non-low birth weight infants. Results for Woodruff et al. (2006, 088758) were based on $PM_{2.5}$ and were converted to PM_{10} assuming $PM_{2.5}/PM_{10} = 0.6$.

action for reproductive changes. Emphasis is placed here on results from different windows of development, i.e., exposure in utero, neonatally or as an adult can affect reproductive outcomes as an adult. In addition, studies evaluating whether fertility is affected in female and/or male animals by a similar exposure, and how exposures are transmitted to the fertility of the F_1 offspring, are summarized. Hormonal changes which can lead to decreased sperm count or changes in the estrous cycle are also of interest. Studies of pregnancy losses and placental sufficiency are also reported. Most recently, the role of environmental chemicals in shifting sex ratios (also seen in epidemiologic studies) and in affecting heritable DNA changes have become outcomes of interest.

7.4.2.1. Female Reproductive Effects

Urban Air

Windows of exposure are important in determining reproductive success as an adult. Exposure as a neonate may have a drastically different impact than does a similar adult exposure. To test this, female BALB/C mice were exposed to ambient air in Sao Paulo as neonates or as adults and then were bred to non-exposed males (Mohallem et al., 2005, 088657). Ambient concentrations of the pollutants CO, NO_2, PM_{10}, and SO_2 were 2.2 ± 1.0 ppm, 107.8 ± 42.3 μg/m^3 , 35.5 ± 12.8 μg/m^3, and 11.2 ± 5.3 μg/m^3, respectively. They reported decreased fertility in animals exposed as newborns, but not in adult-exposed female BALB/c mice. There were a significantly higher number of liveborn pups from dams housed in filtered chambers (PM and gaseous components removed) versus animals exposed to ambient air as newborns. There was also a higher incidence of implantation failures in dams reared as newborns in polluted chambers. Sex ratio, number of pregnancies per group, resorptions, fetal deaths, and fetal placental weights did not differ significantly by exposure group. Thus, in these studies, exposure to ambient air pollution affected future reproductive success of females if they were exposed as neonates and not if exposed as adults.

Diesel Exhaust

Significant work has been done in male rodent models to determine the effect of PM exposure on reproductive outcomes, with fewer studies conducted using female rodents. Tsukue et al. (2004, 096643) exposed pregnant C57-BL mice to DE (0.1 mg/m^3) or to clean air (controls) for 8 h/day from GD2-13. The concentration of the gaseous materials including NO, NO_X, NO_2, CO and SO_2 are 2.2 ± 0.34 ppm, 2.5 ± 0.34 ppm, 0.0 ppm, 9.8 ± 0.69 ppm, and <0.1 ppm (not detectable), respectively. At GD14 female fetuses were collected for analysis of mRNA for two genes involved in sexual differentiation (Ad4BP-1/SF-1 and MIS), and found no significant changes. Work by Yoshida et al. (2006, 097015) showed changes in these two transcripts in male ICR fetuses exposed to similar concentrations of DE, albeit with different daily durations of exposure. Further work by Yoshida et al. (2006, 097015) showed that of three mouse strains tested, ICR male fetuses were the most sensitive to DE-dependent changes in these two genes. Nonetheless, strain sensitivity to DE particles may also differ by sex. Thus, it appears that female mice exposed in utero to DE show a lack of response at the mRNA level of MIS or Ad4bP-1/SF-1, important genes in male sexual differentiation that showed DE-dependent changes in male pups from dams exposed in utero. Female fetuses have shown a decrease in BMP-15, which is related to oocyte development (Tsukue et al., 2004, 096643).

A sensitive measure of androgenic activity in male rodents is anogenital distance (AGD), i.e., decreased AGD is seen with exposure to anti-androgenic environmental chemicals, the phthalates (Foster et al., 1980, 094701; Foster et al., 2001, 156442). To assess the role of DE exposure on reproductive success and anti-androgenic effects on offspring, Tsukue et al. (2002, 030593) exposed 6 week-old female C57-Bl mice to 4 mo of DE (0.3, 1.0, or 3.0 mg/m^3; PM MMAD of 0.4 μm) or filtered air. DE-exposed estrous females had significantly decreased uterine weight (1.0 mg/m^3). Some of the DE-exposed females were bred to unexposed males and DE-exposure led to increased, albeit not significantly increased, rates of pregnancy loss in mated females (up to 25%). Offspring were weighed after birth and decreases in body weight were observed at 6 and 8 wk (males and females, 1.0 and 3.0 mg/m^3) and 9 wk (females, 1.0 and 3.0 mg/m^3). Anogenital distance was decreased in 70-day old DE-exposed male offspring (0.3 mg/m^3). In female offspring at 70 days of

age, lower organ weights (adrenals, liver, and thymus) were observed (1.0 mg/m^3) compared to controls; thymus weight of the 0.3 mg/m^3 females was also lower at 70 days. Crown to rump length in females from dams exposed to DE (1.0 and 3.0 mg/m^3) was less than the control group. In conclusion, adult exposure to DE led to maternal-dependent reproductive changes that affected outcomes in offspring that manifested as decreased pup body weight, anti-androgenic effects like decreased AGD and decreased organ weight (which may have been confounded by changes in body weight because weights were not reported as relative organ weights).

7.4.2.2. Male Reproductive Effects

Diesel Exhaust

Studies were performed to determine PM-dependent strain sensitivity of the male reproductive tract using male steroidogenic enzymes as the model pathway. Three strains of pregnant mice (ICR, C57Bl/6J or ddY mice) were continuously exposed to DE at 0.1 mg/m^3 via inhalation or clean air over gestational days 2-13 (Yoshida et al., 2006, 156170). At GD14, dams were euthanized and fetuses were collected. Male fetuses were collected from each dam for mRNA analysis of genes related to male gonad development including Mullerian inhibiting substance (MIS; crucial for sexual differentiation including Mullerian duct regression in males), steroid transgenic factor (Ad4BP/SF-1, an enzyme in the testosterone synthesis pathway), cytochrome P450 cholesterol side chain cleavage enzyme (P450scc), and other steroidogenic enzymes [17β-hydroxysteroid dehydrogenase (HSD), cytochrome P450 17-α-hydroxylase (P450c17), and 3-βhydroxysteroid dehydrogenase (3βHSD)]. There were significant decreases in MIS (ICR and C57BL/6 mice) and Ad4BP/SF-1 (ICR mice) compared to the control groups. The ddY strain demonstrated no changes in Ad4BP/SF-1 or MIS, which may be due to marked changes in 3β-hD expression compared to non-DE exposed controls. From these studies, it appears that mouse strains with in utero exposure to DE show differential sensitivity in gonadal differentiation genes (mRNA) expression in male offspring; ICR are the most sensitive, followed by C57BL/6, with ddY mice being the least sensitive.

Yoshida et al. (2006, 097015) also monitored changes in the male reproductive tract after in utero exposure to DE. Timed-pregnant ICR dams were exposed during gestation (2 days post-coitus [dpc]-16 dpc) to continuous DE (0.3, 1.0 or 3.0 mg/m^3) or clean air. The reproductive tracts of male offspring were monitored at 4 wk postnatally. These pups received possible continued exposure through lactation as dams were exposed to DE during gestation and nursed pups. Exposure to 0.3 mg/m^3 of DE had no effect on male reproductive organ weight or serum testosterone. The intermediate concentration of 1.0 mg/m^3 induced increases in serum testosterone. Exposure to the higher concentration (1.0 and 3.0 mg/m^3) of DE led to significant increases in reproductive gland weight (testis, prostate, and coagulating gland). The organ weights are presented as absolute numbers and not adjusted for body weight, which is sometimes problematic for complete representation of hormonal changes, as body weight may confound absolute organ weight changes. Transcripts relating to male sexual differentiation (MIS and AD4BP/SF-1, 1.0 and 3.0 mg/m^3) were also significantly decreased. Sexual differentiation is a tightly regulated process and these changes in transcription may lead to changes that can affect genitalia development.

The effects of DE exposure on male spermatogenesis have also been demonstrated. Exposure of pregnant ICR mice to DE (2-16 dpc continuous inhalation exposure to 1.0 mg/m^3 or filtered clean air) led to impaired spermatogenesis in offspring (Ono et al., 2007, 156007). Male offspring were followed at PND 8, 16, 21 (3 wk), 35 (5 wk) and 84 (12 wk). After 16 dpc, but before termination of the study, all of the animals were transferred to a regular animal care facility and received clean air exposure until the termination of the study. No cross fostering was performed in this experiment, so pups that were born to DE-exposed dams were also nursed on these dams and may have received lactational exposure to DE. The gaseous components of the diluted DE included NO, NO_2, SO_2, and CO_2 at concentrations of 11.75 ± 1.18, 4.62 ± 0.36, 0.21 ± 0.01, and 4922 ± 244 ppm, respectively. Body weight was significantly depressed at PNDs 8 and 35. Accessory gland relative weight was significantly increased at PND8 and PND16 only. Serum testosterone was significantly decreased at 3 wk and was significantly increased at 12 wk. At 5 and 12 wk, daily sperm production (DSP) was significantly decreased. FSH receptor and StAR mRNA levels were significantly increased at 5 and 12 wk, respectively. Relative testis weight and relative epididymal weight were unchanged at all

time points. Histological changes showed sertoli cells with partial vacuolization and a significant increase in testicular multinucleated giant cells in the seminiferous tubules of DE-exposed animals compared to control. This study indicates that in utero exposure to DE had effects on spermatogenesis in offspring at the histological, hormonal and functional levels.

In utero exposure to DE and its effect on adult body weight, sex ratio, and male reproductive gland weight was measured by Yoshida et al. (2006, 097015). Pregnant ICR mice were exposed by inhalation to DE (0.3, 1.0 or 3.0 mg/m^3) or clean air from 2 dpc to 16 dpc. Pups were allowed to nurse in clean air on exposed dams until weaning and at PND28, male pups were sacrificed. At this time, serum testosterone and pup reproductive gland weight was determined. Significant increases in relative reproductive organ weights were reported at 1.0 and 3.0 mg/m^3 for the seminal vesicle, testis, epididymis, coagulating gland, prostate and liver. Male pup serum testosterone was significantly increased at 1.0 mg/m^3. Mean testosterone positively correlated with testis weight, DSP, aromatase and steroidogenic enzyme message levels (P450cc, c17 lyase, and P450 aromatase). Sex ratio did not differ in DE-exposed animals versus control. Male pup body weight of DE-exposed animals was significantly increased at PND28 (1.0 and 3.0 mg/m^3). These studies show that in utero DE-exposure led to increased serum testosterone and increased reproductive gland weight in male offspring early in life.

The effects of DE on murine adult male reproductive function were studied by exposing ICR male mice (6 wk of age) to DE (clean air control, 0.3, 1.0 or 3.0 mg/m^3) for 12 h/day for 6 mo with another group receiving a 1-mo recovery of clean air post-exposure (Yoshida and Takedab, 2004, 097760). After 6 mo of DE exposure, there was a concentration-dependent increase in degeneration of seminiferous tubules and a decrease in DSP/g of testis tissue. After 6 mo exposure to DE particles plus 1 mo of recovery in clean air, significant decreases remained in DSP at the two highest concentrations. The effect of ingestion of deposited PM on the fur with grooming cannot be ruled out as a possible exposure pathway in this experiment.

To expand on PM-dependent changes in spermatogenesis, an eloquent DE-exposure model was designed to determine if PM or the gaseous phase of DE was responsible for changes in sperm production in rodents (Watanabe, 2005, 087985). Pregnant dams (F344/DuCrj rats) exposed to DE (6 h/day exposure to 0.17 or 1.71 mg/m^3; <90% of PM less than 0.5 μm; NO_2 concentrations 0.10 and 0.79 ppm, respectively) or filtered air (removing PM only, low concentration filtered air and high concentration filtered air) from GD7 to parturition produced adult male offspring with a decreased number of sertoli cells and decreased DSP (PND 96) when compared to control mice exposed to clean air. The concentrations of NO_2 for the low and high filtered exposure groups were 0.1 and 0.8 ppm, respectively. Because both PM-filtered and DE-exposure groups showed the same outcomes, the effects are likely due to gaseous components of DE.

Motorcycle Exhaust

Adult male (8-wk old) Wistar rats were exposed to motorcycle exhaust (ME) for 1 h in the morning and 1 h in the afternoon (5 day/wk) at 1:50 dilution for 4 wk (group A), 1:10 dilution for 2 wk (group B) or 4 wk (group C), or to clean air (Huang et al., 2008, 156574). After 4 wk of exposure, both exposed groups had significantly decreased body weight compared to the control group. All three ME exposure groups showed a decreased number of spermatids in the testis. Both 1:10 exposure groups also demonstrated decreased caudal epididymal sperm counts. Group C had significant decreased testicular weight, decreased mRNA expression for the cytochrome P450 substrate 7-ehtoxycoumarin O-de-ethylase, and increased IL-6, IL-1β, and COX-2 mRNA levels. Decreased protein levels of the antioxidant, superoxide dismutase, and increased IL-6 protein were reported for group C when compared to control. In addition, serum testosterone was significantly decreased in group C. Co-treatment with the antioxidant vitamin E resulted in partial attenuation of serum testosterone levels and caudal epididymal sperm counts, and returned IL-6, IL-1β, and COX-2 ME exposure-dependent message levels to baseline. The glutathione antioxidant system and lipid peroxidation were unchanged. In conclusion, male animals exposed to ME showed significant decrements in body weight, spermatid number, and serum testosterone with an increase in inflammatory cytokines. Vitamin E co-treatment with ME-exposure led to an attenuation of inflammation and a partial rescue of testosterone levels and sperm numbers.

Summary of Toxicological Study Findings for Male Reproductive Effects

In summary, laboratory animals exposed to DE in utero or as adults manifest with abnormal effects on the male reproductive system. In utero exposure to DE induced increased reproductive gland weight and increased serum testosterone in early life (PND28), which may lead to early puberty (albeit not measured in this study). With similar in utero DE exposures, later life outcomes include decreased DSP, aberrant sperm morphology, and hormonal changes (testosterone and FSHr decrements). Chronic exposure of adult mice to DE also induced decreased DSP and seminiferous tubule degeneration. DE-dependent effects on male reproductive function have been reported in multiple animal models, with only one model separating exposure based on particulate versus gaseous components. DE and filtered air (gaseous phase only) exposure in utero induced sertoli cell and DSP decrements in both groups, indicating that the gaseous phase of DE was causative. Adult male rats exposed to ME manifested with decreased spermatid number, serum testosterone, and an increase in inflammatory cytokines. Significant effects on the male reproductive system have been demonstrated after exposure to ambient PM sources (DE or ME). Nonetheless, these models often include a complex mixture of gaseous component and PM exposure, which makes interpreting the contribution from PM alone difficult.

7.4.2.3. Multiple Generation Effects

Urban Air

Veras et al. (2009, 190496) investigated pregnancy and female reproductive outcomes in BALB/c female mice exposed to ambient air or PM-filtered ambient air at one of two different time periods (before conception and during pregnancy) near an area of high traffic density in Sao Paulo, Brazil. Exposures were 27.5 and 6.5 $\mu g/m^3$ $PM_{2.5}$ for ambient and PM-filtered air chambers, respectively, with 101 $\mu g/m^3$ NO_2, 1.81 $\mu g/m^3$ CO, and 7.66 ppm SO_2 in both chambers. Two groups of 2nd generation (G2) nulliparous female mice were continuously exposed from birth. Estrous cyclicity and ovarian follicle classification were followed at PND60 (reproductive maturation) in one group. A further group was subdivided into four groups by exposures during pregnancy following reproductive capability and pregnancy outcomes of the G2 mice. Animals exposed to ambient air versus PM-filtered air had an extended time in estrous and thus, a reduction in the number of cycles during the study period. The number of antral follicles was significantly decreased in the ambient air versus the PM-filtered air animals. Other follicular quantification (number of small, growing or preovulatory follicles) showed no differences between the two chambers. There was an increase in the time necessary for mating, a decrease in the fertility index, and an increase in the pregnancy index in the ambient air group versus the PM-filtered group. Specifically, in the ambient air groups, there was a significant increase in rate of the post-implantation loss in G1 and G2 groups. However, there was no statistically significant change in number of pups in the litter. Fetal weight was decreased in all treatment groups (ambient air groups G1 and G2, and PM-filtered G2) when compared to the PM-filtered G1 group or animals raised entirely in filtered air, showing that fetal weight was affected by both pre-gestational and gestational PM exposure.

PM exposure prior to conception is associated with increased time in estrous, which in other animal models can be related to ovarian hormone dysfunction and ovulatory problems. These estrous alterations can contribute to fecundity issues. There was no significant difference in number of preovulatory follicles in the above model, but there was a statistically significant decrease in the number of antral follicles (Veras et al., 2009, 190496). Antral follicles are the last stage in follicle development prior to ovulation, and a decrease in antral follicle number can be related to premature reproductive senescence, premature ovarian failure, or early menopause, which were not followed in this study.

In this study (Veras et al., 2009, 190496), the males that were used to generate the G1 and G2 groups were also exposed to ambient air or PM-filtered ambient air, and thus the reproductive contribution of these males to the overall fertility and mating changes in the females cannot be totally eliminated as a possible confounder to the observed effects. Thus, these effects are hard to differentiate as male- or female-dependent and likely indicate a general loss of reproductive fitness. Interestingly, both pre- and gestational exposure to ambient air induced a significant loss in post-

implantation of fetuses and this may be related to placental insufficiency as has been described in other work by this lab (Veras et al., 2008, 190493).

7.4.2.4. Receptor Mediated Effects

Arylhydrocarbon Receptor (AhR)

Diesel Exhaust Particles

The AhR is often activated by chemicals classified as endocrine disrupting compounds (EDCs), exogenous chemicals that behave as hormonally active agents, disrupting the physiological function of endogenous hormones. DE particles are known to activate the AhR. A recent study by Izawa et al. (2007, 190387) showed that certain polyphenols (quercetin from the onion) and food extracts (Ginkgo biloba extract) are able to attenuate DE particle-dependent AhR activation when measured with the Ah-Immunoassay, thus possibly attenuating the EDC activity of DE particles.

7.4.2.5. Developmental Effects

Sex Ratio

Urban Air

A correlation between PM_{10} exposure and a decrease in standardized sex ratios (SSRs) has been reported in humans exposed to air pollution (Lichtenfels et al., 2007, 097041; Wilson et al., 2000, 010288), with fewer numbers of male births reported. To understand this shift, two groups (control and exposed) of male Swiss mice were housed concurrently in Sao Paulo and received either ambient air exposure or filtered air (chemical and particulate filtering) from PND10 for 4 mo (Lichtenfels et al., 2007, 097041). Filtration efficiency for $PM_{2.5}$, CB, and NO_2 inside the chamber was found to be 55%, 100%, and 35%, respectively. After this exposure, non-exposed females were placed in either chamber to mate. After mating, the males were sacrificed and testes collected; males exposed to ambient air showed decreased testicular and epididymal sperm counts, decreased total number of germ cells, and decreased elongated spermatids, but no significant change in litter size. Females were housed in the chambers and sacrificed on GD19 when the number of pups born alive and the sex ratio were obtained. There was a significant decrease in the SSR for pups born after living in the ambient air-exposed chamber compared to the filtered chamber. In this study, a shift in SSR has been shown for both humans and rodents exposed to air pollution, but other studies with DE exposure (Yoshida et al., 2006, 156170) or ambient air in Sao Paulo (Mohallem et al., 2005, 088657) showed no changes in rodent sex ratio. Possible exposure to PM and other components of ambient air via ingestion during grooming cannot be ruled out in this rodent model.

Immunological Effects: Placenta

Diesel Exhaust

Placental insufficiency can lead to the loss of a pregnancy or to adverse fetal outcomes. DE-exposure has been shown to induce inflammation in various models. Fujimoto et al. (2005, 096556) assessed cytokine/immunological changes of DE-dependent inhalation exposure on the placenta during pregnancy. Pregnant Slc:CR mice were exposed to DE (0.3, 1.0, or 3.0 mg/m^3; PM MMAD of 0.4 µm) or clean air from 2 to 13 dpc and dams, placenta, and pups were collected at 14 dpc. There was a significant increase in the number of absorbed placentas in DE-exposed animals (0.3

and 3.0 mg/m^3) with a significant decrease in the number of absorbed placentas in DE-exposed animals at the middle concentration (1.0 mg/m^3). Absorbed placentas from DE exposed mice had undetectable levels of CYP1A1 and twofold increases in TNF-α; CYP1A1 placental mRNA from healthy placentas of DE-exposed mice was unchanged versus control. IL-2, IL-5, IL-12α, IL-12β and GM-CSF mRNA significantly increased in placentas of DE-exposed animals (0.3 and 3.0 mg/m^3). Fujimoto et al. (2005, 096556) reported DE-induced significant increases in multiple inflammatory markers in the placenta with significant increases in the number of absorbed placentas.

Immunological Effects: Asthma

Model Particles

In utero exposure may confer susceptibility to PM-induced asthmatic responses in offspring. Exposure of pregnant BALB/c mice to aerosolized ROFA leachate by inhalation or to DE particles intranasally increases asthma susceptibility to their offspring (Fedulov et al., 2008, 097482; Hamada et al., 2007, 091235). The offspring from dams exposed for 30 min to 50 mg/mL ROFA 1, 3, or 5 days prior to delivery responded to OVA immunization and aerosol challenge with airway hyperreactivity and increased antigen-specific IgE and IgG1 antibodies (Hamada et al., 2007, 091235). Airway hyperreactivity was also observed in the offspring of dams intranasally instilled with 50 µg of DE particles or TiO_2, or 250 µg CB, indicating that the same effect could be demonstrated using relatively "inert" particles (Fedulov et al., 2008, 097482). Pregnant mice were particularly sensitive to exposure to DE or TiO_2 particles, and genetic analysis indicated differential expression of 80 genes in response to TiO_2 in pregnant dams. Thus pregnancy and in utero exposure may enhance responses to PM, and exposure to even relatively inert particles may result in offspring predisposed to asthma.

Placental Morphology

Urban Air

Exposure to ambient air pollution during pregnancy is associated with reduced fetal weight in both human and animal models. The effect of particulate urban air pollution on the functional morphology of the mouse placenta was explored by exposing second generation mice in one of four groups to urban Sao Paulo air (PM was 67% $PM_{2.5}$, mainly of vehicular origin) or filtered air (Veras et al., 2008, 190493). Experimental design was: group F-F comprised of mice that were raised in filtered air chambers and completed pregnancy in filtered air chambers; group F-nF raised in filtered air and pregnant in ambient air; group nF-nF raised and completed pregnancy in non-filtered air chambers; and group nF-F mice raised in ambient air and received filtered air during pregnancy. Mean $PM_{2.5}$ concentrations in the F and nF chambers were 6.5 and 27.5 µg/m^3, respectively. Exposure was from PND20-PND60. After this exposure, the animals were mated and then maintained in their respective chambers during pregnancy. Pregnancy was terminated at GD8 (near term) with placentas and fetuses collected for analysis.

Exposure to ambient PM pre-gestationally or gestationally led to significantly smaller fetal weight (total litter weight). Pregestational exposure to ambient air induced significant increases in fetal capillary surface area and total mass-specific conductance, but this may be explained by reduced maternal/dam blood space and diameters. Gestational exposure to non-filtered air was associated with reduced volume, diameter (caliber) and surface area of maternal blood space with compensatory greater fetal capillary surface and oxygen diffusion conduction rates. Intravascular barrier thickness, a quantitative relationship between trophoblast volume and the combined surfaces of maternal blood spaces and fetal capillaries, was not reduced with ambient air exposure. This study provides evidence that fetal/placental circulatory adaptation to maternal blood deficits after ambient PM exposure may not be sufficient to overcome PM-dependent birth weight deficits in mice exposed to ambient air, with the magnitude of this effect greater in the gestationally-exposed groups.

Placental Weights and Birth Outcomes

Urban Air

Pregnant female Swiss mice were exposed to ambient air (Sao Paulo) or filtered air over various portions of gestation to determine if there was an association between fetal or placental weight or birth outcomes with exposure to air pollution (Rocha et al., 2008, 096685). The reported ambient concentrations of PM_{10} (42 ± 17 μg/m^3), NO_2 (97 ± 39 μg/m^3), and SO_2 (9 ± 4 μg/m^3) were measured 100 m away from the rodent exposure chambers. By using six time windows of exposure that covered 1-3 wk of gestation (the entire gestation period in a mouse), a significant decrease in near-term fetal weight (GD19) was induced by ambient air-exposure during the first week of gestation. Decreased placental weight could be induced by ambient air exposure during any of the 3 wk of gestation. This study points to possible windows of exposure that may be important in evaluating epidemiologic study results.

Neurodevelopmental Effects

Diesel Exhaust

The diagnosis of autism is on the rise in the Western world with its etiology mostly unknown. Autism-associated cell loss is brain region-specific and hypothesized to be developmental in origin. Sugamata et al. (2006, 097166) exposed pregnant ICR mice to DE (0.3 mg/m^3) continuously from 2 dpc to 16 dpc. Pups with in utero exposure to DE were nursed in clean air chambers, but may have received gastro-intestinal exposure via lactational transfer of various components of DE. At 11 wk of age, cerebellar brain tissue was collected. Earlier work has shown that DE particles (<0.1 μm) have been detected in the brains (cerebral cortex and hippocampus) of newborn pups who were born to dams exposed to DE during pregnancy (Sugamata et al., 2006, 097166). Histological analysis of DE-exposed pup cerebella revealed significant increases in caspase-3 (c-3) positive cells compared to control and significant decreases in cerebella Purkinje cell numbers in DE-exposed animals versus control. The ratio of cells positive for apoptosis (c-3 positive) showed a nearly significant sex difference with males displaying increased apoptosis versus females ($p = 0.09$). In humans with autism, the cerebellum has a decreased number of Purkinje cells, which is thought to be fetal and developmental in origin; further, these authors speculate that humans may be more sensitive to DE-dependent neuronal brain changes, as the human placenta is two-layers thick compared to the mouse placenta that is four layers thick.

Behavioral Effects

Diesel Exhaust Particles

Body weight decrements at birth have recently been associated through the Barker hypothesis with adverse adult outcomes. Thus, many publications have begun to focus on decreased birth weight for gestational age and associated adult changes. Hougaard et al. (2008, 156570) exposed 40 timed-pregnant C57BL/6 dams to DE particles reference materials (SRM 2975) via inhalation over GD7-GD19 of pregnancy. They found significantly decreased pup weight at weaning, albeit not at birth. PM-dependent liver changes were monitored by following various inflammatory and genotoxicity-related mRNA transcripts and there were no significant differences in pups at PND2. The comet assay from PND2 pup livers showed no significant differences in DNA damage between DE particle-exposed and control animals. The prohormone, thyroxine, was unchanged in control and DE particle-exposed dams and offspring at weaning. At 2 mo, female DE particle-exposed pups required less time than controls to locate the platform in its new location during the first trial of the spatial reversal learning task in the Morris water maze. Thus, DE particle exposure during in utero development led to behavioral changes without body weight at weaning or changes in inflammatory markers or thyroid hormone levels.

Diesel Exhaust

The effect of in utero DE exposure on CNS motor function was evaluated in male pups (ICR mice) after dams received DE exposure (8h/d×5d/wk) from GD2-GD17 (Yokota et al., 2009, 190518). The exposure atmosphere contained concentrations of 1.0 mg/m^3 for particle mass, 2.67 ppm CO, 0.23 ppm NO_2, and <0.01 ppm SO_2. Spontaneous motor activity was significantly decreased in pups (PND35), as was the dopamine metabolite homovanillic acid measured in the striatum and nucleus accumbens, indicating decreased dopamine (DA) turnover. However, DA levels were unchanged in the same areas of the brain. The authors conclude that these data demonstrate that maternal exposure to DE induced hypolocomotion, similar to earlier studies with adult and neonatal DE particle exposure (Peters et al., 2000, 001756), with decreased extracellular DA release.

Lactation

Diesel Exhaust

Tozuka et al. (2004, 090864) monitored the transfer of PAHs to fetuses and breast milk of F344 rats exposed to DE (6h/day) for 2 wk from GD7-GD 20 (minus 4 days for the weekend when no exposure occurred) with PM_{10} concentration of 1.73 mg/m^3. At PND 14, breast milk was collected. Fifteen PAHs were monitored in the DE exposure chamber and seven were quantified in dam blood with levels of phenanthrene (Phe), anthracene (Ant) and benz[a]anthracene (BaA) in the DE group being significantly higher than the control group. In breast milk, Ant, fluoranthene (Flu), pyrene (Pyr), and chrysene (Chr) showed significant increases in the DE group compared to the control group. BaA tended to be about fourfold higher than the control group in breast milk, but the increase was not significant. PAHs in dam livers of DE versus control were not significantly different. The results of this study demonstrate that PAHs derived from DE are transferred across the placenta from the DE-exposed dam to the fetus. Lactational transfer through the breast milk is also likely as PAHs were detected in dam breast milk, but this should be confirmed in future studies that cross foster control and exposed dams and pups. The lipophilicity of the PAH based on its structure likely affected its uptake in the dam, as PAHs with 3 or 4 rings were found in maternal blood and PAHs with 5 or 6 rings were not detected.

Heritable DNA Changes and Epigenetic Changes

Ambient Air

To address the role of ambient air exposure on heritable changes, Somers et al. (2004, 078098) exposed mice to ambient air in at a rural Canadian site or at an urban site near a steel mill. They showed that offspring of mice exposed to ambient air in urban regions inherited paternal-origin expanded simple tandem repeat (ESTR) mutations 1.9-2.1 times more frequently than offspring of mice exposed to HEPA filtered air or those exposed to rural ambient air. Mouse expanded simple tandem repeat (ESTR) DNA is composed of short base pair repeats which are unstable in the germline and tend to mutate by insertion or deletion of repeat units. In vivo and in situ studies have shown that murine ESTR loci are susceptible to ionizing radiation, and other environmental mutatgen-dependent germline mutations, and are thus good markers of exposure to environmental contaminants.

Expanding upon the above work and to determine if PM or the gaseous phase of the urban air was responsible for heritable mutations, Yauk et al. (2008, 157164) exposed mature male C57Bl×CBA F1 hybrid mice to either HEPA-filtered air or to ambient air in Hamilton, Ontario, Canada for 3 or 10 wk, or 10 wk plus 6 wk of clean air exposure (16 wk). Sperm DNA was monitored for expanded simple tandem repeat (ESTR) mutations. In addition, male-germ line (spermatogonial stem cell) DNA methylation was monitored post-exposure. This area in Hamilton is near two steel mills and a major highway. Air quality data provided by the Ontario Ministry of the Environment showed the highest concentrations of TSP and metals at week 4 (93.8 ± 17 and 3.6 ± 0.7 μg/m^3, respectively) and PAH at week 3 (8.3 ± 1.7 ng/m^3). Mutation frequency at ESTR

Ms6-hm locus in sperm DNA from mice exposed 3 or 10 wk did not show elevated ESTR mutation frequencies, but there was a significant increase in ESTR mutation frequency at 16 wk in ambient air-exposed males versus HEPA filter-exposed animals, pointing to a PM-dependent mechanism of action. When compared to HEPA filter air-exposed males, ambient air-exposed males manifested with hypermethylation of germ-line DNA at 10 and 16 wk. These PM-dependent epigenetic modifications (hypermethylation) were not seen in the halploid stage (3 wk) of spermatogenesis, but were nonetheless seen in early stages of spermatogenesis (10 wk) and remained significantly elevated in mature sperm even after removal of the mouse from the environmental exposure (16 wk). Thus, these studies indicate that the ambient PM phase and not the gaseous phase is responsible for the increased frequency of heritable DNA mutations and epigenetic modifications.

7.4.3. Summary and Causal Determinations

7.4.3.1. $PM_{2.5}$

The 1996 PM AQCD concluded that while few studies had been conducted on the link between PM and infant mortality, the research "suggested an association," particularly for post-neonates (U.S. EPA, 1996, 079380). In the 2004 PM AQCD, additional evidence was available on PM's effect on fetal and early postnatal development and mortality and while some studies indicated a relationship between PM and pregnancy outcomes, others did not (U.S. EPA, 2004, 056905). Studies identifying associations found that exposure to PM_{10} early during pregnancy (first month of pregnancy) or late in the pregnancy (6 wk prior to birth) were linked with higher risk of preterm birth, including models adjusted for other pollutants, and that $PM_{2.5}$ during the first month of pregnancy was associated with IUGR. However, other work did not identify relationships between PM_{10} exposure and low birth weight. The state of the science at that time, as indicated in the 2004 PM AQCD, was that the research provided mixed results based on studies from multiple countries.

Building on the evidence characterized in the previous AQCDs, recent epidemiologic studies conducted in the U.S. and Europe were able to examine the effects of $PM_{2.5}$, and all found an increased risk of low birth weight (Section 7.4.1). Exposure to $PM_{2.5}$ was usually associated with greater reductions in birth weight than exposure to PM_{10}. All of the studies that examined the relationship between $PM_{2.5}$ and preterm birth report positive associations, and most were statistically significant. The studies evaluating the association between $PM_{2.5}$ and growth restriction all found positive associations, with the strongest evidence coming when exposure was assessed during the first or second trimester (Section 7.4.1). For infant mortality (<1 yr), several studies examined $PM_{2.5}$ and found positive associations (Section 7.4.1).

Animal toxicological studies reported effects including decreased uterine weight, limited evidence of male reproductive effects, and conflicting reports of reproductive outcomes in male offspring, particularly in studies of DE (Section 7.4.2). Toxicological studies also reported effects for several development outcomes, including immunological effects (placental and related to asthma), neurodevelopmental and behavioral effects (Section 7.4.2).

In summary evidence is accumulating from epidemiologic studies for effects on low birth weight and infant mortality, especially due to respiratory causes during the post-neonatal period. The mean $PM_{2.5}$ concentrations during the study periods ranged from 5.3-27.4 $\mu g/m^3$. Exposure to $PM_{2.5}$ was usually associated with greater reductions in birth weight than exposure to PM_{10}. Several U.S. studies of PM_{10} investigating fetal growth reported 11-g decrements in birth weight associated with PM_{10} exposure. Most of these studies were conducted in California, where $PM_{2.5}$ and $PM_{10-2.5}$ contribute almost equally to the PM_{10} mass concentration. So while these results can not be attributed to one size fraction or the other, the consistency of the results strengthens the interpretation that particle exposure may be causally related to reductions in birth weight. Similarly, animal evidence supported an association between $PM_{2.5}$ and PM_{10} exposure and adverse reproductive and developmental outcomes, but provided little mechanistic information or biological plausibility for an association between long-term PM exposure and adverse birth outcomes, including low birth weight, or infant mortality. Epidemiologic studies do not consistently report associations between PM exposure and preterm birth, growth restriction, birth defects or decreased sperm quality. New evidence from animal toxicological studies on heritable mutations is of great interest, and warrants further investigation. Overall, the epidemiologic and toxicological evidence is **suggestive of a**

causal relationship between long-term exposures to $PM_{2.5}$ and reproductive and developmental outcomes.

7.4.3.2. $PM_{10-2.5}$

Evidence is **inadequate to determine if a causal relationship exists between long-term exposure to $PM_{10-2.5}$ and developmental and reproductive outcomes** because studies have not been conducted in sufficient quantity or quality to draw any conclusion. A single study found an association between $PM_{10-2.5}$ and birthweight (-13 g [95% CI: -18.3 to -7.6] per 10 $\mu g/m^3$ increase), but no such association for $PM_{2.5}$ (Parker et al., 2008, 156013).

7.4.3.3. UFPs

The 2004 PM AQCD did not report long-term exposure studies for UFPs. No epidemiologic or animal toxicology studies have been conducted to evaluate the effects of long-term UFP exposure and reproductive and developmental effects. Ambient air exposures, which likely include UFPs, are reported in this ISA but there is no delineation of the separate contribution from UFPs. The evidence is **inadequate to determine if a causal relationship exists between long-term UFP exposures and reproductive and developmental effects**.

7.5. Cancer, Mutagenicity, and Genotoxicity

Evidence from epidemiologic and animal toxicological studies has been accumulating for more than three decades regarding the mutagenicity and carcinogenicity of PM in the ambient air. DE has been identified as one source of PM in ambient air, and has been extensively studied for its carcinogenic potential. In 1989, the International Agency for Research on Cancer (IARC) found that there was sufficient evidence that extracts of DE particles were carcinogenic in experimental animals and that there was limited evidence for the carcinogenic effect of DE in humans (IARC, 1989, 002958). This conclusion was based on studies in which organic extracts of DE particles were used to evaluate the effects of concentrates of the organic compounds associated with carbonaceous soot particles. These extracts were applied to the skin or administered by IT instillation or intrapulmonary implantation to mice, rats, or Syrian hamsters and an excess of tumors on the skin, lung or at the site of injection were observed.

In 2002, the U.S. EPA reviewed over 30 epidemiologic studies that investigated the potential carcinogenicity of DE. These studies, on average, found that long-term occupational exposures to DE were associated with a 40% increase in the relative risk of lung cancer (U.S. EPA, 2002, 042866). In the same report the U.S. EPA concluded that extensive studies with salmonella had unequivocally demonstrated mutagenic activity in both particulate and gaseous fractions of DE. They further concluded that DE may present a lung cancer hazard to humans (U.S. EPA, 2002, 042866). The particulate phase appeared to have the greatest contribution to the carcinogenic effect. Both the particle core and the associated organic compounds demonstrated carcinogenic properties, although a role for the gas-phase components of DE could not be ruled out. Almost the entire diesel particle mass is $\leq$ 10 μm in diameter (PM_{10}), with approximately 94% of the mass of these particles <2.5 μm in diameter ($PM_{2.5}$), including a subgroup with a large number of UFPs (U.S. EPA, 2002, 042866). U.S. EPA considered the weight of evidence for potential human carcinogenicity for DE to be strong, even though inferences were involved in the overall assessment, and concluded that DE is "likely to be carcinogenic to humans by inhalation" and that this hazard applies to environmental exposures (U.S. EPA, 2002, 042866).

Two recent reviews of the mutagenicity (Claxton et al., 2004, 089008) and carcinogenicity (Claxton and Woodall, 2007, 180391) of ambient air have characterized the animal toxicological literature on ambient air pollution and cancer. The majority of these toxicological studies have been conducted using IT instillation or dermal routes of exposure. Generally, the toxicological evidence reviewed in this ISA has been limited to inhalation studies conducted with lower concentrations of

PM (<2 mg/m^3), relevant to current ambient concentrations and the current regulatory standard (Section 1.3). Because this ISA focuses on toxicological studies which use the inhalation route of exposure, it is possible that important evidence for the role of PM in mutagenicity, tumorigenicity, and/or carcinogenicity may be missed. In order to accurately characterize the relationship between PM and cancer and be consistent with the EPA Guidelines for Carcinogen Risk Assessment (U.S. EPA, 2005, 086237), these reviews (that include studies that employ IT instillation and dermal routes of exposure) are summarized briefly.

Claxton et al. (2004, 089008) reviewed the mutagenicity of air in the Salmonella (Ames) assay, and showed that hundreds of compounds identified in ambient air from varying chemical classes are mutagenic and that the commonly monitored PAHs could not account for the majority of mutagenicity associated with most airborne particles. They concluded that the smallest particles have the highest toxicity per particulate mass, with the $PM_{2.5}$ size fraction having greater mutagenic and cytotoxic potential than the PM_{10} size fraction, which had a higher mutagenic potential than the TSP size fraction. One study reviewed by Claxton et al. (2004, 089008) found that the cytotoxic potential of $PM_{2.5}$ was higher in wintertime samples than in summertime samples. A series of studies on source apportionment for ambient particle mutagenic activity reviewed by Claxton et al. (2004, 089008) indicate that mobile sources (cars and diesel trucks) account for most of the mutagenic activity.

Claxton and Woodall (2007, 180391) reviewed many studies that examined the rodent carcinogenicity of extracts of ambient PM samples; the PM was of various size classes, often from TSP samples. Among a variety of mouse and rat strains, application methods, and samples employed, the authors found no pattern that would suggest the routine use of a particular strain or protocol would be more informative than another. The primary conclusion that comes from the analysis of rodent carcinogenicity studies is that the most polluted urban air samples tested to date are carcinogenic; the contribution of PM and different size classes of PM to the carcinogenic effects of ambient air has not been delineated. The differences in response by the various strains of inbred mice indicate that the genetic background of an individual can influence tumorigenic response. Studies examining different components of ambient PM (e.g., PAHs) confirm that ambient air contains multiple carcinogens, and that the carcinogenic potential of particles from different airsheds can be quite different. Therefore, one would expect the incidence of cancers related to ambient air exposure in different metropolitan areas to differ.

Numerous epidemiologic and animal toxicological studies of ambient PM and their contributing sources have been conducted to assess the relative mutagenic or genotoxic potential. Studies previously reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905) provide evidence that ambient PM as well as PM from specific combustion sources (e.g., fossil fuels) is mutagenic in vivo and in vitro. Building on these results, data from recent epidemiologic and animal toxicological studies that evaluated the carcinogenic, mutagenic and/or genotoxic effects of PM, PM-constituents, and combustion emission source particles are reviewed in this section.

7.5.1. Epidemiologic Studies

The 2004 PM AQCD reported on original and follow-up analyses for three prospective cohort studies that examined the relationship between PM and lung cancer incidence and mortality. Based on these findings, as well as on the results from case-control and ecologic studies, the 2004 PM AQCD concluded that long-term PM exposure may increase the risk of lung cancer incidence and mortality. The largest of the three prospective cohort studies included in the 2004 PM AQCD was the ACS study (Pope et al., 2002, 024689). This study was the follow-up to the original ACS study (Pope et al., 1995, 045159), and included a longer follow-up period and reported a statistically significant association between $PM_{2.5}$ exposure and lung cancer mortality.

A 14- to 16-yr prospective study conducted using the Six Cities Study cohort reported a slightly elevated risk of lung cancer mortality for individuals living in the most polluted city (mean PM_{10}: 46.5 µg/m^3; mean $PM_{2.5}$ 29.6 µg/m^3) as compared to the least polluted city (mean PM_{10}: 18.2 µg/m^3; mean $PM_{2.5}$ 11.0 µg/m^3) but the association was not statistically significant (Dockery et al., 1993, 044457).

Re-analysis of the AHSMOG cohort, a study of non-smoking whites living in California, concluded that elevated long-term exposure to PM_{10} was associated with lung cancer incidence among both men and women (Beeson et al., 1998, 048890). The original study had reported an excess of incident lung cancers only among women (Abbey et al., 1991, 042668). Further reanalysis

of this cohort revealed an association between PM_{10} and lung cancer mortality among men but no association among women (Abbey et al., 1999, 047559). In addition, McDonnell et al. (2000, 010319) reported increases in lung cancer mortality with long-term exposure to $PM_{2.5}$ in the AHSMOG cohort; no association was seen for $PM_{10-2.5}$.

7.5.1.1. Lung Cancer Mortality and Incidence

The following sections will examine extensions of the above mentioned cohort studies and new studies published since the 2004 PM AQCD. The section includes discussion of both lung cancer incidence and mortality, as well as markers of exposure/susceptibility. A summary of the mean PM concentrations reported for the new studies is presented in Table 7-6. In addition, a summary of the associations for lung cancer mortality and incidence are presented in Table 7-7 and Figure 7-7 (Section 7.6) Further discussion of all-cause and cause-specific mortality is presented in Section 7.6.

Table 7-6. Characterization of ambient PM concentrations from recent studies of cancer and long-term exposures to PM.

Study	Location	Pollutant	Mean Annual Concentration ($\mu g/m^3$)	Upper Percentile Concentrations ($\mu g/m^3$)
Brunekreef et al. (2009, 191947)	The Netherlands	$PM_{2.5}$	28.3	Max: 36.8
Bonner et al. (2005, 088993)	Western NY State	TSP	44	
Jerret et al. (2005, 087600)	Los Angeles, California	$PM_{2.5}$		Max:27.1
Laden et al. (2006, 087605)	6 U.S. cities	$PM_{2.5}$	Range of means across sites: 10.2-29.0 Avg of means across sites: 16.4	
Naess et al. (2007, 090736)	Oslo, Norway	$PM_{2.5}$	15	Max: 22
		PM_{10}	19	Max: 30
Palli et al. (2008, 156837)	Florence, Italy	PM_{10}	NR	
Pedersen et al. (2006, 156848)	Czech Republic	$PM_{2.5}$		Max: 46-120
		PM_{10}		Max: 120-238.6
Sorensen et al. (2005, 083053)	Copenhagen, Denmark	$PM_{2.5}$	Range of means across sites: 12.6-20.7 Avg of means across sites: 16.7	75th: 24.3-27.7
Sram et al. (2007, 188457)	Czech Republic	PM_{10}		Max: 55
		$PM_{2.5}$		Max: 38
Sram et al. (2007, 192084)	Czech Republic	PM_{10}	Range of means across sites: 36.4-55.6 Avg of means across sites: 46.0	
		$PM_{2.5}$	Range of means across sites: 24.8-44.4 Avg of means across sites: 34.6	
Vineis et al. (2006, 192089)	Multi-city, Europe	PM_{10}	Range of means across sites: 19.9-73.4 Avg of means across sites: 35.4	
Vinzents et al. (2005, 087482)	Copenhagen, Denmark	PM_{10}	Range of means across sites: 16.9-23.5 Avg of means across sites: 20.2	

A subset of the ACS cohort study from 1982 to 2000 that included only residents of Los Angeles, California was used to examine the association between $PM_{2.5}$ and lung cancer mortality while adjusting for both individual and neighborhood covariates (Jerrett et al., 2005, 087600). There was a positive association between $PM_{2.5}$ and lung cancer mortality when adjusting for 44 individual covariates (RR 1.44 [95% CI: 0.98-2.11] per 10 $\mu g/m^3$ increase in $PM_{2.5}$). However, including all potential individual and neighborhood covariates associated with mortality reduced the association

(RR 1.20 [95% CI: 0.79-1.82] per 10 μg/m^3 increase in $PM_{2.5}$). A recent re-analysis of the full ACS cohort also demonstrated a positive association between $PM_{2.5}$ and lung cancer mortality (RR 1.11 [95% CI: 1.04-1.18]) (Krewski et al., 2009, 191193). The authors observed modification of this risk by educational attainment, with those completing a high school degree or less having greater risk. In addition to utilizing the ACS cohort for a nationwide analysis, this same study conducted two regional assessments, one in the New York City area and the other in the Los Angeles area. No association was detected between $PM_{2.5}$ and lung cancer mortality in the analysis of the region included in the New York City analysis. A positive association was observed in the Los Angeles-area analysis using an unadjusted model, but this association did not persist after control for individual, ecologic, and copollutant covariates.

The Six Cities Study was extended to include data from 1990-1998, a period including 1,368 deaths and 54,735 person-years (Laden et al., 2006, 087605). An elevated risk ratio for lung cancer mortality was reported when the entire follow-up period (1974-1998) was included in the analysis (RR 1.27 [95% CI 0.96-1.69] per 10 μg/m^3 increase in average annual $PM_{2.5}$). However, estimated decreases in $PM_{2.5}$ were not associated with reduced lung cancer mortality (RR 1.06 (95% CI: 0.43-2.62] for every 10 μg/m^3 reduction in $PM_{2.5}$).

Naess et al. (2007, 090736) studied individuals aged 51-90 yr living in Oslo, Norway in 1992. Death certificate data were obtained for 1992-1998 and information on PM was collected from 1992-1995. Women had a larger association of lung cancer mortality with $PM_{2.5}$ compared to men. Similar results were reported for PM_{10}.

Most recently, Brunekreef et al. (2009, 191947) used the Netherlands cohort study (NLCS) on diet and cancer to conduct a re-analysis of the research performed by Beelen et al. (2008, 156263) examining the association between PM and both lung cancer mortality and incidence. After 10 yr of follow-up, there was no association between $PM_{2.5}$ and lung cancer mortality for either the analysis of the full cohort (n = 105,296) (RR 1.06 [95% CI: 0.82-1.38] per 10 μg/m^3 increase in $PM_{2.5}$) or the case-cohort (n = 4,075) (RR 0.87 [95% CI: 0.52-1.47]). There was also no association with black smoke or traffic density variables, although living near a major roadway was associated with an elevated relative risk for lung cancer in the full cohort analysis (RR 1.20 [95% CI: 0.98-1.47]). The association was not present in the case-cohort analysis (RR 1.07 [95% CI: 0.70-1.64]).

In addition to lung cancer mortality, Brunekreef et al. (2009, 191947) also examined the association with lung cancer incidence using 11.3 yr of follow-up data. In both the full cohort and the case-cohort analyses no association was reported between $PM_{2.5}$ and lung cancer incidence (full cohort: RR 0.81 [95% CI: 0.63-1.04]; case-cohort: RR 0.67 [95% CI: 0.41-1.10] per 10 μg/m^3 increase in $PM_{2.5}$). The same was true for analyses of BS and traffic density variables.

The association between PM and incident lung cancers was examined in the European Prospective Investigation into Cancer and Nutrition study (EPIC) (Vineis et al., 2006, 192089). Within this cohort, a nested case-control study, the GenAir study, included cases of incident cancer and controls matched on age, gender, smoking status, country of recruitment, and time between recruitment and diagnosis. Only non-smokers and former smokers who had quit smoking at least 10 yr prior were included. The study included 113 cases and 312 controls. No association was seen between PM_{10} and lung cancer (OR 0.91 [95% CI: 0.70-1.18] per 10 μg/m^3). The OR was elevated when cotinine, a marker for cigarette exposure, was included in the model but the authors state that this is probably due to small study size (OR 2.85 [95% CI: 0.97-8.33] comparing ≥ 11 μg/m^3 to <11 μg/m^3). Control for other potential confounders, such as BMI, education level, and intake of fruit and vegetables, did not have a large impact on the estimate.

Table 7-7. Associations* between ambient PM concentrations from select studies of lung cancer mortality and incidence.

Study	Cohort	Location	Years	Analysis subgroup	Effect Estimate (95% CI)
MORTALITY - $PM_{2.5}$					
Dockery et al. (1993, 044457)‡	Six-Cities	Six cities across the U.S.	1974-1991		1.18 (0.89-1.57)
Krewski et al. (2000, 012281)‡	Six-Cities-Re-analysis	Six cities across the U.S.	1974-1991		1.16 (0.86-1.23)
Laden et al. (2006, 087605)	Six-Cities	Six cities across the U.S.	1974-1998		1.27 (0.96-1.69)
Beelen et al. (2008, 156263)	NLCS	Netherlands	1987-1996	Full Cohort	1.06 (0.82-1.38)
Beelen et al. (2008, 156263)	NLCS	Netherlands	1987-1996	Case Cohort	0.87 (0.52-1.47)
Brunekreef et al. (2009, 191947)	NLCS-Re-analysis	Netherlands	1987-1996	Full Cohort	1.06 (0.82-1.38)
Brunekreef et al. (2009, 191947)	NLCS-Re-analysis	Netherlands	1987-1996	Case Cohort	0.87 (0.52-1.47)
Pope et al. (1995, 045159)‡	ACS	U.S.	1982-1989		1.01 (0.91-1.12)
Pope et al. (2002, 024689)‡	ACS	U.S.	1982-2000		1.13 (1.04-1.22)
Jerret et al. (2005, 087600)	ACS-LA	Los Angeles	1982-2000	Intra-metro Los Angeles	1.44 (0.98-2.11)
Krewski et al. (2009, 191193)	ACS-Re-analysis	U.S.	1982-2000		1.11 (1.04-1.18)
Krewski et al. (2009, 191193)	ACS-Re-analysis	New York City	1982-2000	Intra-metro New York City	0.90 (0.29-2.78)
Krewski et al. (2009, 191193)	ACS-Re-analysis	Los Angeles	1982-2000	Intra-metro Los Angeles	1.31 (0.90-1.92)
McDonnell et al. (2000, 010319) †	AHSMOG	California	1973-1977	Men	1.39 (0.79-2.46)
Naess et al. (2007, 090736)		Oslo, Norway	1992-1998	Men, 51-70 yrs	1.18 (0.93-1.52)
Naess et al. (2007, 090736)		Oslo, Norway	1992-1998	Men, 71-90 yrs	1.18 (0.93-1.52)
Naess et al. (2007, 090736)		Oslo, Norway	1992-1998	Women, 51-70 yrs	1.83 (1.36-2.47)
Naess et al. (2007, 090736)		Oslo, Norway	1992-1998	Women, 71-90 yrs	1.45 (1.05-2.02)
MORTALITY - PM_{10}					
McDonnell et al. (2000, 010319) †	AHSMOG	California	1973-1977	Men	1.23 (0.84-1.80)
Naess et al. (2007, 090736) †		Oslo, Norway	1992-1998	Men, 51-70 yrs	1.12 (0.95-1.33)
Naess et al. (2007, 090736)		Oslo, Norway	1992-1998	Men, 71-90 yrs	1.14 (0.97-1.36)
Naess et al. (2007, 090736) †		Oslo, Norway	1992-1998	Women, 51-70 yrs	1.50 (1.23-1.84)
Naess et al. (2007, 090736) †		Oslo, Norway	1992-1998	Women, 71-90 yrs	1.29 (1.03-1.60)
INCIDENCE - $PM_{2.5}$					
Beelen et al. (2008, 155681)	NLCS	Netherlands	1987-1996	Full Cohort	0.81 (0.63-1.04)
Beelen et al. (2008, 155681)	NLCS	Netherlands	1987-1996	Case Cohort	0.65 (0.41-1.04)
Brunekreef et al. (2009, 191947)	NLCS-Re-analysis	Netherlands	1987-1996	Full Cohort	0.81 (0.63-1.04)
Brunekreef et al. (2009, 191947)	NLCS-Re-analysis	Netherlands	1987-1996	Case Cohort	0.67 (0.41-1.10)
INCIDENCE – PM_{10}					
Beeson et al. (1998, 048890)	AHSMOG	California	1977-1992	Men	1.99 (1.32-3.00)
Vineis et al. (2006, 192089)	GenAir	Europe	1993-1999	Case-Control	0.91 (0.70-1.18)

*per 10 $\mu g/m^3$ increase

†Results from the paper were standardized to10 $\mu g/m^3$ [For McDonnell et al. (2000, 010319) the non-standardized results were reported based on IQR increments (24.3 $\mu g/m^3$ for $PM_{2.5}$ and 29.5 $\mu g/m^3$ for PM_{10}). For Naess et al. (2007, 090736) the original hazard ratios were calculated based on quartiles of PM exposure. The results were converted to10 $\mu g/m^3$ using the mean range of the four quartiles (3.95 $\mu g/m^3$ for $PM_{2.5}$ and 5.88 $\mu g/m^3$ for PM_{10})].

‡Study was included in the 2004 PM AQCD

7.5.1.2. Other Cancers

Bonner et al. (2005, 088993) conducted a population-based, case-control study of the association between ambient exposure to PAHs in early life and breast cancer incidence among women living in Erie and Niagara counties in the state of New York. Cases (n = 1,166 of which 841 were post-menopausal) were women with primary breast cancer, and controls (n = 2,105 of which 1,495 were post-menopausal) were frequency matched to the cases by age, race, and county of residence. TSP was used as a proxy for PAH exposure. Annual average TSP concentrations (1959-1997) were obtained from the New York State Department of Environmental Conservation for Erie and Niagara Counties. Among postmenopausal women, exposure to high concentrations of TSP (>140 $\mu g/m^3$) at birth was associated with an OR of 2.42 for breast cancer (95% CI: 0.97-6.09) relative to low concentrations of TSP (<84 $\mu g/m^3$). ORs were elevated for pollution exposures at age of menarche (OR: 1.45 [95% CI: 0.74-2.87]) and age at first birth (OR: 1.33 [95% CI: 0.87-2.06]) among postmenopausal women. Among premenopausal women, exposure to high concentrations of TSP at birth was associated with an OR for breast cancer incidence of 1.79 (95% CI: 0.62-5.10) relative to low exposure levels, exposure at age of menarche was associated with an OR of 0.66 (95% CI: 0.38-1.16), and exposure at age of first birth was associated with an OR of 0.52 (95% CI: 0.22-1.20).

7.5.1.3. Markers of Exposure or Susceptibility

Several studies looked at markers of exposure or susceptibility as the outcome associated with short-term exposure. These studies are included here because they may be relevant to the mechanism that leads to cancer associated with long-term exposures. For example, inflammation can contribute to carcinogenesis by inducing genomic instability, which can then lead to altered gene expression, enhanced proliferation, and resistance to apoptotic signals. Reactive oxygen and nitrogen species, provided by PM components or inflammation pathways, can cause molecular damage leading to cellular transformation. Elevated inflammatory cytokines, chemokines, and prostaglandins promote tumor growth and angiogenesis, which in turn promotes metastasis and malignant invasion. In particular, IL-6, IL-8, IL-1β, COX-2, and TNF-α have been implicated in these processes (Kundu and Surh, 2008, 198840). Several lines of evidence support the involvement of COX-2 in the pathogenesis of lung cancer (Lee et al., 2008, 198811). Both short- and long-term exposure studies demonstrate relationships between various forms of PM and increased production of these inflammatory mediators, both in the lungs and circulation. Additionally, limited evidence suggests that exposure to PM (Chen and Schwartz, 2008, 190106), or traffic (Williams et al., 2009, 191945), or residence in a polluted airshed (Calderon-Garciduenas et al., 2007, 091252; Calderón-Garcidueñas et al., 2009, 192107) are associated with decreases in the number or function of natural killer cells or other white blood cells, indicating suppression of anti-tumor defenses.

A study performed in the Czech Republic compared 53 male policemen working at least 8 hours per day outdoors in urban air with age- and sex-matched controls who spent at least 90% of their day indoors (n = 52) (Sram et al., 2007, 188457). During the sampling period, two monitors from downtown and suburban areas detected levels of air pollutants in the following ranges: PM_{10} 32-55 $\mu g/m^3$, $PM_{2.5}$ 27-38 $\mu g/m^3$, c-PAHs 18-22 ng/m^3, and B[a]P 2.5-3.1 ng/m^3 using a VAPS monitor (measurements taken with a HiVol monitor, which has a lower flow rate, had a mean for PM_{10} of 62.6 $\mu g/m^3$). c-PAHs detected on personal monitors during sampling days had a mean of 12.04 ng/m^3 among the policemen and 6.17 ng/m^3 among the controls. No difference in percent of chromosomal aberrations was observed between the policemen and control group using conventional cytogenetic analysis. However, using fluorescent in situ hybridization (FISH), a difference in chromosomal aberrations between the policemen and control group was reported. For example, the percentage of aberrant cells, as well as the genomic frequency of translocations per 100 cells, was about 1.4-fold greater in the policemen. This was largely driven by a difference in chromosomal aberrations between nonsmoking policemen and nonsmoking controls. A similar study that included only the policemen (n = 60), reported that the mean exposure to c-PAHs and B[a]P for 40-50 days before sampling was associated with chromosomal aberrations when analyzed with FISH (Sram et al., 2007, 192084). However, when included in a model with other covariates, the association with these variables was null. No association was present with use of conventional cytogenetic analysis.

Palli et al. (2008, 156837) investigated the correlation between ambient PM_{10} concentrations and individual levels of DNA bulky adducts. Study participants were 214 healthy adults aged

35-64 yr at enrollment who resided in the city of Florence, Italy. This study was conducted between 1993 and 1998. PM_{10} exposure levels were based on daily environmental measures provided by two types of urban monitoring stations (high-traffic and low-traffic). The researchers assessed correlation between DNA bulky adducts measured in blood samples and PM_{10} concentrations prior to blood sample collection. Time windows of PM_{10} exposure evaluated in this study were 0-5 days, 0-10 days, 0-15 days, 0-30 days, 0-60 days, and 0-90 days prior to blood sample collection. Overall, average PM_{10} concentrations decreased during the study period, with some fluctuations. Quantitative values were not reported, but PM_{10} appeared to range between approximately 30 and 100 $\mu g/m^3$ for high-traffic stations, and between approximately 20 and 50 $\mu g/m^3$ for low-traffic stations. This study found that levels of DNA bulky adducts among non-smoking workers with occupational traffic exposure were positively correlated with cumulative PM_{10} levels from high-traffic stations during approximately 2 wk preceding blood sample collection (0-5 days: $r = 0.55$, $p = 0.03$; 0-10 days: $r = 0.58$, $p = 0.02$; 0-15 days: $r = 0.56$, $p = 0.02$). DNA bulky adducts were not associated with PM_{10} levels among Florence residents with no occupational exposure to vehicle emissions or among smokers. DNA bulky adducts were not associated with PM_{10} levels assessed by low-traffic urban monitoring stations.

The association between personal exposure to water-soluble transition metals in $PM_{2.5}$ and oxidative stress-induced DNA damage was investigated among 49 students from Central Copenhagen, Denmark (Sorensen et al., 2005, 083053). Researchers assessed $PM_{2.5}$ exposure by personal sampling over two weekday periods twice in one year (November 1999 and August 2000), and determined the concentration of water-soluble transition metals (V, Cr, Fe, Ni, Cu and Pt) in these samples. In addition, lymphocyte and 24-h urine samples were analyzed for DNA damage by measuring 7-hydro-8-oxo-2'-deoxyguanosine (8-oxodG). Mean concentrations and corresponding IQR of these metals differed between months of sample collection. This study found that 8-oxodG concentration in lymphocytes was significantly associated with V and Cr concentrations, with a 1.9% increase in 8-oxodG per 1 µg/L increase in V concentration and a 2.2% increase in 8-oxodG per 1 µg/L increase in Cr concentration; these associations were independent of the $PM_{2.5}$ mass concentration. The other transition metals were not significantly associated with the 8-oxodG concentration in lymphocytes, and none of the six measured transition metals was associated with the 8-oxodG concentration in urine.

Vinzents et al. (2005, 087482) investigated the association between UFP and PM_{10} concentrations with levels of purine oxidation and strand breaks in DNA using a crossover design in Copenhagen, Denmark. Study participants were 15 healthy nonsmoking individuals with a mean age of 25 yr. UFP exposure was evaluated using number concentration obtained in the breathing zone by portable instruments in six 18-h weekday periods from March to June 2003. Ambient concentrations for PM_{10} and UFP were also measured on all exposure days at curbside street stations and at one urban background station. Oxidative DNA damage was assessed by evaluating strand breaks and oxidized purines in mononuclear cells isolated from venous blood the morning after exposure measurement. Mean number concentration of UFPs (street station) was 30.4×10^3 UFPs/mL (standard deviation [SD]: 1.38), mean mass concentration of PM_{10} at a background monitoring station was 16.9 $\mu g/m^3$ (SD: 1.53), and mean mass concentration of PM_{10} at a street station was 23.5 $\mu g/m^3$ (SD: 1.48). Mean personal exposure to UFPs was 32.4×10^3 UFPs/mL (SD: 1.49) while bicycling (5 occasions), 19.6×10^3 UFPs/mL (SD: 1.78) during other outdoor activities (6 occasions), and 13.4×10^3 UFPs/mL (SD: 1.96) while indoors (6 occasions). The regression coefficients of the mixed-effects models looking at level of purine oxidation were estimated as 1.50×10^{-3} (95% CI: 0.59×10^{-3} to 2.42×10^{-3}; $p = 0.002$) for cumulative outdoor exposure and 1.07×10^{-3} (95% CI: 0.37×10^{-3} to 1.77×10^{-3}; $p = 0.003$) for cumulative indoor exposure. Neither cumulative outdoor nor cumulative indoor exposures to UFPs were associated with strand breaks. Neither ambient air concentrations of PM_{10} nor number concentrations of UFPs at monitoring stations were significant predictors of DNA damage.

Additionally, a number of studies employed ecologic study designs, comparing the prevalence of biomarkers in populations from more polluted locations to those in less polluted locations. In a pilot study conducted in the Czech Republic (Pedersen et al., 2006, 156848), children age 5-11 yr provided 5 mL blood samples and the frequency of micronuclei (MN) in peripheral blood lymphocytes was analyzed as a measure of cytogenetic effects. Significantly higher frequencies of MN were found in younger children living in Teplice ($PM_{2.5}$ concentration = 120 $\mu g/m^3$) than in Prachatice ($PM_{2.5}$ concentration = 46 $\mu g/m^3$). The levels of c-PAHs were also much higher in Teplice (nearly 30 ng/m^3 in Teplice and about 15 ng/m^3 in Prachatice). The difference in MN frequencies

observed in the children from the two locations may be attributable to differences in exposure to air pollution, but could also be due to differences in diet or other environmental exposures. This finding is noteworthy considering MN formation in peripheral blood lymphocytes is thought to be biologically relevant for carcinogenesis.

Avogbe et al. (2005, 087811) showed a correlation between the level of oxidative DNA damage in individuals and exposure to ambient UFPs. Formamidopyrimidine DNA glycosylase sensitive sites and the presence of DNA strand breaks were assessed in blood and urine samples obtained from healthy, non-smoking male volunteers that lived and worked in different areas of Cotonou, Benin. Exposure to benzene was assessed by urinary excretion of S-phenylmercapturic acid. There was a high degree of correlation between exposure to benzene and UFPs and the presence of DNA strand breaks and formamidopyrimidine DNA glycosylase sensitive sites (rural subjects < suburban subjects < residents living near high traffic roads < taxi drivers). Genotyping studies showed that the magnitude of the effects of benzene and UFPs may be modified by polymorphisms in GSTP1 and NQO1 genes.

Tovalin et al. (2006, 091322) evaluated the association between exposure to air pollutants and the level of DNA damage using the single cell gel electrophoresis (comet) assay. Mononuclear lymphocytes from outdoor and indoor workers from two areas in Mexico, Mexico City (large city) and Puebla (medium size city), were evaluated. The outcomes showed that the outdoor workers in Mexico City exhibited greater DNA damage than indoor workers in the same region. Similar levels of DNA damage were observed between indoor and outdoor workers in Puebla. The level of observed DNA damage was correlated with exposure to O_3 and $PM_{2.5}$.

In summary, several recent studies have reported an association between lung cancer mortality and long-term $PM_{2.5}$ exposure. Although many of the estimates include the null in the confidence interval, overall the results have shown a positive relationship. The two recent studies that looked at lung cancer incidence did not report an association with $PM_{2.5}$ (Brunekreef et al., 2009, 191947) or PM_{10} (Vineis et al., 2006, 192089). Studies of exposure/susceptibility markers have reported inconsistent outcomes, with some markers being associated with PM and others not.

7.5.2. Toxicological Studies

Over the past 30 yr numerous mutagenicity and genotoxicity studies of ambient PM and their contributing sources have been conducted to assess the relative mutagenic or genotoxic potential. Studies previously reviewed in the 2004 PM AQCD (U.S. EPA, 2004, 056905) provide compelling evidence that ambient PM and PM from specific combustion sources (e.g., fossil fuels) are mutagenic in vivo and in vitro. Research cited in the 2004 AQCD demonstrated mutagenic activity of ambient PM from urban centers in California, Germany and the Netherlands. These studies suggested that ubiquitous emission sources, particularly motor vehicle emissions, rather than isolated point sources were largely responsible for the mutagenic effects. In addition, the mutagenicity was dependent upon the chemical composition of the PM with unsubstituted polyaromatic compounds and semi-polar compounds being highly mutagenic. Mutagenicity was also dependent on size, with the fine fraction of urban PM having greater effects than the coarse fraction. Genotoxic activity was demonstrated for ambient PM from two high traffic areas (one upwind and one downwind) and a rural site. In addition, the 2004 AQCD reported that exhausts from gasoline and diesel engines were mutagenic and that DE was more potent. More mutagenicity was observed for exhaust from cold starts than starts at room temperature. Both gaseous and particulate fractions of DE were found to be mutagenic. Sequential fractionation of extracts from gasoline and DE implicated the polar fractions, especially nitrated polynuclear aromatic compounds, as contributing greatly to mutagenicity. Among some of the other mutagenically active compounds found in the gas phase of DE are ethylene, benzene, 1,3-butadiene, acrolein and several PAHs, all of which are also present in gasoline exhaust. Also cited in the 2004 AQCD were studies demonstrating mutagenic effects of emissions from wood/biomass burning, which were primarily attributable to the organic fraction and not the condensate. It was noted that wood smoke induced both frameshift mutations and base pair substitution but not DNA adducts. Further, emissions from coal combustion in China were found to be mutagenic, with both polar and aromatic fractions contributing to effects. Little data were available on the mutagenicity of coal fly ash emissions from U.S. conventional combustion plants. In conclusion, these studies provide evidence that ambient PM and combustion-derived PM are mutagenic/genotoxic. The 2004 AQCD noted that there is not a simple relationship between

mutagenic potential and carcinogenic potential in animals or humans. No studies evaluating carcinogenic effects of PM were reported in the 2004 AQCD.

Building on results of earlier studies in the 2004 PM AQCD, data from newly published studies that evaluated the mutagenic, genotoxic and carcinogenic effects of PM, PM-constituents, and combustion emission source particles are reviewed. Pertinent studies are described briefly in the following paragraphs. A summary table is provided in Annex D, Tables D7 and D8).

7.5.2.1. Mutagenesis and Genotoxicity

In Vitro Studies

In general, studies have focused on PM and PM extracts for mutagenicity testing using bacteria and mammalian cell lines. PM and/or PM extracts from ambient air samples, wood smoke, and coal, diesel, or gasoline combustion have all been reported to induce mutation in *S. typhimurium* and in cultured human cells (Abou et al., 2007, 098819; Gabelová et al., 2007, 156457; Gabelová et al., 2007, 156458; Hannigan et al., 1997, 083598; Hornberg et al., 1998, 095741). In addition, effects associated with PM and PM-associated constituents include induction of MN formation, DNA adduct formation, SCE, DNA strand breaks, frameshifts and inhibition of gap-junction intercellular communication (Alink et al., 1998, 087159; Arlt et al., 2007, 097257; Avogbe et al., 2005, 087811; Gabelová et al., 2007, 156457; Gabelová et al., 2007, 156458; Healey et al., 2006, 156532; Hornberg et al., 1996, 087164; Hornberg et al., 1998, 095741; Sevastyanova et al., 2007, 156969).

Constituents adsorbed onto individual particles play a large role in the genotoxic potential of PM. Poma et al. (2006, 096903) showed that fine CB particles were consistently less genotoxic than similar concentrations of $PM_{2.5}$ extracts, suggesting that the adsorbed components play a role in the genotoxic potential of PM. Total PAH and carcinogenic PAH content were correlated with the genotoxic effects of PM (De Kok et al., 2005, 088656; Sevastyanova et al., 2007, 156969). Comparison of different extracts (water-soluble versus organic) by Gutierrez-Castillo et al. (2006, 089030) indicated that water-soluble extracts were more genotoxic than the corresponding organic extracts. Sharma et al. (2007, 156975) reported that mutagenic activity of extracted PM samples collected in and around a waste incineration plant was attributed to the moderately polar and polar fractions. The polar and crude fractions were mutagenic without metabolic activation, suggesting a direct mutagenic effect. No mutagenic activity was observed from any of the nonpolar samples evaluated. Arlt and colleagues (2007, 097257) have shown that the PM constituents 2-nitrobenzanthrone (2-NB) and 3-nitrobenzanthrone were genotoxic in a variety of bacterial and mammalian cell systems.

Conflicting data have been reported on the role of metabolic enzymes in the genotoxicity of PM and their adsorbed constituents. Arlt et al. (2007, 097257) reported that the PM constituent 2-NB was genotoxic in bacterial and mammalian cells. However, metabolic activation with the human N-acetyltransferase 2 or sulfotransferase (SULT1A1) enzyme was needed for the effect to be observed in human cells. Erdinger et al. (2005, 156423) demonstrated that mutagenic activity was not affected when metabolism was induced. de Kok et al. (2005, 088656) evaluated the relationship between the physical, chemical, and genotoxic effects of ambient PM. TSP, PM_{10}, and $PM_{2.5}$ were sampled at different locations and the extracts were assessed for mutagenicity and induction of DNA adducts in cells. Overall, induction of rat liver S9 metabolism generally reduced the mutagenic potential via the Ames assay of the particle fractions and DNA reactivity (induction of DNA adducts) was generally higher after metabolic activation. Binková et al. (2003, 156274) found that the addition of S9 increased PM_{10}-dependent DNA adduct formation.

Ambient Air

A limited number of studies evaluated the impact of the season on the genotoxic effects of ambient PM. A few studies have indicated that greater genotoxic effects were associated with samples collected during the winter months compared to those collected in the summer (Abou et al., 2007, 098819; Gabelová et al., 2007, 156457; Gabelová et al., 2007, 156458). In contrast, Hannigan et al. (1997, 083598) indicated that no seasonal variation was observed. Studies have also shown that greater genotoxic effects were associated with smaller particle size extracts (e.g., $PM_{2.5}$>PM_{10}) and

from samples collected in urban areas or closer to higher trafficked areas (Abou et al., 2007, 098819; Hornberg et al., 1998, 095741).

de Kok et al. (2005, 088656) found the direct mutagenicity (Ames assay) and the direct DNA reactivity (DNA adduct formation) of the $PM_{2.5}$ size fraction was significantly higher than that of the larger size fractions (TSP, PM_{10}) at most locations.

DNA damage was assessed by the Comet assay in A549 cells exposed to PM collected from a high traffic area in Copenhagen, Denmark (TSP approximately 30 µg/m^3) and compared to the results from exposure of A549 cells to standard reference materials (SRM1650 or SRM2975) at the same concentrations (2.5-250 µg/ml) (Danielsen et al., 2008, 192092). All three particles induced strand breaks and oxidized purines in a dose-dependent manner and there were no obvious differences in potency. In contrast, only the ambient PM formed 8-oxodG when incubated with calf thymus DNA , which may be due to the concentration of transition metals.

Diesel and Gasoline Exhaust

Automobile DE particles (A-DE particles) was tested in *S. typhimurium* strains TA98, TA100, and its derivatives (e.g., TA98NR and YG1021) and found to be more mutagenic than forklift DE particles (f-DE particles, derivative SRM2975), based on PM mass. A-DE particles had 227 times more PAH-type mutagenic activity and 8-45 times more nitroarene-type mutagenic activity (DeMarini et al., 2004, 066329). Using a diesel engine without an oxidation catalytic converter (OCC), the diesel engine exhaust particle extract produced the highest number of revertant colonies in strains TA98 and TA100 with and without S9 at several tested loads when compared to extracts from low-sulfur diesel fuel (LSDF), rapeseed oil methyl ester (RME), and soybean oil methyl ester (SME). When an OCC was installed in the exhaust pipe of the engine, all extracts reduced the number of revertant colonies in both strains with and without S9 at partial loads but increased the number of revertant colonies without S9 at rated power. At idling, DE particles extracts increased the number of revertant colonies with and without S9 (Bunger et al., 2006, 156303). In a separate study, engine emissions (particle extracts and condensates) from rapeseed (canola) oil were found to produce greater mutagenic effects in *S typhimurium* strains TA98 and TA100 than DE particles (Bunger et al., 2007, 156304). Additionally, DE extract (DEE) from diesel fuel containing various percentages of ethanol was also observed to induce mutational response in two Salmonella strains. Base diesel fuel DEE and DEE from fuel with 20% ethanol caused more significant DNA damage in rat fibrocytes L-929 cells than extracts containing 5, 10, or 15% ethanol (Song et al., 2007, 155306).

DE and gasoline engine exhaust particles, as well as their semi-volatile organic compound (SVOC) extracts, induced mutations in the two *S. typhimurium* strains YG1024 and YG1029 in the absence and presence of S9; the PM extracts were more mutagenic than the SVOC extracts. Additionally, all extracts except the DE extract induced DNA damage and MN formation in Chinese hamster lung V79 cells (Liu et al., 2005, 097019). Another study demonstrated that gasoline engine exhaust significantly increased colony formation in TA98 with and without S9 (Zhang et al., 2007, 157186).

Jacobsen et al. (2008, 156597) used the FE1-Muta™ Mouse lung epithelial cell line to investigate putative mechanisms of DE particle-induced mutagenicity. Mutation ion frequencies and ROS were determined after cells were incubated with 37.5 or 75 µg/ml DE particles (SRM1650) for 72-h (n = 8). The mutation frequency at the 75 µg/ml dose was significantly increased (1.55-fold; $p<0.001$) in contrast to cells treated with 37.5 µg/ml DE particles. DE particles-induced ROS generation 1.6- to 1.9-fold in the epithelial cell cultures after 3 h of exposure compared with the 3- to 10-fold increase in ROS production previously reported for CB. The authors concluded that the mutagenic activity of DE particles is likely attributable to activity from the organic fraction that both contains reactive species and can generate ROS.

In human A549 and CHO-K1 cells, the organic fraction of DE particles significantly increased the amount of Comet and MN formation, respectively, in the presence and absence of SKF-525A (a CYP450 inhibitor) and S9, respectively (Oh and Chung, 2006, 088296). The organic base and neutral fractions of DE particles also significantly induced DNA damage but only without SKF-525A, and all fractions but the moderately polar fraction (phthalates and PAH oxyderivatives) induced MN formation with and without S9 (Bao et al., 2007, 097258). Gasoline engine exhaust significantly induced DNA damage as measured in the Comet assay and increased the frequency of MN in human A549 cells (Zhang et al., 2007, 157186). In human-hamster hybrid (A_L) cells, DE particles (SRM 2975) dose-dependently increased the mutation yield at the *CD59* locus; this was

significantly reduced by simultaneous treatment with phagocytosis inhibitors (Bao et al., 2007, 097258).

Wood Smoke

The mutagenicity of wood smoke and cigarette smoke (CS) extracts was assayed in *S. typhimurium* strains TA98 and TA100 (Ames assay) using the pre-incubation assay with exogenous metabolic activation (rat liver S-9). Extracts of both samples (62.5 or 125 µg total PM equivalent/ml) were equally mutagenic to strain TA98 but the wood smoke extract was less mutagenic than the CS extracts in strain TA100 (Iba et al., 2006, 156582).

In Vivo studies

Ambient Air

The contribution of ambient urban roadside air exposure (4, 12, 24, 48 or 60 wk) to DNA damage was examined in the lungs, nasal mucosa, and livers of adult male Wistar rats in Kawasaki, Japan (Sato et al., 2003, 096615). Messenger RNA levels of CYP450 enzymes that catalyze the transformation of PAHs to reactive metabolites were also evaluated. Concentrations of gases were reported to be 12-182 ppb NO and 0-9 ppb NO_2 in the filtered air chamber and 33-280 ppb NO and 42-81 ppb NO_2 in the experimental group chamber. Suspended PM concentrations were 11-19 µg/m^3 in the filtered air chamber and 42-100 µg/m^3 (average 63 µg/m^3) in the experimental group chamber. Body weight significantly decreased in exposed animals at 24, 48 and 60 wk. A 4-wk exposure to urban roadside air resulted in significant increases in multiple DNA adducts (lung, nasal, and liver DNA adducts). With longer exposures, there were significant increases in lung (48 wk), nasal (60 wk), and liver DNA adducts (60 wk). Changes were seen in CYP1A2 mRNA at 4 wk with a 2.3-fold increase in exposed animals compared to the control group with no change observed at 60 wk; CYP1A1 mRNA was unchanged. These results indicate that exposure to ambient air in this roadside area could induce DNA adduct formation, which may be important for carcinogenicity. Earlier studies (Ichinose et al., 1997, 053264) have shown that 8-oxodG, a DNA adduct, is elevated along with tumor formation in a dose-dependent manner in mice administered DE particles. The finding of adducts in the liver indicated that deposition of PM and its associated PAHs in the lung can have indirect effects on extrapulmonary organs. It should be noted that PM deposition on the fur and ingestion during grooming cannot be ruled out as a possible exposure route.

Another animal toxicological study employed "non-carcinogenic" particles obtained from pooled non-cancerous lung tissue collected during surgical lung resection from three non-smoking male patients diagnosed with lung adenocarcinomas (Tokiwa et al., 2005, 191952). Particles were partially purified to remove organic compounds. Morphologically the particles were similar to DE or ambient air PM and the organic extracts from the particles were directly mutagenic in S. typhimurium tester strains TA98, YG1021 and YG1024. BALB/c and ICR mice were intratracheally instilled with particles at doses of 0.25, 0.5, 1.0, or 2.0 mg/mouse. After 24 h, 8-oxodG was measured in lung DNA and found to be increased in ICR mice in a dose-dependent manner, reaching a maximum of ~2.75 8-oxodG/10^5 dG at the 2.0 mg dose. The response was statistically significant at doses of 0.5, 1.0, and 2.0 mg. The increased 8-oxodG levels observed in vivo was reported to be likely due to hydroxyl radicals presumed to be involved in phagocytosis of non-mutagenic particles by inflammatory cells that could induce hydroxylation of guanine residue on DNA.

Diesel Exhaust

An in vivo study employed *gtp* delta transgenic mice carrying the lambda EG10 on each Chromosome 17 from a C57BL/6J background to investigate the effects of DE particles on mutation frequency (Hashimoto et al., 2007, 097261). Mice were exposed via inhalation to DE particles or via IT instillation to DE particles or DE particle extract and lambda EG10 phages were rescued; *E. coli YG6020* was infected with the phage and screened for 6-thioguanine resistance. The mutagenic potency (mutation frequency per mg) caused by DE particle extract was twice that of DE particles, suggesting that the mutagenicity of DE particles is attributed primarily to compounds in the extract,

since ≈50% of the weight of DE particles was provided by the extract. There was no difference in mutation frequency between the 1 and 3 mg/m^3 DE particle groups after 12 wk of exposure.

Wood Smoke

One recent study measured the effect of freshly generated hardwood smoke on CYP1A1 activity based on ethoxyresorufin O-deethylase in pulmonary microsomes recovered from male Sprague-Dawley rats exposed to hardwood smoke by nose-only inhalation exposure (Iba et al., 2006, 156582). CYP1A1 activity in rat lung explants treated with extracts of the total PM (TPM) from hardwood smoke samples and from freshly generated cigarette smoke (CS) was also evaluated. Unlike CS, hardwood smoke did not induce pulmonary CYP1A1 activity or mRNA (assessed by northern blot analysis) nor did extracts of hardwood smoke TPM induce CYP1A1 protein (assessed by western blot analysis) in cultured rat lung explants. The results suggest that unique constituents that are activated by CYP1A1 may be present in CS but not hardwood smoke.

7.5.2.2. Carcinogenesis

Studies published prior to the 2004 AQCD that evaluated the carcinogenicity of ambient air were reviewed by Claxton and Woodall (2007, 180391). Five studies involved chronic inhalation exposures in rodents. No statistically significant increase in tumorigenesis was observed following chronic exposure to urban air pollution in Los Angeles (Gardner, 1966, 015129; Gardner et al., 1969, 015130; Wayne and Chambers, 1968, 038537). However in a study conducted in Brazil, urban air pollution was found to enhance the formation of urethane-induced lung tumors in mice (Cury et al., 2000, 192100; Reymao et al., 1997, 084653).

Two recent studies evaluated the carcinogenic potential of chronic inhalation exposures to DE (Reed et al., 2004, 055625) and hardwood smoke (Reed et al., 2006, 156043). Two indicators of carcinogenic potential, formation of MN and tumorigenesis were measured in strain A/J mice, which is a mouse model that spontaneously develops lung tumors. Exposure to DE or hardwood smoke at concentrations of 1,000 μg/m^3 and below did not cause increased formation of MN or an increased rate of lung tumors in this cancer-prone rodent model. These studies are described below.

Diesel Exhaust

A/J mice were exposed to 30, 100, 300 and 1000 μg/m^3 DE for 6 h/day and 7 days/wk for 6 mo (Reed et al., 2004, 055625). The concentration of gases in this including NO_X, NO_2, CO, SO_2, NH_3, methane, non-methane VOC, and FID total hydrocarbon ranged from control to high dose group values of 0 to 50.4 ± 0.6 ppm, 0.2 ± 0.2 to 6.9 ± 3.3 ppm, 0.3 ± 0.1 to 30.9 ± 4.5 ppm, not detectable to 955.2 ± 58.4 ppb, 176.5 ± 8.8 to 9.1 ± 0.2 μg/m^3, 1406.5 ± 253.2 to 2642.1 ± 455.9 μg/m^3, 134.0 ± 52.1 to 1578.6 ± 256.2 μg/m^3, 0.1 ± 0.1 to 2.2 ± 0.2 ppm, respectively. Particle sizes in the four exposure groups ranged from 0.10-0.15 μm MMAD with geometric standard deviations of 1.4-1.8. Following the 6-mo exposure and a 6-mo recovery period, mice were collected and MN formation in blood and tumor multiplicity and tumor incidence were measured in lungs. No increases in formation of MN or numbers of lung adenomas were observed in DE-exposed mice compared with controls.

Wood Smoke

A/J mice were exposed to 30, 100, 300 and 1,000 μg/m^3 hardwood smoke or to 30, 100, 300 and 1,000 μg/m^3 DE for 6 h/day and 7 days/wk for 6 mo (Reed et al., 2006, 156043). Gaseous components of the hardwood smoke included CO, NH_3, and non-methane VOC with concentrations from control levels to high dose hardwood smoke exposure ranging from 229 ± 31 to 14887.6 ± 832.3 ppm, 139.3 ± 2.3 to 54.9 ± 1.2 μg/m^3 and 177.6 ± 10.4 to 3455.0 ± 557.2 μg/m^3, respectively. Concentrations of NO_X, NO_2 and SO_2 were reported to be null. Particle sizes in the four exposure groups ranged from 0.25-0.36 μm MMAD with geometric standard deviations of 2.0-3.3. Following the 6-mo exposure and a 6-mo recovery period, mice were collected and MN formation in blood and tumor multiplicity and tumor incidence were measured in lungs. No increases in formation of MN or

numbers of lung adenomas were observed in hardwood smoke-exposed mice compared with controls. However, hardwood smoke from this study was mutagenic in the Ames reverse mutation assay.

7.5.2.3. Summary of Toxicological Studies

In summary, numerous new in vitro studies confirm and extend findings reported in the 2004 AQCD that ambient PM from urban sites and combustion-derived PM are mutagenic and genotoxic. A small number of new studies were conducted in vivo. One of these studies demonstrated increased mutagenic potency in mice exposed to DE particles and DE particle extract. Another study found increased formation of 8-oxodG, a DNA adduct, following IT instillation of PM in mice. A chronic inhalation study of rats exposed to urban roadside air reported increased formation of DNA adducts in nose, lung, and liver and induction of CYP1A2. Inhalation exposure of rats to hardwood smoke failed to induce CYP1A1 in another study. Finally, two chronic inhalation studies found no evidence of carcinogenic potential for DE and hardwood smoke in a cancer-prone mouse model. Collectively, these results provide some evidence, mainly from in vitro studies, to support the biological plausibility of ambient PM-lung cancer relationships observed in epidemiology studies.

7.5.3. Epigenetic Studies and Other Heritable DNA mutations

Two epidemiologic epigenetic studies examined the effect of PM on DNA methylation. Both studies examined methylation of Alu and long interspersed nuclear element-1 (LINE-1) sequences, which are located in repetitive elements. In previous studies, methylation of these sequences has been linked to global genomic DNA methylation content (Weisenberger et al., 2005, 192101; Yang et al., 2004, 192102).

The first study included men age 55 and older who were part of the Normative Aging Study in the Boston area (Baccarelli et al., 2009, 192155). A stationary monitoring site located 1 km from the examination site was used to estimate ambient $PM_{2.5}$ exposure for the duration of the study (1999-2007). During the study period, the median level of $PM_{2.5}$, averaged over 7-day periods, was 9.8 $\mu g/m^3$ (interquartile range 8.0-12.0 $\mu g/m^3$). There was no association between $PM_{2.5}$ and Alu methylation. LINE-1 methylation was associated with $PM_{2.5}$ measured over the 7 days before the examinations.

The second study included 63 healthy men aged 27-55 yr working at an electric furnace steel plant (Tarantini et al., 2009, 192010). Blood samples were taken twice, once in the morning after 2 days of not working and once in the morning after 3 full days of work. PM_{10} was measured in 11 work areas and individuals completed daily logs about the amount of time spent in each area. On average, individuals had an estimated exposure of 233.4 $\mu g/m^3$ PM_{10} (range 73.4-1220.2 $\mu g/m^3$). Short-term exposure did not alter the methylation of Alu and LINE-1. To examine effects of long-term exposure, both blood samples were considered independent of time, and Alu and LINE-1 were examined with respect to overall estimated PM_{10} exposure using mixed effects models. There was a negative association between increasing levels of PM_{10} exposure and Alu and LINE-1 methylation, indicating that PM_{10} causes epigenetic changes to occur with long-term exposure. This study also looked at levels of iNOS gene, which is a gene suppressed by DNA methylation. iNOS expression was not associated with long term exposure to PM_{10} but was affected by methylation in the short term.

Animal toxicology studies evaluating the effect of PM exposure on changes in the epigenome and other non-epigenetic heritable DNA changes have only recently been conducted. After earlier work showed increased germline mutation rates in herring gulls nesting near steel mills on Lake Ontario (Yauk and Quinn, 1996, 089093) further work was conducted to address air-dependent contribution to germline mutations by housing male and female Swiss Webster mice in the same area and comparing mutation rates in those animals with mutation rates of animals housed in a rural setting with less air pollution (Somers et al., 2002, 078100). To determine if PM or the gaseous phase of the urban air was responsible for heritable mutations, Yauk et al. (2008, 157164) exposed mature male C57Bl×CBA F1 hybrid mice to either HEPA-filtered air or to ambient air in Hamilton, Ontario, Canada for 3 or 10 wk, or 10 wk plus 6 wk of clean air exposure (16 wk) (also discussed in Section 7.4.2.5). Sperm DNA was monitored for ESTR mutations, testicular sample bulky DNA adducts, and DNA single or double strand breaks. In addition, male-germ line (spermatogonial stem

cell) DNA methylation was monitored post-exposure. This area in Hamilton is near two steel mills and a major highway. Air composition showed mean concentrations for TSP of 93.8 ± 17 μg/m^3, PAH of 8.3 ± 1.7 ng/m^3, and metal of 3.6 ± 0.7 μg/m^3. Mutation frequency at ESTR Ms6-hm locus in sperm DNA from mice exposed 3 or 10 wk did not show elevated ESTR mutation frequencies, but there was a significant increase in ESTR mutation frequency at 16 wk compared to HEPA-filter control animals, pointing to a PM-dependent mechanism of action. No detectable DNA adducts were observed in testes samples at any of the time points monitored. To verify inhalation exposure to particles, DNA adducts were reported in the lungs of mice exposed for 3 wk to ambient air; no other time points showed detectable DNA adduct formation. Hypermethylation of germ-line DNA was also observed in mice exposed to ambient air for 10 and 16 wk. These PM-dependent epigenetic modifications (hypermethylation) were not seen in the halploid stage (3 wk) of spermatogenesis, but were nonetheless seen in early stages of spermatogenesis (10 wk) and remained significantly elevated in mature sperm even after removal of the mouse from the environmental exposure (16 wk). Thus, these studies indicate that the ambient PM phase and not the gaseous phase is responsible for the increased frequency of heritable DNA mutations and epigenetic modifications.

Based on the limited evidence from these epigenetics studies, long-term exposure to PM_{10} may result in epigenetic changes. $PM_{2.5}$ also potentially affects some DNA methylation content. As epigenetic research progresses, future studies examining the relationship between PM and DNA methylation will be important in more thoroughly characterizing these associations.

The effect of ambient PM on heritable DNA mutations and the epigenome has been well characterized in a Canadian steel mill area. Mice exposed to ambient PM plus gases developed paternally-derived heritable DNA mutations and epigenetic changes in sperm DNA that were not observed in mice exposed to ambient air that was HEPA-filtered. This is the first animal toxicology study showing heritable effects of PM exposure on DNA mutation and the epigenome. Because the epigenetics field is so new, further work in this emerging area will expand on these PM-dependent methylation changes to determine if the results can be recapitulated at other urban sites.

7.5.4. Summary and Causal Determinations

7.5.4.1. $PM_{2.5}$

The 2004 PM AQCD reported on original and follow-up analyses for three prospective cohort studies that reported positive relationships between $PM_{2.5}$ and lung cancer mortality. Several recent, well-conducted epidemiologic studies have extended the evidence for a positive association between $PM_{2.5}$ and lung cancer mortality (Section 7.5.1.1). Generally, studies have not reported associations between long-term exposure to $PM_{2.5}$ or PM_{10} and lung cancer incidence (Section 7.5.1.1). Animal toxicological studies did not focus on specific size fractions of PM, but rather examined ambient PM, wood smoke, and DE particles (Section 7.5.2). A number of recent studies indicate that ambient urban PM, emissions from wood/biomass burning, emissions from coal combustion, and gasoline and DE are mutagenic and that PAHs are genotoxic (Section 7.5.2). These findings are consistent with earlier studies that concluded that ambient PM and PM from specific combustion sources are mutagenic and genotoxic and provide biological plausibility for the results observed in the epidemiologic studies. A limited number of epidemiologic and toxicological studies on the epigenome demonstrate that PM induces changes in methylation (Section 7.5.3), a new area of research that will likely be expanded in the future. However, it has yet to be determined how these alterations in the genome could influence the initiation and promotion of cancer. Overall, the evidence is **suggestive of a causal relationship between relevant $PM_{2.5}$ exposures and cancer, with the strongest evidence from the epidemiologic studies of lung cancer mortality.** This evidence is limited by the non-specific measure of PM size fraction in some of the epidemiologic studies and most of the animal toxicological studies, and the inconsistency in evidence with recent epidemiologic studies for an effect on cancer incidence. There is no epidemiologic evidence for cancer related to long-term exposure to PM in organs or systems other than the lung.

7.5.4.2. $PM_{10-2.5}$

The 2004 PM AQCD did not report long-term exposure studies for $PM_{10-2.5}$. No epidemiologic studies have been conducted to evaluate the effects of long-term $PM_{10-2.5}$ exposure and cancer. The evidence is **inadequate to assess the association between $PM_{10-2.5}$ and UFP exposures and cancer.**

7.5.4.3. UFPs

The 2004 PM AQCD did not report long-term exposure studies for UFPs. No epidemiologic studies have been conducted to evaluate the effects of long-term UFP and cancer. The evidence is **inadequate to determine if a causal relationship exists between long-term UFP exposures and cancer**.

7.6. Mortality

In the 1996 PM AQCD, results were presented for three prospective cohort studies of adult populations: the Six Cities Study (Dockery et al., 1993, 044457); the ACS Study (Pope et al., 1995, 045159); and the AHSMOG Study (Abbey et al., 1995, 000669). The 1996 AQCD concluded that the chronic exposure studies, taken together, suggested associations between increases in mortality and long-term exposure to $PM_{2.5}$, though there was no evidence to support an association with $PM_{10-2.5}$ (U.S. EPA, 1996, 079380).

Discussions of mortality and long-term exposure to PM in the 2004 PM AQCD emphasized the results of four U.S. prospective cohort studies, but the greatest weight was placed on the findings of the ACS and the Harvard Six Cities studies, which had each undergone extensive independent reanalysis, and which were based on cohorts that were broadly representative of the U.S. population. The 2004 PM AQCD concluded that the results from the Seventh-Day Adventist (AHSMOG) cohort provided some suggestive (but less conclusive) evidence for associations, while results from the Veterans Cohort provided inconsistent evidence for associations between long-term exposures to $PM_{2.5}$ and mortality. Collectively, the 2004 PM AQCD found that these studies provided strong evidence that long-term exposure to $PM_{2.5}$ was associated with increased risk of human mortality. Effect estimates for all-cause mortality ranged from 6 to 13% increased risk per 10 $\mu g/m^3$ $PM_{2.5}$, while effect estimates for cardiopulmonary mortality ranged from 6 to 19% per 10 $\mu g/m^3$ $PM_{2.5}$. For lung cancer mortality, the effect estimate was a 13% increase per 10 $\mu g/m^3$ $PM_{2.5}$, based upon the results of the extended analysis from the ACS cohort (Pope et al., 2002, 024689). With regard to $PM_{10-2.5}$, the 2004 PM AQCD reported that no association was observed between mortality and long-term exposure to $PM_{10-2.5}$ in the ACS study (Pope et al., 2002, 024689), while a positive but statistically non-significant association was reported in males in the AHSMOG cohort (McDonnell et al., 2000, 010319). Thus, the 2004 PM AQCD concluded that there was insufficient evidence for associations between long-term exposure to $PM_{10-2.5}$ and mortality. Overall, the 2004 PM AQCD concluded that there was strong epidemiologic evidence for associations between long-term exposures to $PM_{2.5}$ and excess all-cause and cardiopulmonary mortality.

At the time of the 2004 PM AQCD, only a limited number of the chronic-exposure cohort studies had considered direct measurements of constituents of PM, other than sulfates. With regard to source-oriented evaluations of mortality associations with long-term exposure, the 2004 PM AQCD noted only the study by Hoek et al. (2002, 042364), in which the authors concluded that long-term exposure to traffic-related air pollution may shorten life expectancy. However, Hoek et al. (2002, 042364) also noted that living near a major road might include other factors that contribute to mortality associations. There was not sufficient evidence at the time of the 2004 PM AQCD to draw conclusions on effects associated with specific components or sources of PM.

New epidemiologic evidence reports a consistent association between long-term exposure to $PM_{2.5}$ and increased risk of mortality. There is little evidence for the long-term effects of $PM_{10-2.5}$ on mortality. Although this section focuses on mortality outcomes in response to long-term exposure to PM, it does not evaluate studies that examine the association between PM and infant mortality.

These studies are evaluated in Section 7.5 because it is possible that in utero exposures contribute to infant mortality. A summary of the mean PM concentrations reported for the studies characterized in this section is presented in Table 7-8.

Table 7-8. Characterization of ambient PM concentrations from studies of mortality and long-term exposures to PM.

Study	Location	Mean Concentration ($\mu g/m^3$)	Upper Percentile Concentrations ($\mu g/m^3$)
$PM_{2.5}$			
Brunekreef et al. (2009, 191947)	The Netherlands	28	95th: 32 99th: 33 Max: 37
Chen et al. (2005, 087942)	Multicity, CA	29.0	
Eftim et al. (2008, 099104)	U.S.	13.6-14.1	Max: 19.1-25.1
Enstrom (2005, 087356)	CA	23.4	Max: 36.1
Goss et al. (2004, 055624)	U.S.	13.7	75th: 15.9
Janes et al. (2007, 090927)	U.S.	14.0	
Jerrett et al. (2005, 087600)	Los Angeles, CA		Max: 27.1
Krewski et al. (2009, 191193)	U.S.	14.02	75^{th}: 16.00 90th: 26.75 95th: 27.89 Max: 30.01
Laden et al. (2006, 087605)	Multicity, U.S.	10.2-29.0	
Lipfert et al. (2006, 088218)	U.S.	14.3	
Miller et al. (2007, 090130)	U.S.	13.5	75th: 18.3 Max: 28.3
Pope et al. (2004, 055880)	U.S.	17.1	
Schwartz et al. (2008, 156963)	Multicity, U.S.	17.5	Max: 40
Zeger et al. (2007, 157176)	U.S.		17.0
Zeger et al. (2008, 191951)	U.S.	13.2	75th: 14.9
$PM_{10-2.5}$			
Chen et al. (2005, 087942)	Multicity, CA	25.4	
Lipfert et al. (2006, 088218)	U.S.	16.0	
PM_{10}			
Chen et al. (2005, 087942)	Multicity, CA	52.6	
Gehring et al. (2006, 089797)	North Rhine, Germany	43.7-48.0	Max: 52.5-56.1
Goss et al. (2004, 055624)	U.S.	24.8	75th: 28.9
Puett et al. (2008, 156891)	NE U.S.	21.6	
Zanobetti et al. (2008, 156177)	U.S.	29.4	

7.6.1. Recent Studies of Long-Term Exposure to PM and Mortality

Studies since the last PM AQCD include results of new analyses and insights for the ACS and Harvard Six Cities studies, further analyses from the AHSMOG and Veterans study cohorts, as well as analyses of a Cystic Fibrosis cohort and subsets of the ACS from Los Angeles and New York City. In the original analyses of the Six Cities and ACS cohort studies, no associations were found between long-term exposure to $PM_{10-2.5}$ and mortality, and the extended and follow-up analyses did not evaluate associations with $PM_{10-2.5}$. The historical and more recent results for $PM_{2.5}$ of both the ACS and the Harvard Six Cities studies are compiled in Figure 7-6. Moreover, since the last PM AQCD, there is a major new cohort that investigates the effects of $PM_{2.5}$ on cardiovascular mortality in the literature: the WHI study (Miller et al., 2007, 090130). Most recently, an ecologic cohort study of the nation's Medicare population has been completed (Eftim et al., 2008, 099104). These new findings further strengthen the evidence linking long-term exposure to $PM_{2.5}$ and mortality, while providing indications that the magnitude of the $PM_{2.5}$-mortality association is larger than previously estimated (Figure 7-7). Two recent reports from the AHSMOG and Veterans study cohorts have provided some limited evidence for associations between long-term exposure to $PM_{10-2.5}$ and mortality. The original analyses of the AHSMOG cohort study found positive associations between long-term concentrations of PM_{10} and 15-yr mortality due to natural causes and lung cancer (Abbey et al., 1999, 047559). McDonnell et al. (2000, 010319) reanalyzed these data and concluded that previously observed association of long-term ambient PM_{10} concentrations with mortality for males were best explained by a relationship of mortality with the fine fraction of PM_{10} rather than the thoracic coarse fraction of PM_{10}. Recent reports from the AHSMOG study cohort, as well as the Nurses' Health Study and a cohort of women in Germany have provided some evidence for associations between long-term exposure to PM_{10} and mortality among women.

Harvard Six Cities: A follow-up study has used updated air pollution and mortality data; an additional 1,368 deaths occurred during the follow-up period (1990-1998) versus 1,364 deaths in the original study period (1974-1989) (Laden et al., 2006, 087605). Statistically significant associations are reported between long-term exposure to $PM_{2.5}$ and mortality for data for the two periods (RR = 1.16 [95% CI: 1.07-1.26] per 10 $\mu g/m^3$ $PM_{2.5}$). Of special note is a statistically significant reduction in mortality risk reported with reduced long-term $PM_{2.5}$ concentrations (RR = 0.73 [95% CI: 0.57-0.95] per 10 $\mu g/m^3$ $PM_{2.5}$). This is equivalent to an RR of 1.27 for reduced mortality risks with reduced long-term $PM_{2.5}$ concentrations. This reduced mortality risk was observed for deaths due to cardiovascular and respiratory causes, but not for lung cancer deaths. The $PM_{2.5}$ concentrations for recent years were estimated from visibility data, which introduces some uncertainty in the interpretation of the results from this study. Coupled with the results of the original analysis (Dockery et al., 1993, 044457), this study strongly suggests that a reduction in $PM_{2.5}$ pollution yields positive health benefits.

ACS Extended Analyses/Reanalysis II: Two new analyses further evaluated the associations of long-term $PM_{2.5}$ exposures with risk of mortality in 50 U.S. cities reported by Pope and colleagues (2002, 024689), adding new details about deaths from specific cardiovascular and respiratory causes (Krewski, 2009, 190075; Pope et al., 2004, 055880). Pope et al. (2004, 055880) reported positive associations with deaths from specific cardiovascular diseases, particularly ischemic heart disease (IHD), and a group of cardiac conditions including dysrhythmia, heart failure and cardiac arrest (RR for cardiovascular mortality = 1.12, 95% CI 1.08-1.15 per 10 $\mu g/m^3$ $PM_{2.5}$), but no PM associations were found with respiratory mortality.

In an additional reanalysis that extended the follow-up period for the ACS cohort to 18 yr (1982-2000) (Krewski et al., 2009, 191193), investigators found effect estimates that were similar, though generally higher, than those reported in previous ACS analyses. This reanalysis also included data for seven ecologic (neighborhood-level) contextual (i.e., not individual-level) covariates, each of which represents local factors known or suspected to influence mortality, such as poverty level, educational attainment, and unemployment. The effect estimate for all cause mortality, based on $PM_{2.5}$ concentrations measured in 1999-2000 was 1.03 (95% CI: 1.01-1.05). The corresponding effect estimates for deaths due to IHD and lung cancer were 1.15 (95% CI: 1.04-1.18) and 1.11 (95% CI: 1.04-1.18), respectively. In earlier analyses of this cohort, investigators found that increasing education levels appeared to reduce the effect of $PM_{2.5}$ exposure on mortality. Results from this reanalysis show a similar pattern, although with somewhat less certainty, for all causes of death except IHD, for which the pattern was reversed. Overall, although the addition of random effects modeling and contextual covariates to the ACS model made most effect estimates higher (but

some lower), they were not statistically different from the earlier ACS effect estimates. Thus, these new analyses, with their more extensive consideration of potentially confounding factors, confirm the published ACS $PM_{2.5}$-mortality results to be robust.

California Cancer Prevention Study: In a cohort of elderly people in 11 California counties (mean age 73 yr in 1983), an association was reported for long-term $PM_{2.5}$ exposure with all-cause deaths from 1973-1982 (RR = 1.04 [95% CI: 1.01-1.07] per 10 $\mu g/m^3$ $PM_{2.5}$) (Enstrom, 2005, 087356). However, no significant associations were reported with deaths in later time periods when $PM_{2.5}$ levels had decreased in the most polluted counties (1983-2002) (RR = 1.00 [95% CI: 0.98-1.02] per 10 $\mu g/m^3$ $PM_{2.5}$). The $PM_{2.5}$ data were obtained from the EPA's Inhalation Particle Network (collected 1979-1983), and the locations represented a subset of data used in the 50-city ACS study (Pope et al., 1995, 045159). However, the use of average values for California counties as exposure surrogates likely leads to significant exposure error, as many California counties are large and quite topographically variable.

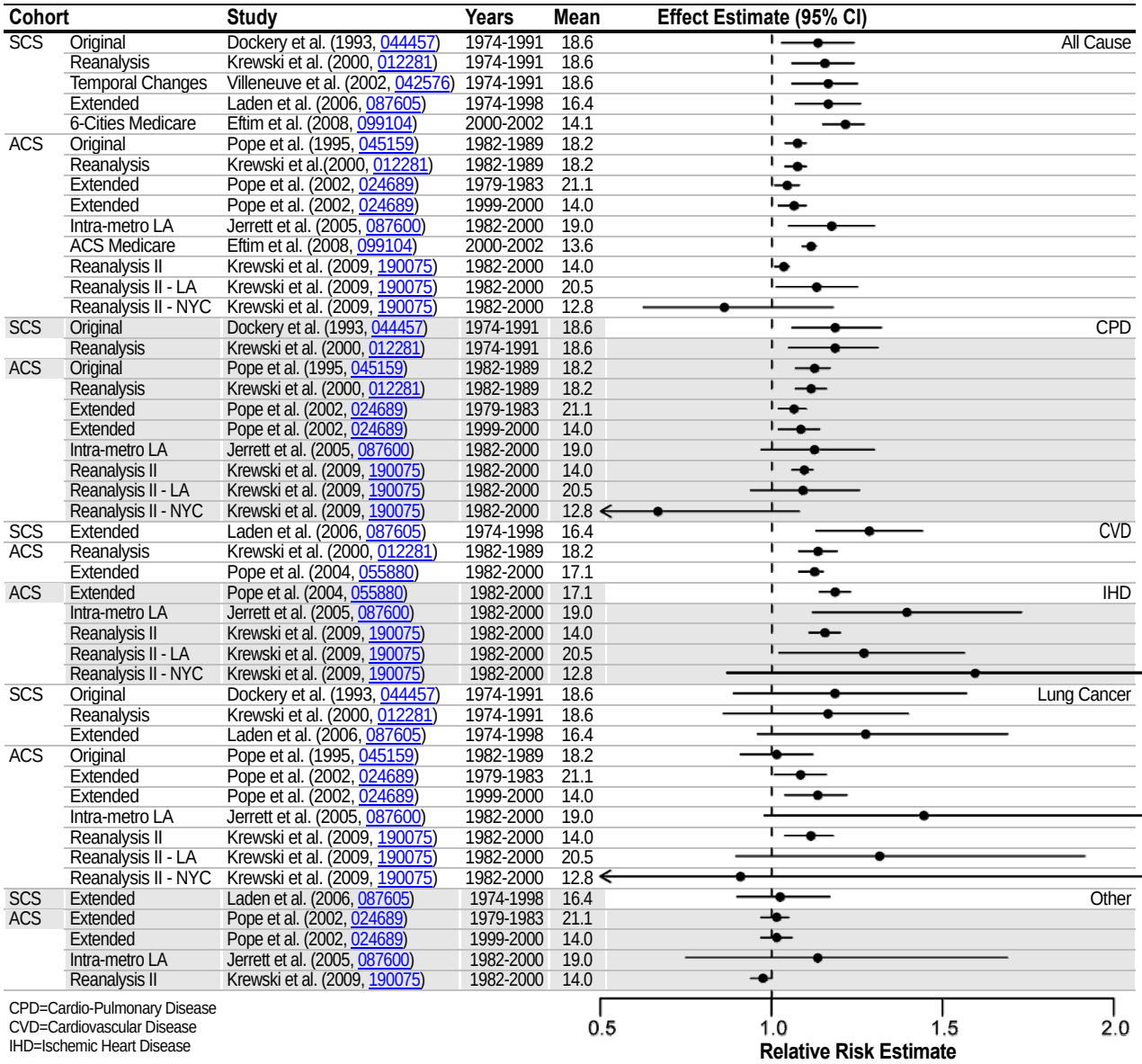
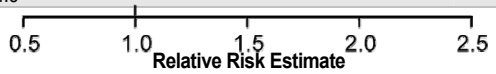


Figure 7-6. Mortality risk estimates associated with long-term exposure to $PM_{2.5}$ from the Harvard Six Cities Study (SCS) and the American Cancer Society Study (ACS).

Study	Cohort	Subset	Mean	Effect Estimate (95% CI)	
McDonnell et al. (2000, 010319)	AHSMOG	Males	32.0		All Cause
Brunekreef et al. (2009, 191947)	NLCS-AIR	Full Cohort	28.3		
		Case Cohort	28.3		
Enstrom (2005, 087356)	CA Cancer Prevention	1973-1982	23.4		
		1983-2002	23.4*		
		1973-2002	23.4*		
Jerrett et al. (2005, 087600)	ACS-LA		19.0		
Krewski et al. (2009, 191193)	ACS Reanalysis II-LA		20.5		
Laden et al. (2006, 087605)	Harvard 6-Cities		16.4		
Lipfert et al. (2006, 088218)	Veterans Cohort		14.3		
			14.3		
Eftim et al. (2008, 099104)	Medicare Cohort	ACS Sites	13.6		
		6-Cities sites	14.1		
Krewski et al. (2009, 191193)	ACS Reanalysis II		14.0		
Goss et al. (2004, 055624)	U.S. Cystic Fibrosis		13.7		
Zeger et al. (2008, 191951)	MCAPS	65+, Eastern	14.0		
		65+, Central	10.7		
		65+, Western	13.1		
		65-74, Eastern	14.0		
		65-74, Central	10.7		
		65-74, Western	13.1		
		65+, Eastern	14.0		
		75-84, Central	10.7		
		75-84, Western	13.1		
		85+, Eastern	14.0		
		85+, Central	10.7		
		85+, Western	13.1		
Krewski et al. (2009, 191193)	ACS Reanalysis II-NYC		12.8		
Brunekreef et al. (2009, 191947)	NLCS-AIR	Full Cohort	28.3		CV
		Case Cohort	28.3		
Pope et al. (2004, 055880)	ACS		17.1		
Laden et al. (2006, 087605)	Harvard 6-Cities		16.4		
Naess et al. (2007, 090736)	Oslo, Norway	Males, 51-70 yrs	14.3		
		Males, 71-90 yrs	14.3		
		Females, 51-70 yrs	14.3		
		Females 71-90 yrs	14.3		
Miller et al. (2007, 090130)	WHI	Females	13.5		
Chen et al. (2005, 087942)	AHSMOG	Females	29.0		CHD
		Males	29.0		
Jerrett et al. (2005, 087600)	ACS-LA		19.0		IHD
Krewski et al. (2009, 190075)	ACS Reanalysis II-LA		20.5		
Pope et al. (2004, 055880)	ACS		17.1		
Krewski et al. (2009, 191193)	ACS Reanalysis II		14.0		
	ACS Reanalysis II-NYC		12.8		
McDonnell et al. (2000, 010319)	AHSMOG	Males	32.0		CPD
Jerrett et al. (2005, 087600)	ACS-LA		19.0		
Krewski et al. (2009, 191193)	ACS Reanalysis II-LA		20.5		
	ACS Reanalysis II		14.0		
	ACS Reanalysis II-NYC		12.8		
Brunekreef et al. (2009, 191947)	NLCS-AIR	Full Cohort	28.3		Respiratory
		Case Cohort	28.3		
Laden et al. (2006, 087605)	Harvard 6-Cities		16.4		
McDonnell et al. (2000, 010319)	AHSMOG	Males	32.0		Lung Cancer
Brunekreef et al. (2009, 191947)	NLCS-AIR	Full Cohort	28.3		
		Case Cohort	28.3		
Jerrett et al. (2005, 087600)	ACS-LA		19.0		
Krewski et al. (2009, 191193)	ACS Reanalysis II-LA		20.5		
Laden et al. (2006, 087605)	Harvard 6-Cities		16.4		
Naess et al. (2007, 090736)	Oslo, Norway	Males, 51-70 yrs	14.3		
		Males 71-90 yrs	14.3		
		Females, 51-70 yrs	14.3		
		Females, 71-90 yrs	14.3		
Krewski et al. (2009, 191193)	ACS Reanalysis II		14.0		
	ACS Reanalysis II-NYC		12.8		
Brunekreef et al. (2009, 191947)	NLCS-AIR	Full Cohort	28.3		Other
		Case Cohort	28.3		
Jerrett et al. (2005, 087600)	ACS-LA		19.0		
Laden et al. (2006, 087605)	Harvard 6-Cities		16.4		
Krewski et al. (2009, 191193)	ACS Reanalysis II		14.0		



CV=Cardiovascular; CHD= Coronary Heart Disease
IHD=Ischemic Heart Disease; CPD=Cardio-Pulmonary Disease
* $PM_{2.5}$ data from 1973-1982 applied to all subsequent time periods

Figure 7-7. Mortality risk estimates, long-term exposure to $PM_{2.5}$ in recent cohort studies.

AHSMOG: In this analysis for the Seventh-Day Adventist cohort in California, a positive, statistically significant, association with coronary heart disease mortality was reported among females (92 deaths; RR = 1.42 [95% CI: 1.06-1.90] per 10 $\mu g/m^3$ $PM_{2.5}$), but not among males (53 deaths; RR = 0.90 [95% CI: 0.76-1.05] per 10 $\mu g/m^3$ $PM_{2.5}$) (Chen et al., 2005, 087942). Associations were strongest in the subset of postmenopausal women (80 deaths; RR = 1.49 [95% CI: 1.17-1.89] per 10 $\mu g/m^3$ $PM_{2.5}$). The authors speculated that females may be more sensitive to air pollution-related effects, based on differences between males and females in dosimetry and exposure. As was found with $PM_{2.5}$, a positive association with coronary heart disease mortality was reported for PM_{10-25} and PM_{10} among females (RR = 1.38 [95% CI: 0.97-1.95] per 10 $\mu g/m^3$ $PM_{10-2.5}$; RR = 1.22 [95% CI: 1.01-1.47] per 10 $\mu g/m^3$ PM_{10}), but not for males (RR = 0.92 [95% CI: 0.66-1.29] per 10 $\mu g/m^3$ $PM_{10-2.5}$; RR = 0.94 [95% CI: 0.82-1.08] per 10 $\mu g/m^3$ PM_{10}); associations were strongest in the subset of postmenopausal women (80 deaths) (Chen et al., 2005, 087942).

U.S. Cystic Fibrosis cohort: A positive, but not statistically significant, association was reported for $PM_{2.5}$ in this study (RR = 1.32 [95% CI: 0.91-1.93] per 10 $\mu g/m^3$ $PM_{2.5}$) that primarily focused on evidence of exacerbation of respiratory symptoms (Goss et al., 2004, 055624). No clear association was reported for PM_{10}. However, only 200 deaths had occurred in the cohort of over 11,000 people (average age in cohort was 18.4 yr), so the power of this study to detect associations was relatively low.

Women's Health Initiative (WHI) Study: This nationwide cohort study considered 65,893 post-menopausal women with no history of cardiovascular disease who lived in 36 U.S. metropolitan areas from 1994 to 1998 (Miller et al., 2007, 090130). The study had a median subject follow-up time of 6 years. Miller and colleagues assessed each woman's exposure to air pollutants using the monitor located nearest to their residence. Hazard ratios were estimated for the first cardiovascular event, adjusting for age, race or ethnic group, smoking status, educational level, household income, body-mass index, and presence or absence of diabetes, hypertension, or hypercholesterolemia. Overall, this study concludes that "long-term exposure to fine particulate air pollution is associated with the incidence of cardiovascular disease and death among postmenopausal women." In terms of effect size, the study found that each increase of 10 $\mu g/m^3$ of $PM_{2.5}$ was associated with a 24% increase in the risk of a cardiovascular event (hazard ratio, 1.24 [95% CI: 1.09-1.41]) and a 76% increase in the risk of death from cardiovascular disease (hazard ratio, 1.76 [95% CI: 1.25-2.47]). While this study found results confirmatory to the ACS and Six Cities Study, it reports much larger relative risk estimates per $\mu g/m^3$ $PM_{2.5}$. In addition, since the study included only women without pre-existing cardiovascular disease, it could potentially be a healthier cohort population than that considered by the ACS and Six Cities Study. Indeed, the WHI Study reported only 216 cardiovascular deaths in 349,643 women-yr of follow-up, or a rate of 0.075% deaths per year (Miller et al., 2007, 090130), while the ACS Study reported that 10% of subjects died of cardiovascular disease over a 16-yr follow-up period, yielding a rate of 0.625% per year, or approximately 8 times the cardiovascular mortality rate of the WHI population (Pope et al., 2004, 055880). Thus, $PM_{2.5}$ impacts may yield higher relative risk estimates in the WHI population because the $PM_{2.5}$ risk is being compared to a much lower prevailing risk of cardiovascular death in this select study population.

The WHI study not only confirms the ACS and Six City Study associations with mortality in yet another well characterized cohort with detailed individual-level information, it also has been able to consider the individual medical records of the thousands of WHI subjects over the period of the study. This has allowed the researchers to examine not only mortality, but also related morbidity in the form of heart problems (cardiovascular events) experienced by the subjects during the study. As reported in this paper, this examination confirmed that there is an increased risk of cardiovascular morbidity, as well (Section 7.2.9). These morbidity co-associations with $PM_{2.5}$ in the same population lend even greater support to the biological plausibility of the air pollution-mortality associations found in this study.

Medicare Cohort Studies: Using Medicare data, Eftim and co-authors (2008, 099104) assessed the association of $PM_{2.5}$ with mortality for the same locations included in the ACS and Six City Study. For these locations, they estimated the chronic effects of $PM_{2.5}$ on mortality for the period 2000-2002 using mortality data for cohorts of Medicare participants and average $PM_{2.5}$ levels from monitors in the same counties included in the two studies. Using aggregate counts of mortality by county for three age groups, they estimated mortality risk associated with air pollution adjusting for age and sex and area-level covariates (education, income level, poverty, and employment), and controlled for potential confounding by cigarette smoking by including standardized mortality ratios

for lung cancer and COPD. This study is, therefore, an ecological analysis, similar to past published cross-sectional analyses, in that area-level covariates (education, income level, poverty, and employment) are employed as controlling variables, since individual level information is not available from the Medicare database (other than age and sex), which includes virtually all Americans aged 65 or greater. Exposures are also ecological in nature, as central site data are used as indices of exposure. These results indicated that a 10 $\mu g/m^3$ increase in the yearly average $PM_{2.5}$ concentration is associated with 10.9% (95% CI: 9.0-12.8) and with 20.8% (95% CI: 14.8-27.1) increases in all-cause mortality for the ACS and Six Cities Study counties, respectively. The estimates are somewhat higher than those reported by the original investigators, and there may be several possible explanations for this apparent increase, especially that this is an older population than the ACS cohort. Perhaps the most likely explanation is that the lack of personal confounder information (e.g., past personal smoking information) led to an insufficient control for the effects of these other variables' effects on mortality, inflating the pollution effect estimates somewhat, similar to what has been found in the ACS analyses when only ecological-level control variables were included. The ability of the Eftim et al. (2008, 099104) study results to qualitatively replicate the original individual-level cohort study (e.g., ACS and Six Cities Study) results suggests that past ecological cross-sectional mortality study results may also provide useful insights into the nature of the association, especially when used for consideration of time trends, or for comparisons of the relative (rather than absolute) sizes of risks between different pollutants or PM components in health effects associations.

Janes et al. (2007, 090927) used the same nationwide Medicare mortality data to examine the association between monthly averages of $PM_{2.5}$ over the preceding 12 mo and monthly mortality rates in 113 U.S. counties from 2000 to 2002. They decomposed the association between $PM_{2.5}$ and mortality into two components: (1) the association between "national trends" in $PM_{2.5}$ and mortality; and (2) the association between "local trends," defined as county-specific deviations from national trends. This second component is posited to provide evidence as to whether counties having steeper declines in $PM_{2.5}$ also have steeper declines in mortality relative to the national trend. They report that the exposure effect estimates are different at these two spatiotemporal scales, raising concerns about confounding bias in these analyses. The authors assert that the association between trends in $PM_{2.5}$ and mortality at the national scale is more likely to be confounded than is the association between trends in $PM_{2.5}$ and mortality at the local scale and, if the association at the national scale is set aside, that there is little evidence of an association between 12-month exposure to $PM_{2.5}$ and mortality in this analysis. However, in response, Pope and Burnett (2007, 090928) point out that such use of long-term time trends as the primary source of exposure variability has been avoided in most other air pollution epidemiology studies because of such concerns about potential confounding of such time-trend associations.

By linking monitoring data to the U.S. Medicare system by county of residence, Zeger et al. (2007, 157176) analyzed Medicare mortality records, comprising over 20 million enrollees in the 250 largest counties during 2000-2002. The authors estimated log-linear regression models having age-specific county level mortality rates as the outcome and, as the main predictor, the average $PM_{2.5}$ pollution level in each county during 2000. Area-level covariates were used to adjust for socio-economic status and smoking. The authors reported results under several degrees of adjustment for spatial confounding and with stratification into eastern, central and western U.S. counties. A 10 $\mu g/m^3$ increase in $PM_{2.5}$ was associated with a 7.6% increase in mortality (95% CI: 4.4-10.8). When adjusted for spatial confounding, the estimated log-relative risks dropped by 50%. Zeger et al. (2007, 157176) found a stronger association in the eastern counties than nationally, with no evidence of an association in western counties.

In a subsequent report, Zeger et al. (2008, 191951) created a new retrospective cohort, the Medicare Cohort Air Pollution Study (MCAPS), consisting of 13.2 million persons residing in 4,568 ZIP codes in urban areas having geographic centroids within 6 miles of a $PM_{2.5}$ monitor. Using this cohort, they investigated the relationship between 6-yr avg exposure to $PM_{2.5}$ and mortality risk over the period 2000-2005. When divided by region, the associations between long-term exposure to $PM_{2.5}$ and mortality for the eastern and central ZIP codes were qualitatively similar to those reported in the ACS and Six Cities Study, with 11.4% (95% CI: 8.8-14.1) and 20.4% (95% CI: 15.0-25.8) increases per 10 $\mu g/m^3$ increase in $PM_{2.5}$ in the eastern and central regions, respectively. The MCAPS results included evidence of differing $PM_{2.5}$ relative risks by age and geographic location, where risk declines with increasing age category until there is no evidence of an association among persons

≥ 85 yr of age, and there is no evidence of a positive association for the 640 urban ZIP codes in the western region of the U.S.

Using hospital discharge data, Zanobetti et al. (2008, 156177) constructed a cohort of persons discharged with COPD using Medicare data between 1985 and 1999. Positive associations in the survival analyses were reported for single year and multiple-year lag exposures, with a hazard ratio for total mortality of 1.22 (95% CI: 1.17-1.27) per 10 $\mu g/m^3$ increase in PM_{10} over the previous 4 years.

Veterans Cohort: A recent reanalysis of the Veterans cohort data focused on exposure to traffic-related air pollution (traffic density based on traffic flow rate data and road segment length) reported a stronger relationship between mortality with long-term exposure to traffic than with $PM_{2.5}$ mass (Lipfert et al., 2006, 088218). A significant association was reported between total mortality and $PM_{2.5}$ in single-pollutant models (RR = 1.12 [95% CI: 1.04-1.20] per 10 $\mu g/m^3$ $PM_{2.5}$). This risk estimate is larger than results reported in a previous study of this cohort. In multipollutant models including traffic density, the association with $PM_{2.5}$ was reduced and lost statistical significance. Traffic emissions contribute to $PM_{2.5}$ so it would be expected that the two would be highly correlated, and, thus, these multipollutant model results should be interpreted with caution. In a companion study, Lipfert et al. (2006, 088218) used data from EPA's fine particle speciation network, and reported findings for $PM_{2.5}$ which were similar to those reported by Lipfert et al. (2006, 088218). In this study (Lipfert et al., 2006, 088218), a significant association was reported between long-term exposure to $PM_{10-2.5}$ and total mortality in a single-pollutant model (RR = 1.07, 95% CI: 1.01-1.12 per 10 $\mu g/m^3$ $PM_{10-2.5}$). However, the association became negative and not statistically significant in a model that included traffic density. As it would be expected that traffic would contribute to the $PM_{10-2.5}$ concentrations, it is difficult to interpret the results of these multipollutant analyses.

Nurses' Health Study Cohort: The Nurses' Health Study (Puett et al., 2008, 156891) is an ongoing prospective cohort study examining the relation of chronic PM_{10} exposures with all-cause mortality and incident and fatal CHD consisting of 66,250 female nurses in MSAs in the northeastern region of the U.S. All cause mortality was statistically significantly associated with average PM_{10} exposures in the time period 3-48 mo preceding death. The association was strongest with average PM_{10} exposure in the 24 mo prior to death (hazard ratio 1.16 [95% CI: 1.05-1.28]) and weakest with exposure in the month prior to death (hazard ratio 1.04 [95% CI: 0.98-1.11]). The association with fatal CHD occurred with the greatest magnitude with mean exposure in the 24 mo prior to death (hazard ratio 1.42 [95% CI: 1.11-1.81]).

Netherlands Cohort Study (NLCS): The Netherlands Cohort Study (Brunekreef et al., 2009, 191947) estimates the effects of traffic-related air pollution on cause specific mortality in a cohort of approximately 120,000 subjects aged 55-69 yr at enrollment. For a 10 $\mu g/m^3$ increase in $PM_{2.5}$ concentration, the relative risk for natural-cause mortality in the full cohort was 1.06 (95% CI: 0.97-1.16), similar in magnitude to the results reported by the ACS. In a case-cohort analysis adjusted for additional potential confounders, there were no associations between air pollution and mortality.

German Cohort: The North Rhine-Westphalia State Environment Agency (LUA NRW) initiated a cohort of approximately 4,800 women, and assessed whether long-term exposure to air pollution originating from motorized traffic and industrial sources was associated with total and cause-specific mortality (Gehring et al., 2006, 089797). They found that cardiopulmonary mortality was associated with PM_{10} (RR = 1.52 [95% CI: 1.09-2.15] per 10 $\mu g/m^3$ PM_{10}).

7.6.2. Composition and Source-Oriented Analyses of PM

As discussed in the 2004 PM AQCD, only a very limited number of the chronic exposure cohort studies have included direct measurements of chemical-specific PM constituents other than sulfates, or assessments of source-oriented effects, in their analyses. One exception is the Veterans Cohort Study, which looked at associations with some constituents, and traffic.

Veterans Cohort: Using data from EPA's fine particle speciation network, Lipfert et al. (2006, 088756) reported a positive association for mortality with sulfates. Using 2002 data from the fine particle speciation network, positive associations were found between mortality and long-term exposures to nitrates, EC, Ni and V, as well as traffic density and peak O_3 concentrations. In

multipollutant models, associations with traffic density remained significant, as did nitrates, Ni and V in some models.

Netherlands Cohort Study: Beelen et al. (2008, 156263) studied the association between long-term exposure to traffic-related air pollution and mortality in a Dutch cohort. They used data from an ongoing cohort study on diet and cancer with 120,852 subjects who were followed from 1987 to 1996. Exposure to BS, NO_2, SO_2, and $PM_{2.5}$, as well as various exposure variables related to traffic, were estimated at the home address. Traffic intensity on the nearest road was independently associated with mortality. Relative risks (CI) for a 10 $\mu g/m^3$ increase in BS concentrations (difference between 5th and 95th percentile) were 1.05 (95% CI: 1.00-1.11) for natural cause, 1.04 (95% CI: 0.95-1.13) for cardiovascular, 1.22 (95% CI: 0.99-1.50) for respiratory, 1.03 (95% CI: 0.88-1.20) for lung cancer, and 1.04 (95% CI: 0.97-1.12) for mortality other than cardiovascular, respiratory, or lung cancer. Results were similar for NO_2 and $PM_{2.5}$, but no associations were found for SO_2. Traffic-related air pollution and several traffic exposure variables were associated with mortality in the full cohort, although the relative risks were generally small. Associations between natural-cause and respiratory mortality were statistically significant for NO_2 and BS. These results add to the evidence that long-term exposure to traffic-related particulate air pollution is associated with increased mortality.

Given the general dearth of published source-oriented studies of the mortality impacts of long-term PM exposure components, and given that the recent Medicare Cohort study now indicates that such ecological cross-sectional studies can be useful for evaluating time trends and/or comparisons across pollution components, it may well be that examining past cross-sectional studies comparing source-oriented components of PM may be informative. In particular, Ozkaynak and Thurston (1987, 072960), utilized the chemical speciation conducted in the Inhalable Particle (IP) Network to conduct a chemical constituent and source-oriented evaluation on long-term PM exposure and mortality in the U.S. They analyzed the 1980 U.S. vital statistics and available ambient air pollution data bases for sulfates and fine, inhalable, and TSP mass. Using multiple regression analyses, they conducted a cross-sectional analysis of the association between various particle measures and total mortality. Results from the various analyses indicated the importance of considering particle size, composition, and source information in modeling of particle pollution health effects. Of the independent mortality predictors considered, particle exposure measures most related to the respirable fraction of the aerosols, such as fine particles and sulfates, were most consistently and significantly associated with the reported SMSA-specific total annual mortality rates. On the other hand, particle mass measures that included $PM_{10-2.5}$ (e.g., total suspended particles and inhalable particles) were often found to be non-significant predictors of total mortality. Furthermore, based on the application of $PM_{2.5}$ source apportionment, particles from industrial sources and from coal combustion were indicated to be more significant contributors to human mortality than fine soil-derived particles.

7.6.3. Within-City Effects of PM Exposure

Much of the exposure gradient in the national-scale cohort studies was due to city-to-city differences in regional air pollution, raising the possibility that some or all of the original PM-survival associations may have been driven instead by city-to-city differences in some unknown (non-pollution) confounder variable. This has been evaluated by three recent studies.

ACS, Los Angeles: To investigate this issue, two new analyses using ACS data focused on neighborhood-to-neighborhood differences in urban air pollutants, using data from 23 $PM_{2.5}$ monitoring stations in the Los Angeles area, and applying interpolation methods (Jerrett et al., 2005, 087600) or land use regression methods (Krewski et al., 2009, 191193) to assign exposure levels to study individuals. This resulted in both improved exposure assessment and an increased focus on local sources of $PM_{2.5}$. Significant associations between $PM_{2.5}$ and mortality from all causes and cardiopulmonary diseases were reported with the magnitude of the relative risks being greater than those reported in previous assessments. In general, the associations for $PM_{2.5}$ and mortality using these two methods for exposure assessment were similar, though the use of land use regression resulted in somewhat smaller hazard ratios and tighter CIs (see Table 7-9). This indicates that city-to-city confounding was not the cause of the associations found in the earlier ACS Cohort studies. This provides evidence that reducing exposure error can result in stronger associations between $PM_{2.5}$ and mortality than generally observed in broader studies having less exposure detail.

Table 7-9. Comparison of results from ACS intra-urban analysis of Los Angeles and New York City using kriging or land use regression to estimate exposure.

Cause of Death	Los Angeles: Hazard Ratio[1] and 95% Confidence Interval Using Kriging[2] (Jerrett et al., 2005, 087600)	Los Angeles: Hazard Ratio[1] and 95% Confidence Interval Using Land Use Regression[3] (Krewski et al., 2009, 191193)	New York City: Hazard Ratio[1] and 95% Confidence Interval Using Land Use Regression[4] (Krewski et al., 2009, 191193)
All Cause	1.11 (0.99-1.25)	1.13 (1.01-1.25)	0.86 (0.63-1.18)
IHD	1.25 (0.99-1.59)	1.26 (1.02-1.56)	1.56 (0.87-2.88)
CPD	1.07 (0.91-1.26)	1.09 (0.94-1.26)	0.66 (0.41-1.08)
Lung Cancer	1.20 (0.79-1.82)	1.31 (0.90-1.92)	0.90 (0.29-2.78)

[1]Hazard ratios presented per 10 μg/m^3 increase in $PM_{2.5}$
[2]Model included parsimonious contextual covariates
[3]Model included parsimonious individual level (23) and ecologic (4) covariates
[4]Model included all 44 individual level and 7 ecologic covariates.

ACS, New York: Krewski et al. (2009, 191193) applied the same techniques used in the land use regression analysis of Los Angeles to an investigation conducted in New York City. Annual average concentrations were calculated for each of 62 monitors from 3 yr of daily monitoring data for 1999-2001. Those data were combined with land-use data collected from traffic counting systems, roadway network maps, satellite photos of the study area, and local government planning and tax-assessment maps to assign estimated exposures to the ACS participants. The investigators did not observe elevated effect estimates for all cause, CPD or lung cancer deaths, but IHD did show a positive association with $PM_{2.5}$ concentration. The difference between the 90th and 10th percentiles of the 3-yr avg $PM_{2.5}$ concentration was 1.5 μg/m^3 and the difference between the minimum and maximum values of the 3-yr avg $PM_{2.5}$ concentration was 7.8 μg/m^3. This narrow range in $PM_{2.5}$ exposure contrasts across the New York City metropolitan area and may well account for the inconclusive results in this city-specific analysis. Relatively uniform exposures would reduce the power of the statistical models to detect patterns of mortality relative to exposure and estimate the association with precision.

WHI Study: This study also investigated the within- versus between-city effects in its cities. As shown in Figure 7-8, similar effects for both the within and between-city analyses demonstrate that this association is not due to some other (non-pollution) confounder differing between the various cities, strengthening confidence in the overall pollution-effect estimates.

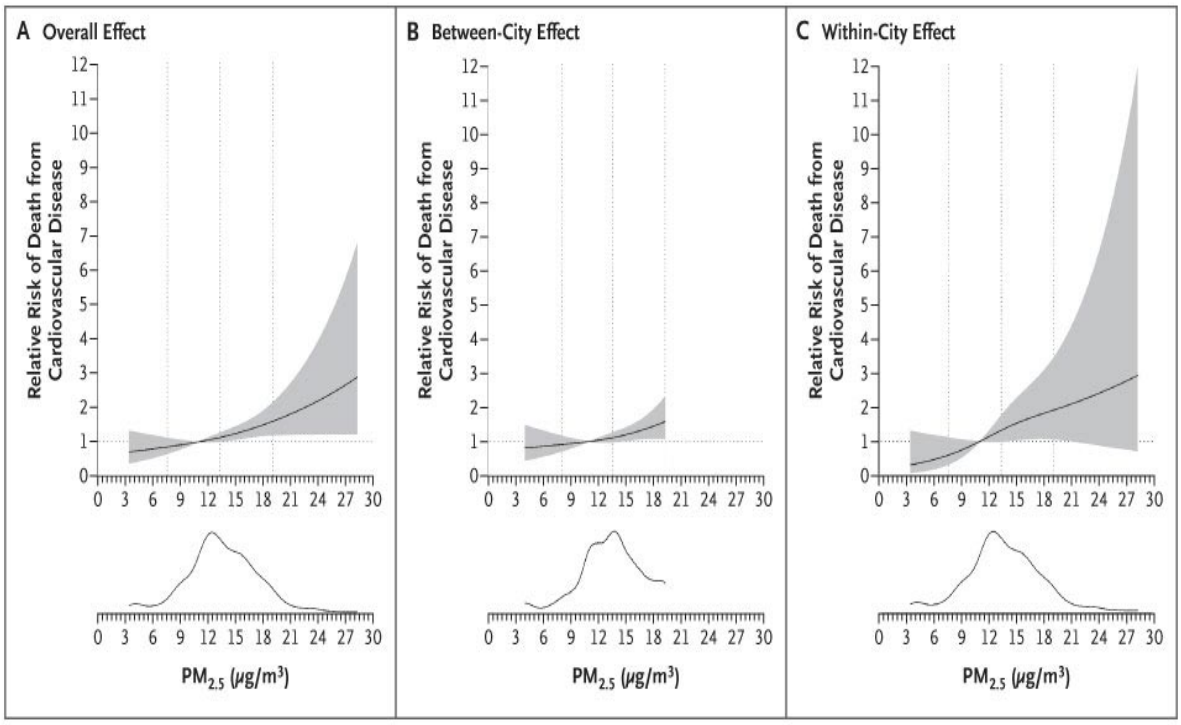
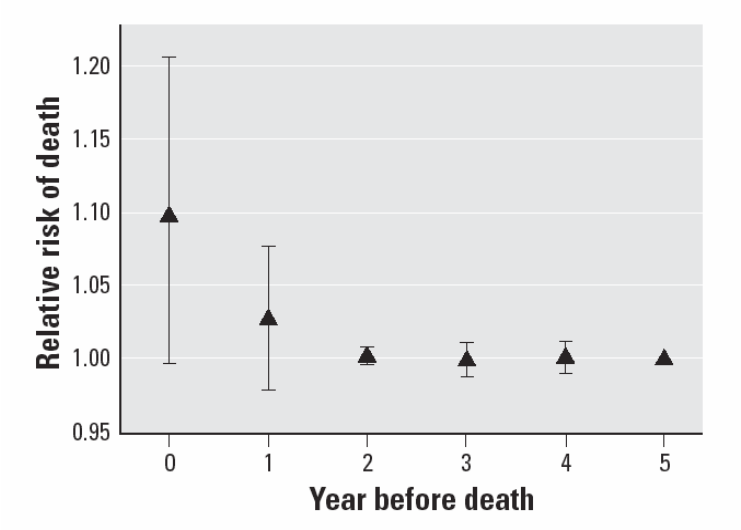


Figure 7-8. Plots of the relative risk of death from cardiovascular disease from the Women's Health Initiative study displaying the between-city and within-city contributions to the overall association between $PM_{2.5}$ and cardiovascular mortality windows of exposure-effects.

7.6.4. Effects of Different Long-term Exposure Windows

The delay between changes in exposure and changes in health has important policy implications. Schwartz et al. (2008, 156963) investigated this issue using an extended follow-up of the Harvard Six Cities Study. Cox proportional hazards models were fit to control for smoking, body mass index, and other covariates. Penalized splines were fit in a flexible functional form to the concentration response to examine its shape, and the degrees of freedom for the curve were selected based on Akaike's information criterion (AIC). The researchers also used model averaging as an alternative approach, where multiple models are fit explicitly and averaged, weighted by their probability of being correct given the data. The lag relationship by model was averaged across a range of unconstrained distributed lag models (i.e., same year, 1 yr prior, 2 yr prior, etc.). Results of the lag comparison are shown in Figure 7-9 indicating that the effects of changes in exposure on mortality are seen within 2 yr. The authors also noted that the concentration-response curve was linear, clearly continuing below the level of the current U.S. air quality standard of 15 $\mu g/m^3$.

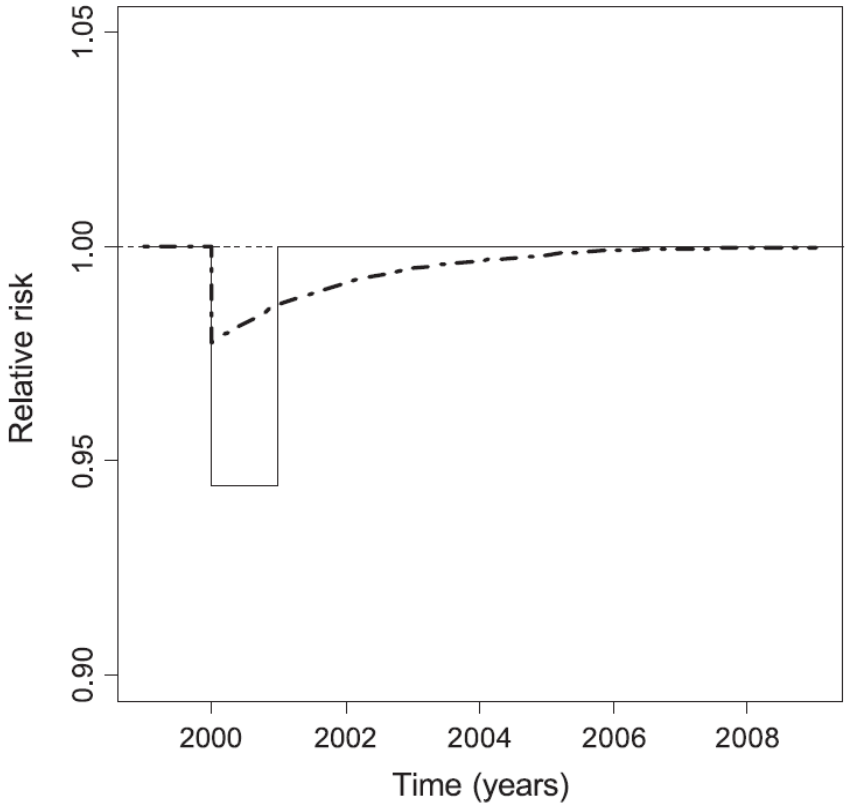


Source: Schwartz et al. (2008, 156963)

Figure 7-9. The model-averaged estimated effect of a 10-μg/m^3 increase in $PM_{2.5}$ on all-cause mortality at different lags (in years) between exposure and death. Each lag is estimated independently of the others. Also shown are the pointwise 95% CIs for each lag, based on jackknife estimates.

Similarly, the effect of long-term exposure to PM_{10} on the risk of death in a large multicity study of elderly subjects discharged alive following an admission for COPD found the effect was not limited to the exposure in each year of follow-up, and had larger cumulative effects spread over the follow-up year and three preceding years (Zanobetti et al., 2008, 156177).

Röösli et al. (2005, 156923) took an alternative approach to determining the window over which the mortality effects of long-term pollution exposures occurred. They fit the model shown in Figure 7-10 using k = 0.5 based on the Utah Steel Strike (Pope, 1989, 044461) and the Ireland coal ban study (Clancy et al., 2002, 035270). They found that roughly 75% of health benefits are observed in the first 5 years, as shown in Table 7-10. These results are consistent with the findings of Schwartz et al. (2008, 156963). Puett et al. (2008, 156891) also compared different long-term exposure lags, with exposure periods ranging from 1 month to 48 mo prior to death. They found statistically significant associations with average PM_{10} exposures in the time period 3-48 mo prior to death, with the strongest associations in the 24 mo prior to death and the weakest with exposure in the 1 mo prior to death.



Source: Reprinted with Permission from Oxford University Press & the International Epidemiological Society from Röösli et al. (2005, 156923)

Figure 7-10. Time course of relative risk of death after a sudden decrease in air pollution exposure during the year 2000, assuming a steady state model (solid line) and a dynamic model (bold dashed line). The thin dashed line refers to the reference scenario.

Table 7-10. Distribution of the effect of a hypothetical reduction of 10 µg/m^3 PM_{10} in 2000 on all-cause mortality 2000-2009 in Switzerland.

Year	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Proportion of total effect (%)	-	39.3	23.9	14.5	8.8	5.3	3.2	2.0	1.2	0.7	0.4
Relative risk (per 10 µg/m^3 reduction in PM_{10})	1.0	0.9775	0.9863	0.9917	0.9950	0.9969	0.9981	0.9989	0.9993	0.9996	0.9997

Relative risk and proportion of total effect in each year are shown, assuming a time constant k of 0.5

Source: Röösli et al. (2005, 156923)

In the reanalysis of the ACS cohort, the investigators calculated time windows of exposure as average concentrations during successive 5-yr periods preceding the date of death (Krewski et al., 2009, 191193). The investigators considered the time window with the best-fitting model (judged by the AIC statistic) to be the period during which pollution had the strongest influence on mortality. Overall, the differences between the time periods were small and demonstrated no definitive patterns. High correlations between exposure levels in the three periods may have reduced the ability of this analysis to detect any differences in the relative importance of the time windows. The investigators did not analyze any time periods smaller than 5 yr, so the results are not directly comparable to those reported by Schwartz et al. (2008, 156963), Röösli et al. (2005, 156923), and Puett et al. (2008, 156891).

Generally, these results indicate a developing coherence of the air pollution mortality literature, suggesting that the health benefits from reducing air pollution do not require a long latency period and would be expected within a few years of intervention.

7.6.5. Summary and Causal Determinations

7.6.5.1. $PM_{2.5}$

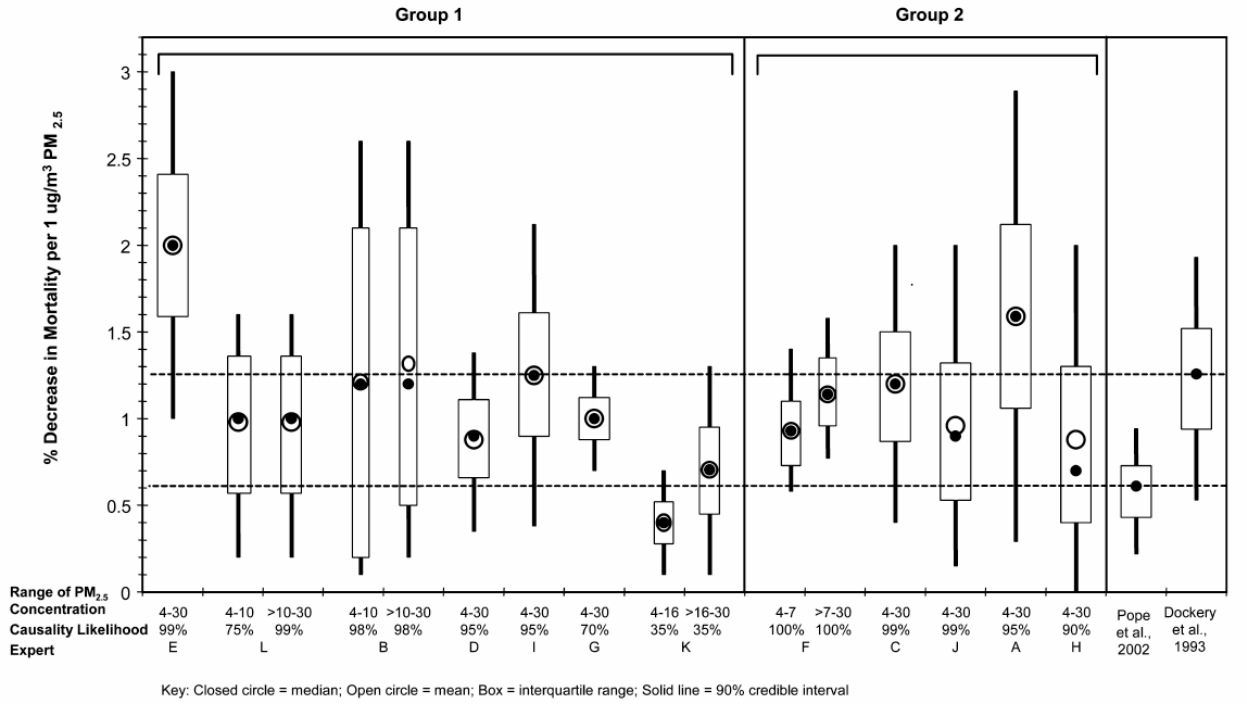
In the 1996 PM AQCD (U.S. EPA, 1996, 079380), results were presented for three prospective cohort studies of adult populations: the Six Cities Study (Dockery et al., 1993, 044457); the ACS Study (Pope et al., 1995, 045159); and the AHSMOG Study (Abbey et al., 1995, 000669). The 1996 AQCD concluded that the chronic exposure studies, taken together, suggested associations between increases in mortality and long-term exposure to $PM_{2.5}$, though there was no evidence to support an association with $PM_{10-2.5}$ (U.S. EPA, 1996, 079380). Discussions of mortality and long-term exposure to PM in the 2004 PM AQCD emphasized the results of four U.S. prospective cohort studies, but the greatest weight was placed on the findings of the ACS and the Harvard Six Cities studies, which had undergone extensive independent reanalysis, and which were based on cohorts that were broadly representative of the U.S. population. Collectively, the 2004 PM AQCD found that these studies provided strong evidence that long-term exposure to $PM_{2.5}$ was associated with increased risk of human mortality.

The recent evidence is largely consistent with past studies, further supporting the evidence of associations between long-term $PM_{2.5}$ exposure and increased risk of human mortality (Section 7.6) in areas with mean concentrations from 13.2 to 29 $\mu g/m^3$ (Figure 7-7). New evidence from the Six Cities cohort study shows a relatively large risk estimate for reduced mortality risk with decreases in $PM_{2.5}$ (Laden et al., 2006, 087605). The results of new analyses from the Six Cities cohort and the ACS study in Los Angeles suggest that previous and current studies may have underestimated the magnitude of the association (Jerrett et al., 2005, 087600). With regard to mortality by cause-of-death, recent ACS analyses indicate that cardiovascular mortality primarily accounts for the total mortality association with $PM_{2.5}$ among adults, and not respiratory mortality. The recent WHI cohort study shows even higher cardiovascular risks per $\mu g/m^3$ than found in the ACS study, but this is likely due to the fact that the study included only post-menopausal women without pre-existing cardiovascular disease (Miller et al., 2007, 090130). There is additional evidence for an association between $PM_{2.5}$ exposure and lung cancer mortality (Section 7.5.1.1). The WHI study also considered within versus between city mortality, as well as morbidity co-associations with $PM_{2.5}$ in the same population. The first showed that the results are not due to between city confounding, and the morbidity analyses show the coherence of the mortality association across health endpoints, supporting the biological plausibility of the air pollution-mortality associations found in these studies.

Results from a new study examining the relationship between life expectancy and $PM_{2.5}$ and the findings from a multiyear expert judgment study that comprehensively characterizes the size and uncertainty in estimates of mortality reductions associated with decreases in $PM_{2.5}$ in the U.S draw conclusions that are consistent with an association between long-term exposure to $PM_{2.5}$ and mortality (Pope et al., 2009, 190107; Roman et al., 2008, 156921). Pope et al. (2009, 190107) report that a decrease of 10 $\mu g/m^3$ in the concentration of $PM_{2.5}$ is associated with an estimated increase in mean (± SE) life expectancy of 0.61 ± 0.20 year. For the approximate period of 1980-2000, the average increase in life expectancy was 2.72 yr among the 211 counties in the analysis. The authors note that reduced air pollution was only one factor contributing to increased life expectancies, with its effects overlapping with those of other factors.

Roman et al. (2008, 156921) applied state-of-the-art expert judgment elicitation techniques to develop probabilistic uncertainty distributions that reflect the broader array of uncertainties in the concentration-response relationship. This study followed best standard practices for expert elicitations based on the body of literature accumulated over the past two decades. The resulting $PM_{2.5}$ effect estimate distributions, elicited from 12 of the world's leading experts on this issue, are shown in Figure 7-11. They indicate both larger central estimates of mortality reductions for decreases in long-term $PM_{2.5}$ exposure in the U.S. (averaging almost 1% per $\mu g/m^3$ $PM_{2.5}$) than reported (for example) by the ACS Study (i.e., 0.6% per $\mu g/m^3$ $PM_{2.5}$ in Pope et al. (2002, 024689),

and a wider distribution of uncertainty by each expert than provided by any one of the $PM_{2.5}$ epidemiologic studies. However, a composite uncertainty range of the overall mean effect estimate (i.e., based upon all 12 experts' estimates, but not provided in Figure 7-11) would be much narrower, and closer to that derived from the ACS study than indicated for any one expert shown in Figure 7-11.



Source: Reprinted with Permission of ACS from Roman et al. (2008, 156921)

Figure 7-11. Experts' mean effect estimates and uncertainty distributions for the $PM_{2.5}$ mortality concentration-response coefficient for a 1 µg/m^3 change in annual average $PM_{2.5}$.

Overall, recent evidence supports the strong evidence reported in the 2004 PM AQCD (U.S. EPA, 2004, 056905) that long-term exposure to $PM_{2.5}$ is associated with an increased risk of human mortality. When looking at the cause of death, the strongest evidence comes from mortality due to cardiovascular disease, with additional evidence supporting an association between $PM_{2.5}$ and lung cancer mortality (Figure 7-7). Fewer studies evaluate the respiratory component of cardiopulmonary mortality, and the evidence to support an association with long-term exposure to $PM_{2.5}$ and respiratory mortality is weak (Figure 7-7). Together these findings are consistent and coherent with the evidence from epidemiologic, controlled human exposure, and animal toxicological studies for the effects of short- and long-term exposure to PM on cardiovascular effects presented in Sections 6.2 and 7.2, respectively. Evidence of short- and long-term exposure to $PM_{2.5}$ and respiratory effects (Sections 6.3 and 7.3, respectively) and infant mortality (Section 7.4) are coherent with the weak respiratory mortality effects. Additionally, the evidence for short- and long-term cardiovascular and respiratory morbidity provides biological plausibility for mortality due to cardiovascular or respiratory disease. The most recent evidence for the association between long-term exposure to $PM_{2.5}$ and mortality is particularly strong for women. Collectively, the evidence is **sufficient to conclude that the relationship between long-term $PM_{2.5}$ exposures and mortality is causal.**

7.6.5.2. $PM_{10-2.5}$

In the 2004 PM AQCD, results from the ACS and Six Cities study analyses indicated that $PM_{10-2.5}$ was not associated with mortality. Evidence is still limited to adequately characterize the association between $PM_{10-2.5}$ and PM sources and/or components. The new findings from AHSMOG and Veterans cohort studies provide limited evidence of associations between long-term exposure to $PM_{10-2.5}$ and mortality in areas with mean concentrations from 16 to 25 $\mu g/m^3$. The evidence **for $PM_{10-2.5}$ is inadequate to determine if a causal relationship exists between long-term exposures and mortality**.

7.6.5.3. UFPs

The 2004 PM AQCD did not report long-term exposure studies for UFPs. No epidemiologic studies have been conducted to evaluate the effects of long-term UFP exposure and mortality. The evidence is **inadequate to determine if a causal relationship exists between long-term UFP exposures and mortality**.

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Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISA) and the Integrated Risk Information System (IRIS).

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Chapter 8. Populations Susceptible to PM-related Health Effects

Interindividual variation in human responses to air pollutants indicates that some populations are at increased risk for the detrimental effects of ambient exposure to an air pollutant (e.g., PM) (Kleeberger and Ohtsuka, 2005, 130489). The NAAQS are intended to provide an adequate margin of safety for both general populations and sensitive subgroups, or those individuals potentially at increased risk for health effects in response to ambient air pollution (see Section 1.1). To facilitate the identification of populations at the greatest risk for PM-related health effects, studies have evaluated factors that contribute to the susceptibility and/or vulnerability of an individual to PM. The definition for both of these terms has been found to vary across studies, but in most instances susceptibility refers to biological or intrinsic factors (e.g., lifestage, gender) while vulnerability refers to non-biological or extrinsic factors (e.g., socioeconomic status [SES]) (see Table 8-1). Additionally, in some cases, the terms "at-risk" and sensitive populations have been used to encompass these concepts more generally. However, in many cases a factor identified that increases an individual's risk for morbidity or mortality effects from exposure to an air pollutant (e.g., PM) can not be easily categorized as a susceptibility or vulnerability factor. For example, a population that is characterized as having low SES, traditionally defined as a vulnerability factor, may have less access to healthcare resulting in the manifestation of disease (i.e., a susceptibility factor), but they may also reside in a location that results in exposure to higher concentrations of an air pollutant, increasing their vulnerability. Therefore, the terms susceptibility and vulnerability are intertwined and at times can not be distinguished from one another.

As a result of the inconsistencies in the definition of susceptibility and vulnerability presented in the literature as well as the inability to clearly delineate whether an identified factor increases an individual's susceptibility or vulnerability to an air pollutant, in this ISA, the term 'susceptible population' will be used as a blanket term and defined as the following:

> *Populations that have a greater likelihood of experiencing health effects related to exposure to an air pollutant (e.g., PM) due to a variety of factors including, but not limited to: genetic or developmental factors, race, gender, lifestage, lifestyle (e.g., smoking status and nutrition) or preexisting disease; as well as, population-level factors that can increase an individual's exposure to an air pollutant (e.g., PM) such as socioeconomic status [SES], which encompasses reduced access to health care, low educational attainment, residential location, and other factors.*

Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISA) and the Integrated Risk Information System (IRIS).

Table 8-1. Definitions of susceptible and vulnerable in the PM literature.

Definition	Reference
Susceptible: predisposed to develop a noninfectious disease Vulnerable: capable of being hurt: susceptible to injury or disease	Merriam-Webster (2009, 192146)
Susceptible: greater likelihood of an adverse outcome given a specific exposure, in comparison with the general population. Includes both host and environmental factors (e.g., genetics, diet, physiological state, age, gender, social, economic, and geographic attributes). Vulnerable: periods during an individual's life when they are more susceptible to environmental exposures.	American Lung Association (2001, 016626)
Susceptible: innate (e.g., genetic or developmental) or acquired (e.g., age, disease or smoking or smoking) factors that make individuals more likely to experience effects with exposure to PM. Vulnerable: PM-related effects due to factors including socioeconomic status (e.g., reduced access to health care) or particularly elevated exposure levels.	U.S. EPA. (2008, 157072)
Susceptible: greater or lesser biological response to exposure. Vulnerable: more or less exposed.	U.S. EPA (2009, 192149)
Vulnerable: to be susceptible to harm or neglect, that is, acts of commission or omission on the part of others that can wound.	Aday, LA. (2001, 192150)
Susceptible:may be those who are significantly more liable than the general population to be affected by a stressor due to life stage (e.g., children, the elderly, or pregnant women), genetic polymorphisms (e.g., the small but significant percentage of the population who have genetic susceptibilities), prior immune reactions (e.g., individuals who have been "sensitized" to a particular chemical), disease state (e.g., asthmatics), or prior damage to cells or systems (e.g., individuals with damaged ear structures due to prior exposure to toluene, making them more sensitive to damage by high noise levels). Vulnerable: differential exposure and differential preparedness (e.g., immunization).	U.S. EPA (2003, 192145)
Susceptible: intrinsic (e.g., age, gender, pre-existing disease (e.g., asthma) and genetics) and extrinsic (previous exposure and nutritional status) factors.	Kleeberger and Ohtsuka (2005, 130489)
Susceptible:characteristics that contribute to increased risk of PM-related health effects (e.g., genetics, pre-existing disease, age, gender, race, socioeconomic status, healthcare availability, educational attainment, and housing characteristics).	Pope and Dockery (2006, 156881)

To examine whether air pollutants (e.g., PM) differentially affect certain populations, epidemiologic studies conduct stratified analyses to identify the presence or absence of effect modification. A thorough evaluation of potential effect modifiers may help identify populations that are more susceptible to an air pollutant (e.g., PM). Although the design of toxicological and controlled human exposure studies do not allow for an extensive examination of effect modifiers, the use of animal models of disease and the study of individuals with underlying disease or genetic polymorphisms do allow for comparisons between subgroups. Therefore, the results from these studies, combined with those results obtained through stratified analyses in epidemiologic studies, contribute to the overall weight of evidence for the increased susceptibility of specific populations to an air pollutant (e.g., PM).

This chapter discusses the epidemiologic, controlled human exposure, and toxicological studies evaluated in Chapters 6 and 7 that provide information on potentially susceptible populations. The studies highlighted include only those studies that present stratified results (e.g., males vs. females or <65 vs. ≥ 65). This approach allowed for a comparison between populations exposed to similar PM concentrations and within the same study design. In addition, numerous studies that focus on only one potentially susceptible population can provide supporting evidence on whether a population is susceptible to PM exposure and are described in Chapters 6 and 7, but these studies are not discussed in detail in this chapter. Table 8-2 provides an overview of the factors examined in the current toxicological, controlled human exposure, and epidemiologic literature and the direction of the underlying evidence in determining whether a factor increases the susceptibility of a population to PM-related health effects.

Table 8-2. Susceptibility factors evaluated.

Factor	Collective Evidence (+/-)[2]
Older Adults (≥ 65)	+
Children (<18)[1]	+
Pregnancy and Developmental Effects	+*
Gender	-
Race/Ethnicity	-
Genetic factors - Genetic polymorphisms - Epigenetics	+
Cardiovascular Diseases	+
Respiratory Illnesses	+
Respiratory Contributions to Cardiovascular Effects	-*
Diabetes	+*
Obesity	+*
Socioeconomic Status (SES)	+
Educational Attainment[3]	+
Residential Location[3]	+
Health Status (e.g., Nutrition)[3]	+*

[1] The age range that defines a child varies from study to study. In some cases it is <21 years old while in others it is <18 years old (Firestone et al., 2007, 192071). For the purposes of this exercise children are defined as those individuals <18 years old because the majority of epidemiologic studies consider individuals under the age of 18 children.

2 This column identifies whether the "collective" evidence from studies evaluated found that a specific factor increased (+) or did not increase (-) a population's susceptiblity to PM exposure (i.e., PM exposure to all size fractions combined). In instances where only a few studies were evaluated for a speicifc factor it was not possible to clearly assign a (+) or (-) as a result the direction of the preliminary evidence is identified along with (*) to represent that more information is warranted.

3 These factors are surrogates of socioeconomic status and are discussed within this subsection of the chapter.

8.1. Potentially Susceptible Populations

8.1.1. Lifestage

8.1.1.1. Older Adults

Evidence for PM-related health effects in older adults spans epidemiologic, controlled human exposure, and toxicological studies. The 2004 PM AQCD found evidence for increased risk of cardiovascular effects in older adults exposed to PM (U.S. EPA, 2004, 056905). Older adults represent a potentially susceptible population due to the higher prevalence of pre-existing cardiovascular and respiratory diseases found in this age range compared to younger age groups. The increased susceptibility in this population can primarily be attributed to the gradual decline in physiological processes as part of the aging process (U.S. EPA, 2006, 192082). Therefore, some overlap exists between potentially susceptible older adults and the population that encompases individuals with pre-existing diseases (Kan et al., 2008, 156621). Epidemiologic studies that conduct age stratified analyses primarily focus on the association between short-term exposure to PM and cardiovascular morbidity, but additional studies have examined the association between PM and respiratory morbidity and mortality.

In recent publications, the epidemiologic evidence for cardiovascular effects in older adults in response to short-term exposure to $PM_{10-2.5}$ and $PM_{2.5}$ is limited, but taken together with evidence from studies of PM_{10} (e.g., Larrieu et al., 2007, 093031; Le Tertre et al., 2002, 023746), supports the increased risk of cardiovascular morbidity in older adults. Host et al. (2007, 155851) found an increase in cardiovascular disease (CVD) hospital admissions in individuals >65 yr compared to all ages for short-term exposure to both $PM_{10-2.5}$ and $PM_{2.5}$. Barnett et al. (2006, 089770) analyzed data from several cities across Australia and New Zealand and found that the excess risk of hospitalizations for cardiac diseases, congestive heart failure (CHF), ischemic heart disease (IHD), myocardial infarction (MI), and all CVD was greater among patients aged ≥ 65 yr as compared to those individuals <65 years in response to short-term exposure to $PM_{2.5}$. U.S.- and Canadian-based studies that examined the association between short-term exposure to PM and cardiovascular morbidity primarily found no evidence for increased risk among older adults. Metzger et al. (2004, 044222) found no evidence of effect modification by age for cardiovascular outcomes and short-term exposure to $PM_{2.5}$ in Atlanta, Georgia, which is supported by the results from other studies that focused on short-term exposure to PM_{10} (Fung et al., 2005, 074322; Zanobetti and Schwartz, 2005, 088069). However, Pope et al. (2008, 191969) observed an increased risk of HF hospital admissions in older adults (i.e., ≥ 65 yr) in Utah, but the study used a 14-day lagged cumulative moving average of $PM_{2.5}$, which is much longer than the lags examined by the other U.S.- and Canadian-based studies. Although studies have not consistently found an association between short-term exposure to PM and respiratory-related health effects in older adults, some studies have reported an increase in respiratory hospital admissions in individuals 65 years of age and older (e.g., Fung et al., 2005, 093262).

Additional evidence for an increase in cardiovascular and respiratory effects among older adults has been observed in controlled human exposure and dosimetry studies. Devlin et al. (2003, 087348) found that older subjects exposed to $PM_{2.5}$ concentrated ambient particles (CAPs) experienced significant decreases in heart rate variability (HRV) (both in time and frequency) immediately following exposure, when compared to healthy young subjects. In addition, Gong et al (2004, 055628) reported that older subjects demonstrated significant decreases in HRV when exposed to $PM_{2.5}$ CAPs, but this study did not compare the response in older subjects to those elicited by young, healthy individuals. However, the study did find that healthy older adults were more susceptible to decreases in HRV compared to those with an underlying health condition (i.e., chronic obstructive pulmonary disease [COPD]) in response to PM exposure (Gong et al., 2004, 055628). Dosimetry studies have shown a depression of $PM_{2.5}$ and $PM_{10-2.5}$ clearance in all regions of the respiratory tract with increasing age beyond young adulthood in humans and laboratory animals. These results suggest that older adults are also susceptible to PM-related respiratory health effects (Section 4.3.4.1).

Animal toxicological studies have attempted to characterize the relationship between age and PM-related health effects through the development of models that mimic the physiological conditions associated with older individuals. For example, Nadziejko et al. (2004, 055632) observed arrhythmias in older, but not younger, rats exposed to $PM_{2.5}$ CAPs. In addition, another study (Tankersley et al., 2004, 094378) that used a mouse model of terminal senescence demonstrated altered baseline autonomic tone in response to carbon black exposure, which may subsequently affect the quality and severity of cardiovascular responses (Tankersley et al., 2007, 097910). Reductions in cardiac fractional shortening and significant pulmonary vascular congestion upon exposure to carbon black were also reported in older mice (Tankersley et al., 2008, 157043). Overall, these studies provide biological plausibility for the increase in cardiovascular effects in older adults observed in the controlled human exposure and epidemiologic studies.

Recent epidemiologic studies have also found that individuals >65 years of age are more susceptible to all-cause (nonaccidental) mortality upon short-term exposure to both $PM_{2.5}$ (Ostro et al., 2006, 087991) and PM_{10} (Samoli et al., 2008, 188455; Zeka et al., 2006, 088749), which is consistent with the findings of the 2004 PM AQCD. Of note are the results from Ostro et al. (2006, 087991) that reported a slight increase in mortality for older adults compared to all ages in single-pollutant models, but a robust effect estimate in co-pollutant models with gaseous pollutants (i.e., $PM_{2.5}$+CO and $PM_{2.5}$+NO_2). These results differ from those in the all ages model (i.e., attenuation of the effect estimate in co-pollutant models with CO and NO_2), which suggests that older adults are more susceptible to PM exposures, even though the age-stratified effect estimates in single-pollutant models did not significantly differ. Epidemiologic studies that examined the association between mortality and long-term exposure to PM (i.e., $PM_{2.5}$) have found results

contradictory to those obtained in the short-term exposure studies. Villeneuve et al. (2002, 042576), Naess et al. (2007, 090736) and Zeger et al. (2008, 191951) report evidence of differing $PM_{2.5}$ relative risks by age, where risk declines with increasing age starting at age 60 until there is no evidence of an association among persons ≥ 85 yr.

The evidence from epidemiologic, controlled human exposure, and toxicological studies that focused on exposures to $PM_{2.5}$, $PM_{10-2.5}$, and PM_{10}, provide coherence and biological plausibility for the association between PM and cardiovascular morbidity in older adults. The clear pattern of positive associations only being observed in epidemiologic studies conducted in non-U.S. locations brings into question the influence of PM composition on health effects. However, the difference in effects observed between U.S. and Canadian, and international studies could also be due to possible differences in the identification of CVD-related morbidity and mortality between the studies evaluated. Although most studies examined the effect of PM on CVD outcomes in older adults, the additional evidence from epidemiologic studies that focus on respiratory morbidity and mortality in response to short-term exposure to PM also indicate that older adults represent a susceptible population. As the demographics of the U.S. population shift over the next 20 years with a larger percentage of the population (i.e., 13% of the population in 2011 and a projected 20% in 2030) encompassing individuals ≥ 65 yr (U.S. Census, 2000, 157064), an increase in the number of PM-related health effects (e.g., cardiovascular and respiratory morbidity, and mortality) in individuals ≥ 65 years of age could occur.

8.1.1.2. Children

Children have generally been considered more susceptible to PM exposure due to multiple factors including more time spent outdoors, greater activity levels, exposures resulting in higher doses per body weight and lung surface area, and the potential for irreversible effects on the developing lung (U.S. EPA, 2004, 056905). The 2004 PM AQCD found that studies which stratify results by age typically report associations between PM and respiratory-related health effects in children, specifically asthma (U.S. EPA, 2004, 056905). Of the recent epidemiologic studies evaluated, only a few have examined the association between $PM_{10-2.5}$ and $PM_{2.5}$ and respiratory effects in children. Mar et al. (2004, 057309) found increased respiratory effects (e.g., wheeze, cough, lower respiratory symptoms) in children 7-12 years of age compared to individuals 20-51 years of age in response to exposure to both $PM_{10-2.5}$ and $PM_{2.5}$ in Spokane, Washingon. In addition, Host et al. (2007, 155851) found an increase in respiratory-related hospital admissions with short-term exposure to $PM_{10-2.5}$ among children ages 0-14 yr in 6 French cities. An examination of studies that also focused on PM_{10} provide additional support for PM-induced respiratory effects in children (Mar et al., 2004, 057309; Peel et al., 2005, 056305). A recent toxicological study provides biological plausibility for the increase in PM-related respiratory effects in children observed in the epidemiologic studies. Mauad et al. (2008, 156743) using both prenatal and postnatal mice exposed to ambient $PM_{2.5}$ in a "polluted chamber" found evidence for changes in lung function and pulmonary injury (e.g., incomplete alveolarization). Additionally, Pinkerton et al. (2004, 087465; 2008, 190471) found evidence suggesting that the developing lung is more susceptible to PM by demonstrating that neonatal rats exposed to iron-soot PM had a reduction in cell proliferation in the lung. Overall, the evidence from epidemiologic studies that have examined the health effects associated with all size fractions of PM and toxicological studies that have examined individual PM components provide additional support to the hypothesis that children are more susceptible to respiratory effects from exposure to PM.

8.1.2. Pregnancy and Developmental Effects

While the majority of the literature focuses on epidemiologic studies that examine the potential health effects (e.g., low birth weight, growth restriction) attributed to in utero exposure to PM (see Section 7.4), it is unclear if the health effects observed are due to soluble fractions of PM that cross the placenta or physiological alterations in the pregnant woman. In the case of exposure to PM, adverse health effects in the offspring could be mediated by potentially greater susceptibility in the pregnant woman. For example, an inflammatory response leads to differential activation of multiple genes involved in immune response and regulation, cell metabolism, and proliferation all of which can lead to health effects in the developing fetus (Fedulov et al., 2008, 097482). Toxicological

studies have recently examined whether exposure to air pollutants during pregnancy leads to increased allergic susceptibility in the offspring. Fedulov et al. (2008, 097482) used an animal model to examine the effect of diesel exhaust particles (DEPs) along with an immunologically "inert" particle (TiO_2) on pregnant mice. The authors found that pregnant mice exhibited a local and systemic inflammatory response when exposed to either DEP or TiO_2, which was not observed in control, non-pregnant mice. In addition, the offspring of exposed pregnant mice developed AHR and allergic inflammation. This study suggests that exposure to $PM_{2.5}$, and even relatively inert particles, during pregnancy can potentially lead to increased allergic susceptibility in offspring and subsequently the development of asthma.

8.1.3. Gender

The 2004 PM AQCD did not find consistent evidence for a difference in health effects by gender. However, there appeared to be gender differences in the localization of particles when deposited in the respiratory tract and the deposition rate due to differences in body size, conductive airway size, and ventilatory parameters (U.S. EPA, 2004, 056905). For example, females have proportionally smaller airways and slightly greater airway reactivity than males (Yunginger et al., 1992, 192074).

Few recent epidemiologic studies have conducted gender-stratified analyses when examining the association between either short- or long-term exposure to $PM_{10-2.5}$ or $PM_{2.5}$. Similar to the studies evaluated in the 2004 PM AQCD, the current literature has not found a consistent pattern of associations by gender for any health outcome. Pope et al. (2006, 091246) observed a slightly larger, non-significant, association between short-term exposure to $PM_{2.5}$ and daily hospital admission for acute IHD events in males. An examination of gender-specific effects by both Ostro et al. (2006, 087991) and Franklin et al. (2007, 091257) found conflicting associations by gender for multiple cause-specific mortality outcomes. The inconsistency in associations between males and females is further highlighted in studies that examined the health effects associated with long-term exposure to $PM_{10-2.5}$ and $PM_{2.5}$. Chen et al. (2005, 087942) found larger effects in females for congestive heart disease (CHD) mortality upon long-term exposure to $PM_{10-2.5}$ in three California cities. Naess et al. (2007, 090736), also observed slightly larger effect estimates in females for CVD and lung cancer mortality upon long-term exposure to $PM_{2.5}$, but for COPD mortality the greatest association was found in males.

The majority of the epidemiologic studies that examined the association between exposure to PM and gender focused on exposure to PM_{10}. Although most of these studies do not attribute the association to specific size fractions (i.e., $PM_{10-2.5}$ or $PM_{2.5}$) or provide insight as to whether one size fraction may be driving the observed effect, the studies of PM_{10} provide further support that gender does not appear to differentially affect PM-related health outcomes. Neither Zanobetti and Schwartz (2005, 088069) nor Wellenius et al. (2006, 088748) found gender to be a significant effect modifier of the risk estimates associated with short-term exposure to PM_{10} and cardiovascular hospital admissions. These results are consistent with those found in other studies that examined the association between short-term exposure to PM_{10} and both cardiovascular and respiratory hospital admissions (Luginaah et al., 2005, 057327; Middleton et al., 2008, 156760). Additional studies that examined the effects of short-term and long-term exposure to PM_{10} on respiratory morbidity and mortality (Boezen et al., 2005, 087396; Chen et al., 2005, 087942; Zanobetti and Schwartz, 2005, 088069; Zeka et al., 2006, 088749) found results that are consistent with those reported in studies of $PM_{10-2.5}$ and $PM_{2.5}$ (i.e., gender is not likely to be an effect modifier).

Although human clinical studies are not typically powered to detect differences in response between males and females, one study did report significantly greater decreases in blood monocytes, basophils, and eosinophils in females compared to males following controlled exposures to UF EC (Frampton et al., 2006, 088665). Overall, the evidence from primarily epidemiologic studies that examined the association between short- and long-term exposure to $PM_{10-2.5}$ and $PM_{2.5}$, along with the supporting evidence from PM_{10} studies, further confirms that although differences in dosimetry exist between males and females, neither gender consistently exhibits a higher disposition for PM-related health effects.

8.1.4. Race/Ethnicity

The 2004 PM AQCD (U.S. EPA, 2004, 056905) did not evaluate the potential susceptibility of individuals of different races and ethnicities to PM exposure. The results from epidemiologic studies evaluated in this review that examined the potential effect modification of the PM-morbidity and -mortality relationships by race and ethnicity varied depending on the study location. In an analysis of the $PM_{2.5}$-mortality relationship, Ostro et al. (2006, 087991) stratified the association by race and ethnicity, and observed a positive and marginally significant effect for whites and Hispanics, but not for blacks, in response to short-term exposure to $PM_{2.5}$ in 9 California counties. An additional analysis performed by Ostro et al. (2008, 097971) in 6 California counties using $PM_{2.5}$ and various $PM_{2.5}$ components, also found a significant association between mortality, specifically cardiovascular mortality, and Hispanic ethnicity (Ostro et al., 2008, 097971). It should be noted that neither study, Ostro et al. (2006, 087991) nor Ostro et al. (2008, 097971), controlled for potential confounders (e.g., SES factors and location of residence) of the association observed between $PM_{2.5}$ exposure and Hispanic ethnicity. As a result, Ostro et al (2008, 097971) speculated that the increased $PM_{2.5}$-mortality risks observed for Hispanics could be due to a variety of factors including, higher rates of: non-high school graduates, obesity, no leisure-time activity, and alcohol consumption within the Hispanic population in California. Additional evidence for the potential susceptibility of individuals by race and ethnicity were derived from studies on the health effects associated with short-term exposure to PM_{10}. Wellenius et al. (2006, 088748) observed that race (i.e., white vs. other) did not significantly modify the association between short-term exposure to PM_{10} and CHF hospital admissions. Additionally, Zeka et al. (2006, 088749) did not observe any difference in mortality effect estimates when stratifying by race (i.e., black and white) upon short-term exposure to PM_{10}. To date, dosimetry studies have not extensively examined differences in particle deposition between races or ethnicities to confirm the epidemiologic findings. Although not extensively analyzed, toxicological studies have examined PM responses in different mouse and rat strains, and reported greater CV effects (Kodavanti et al., 2003, 051325; Tankersley et al., 2007, 097910) and compromised host defense (Ohtsuka et al., 2000, 004409) for some strains. These studies provide some support, in terms of biological plausibility, for differences in PM-induced health effects by race or ethnicity. However, it is unclear how the difference in the response to PM in different mouse or rat strains extrapolates to PM-induced differences between races or ethnicities. Overall, the results from the studies that examined the potential effect modification of PM associations by race and ethnicity provide some evidence for increased risk of mortality in Hispanics upon short-term exposure to $PM_{2.5}$. However, the evidence for this association is derived from two studies conducted in California, and it is unclear if the studies adequately controlled for potential confounders. Additional studies conducted in other locations that stratify results by ethnicity have not yet been conducted to substantiate these results.

8.1.5. Gene-Environment Interaction

A consensus now exists that gene-environment interactions merit serious consideration when examining the relationship between ambient exposures to air pollutants and the development of health effects (Gilliland et al., 1999, 155792; Kauffmann et al., 2004, 090968). These potential interactions were not evaluated in the 2004 PM AQCD. Inter-individual variation in human responses to air pollutants suggests that some populations are at increased risk of detrimental effects due to pollutant exposure, and it has become clear that the genetic makeup of an individual can increase their susceptibility (Kleeberger and Ohtsuka, 2005, 130489). Gene-environment interactions can result in health effects due to: genetic polymorphisms, which result in the lack of a protein or a change that makes a functionally important protein dysfunctional; or genetic damage in response to an exposure which potentially leads to a health response (e.g., formation of benzo [a] pyrene DNA adducts in response to PM exposure). In this review, the majority of studies examine gene-environment interactions due to genetic polymorphisms. In order to establish useful links between polymorphisms in candidate genes and adverse health effects, several criteria must be satisfied: the product of the candidate gene must be significantly involved in the pathogenesis of the adverse effect of interest; and polymorphisms in the gene must produce a functional change in either the protein product or in the level of expression of the protein (U.S. EPA, 2008, 157075). Further, the issue of confounding by other environmental exposures must be carefully considered.

It has been hypothesized that the cardiovascular and respiratory health effects that occur in response to short-term PM exposure are mediated by oxidative stress (see Section 5.1.1). Research has examined this hypothesis by primarily focusing on the glutathione-S transferase (GST) genes because they have common, functionally important polymorphic alleles that significantly affect antioxidant defense function in the lung, and approximately half of the white population has a polymorphic null allele, resulting a large potential study population (Schwartz et al., 2005, 086296). Exposure to free radicals and oxidants in air pollution leads to a cascade of events, which can result in a reduction in glutathione (GSH), and an increase in the transcription of GSTs. Individuals with genotypes that result in reduced or absent enzymatic activity are likely to have reduced antioxidant defenses and potentially increased susceptibility to inhaled oxidants and free radicals.

Numerous studies have examined the role of genetic polymorphisms on PM-related cardiovascular health effects using the Normative Aging Study cohort. Schwartz et al. (2005, 086296) and Chahine et al. (2007, 156327) found that individuals with null GSTM1 alleles had a larger decrease in HRV upon short-term exposure to $PM_{2.5}$ compared to individuals with at least one allele. Polymorphisms in the HO-1 promoter resulted in lowered HRV upon short-term exposure to $PM_{2.5}$ in individuals with the long repeat polymorphism compared to those individuals with the short repeat polymorphism (Chahine et al., 2007, 156327). In addition, Schneider et al. (2008, 191985) found that diabetic individuals with null GSTM1 alleles had larger decrements in FMD (i.e., flow-mediated dialation of the brachial artery), suggesting alterations in endothelial function. A controlled human exposure study (Gilliland et al., 2004, 156471) also examined whether genetic polymorphisms increase the susceptibility of individuals to respiratory morbidity in response to PM exposure. Gilliland et al. (2004, 156471) examined the effect of allergens and DEPs on individuals with either null genotypes for GSTM1 and GSTT1 or GSTP1 codon 105 variants. The authors found that individuals with the GSTM1 null or the GSTP1 I105 wildtype genotypes were more susceptible to allergic inflammation upon exposure to allergen and DEPs. Additional genes within the GST pathway have also been examined (e.g., NQO1), but the sample sizes are relatively small, which prohibits the analysis of the potential effect modification of PM-related health effects by these genes (e.g., Schneider et al., 2008, 191985).

The interaction between GST genes and PM exposure has recently been extended to studies that examined the effect of PM exposure on birth outcomes. A recent study (Suh et al., 2008, 192077) that examined the effect of high PM_{10} exposures during the third trimester of pregnancy on the risk of preterm delivery, found that women with the GSTM1 null genotype were at an increased risk of preterm birth. When examining the interaction between high PM_{10} concentrations during the third trimester of pregnancy and the presence of the GSTM1 null genotype on the risk of preterm delivery, there was evidence for a synergistic gene-environment interaction in pregnant women. This effect could occur due to oxidative stress induced by metals contained in PM_{10}, and subsequently could be modified by polymorphisms of the GSTM1 gene. This oxidative stress causes oxidative DNA damage in fetal tissues, which may lead to preterm delivery via a reduction in placental blood flow.

An examination of other genes outside the GST pathway have also been conducted to determine if specific polymorphisms increase the susceptibility of individuals to PM. Baccarelli et al. (2008, 157984) in the Normative Aging Study observed that individuals with polymorphisms in MTHFR (C677T methylenetetrahydrofolate reductase), an alteration associated with reduced enzyme activity, and cSHMT (cytoplasmic serine hydroxymethyltransferase) (i.e., [CT/TT] MTHFR and [CC] cSHMT genotypes), alterations associated with higher homocysteine levels, have a reduction in SDNN, upon exposure to $PM_{2.5}$. Peters et al. (2009, 191992) examined single nucleotide polymorphisms (SNPs) in the fibrinogen gene in myocardial infarction survivors to assess whether exposure to PM_{10} altered steady state levels of fibrinogen, which has been implicated in promoting atherothrombosis. The authors found that individuals with single nucleotide polymorphisms (SNPs) in the fibrinogen gene have higher baseline fibrinogen levels which when combined with the inflammatory effects (i.e., increased fibrinogen levels) associated with exposure to PM could increase their risk of PM-related cardiovascular health effects. These results taken together suggest that individuals with null alleles or specific polymorphisms in genes that mediate the antioxidant response to oxidative stress, regulate enzyme activity, or regulate levels of procoagulants are more susceptible to PM. However, in some cases genetic polymorphisms may actually reduce an individual's susceptibility to PM-related health effects. For example, Park et al. (2006, 091245) found that individuals with two hemochromatosis (HFE) polymorphisms (C282Y and H63D), which result in an increase in iron uptake, had smaller reductions in HRV upon exposure to $PM_{2.5}$. This

effect could possibly be due to the reduction in free iron that enters oxidation-reduction (redox) reactions and the subsequent reduction in reactive oxygen species (ROS).

More recently, studies have begun to focus on epigenetic effects associated with PM exposure (i.e., the effect of PM on DNA methylation) due to the fact that DNA methylation can result in gene alterations. The limited number of epidemiologic studies that examined epigenetic effects have found some evidence that long-term exposure to $PM_{2.5}$ and PM_{10} can influence DNA methylation (Baccarelli et al., 2009, 188183; Tarantini et al., 2009, 192010). Additionally, a toxicological study found some evidence of hypermethylation of spermatogonial stem cells in response to the PM component of ambient urban air (Yauk et al., 2008, 157164). Although epigenetic effects have been observed in response to PM exposure in some studies additional research is needed to more accurately characterize these associations.

Overall, the evidence suggests that specific genetic polymorphisms can potentially increase the susceptibility of an individual to PM exposure, but protective polymorphisms also exist, which may diminish the health effects attributed to PM exposure in some individuals. In addition, the studies that examine genetic polymorphisms or epigenetics can potentially provide additional information that can aid in identifying the specific pathways and mechanisms by which PM initiates health effects.

8.1.6. Pre-Existing Disease

In 2004, the National Research Council (NRC) published a report that emphasized the need to evaluate the effect of air pollution on susceptible populations, including those with respiratory illnesses and cardiovascular diseases (NRC, 2004, 156814). The 2004 PM AQCD included epidemiologic evidence suggesting that individuals with pre-existing heart and lung diseases, as well as diabetes may be more susceptible to PM exposure. In addition, toxicological studies that used animal models of cardiopulmonary diseases and heightened allergic sensitivity found evidence of enhanced susceptibility. More recent epidemiologic and human clinical studies have directly examined the effect of PM on individuals with pre-existing diseases and toxicological studies have employed disease models to identify whether exposure to PM disproportionately effects certain populations.

8.1.6.1. Cardiovascular Diseases

The potential effect of underlying cardiovascular diseases on PM-related health responses has been examined using epidemiologic studies that stratify effect estimates by underlying conditions or secondary diagnoses, and toxicological studies that use animal models to mimic the physiological conditions associated with various cardiovascular diseases (e.g., MI, ischemia, and atherosclerosis). A limited number of controlled human exposure studies have also examined the potential relationship between CVD and exposure to PM in individuals with underlying cardiovascular conditions, but these studies have provided somewhat inconsistent evidence for these associations.

The majority of the epidemiologic literature that examined the association between short-term exposure to PM and cardiovascular outcomes focuses on cardiovascular-related hospital admissions and emergency department (ED) visits. Hypertension is the pre-existing condition that has been considered to the greatest extent when examining the association between short-term exposure to PM and cardiovascular-related HAs and ED visits. Pope et al. (2006, 091246) found no evidence of effect modification of the IHD ED visit association with $PM_{2.5}$ in individuals with secondary hypertension in Utah. This is consistent with the results of both Wellenius et al. (2006, 088748) in 7 U.S. cities and Lee et al. (2008, 192076) in Taipei, which found that hypertension did not modify the association between PM_{10} and cardiovascular-related health outcomes. These results differ from those presented by Peel et al. (2007, 090442), in Atlanta, which observed that exposure to PM_{10} resulted in an increase in ED visits for arrhythmias and CHF in individuals with underlying hypertension. An additional study conducted by Park et al. (2005, 057331) in Boston found that underlying hypertension increased associations between HRV, specifically a reduction in the HF parameter, and short-term exposure to $PM_{2.5}$.

Park et al. (2005, 057331), in the analysis mentioned above, examined other underlying cardiovascular conditions and found associations between $PM_{2.5}$ and HRV in individuals with pre-existing IHD. In a toxicological study, Wellenius et al. (2003, 055691) examined the effects of

$PM_{2.5}$ CAPs exposure on induced myocardial ischemia in dogs, which mimics the effects associated with IHD. The authors found that exposure to $PM_{2.5}$ prior to the induced ischemia increased ST-segment elevation, indicating greater ischemia than air-exposed animals (Wellenius et al., 2003, 055691). A follow-up study implicated impaired myocardial blood flow in the response (Bartoli et al., 2009, 179904).

Additional studies examined the effects of PM on cardiac function in individuals with dysrhythmia. Peel et al. (2007, 090442) observed some evidence for an increase in ED visits for IHD for individuals with secondary dysrhythmia and PM_{10} exposure. However, when examining CHF hospital admissions in 7 U.S. cities, Wellenius et al. (2006, 088748) found no evidence for effect modification of PM_{10} exposure in individuals with secondary dysrhythmia.

Limited evidence is available from epidemiologic studies that examined other pre-existing cardiovascular conditions, such as CHF and MI. Pope et al. (2006, 091246) observed an increase in hospital admissions for acute IHD in individuals with underlying CHF upon short-term exposure to $PM_{2.5}$. However, Peel et al. (2007, 090442) did not find that underlying CHF contributed to an increase in the association between IHD ED visits and short-term exposure to PM_{10}. Zanobetti and Schwartz (2005, 088069) also examined the potential effect modification of the association between PM_{10} and cardiovascular-related health effects in individuals with CHF, but used MI hospital admissions as the outcome of interest. Underlying CHF was not found to increase MI hospital admissions for exposure to PM_{10} in the cohort of more than 300,000 hospital admissions.

Wellenius et al. (2006, 088748) examined the effect of previous diagnoses of acute MI on the association between CHF hospital admissions and short-term exposure to PM_{10} in 7 U.S. cities. In this study, Wellenius et al. (2006, 088748) found no evidence of effect modification of the relationship between PM_{10} and CHF hospital admissions by previous acute MI. Toxicological studies have provided additional evidence for the cardiovascular health effects associated with exposure to PM in individuals with underlying MI. Anselme et al. (2007, 097084) and Wellenius et al. (2006, 156152) examined the arrhythmic effects of PM on rats that experienced an MI using two different models. Wellenius et al. (2006, 156152) used a post-myocardium sensitivity model (acute MI) and observed that exposure to $PM_{2.5}$ CAPs decreased ventricular premature beats and spontaneous supraventricular ectopic beats. In contrast, the MI model of chronic heart failure (i.e., rats that experienced an MI 3 mo prior to exposure), demonstrated a prominent increase in the incidence of premature ventricular contraction when exposed to DE (Anselme et al., 2007, 097084). The discrepancy in effects observed between studies could be due to differences in the MI model or the PM exposure (i.e., CAPs vs. DE).

Additional toxicological studies examined the association between PM and pre-existing cardiovascular diseases using a murine model of atherosclerosis ($ApoE^{-/-}$ mouse). For example, Campen et al. (2005, 083977; 2006, 096879) examined the heart rate and ECG effects of acute exposure to PM on $ApoE^{-/-}$ mice. With DE, dramatic bradycardia and T-wave depression were observed that were attributable to the gases (Campen et al., 2005, 083977), while whole gasoline emissions induced T-wave alterations that required particles (Campen et al., 2006, 096879). However, these studies along with others that used this mouse model (see Section 6.2 and 7.2) did not compare the effects observed with the $ApoE^{-/-}$ mouse to other non-diseased mouse models, so it is unclear if the responses would differ if other strains were used in the same experimental protocol.

Controlled human exposure studies that examined the effect of pre-existing diseases on cardiovascular outcomes with exposure to PM are less consistent and difficult to interpret in the context of the results from the epidemiologic and toxicological studies. Mills et al. (2007, 091206; 2008, 156766) investigated the effects of dilute DE, or fine and ultrafine CAPs, respectively, on subjects with coronary artery disease and prior MI. Exposure to dilute DE was found to promote exercise-induced ST-segment changes indicating myocardial ischemia, as well as inhibit endogenous fibrinolytic capacity (Mills et al., 2007, 091206). The physiological responses observed in Mills et al. (2007, 091206) provides a measure of coherency with the cardiovascular effects observed in epidemiologic studies, including increases in hospital admissions and ED visits for IHD and stroke associated with exposure to PM. An examination of fine and ultrafine CAPs that were low in combustion derived particles, were not found to exhibit any significant effects on vascular function (Mills et al., 2008, 156766). Routledge et al. (2006, 088674) reported no change in HRV in a group of adults with coronary artery disease following exposure to ultrafine carbon particles, which may be explained in part by the use of medication (beta blockers) among the majority of the subjects. Although the epidemiologic studies did not examine potential effect modification of pre-existing cardiovascular conditions on effects associated with long-term exposure to PM, a few

toxicological studies exposed animals with underlying cardiovascular conditions to PM for months. In studies that focused on the cardiovascular effects following subchronic exposure to PM in ApoE$^{-/-}$ mice, relatively consistent physiological effects were observed across studies. Araujo et al. (2008, 156222) exposed mice to ultrafine CAPs and observed enhanced size of early atherosclerotic lesions. Similarly, Chen and Nadziejko (2005, 087219) and Sun et al. (2005, 087952; 2008, 157033) exposed mice to $PM_{2.5}$ CAPs with the same results. An additional long-term exposure study observed a decreasing trend in heart rate, physical activity, and temperature along with biphasic responses in HRV (SDNN and rMSSD) upon exposure to CAPs (Chen and Hwang, 2005, 087218).

While the majority of the literature examines the potential modification of the association between PM and non-fatal cardiovascular health effects, a few new studies have also examined effect modification in mortality associations. Zeka et al. (2006, 088749) found an increase in risk estimates for associations between PM_{10} and mortality in individuals with underlying stroke, while Bateson et al. (2004, 086244) found evidence for effect modification of the PM-mortality association in individuals with CHF.

Collectively, the evidence from epidemiologic and toxicological, and to a lesser extent, controlled human exposure studies indicates that individuals with underlying cardiovascular diseases are susceptible to PM exposure. Although the evidence for some outcomes was inconsistent across epidemiologic and toxicological studies, this could be due to a variety of issues including the PM size fraction used in the study along with the study location. Even with these caveats, a large proportion of the U.S. population has been diagnosed with cardiovascular diseases (i.e., approximately 51.6 million people with hypertension, 24.1 million with heart disease, and 14.1 million with coronary heart disease [see Table 8-3]), and therefore represents a large population that is potentially more susceptible to PM exposure than the general population.

Table 8-3. Percent of the U.S. population with respiratory diseases, cardiovascular diseases, and diabetes.

			Age				Regional			
	Adults (18+)*		18-44	45-64	65-74	75+	NE	MW	S	W
Chronic Condition/ Disease	Number (x 10^6)	%	%	%	%	%	%	%	%	%
RESPIRATORY DISEASES										
Asthma*	24.2	11.0	11.5	10.5	11.7	9.3	11.7	11.5	10.5	10.8
Asthma (<18 yrs)	6.8*	9.3*	---	---	---	---	---	---	---	---
COPD										
Chronic bronchitis	9.5	4.3	2.9	5.5	5.6	6.7	3.8	4.4	4.9	3.5
Emphysema	4.1	1.8	0.3	2.4	5.0	6.4	1.4	2.3	1.9	1.6
CARDIOVASCULAR DISEASES										
All heart disease	24.1	10.9	3.6	12.3	26.1	36.3	10.8	12.7	10.9	9.2
Coronary heart disease	14.1	6.4	0.9	7.2	18.4	25.5	6.4	7.6	6.6	4.7
Hypertension	51.6	23.4	77	32.4	52.7	53.5	22.2	23.7	25.3	20.6
Stroke	5.6	2.6	0.5	2.4	7.6	11.2	2.1	2.8	2.9	2.2
Diabetes	17.1	7.8	2.6	10.4	18.2	17.9	7.2	8.1	8.0	7.4

* All data for adults except asthma prevalence data for children under 18 years of age, from CDC (2008, 156324; 2008, 156325). For adults prevalence data based off adults responding to "ever told had asthma."

Source: Data from Pleis and Lethbridge-Çejku (2007, 156875); CDC (2008, 156324; 2008, 156325).

8.1.6.2. Respiratory Illnesses

Investigators have examined the effect of pre-existing respiratory illnesses on multiple health outcomes (e.g., mortality, asthma symptoms, CHF) in response to exposure to ambient levels of PM. Animal models have been developed and/or human clinical studies conducted to examine the possible PM effects on pre-existing respiratory conditions in a controlled setting.

Epidemiologic studies have examined the effect of short-term exposure to PM on the respiratory health of asthmatic individuals measuring a variety of respiratory outcomes. Asthmatic individuals were found to have an increase in medication use (Rabinovitch et al., 2006, 088031), respiratory symptoms (i.e., asthma symptoms, cough, shortness of breath, and chest tightness) (Gent et al., 2003, 052885), and asthma symptoms (Delfino et al., 2002, 093740; 2003, 050460) with short-term exposure to $PM_{2.5}$; and morning symptoms (Mortimer et al., 2002, 030281) and asthma attacks (Desqueyroux et al., 2002, 026052) with short-term exposure to PM_{10}.

Toxicological studies that have used ovalbumin-induced allergic airway disease models provide evidence which supports the findings of the epidemiologic literature. Morishita et al. (2004, 087979) used this model to assess the health effects of $PM_{2.5}$ components. In response to short-term exposure to CAPs from Detroit, an area with pediatric asthma rates three times the national average, rats with allergic airway disease were found to preferentially retain PM derived from identified local combustion sources in association with eosinophil influx and BALF protein content after an acute exposure (Morishita et al., 2004, 087979). These findings suggest that individuals with allergic airways conditions are more susceptible to allergic airways responses upon exposure to $PM_{2.5}$, which may be partially attributed to increased pulmonary deposition and localization of particles in the respiratory tract (Morishita et al., 2004, 087979). An additional study (Heidenfelder et al., 2009, 190026) examined whether genes are differentially expressed upon exposure to PM. They found that exposure to CAPs increased the expression of genes associated with inflammation and airway remodeling in rats with allergic airway disease. Although the evidence is much more limited, not all of the toxicological studies evaluated that examined the effect of underlying respiratory conditions on PM-related respiratory morbidity focused on allergic airways disease. Using an animal model of emphysema (i.e., papain-treated mice), Lopes et al. (2009, 190430) found that papain-treated mice exposed to urban ambient PM demonstrated a statistically significant increase in mean linear intercept, a measure of airspace enlargement, compared to saline-treated controls exposed to filtered air. These results provide preliminary evidence, which suggests that non-allergic respiratory morbidities may also increase the susceptibility of an individual to PM-related respiratory effects.

The results from the epidemiologic and toxicological studies that focused on underlying allergic airways disease is supported by a series of controlled human exposure studies which have shown that exposure to DEPs increases the allergic inflammatory response in atopic individuals (Bastain et al., 2003, 098690; Diaz-Sanchez et al., 1997, 051247; Nordenhall et al., 2001, 025185). However, not all controlled human exposure studies have found evidence for differences between the respiratory effects exhibited by healthy and asthmatic individuals. Studies by Gong et al. (2003, 042106; 2004, 055628; Gong et al., 2008, 156483) reported that healthy and asthmatic subjects exposed to coarse, fine and ultrafine CAPs, exhibited similar respiratory responses. However, it should be noted that these studies excluded moderate and severe asthmatics that would be expected to show increased susceptibility to PM exposure.

In addition to examining the association between exposure to PM and respiratory effects in asthmatics, some studies examined whether individuals with COPD represent a potentially susceptible population. Desqueyroux et al. (2002, 026052) did not observe an increase in the exacerbation[1] of COPD in response to short-term exposure to $PM_{2.5}$. However, studies that examined the effect of PM on lung function in individuals with COPD (Lagorio et al., 2006, 089800; Trenga et al., 2006, 155209) observed declines in FEV_1, and FEV_1 and FVC, respectively in response to PM_{10} and/or $PM_{2.5}$. Silkoff et al. (2005, 087471) observed associations between PM_{10} and a reduction in FEV_1 and $PM_{2.5}$ and a reduction in PEF, in those with COPD, but only during one winter of the analysis. Only one controlled human exposure study examined the effects of PM on COPD subjects and found no significant difference in respiratory effects between healthy and individuals with COPD upon exposure to $PM_{2.5}$ CAPs (Gong et al., 2004, 055628). On the other hand the results from dosimetry studies have shown that COPD patients have increased dose rates and impaired

[1] Desqueyroux et al. (2002, 026052) defined a COPD exacerbation as (a) decrease in "vesicular" breath sound, (b) bronchial obstruction, (c) tachycardia or arrhythmia, or (d) cyanosis.

mucociliary clearance relative to age matched healthy subjects, suggesting that individuals with COPD are potentially at a greater risk of PM-related health effects (Sections 4.2.4.5 and 4.3.4.3).

A few of the epidemiologic studies examined the effect of underlying respiratory illnesses on the association between short- and long-term exposure to PM and mortality. Using different pre-existing respiratory illnesses, Zeka et al. (2006, 088749) and De Leon et al. (2003, 055688) found that short-term exposure to PM_{10} increased the risk of nonaccidental mortality for pneumonia and circulatory mortality for all respiratory illnesses, respectively. Additionally, Zanobetti et al. (2008, 156177) observed an association between long-term exposure to PM_{10} and mortality in individuals that had previously been hospitalized for COPD. Although these studies do not examine additional size fractions of PM, together they highlight the potential effect of underlying respiratory illnesses on the PM-mortality relationship.

Overall, the epidemiologic, controlled human exposure, and toxicological studies evaluated provide biological plausibility for the increased health effects observed in epidemiologic studies among asthmatic individuals in response to PM exposure. Although, the evidence from studies that examined associations between PM and health effects in individuals with COPD is inconsistent, taken together individuals with COPD and asthma represent a large percent of the U.S. population (~45 million people), which may be more susceptible to PM-related health effects (Table 8-3).

8.1.6.3. Respiratory Contributions to Cardiovascular Effects

Although the majority of health effects observed in individuals with pre-existing respiratory illnesses were associated with respiratory illness exacerbations, studies also examined whether underlying respiratory illnesses can lead to cardiovascular effects in response to PM exposure. Controlled human exposure and toxicological studies have also observed some cardiovascular effects in individuals with pre-existing respiratory illnesses. Gong et al. (2003, 042106) observed acute responses in the cardiovascular system and systemic circulation among asthmatic individuals after exposure to $PM_{2.5}$ CAPs. However, respiratory disease has not consistently been observed to affect cardiovascular response in controlled human exposure studies. In a toxicological study, Batalha et al. (2002, 088109), using a chronic bronchitis animal model, found that the pulmonary artery lumen-to-wall ratio was decreased in rats exposed to $PM_{2.5}$ CAPs, although the induced bronchitis didn't seem to affect the response. The majority of epidemiologic studies that examined whether underlying respiratory illnesses contributed to the manifestation of PM-related cardiovascular hospital admission or ED visits, did not report increases in effects for a variety of cardiovascular outcomes (e.g., IHD, arrhythmias, CHF, MI) for individuals with underlying respiratory infection (Wellenius et al., 2006, 088748), pneumonia (Zanobetti and Schwartz, 2005, 088069), or COPD (Peel et al., 2007, 090442; Wellenius et al., 2005, 087483). However, Yeatts et al. (2007, 091266), in a panel study, found evidence for cardiovascular effects, specifically reductions in HRV parameters, in asthmatic adults upon short-term exposure to $PM_{10-2.5}$. It must be noted that most of the aforementioned epidemiologic studies focused on exposure to PM_{10}, and, therefore, it is unclear how these results compare to those found in the controlled human exposure and toxicological studies that focused on exposure to $PM_{2.5}$ (e.g., CAPs). Thus, it is unclear if individuals with underlying respiratory illnesses represent a population that is potentially susceptible to PM-related cardiovascular effects.

8.1.6.4. Diabetes and Obesity

It has been hypothesized that the systemic inflammatory cascade leads to an increase in cardiovascular risk (Dubowsky et al., 2006, 088750). As a result, individuals with conditions linked to chronic inflammation (i.e., diabetes and obesity), have been examined to determine whether diabetes or obesity facilitate the manifestation of PM-mediated health effects, and, therefore, represent a potentially susceptible population.

Epidemiologic studies have examined whether diabetes modifies the association between cardiovascular health effects and PM exposure, but these studies have primarily focused on short-term exposure to PM_{10}. Time-series studies have provided evidence through an examination of hospital admission and ED visits and mortality, which suggests an increase in health effects in diabetic individuals in response to PM exposure. Multicity studies have found upwards of 75% greater risk of hospitalization for cardiac diseases in individuals with diabetes upon exposure to PM_{10} (Zanobetti and Schwartz, 2002, 034821). Studies conducted in Atlanta, Georgia have also

found increased risk for cardiovascular-related ED visits in diabetics, specifically for IHD, arrhythmias, and CHF (Peel et al., 2007, 090442). Additional studies found some evidence that individuals with diabetes are at increased risk of mortality upon exposure to PM_{10} (Zeka et al., 2006, 088749) and $PM_{2.5}$ (Goldberg et al., 2006, 088641). However, some studies (both multicity and single-city) have not observed a modification of the risk of cardiovascular ED visits and hospital admissions in response to exposure to PM_{10} in diabetics (Pope et al., 2006, 091246; Wellenius et al., 2006, 088748; Zanobetti and Schwartz, 2005, 088069).

Panel and cohort studies have been conducted to determine the physiological changes that occur in individuals with diabetes in response to PM exposure. These studies examined both changes in inflammatory markers along with specific physiological alterations in the cardiovascular system. Schneider et al. (2008, 191985) in a panel study of 22 individuals with type 2 diabetes mellitus in Chapel Hill, NC found evidence that ambient exposure to $PM_{2.5}$ enhanced the reduction in various markers of endothelial function. Liu et al. (2007, 156705) observed an increase in end-diastolic FMD and end-systolic FMD, and decreases in end-diastolic basal diameter and end-systolic basal diameter in diabetics upon exposure to PM_{10}. The authors also observed positive associations with FMD and blood pressure in diabetic individuals. A controlled human exposure study conducted by Carlsten et al. (2008, 156323) found that DE did not elicit any prothrombotic effects in subjects with metabolic syndrome, which consists of physiological alterations similar to those observed in both diabetic and obese individuals. An examination of biomarkers found mixed results, with Liao et al. (2005, 088677) observing an increase in vWF; Liu et al. (2007, 156705) observing an increase in TBARS, but not CRP or TNF-α; and Dubowsky et al. (2006, 088750) observing an increase in CRP and WBCs. Overall, it is unclear how differences in each of the aforementioned biomarkers contribute to the potential overall cardiovascular effect observed in diabetic individuals; however, an increase in inflammation, oxidative stress, and acute phase response may contribute to cardiovascular effects. A recent toxicological study (Sun et al., 2009, 190487), also demonstrated the potential for PM-related health effects in diabetics. Sun et al. (2009, 190487) found that $PM_{2.5}$ CAPs exposure for 4 mo can exaggerate insulin resistance, visceral adiposity, and inflammation in a diet-induced obesity mouse model.

Overall, epidemiologic studies have reported evidence for increased effects in diabetics in response to PM exposure, with preliminary evidence for pathophysiologic alterations from toxicological studies. This potentially susceptible population is large, with an estimated 17.1 million diabetic individuals in the U.S. (Table 8-3). However, the limited evidence from toxicological and controlled human exposure studies along with the lack of studies that examined additional PM size fractions warrants additional research to confirm the associations observed and to identify the biological pathway(s) that may result in a greater response to PM in diabetics.

In addition to diabetes, obesity has been examined as a health condition with the potential to lead to an increase in PM-related health effects. Only a few recent studies have examined the potential effect modification of PM risk estimates by obesity. Schwartz et al. (2005, 086296) reported a change in HRV in obese (i.e., BMI $\geq$ 30 kg/m^2) compared to non-obese subjects, while Dubowsky et al. (2006, 088750) observed an increase in inflammatory markers (i.e., CRP, IL-6, and WBC) in response to short-term exposure to $PM_{2.5}$ among obese individuals. Additionally, Schneider et al. (2008, 191985) found some evidence for a larger reduction in FMD in individuals with a BMI >30 kg/m^3 in response to $PM_{2.5}$ exposure. These effects could be due, in part, to a higher PM dose rate in obese individuals, which has been demonstrated in children by Bennett and Zeman (2004, 155686). These investigators also reported that tidal volume and resting minute ventilation increased with body mass index. Although a limited amount of research has been conducted to examine PM-related health effects in obese individuals there is an increasing trend of individuals within the U.S. that have been defined as overweight (BMI $\geq$ 25.0) or obese (BMI $\geq$ 25.0), with the prevalence of overweight individuals increasing from 20-74% from 1960 to 2004, and the prevalence of obese individuals increasing from 13.3-32.1% (NCHS, 2006, 198921).

8.1.7. Socioeconomic Status

SES is a composite measure that usually consists of economic status, measured by income; social status measured by education; and work status measured by occupation (Dutton and Levine, 1989, 192052). Based on data from the U.S. Census Bureau in 2006, from among commonly-used indicators of SES, about 12% of individuals and 11% of families are below the poverty line (U.S. Census, 2009, 192147). Although the measure of SES is composed of a multitude of

surrogates, each of these linked factors can influence an individual's susceptibility to PM-related health effects. Additionally, low SES individuals have been found to have a higher prevalence of pre-existing diseases; inadequate medical treatment; and limited access to fresh foods leading to a reduced intake of antioxidant polyunsaturated fatty acids and vitamins, which can increase this population's susceptibility to PM (Kan et al., 2008, 156621).

Surrogates of SES, such as educational attainment, have been shown in some studies to modify health outcomes of PM exposure for a population. Within the U.S. approximately 16% of the population does not have a high school degree and only 27% have a bachelor's degree or higher level of education (U.S. Census, 2009, 192148). Educational attainment generally coincides with an individual's income level, which is correlated to other surrogates of SES, such as residential environment (Jerrett et al., 2004, 087379). Franklin et al. (2008, 097426) noted an increased risk in mortality associated with short-term exposure to $PM_{2.5}$ and its components for individuals with low SES while additional analyses stratified by education level have also observed consistent trends of increased mortality for $PM_{2.5}$ and $PM_{2.5}$ species for individuals with low educational attainment (Ostro et al., 2006, 087991; Ostro et al., 2008, 097971; Zeka et al., 2006, 088749). This is further supported by a reanalysis of the ACS cohort (Krewski et al., 2009, 191193), which found moderate evidence for increased lung cancer mortality in individuals with a high school education or less compared to individuals with more than a high school education in response to long-term exposure to $PM_{2.5}$. However, when examining education level and IHD mortality due to long-term exposure to $PM_{2.5}$ Krewski et al. (2009, 191193) observed an inverse relationship.

Epidemiologic studies have also examined additional surrogates of SES, such as residential location and nutritional status to identify their influence on the susceptibility of a population. Jerrett et al. (2004, 087379) examined the modification of acute mortality effects due to particulate air pollution exposure by residential location in Hamilton, Canada using educational attainment as a surrogate for SES. The authors found that the area of the city with the highest SES characteristics displayed no evidence of effect modification while the area with the lowest SES characteristics had the largest health effects. Likewise, Wilson et al. (2007, 157149) examined the effect of SES on the association between mortality and short-term exposure to PM in Phoenix, but used educational attainment and income to represent SES. When stratifying Phoenix into central, middle, and outer rings of varying urban density central Phoenix, the area with the lowest SES, was found to exhibit the greatest association with $PM_{2.5}$. However, the association with urban density differed when examining $PM_{10-2.5}$, with the greatest effect being observed for the middle ring. Yanosky et al. (2008, 192081) examined whether long-term exposure to traffic-related pollutants, using NO_2 as a surrogate, varied by SES at the block group level. The authors found higher levels of NO_2 associated with lower SES areas, which suggests that lower SES individuals are disproportionately exposed to traffic-related pollutants, which includes PM.

Nutritional deficiencies have been associated with increased susceptibility to a variety of infectious diseases and chronic health effects. Low SES may decrease access to fresh foods, and thus be related to nutritional deficiencies that could increase susceptibility to PM-related health effects. Baccarelli et al. (2008, 157984) examined the association between exposure to $PM_{2.5}$ and HRV in individuals with polymorphisms in MTHFR and cSHMT genes, which are associated with reduced enzyme activity and increased risk of CVD. The authors found that when individuals with these genetic polymorphisms increased their intake (above median levels) of B_6, B_{12}, or methionine no $PM_{2.5}$ effect on HRV was observed.

8.1.8. Summary

Upon evaluating the association between short- and long-term exposure to PM and various health outcomes, studies also attempted to identify populations that are more susceptible to PM. These studies did so by: conducting stratified analyses; examining individuals with an underlying health condition; or developing animal models that mimic the physiological conditions associated with an adverse health effect. These studies identified a multitude of factors that could potentially contribute to whether an individual is susceptible to PM (Table 8-2). Although studies have primarily used exposures to PM_{10} or $PM_{2.5}$, the available evidence suggests that the identified factors may also enhance susceptibility to $PM_{10-2.5}$.

The majority of observations made during the evaluation of the literature reviewed in this ISA are consistent with those reported in the 2004 PM AQCD. An evaluation of age-related health effects suggests that older adults have heightened responses for cardiovascular morbidity with PM exposure.

In addition, epidemiologic and toxicological studies provide evidence, which indicates that children are at an increased risk of PM-related respiratory effects. It should be noted that the health effects observed in children could be initiated by exposures to PM that occurred during key windows of development, such as in utero. Studies that focus on exposures during development have reported inconsistent findings (see Section 7.4.), but a recent toxicological study suggests that inflammatory responses in pregnant women due to exposure to PM could result in health effects in the developing fetus.

Epidemiologic studies have also examined whether additional factors, such as gender, race, or ethnicity modify the association between PM and morbidity and mortality outcomes. Consistent with the findings of the 2004 PM AQCD, gender and race do not seem to modify the association between PM and morbidity and mortality outcomes. However, some evidence, albeit from two studies conducted in California, suggest that Hispanic ethnicity may modify the association between PM and mortality.

Recent epidemiologic and toxicological studies provided evidence that individuals with null alleles or polymorphisms in genes that mediate the antioxidant response to oxidative stress (i.e., GSTM1), regulate enzyme activity (i.e., MTHFR and cSHMT), or regulate levels of procoagulants (i.e., fibrinogen) are more susceptible to PM exposure. However, some studies have shown that polymorphisms in genes (e.g., HFE) can have a protective effect upon PM exposure. Additionally, preliminary evidence suggests that PM exposure can impart epigenetic effects (i.e., DNA methylation), however, this requires further investigation.

Collectively, the evidence from epidemiologic and toxicological, and to a lesser extent, controlled human exposure studies indicate increased susceptibility of individuals with underlying cardiovascular diseases and respiratory illnesses, specifically asthma, to PM exposure. Additional controlled human exposure and toxicological studies provide some evidence for increased PM-related cardiovascular effects in individuals with underlying respiratory health conditions. However, the results are not consistent with epidemiologic studies, resulting in the need for further investigation.

Recently studies have begun to examine the influence of preexisting chronic inflammatory conditions, such as diabetes and obesity, on PM-related health effects. These studies have found some evidence for increased associations for cardiovascular outcomes along with physiological alterations in markers of inflammation, oxidative stress, and acute phase response. However more research is needed to thoroughly examine the effect of PM exposure on obese individuals and to identify the biological pathway(s) that could lead to increased susceptibility of diabetic and obese individuals to PM.

There is also evidence that SES, measured using surrogates such as educational attainment or residential location, modifies the association between PM and morbidity and mortality outcomes. In addition, nutritional status, another surrogate of SES, has been shown to have protective effects against PM exposure in individuals that have a higher intake in some vitamins and nutrients.

Overall, the epidemiologic, controlled human exposure, and toxicological studies evaluated in this review provide evidence for increased susceptibility for various populations. Although the level of evidence varies depending on the factor being evaluated collectively, it can be concluded that some populations are more susceptible to PM than the general population.

Chapter 8 References

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Chapter 9. Welfare Effects

9.1. Introduction

This chapter is a synthesis and evaluation of the most policy-relevant science used to help form the scientific foundation for review of the secondary (welfare-based) NAAQS aimed at protecting against welfare effects of ambient airborne PM. Specifically, Chapter 9 assesses the effects of atmospheric PM on the environment, including: (1) effects on visibility; (2) effects on climate; (3) ecological effects; and (4) effects on materials. These sections initially highlight the conclusions from the 2004 PM AQCD (U.S. EPA, 2004, 056905), followed by an evaluation of recent publications and assessment of the expanded body of evidence. In some sections, few new publications are available, and the discussion is primarily a brief overview of the key conclusions from the previous review.

As discussed in Chapter 1, the effects of particulate NO_X and SO_X have recently been evaluated in the ISA for Oxides of Nitrogen and Sulfur – Ecological Criteria (U.S. EPA, 2008, 157074). That ISA focused on the effects from deposition of gas- and particle-phase pollutants related to ambient NO_X and SO_X concentrations that can lead to acidification and nutrient enrichment, as well as on the potential for increased mercury methylation from SO_4^{2-} deposition. Thus, emphasis in this document is placed on the effects of airborne PM on visibility and climate, and on the deposition effects of PM constituents other than NO_X and SO_X, primarily metals and carbonaceous compounds.

Chapter 2 of this assessment provides an integrative overview of the major welfare effects evaluated. EPA's framework for causality, described in Chapter 1, is applied throughout the evaluation and the causal determinations are highlighted.

9.2. Effects on Visibility

9.2.1. Introduction

In recent years, most visibility research involved characterizing visibility conditions and trends over broad regional scales, improving the understanding of the atmospheric processes and pollutants responsible for the regional impacts, and attribution of visibility-impairing pollutants to emission sources, source types, and regions. The motivation for much of this work has come from the visibility protection provisions of the 1977 Clean Air Act Amendments (CAAA) that called for the development of regulations to address reduction of regional haze in 156 NPs and wilderness areas to natural conditions, and from the subsequent Regional Haze Rule (RHR) promulgated in 1999 by EPA in response to the CAA mandate. Implementation of the RHR entails planned emissions reductions to reach natural haze conditions in these protected areas by 2064 in six 10-year planning steps.

Haze conditions caused solely by PM from natural sources are generally much lower than contemporary conditions. The largest difference is between natural and current conditions for the inorganic salts ammonium sulfate and ammonium nitrate, with natural concentrations taken to be just a few tenths of a $\mu g/m^3$ each (Trijonis et al., 1990, 157058), while current conditions of both over large regions of the country are an order of magnitude or more larger (DeBell, 2006, 156388).

Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISA) and the Integrated Risk Information System (IRIS).

However, natural source PM can be substantial on an episodic basis for crustal mineral PM components during high windblown dust conditions and for carbonaceous PM from biomass combustion during wildfire and prescribed burning episodes. The need for information to generate RHR implementation plans has resulted in extensive use of continental-scale air quality simulation modeling and assessment of expanded ambient monitoring data sets.

Unlike the substantial remote-area visibility investigations that have been conducted in response to the RHR, relatively little work on urban visibility effects has been done in recent years. For example, there has been relatively little new research on the optical and human perceptual aspects of atmospheric visibility over the last decade or more. These topics have been the subjects of numerous earlier investigations that have been summarized in detail elsewhere (Latimer and Ireson, 1980, 035723; Middleton, 1952, 016324; Tombach and McDonald, 2004, 157054; Trijonis et al., 1990, 157058; U.S. EPA, 1979, 157065; Watson et al., 2002, 035623), including past criteria documents on PM, SO_2 and NO_X (U.S. EPA, 1982, 017610; U.S. EPA, 1993, 017649; U.S. EPA, 2004, 056905).

In spite of this fact, the understanding of urban visibility conditions has continued to improve. By applying a well established algorithm that relates PM and haze conditions to data currently collected from routine filter-based PM chemical speciation monitors located in numerous urban areas (Jayanty, 2003, 156605), and to data collected from the more recently deployed high time- and size-resolved PM speciation monitors located in several cities such as those in the PM Supersites program (Solomon and Hopke, 2008, 156997) urban visibility conditions can be better characterized. Comparisons between urban and remote area data in the same region afford the opportunity to differentiate between regional and local visibility impacts. The availability of better size and time resolution PM composition data, compared to that available from the routine monitoring programs, reduces the number of simplifying assumptions required to estimate visibility conditions in these areas, thereby reducing the uncertainty of the estimates. Thus, the state of the science supporting urban visibility assessments continues to improve.

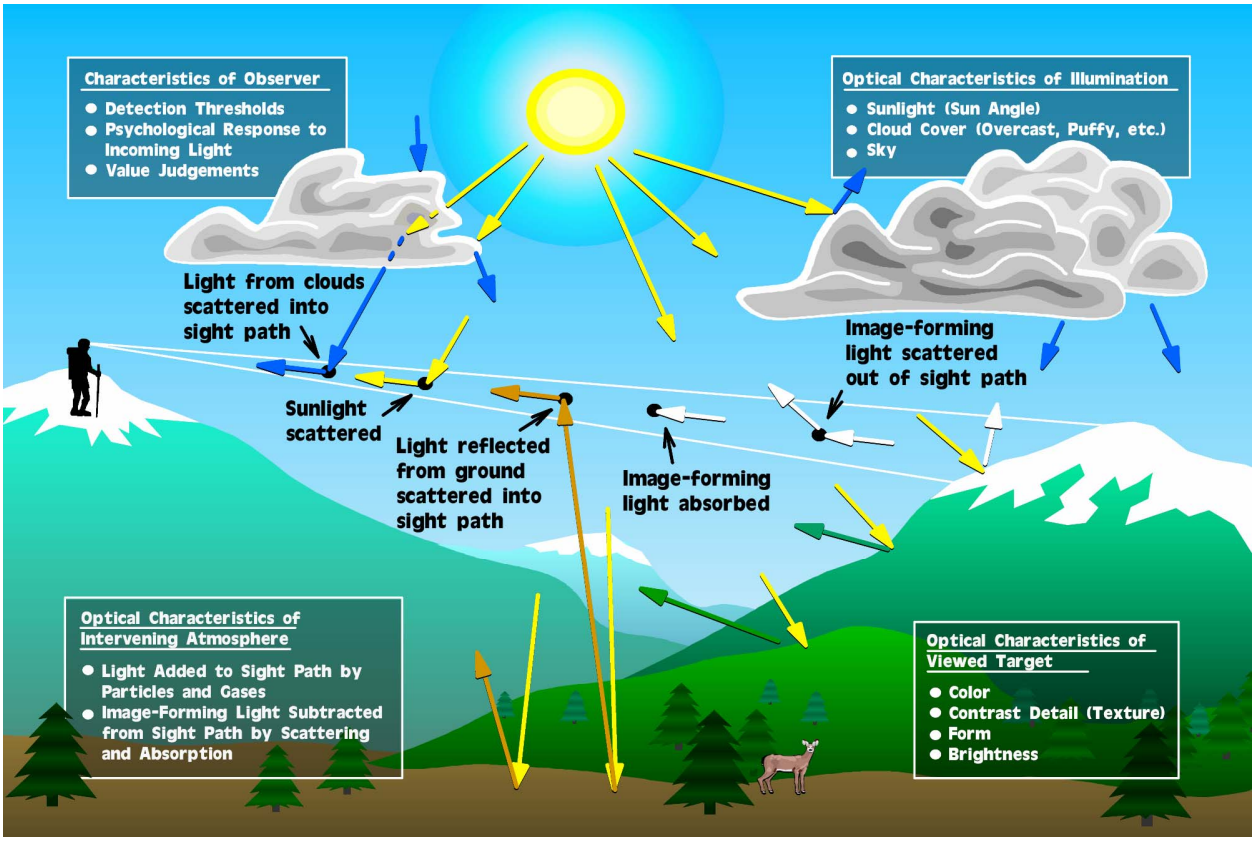
The background section below contains an overview of long-available information to help provide context to the more recently published literature summarized in subsequent sections.

9.2.2. Background

Air pollution-induced visibility impairment is caused by the loss of image-forming light (i.e., signal) and the addition of non-image forming light (i.e., noise) between an observer and the object being viewed. These changes to the light reaching the observer are a result of light being scattered and absorbed by particles and gases in the sight path (see the schematic in Figure 9-1). Electromagnetic theory developed to characterize the interaction of light with matter (Mie, 1908, 155983) permits the calculation of light scattering and absorption by particles and gas molecules where the index of refraction and shape of particles by size are known (Van de Hulst, 1981, 191972).

The ability of human observers to visually detect distant objects or identify changes in their appearance depends on the apparent contrast of the object against its background. The apparent contrast is affected by changes in the physicochemical characteristics of the atmosphere caused by air pollution as well as factors not related to air quality such as length of the sight path, scenic lighting and the physical characteristics of the viewed object and other elements of the scene. To rigorously determine the perceived visual effects of changes in the optical properties of the atmosphere requires the use of radiative transfer modeling to determine changes in light from the field of view experienced by the observer, followed by the use of psychophysical modeling to determine the response to the light by the eye-brain system. The complexity of such an approach discourages its common use.

Atmospheric light extinction is a fundamental atmospheric optics metric used to characterize air pollution impacts on visibility. It is the fractional loss of intensity in a light beam per unit distance due to scattering and absorption by the gases and particles in the air. Light extinction (b_{ext}) can be expressed as the sum of light scattering by particles ($b_{s,p}$), scattering by gases ($b_{s,g}$), absorption by particles ($b_{a,p}$) and absorption by gases ($b_{a,g}$). Light extinction and its components are expressed in units of inverse length, typically either inverse kilometers (km^{-1}) or, as will be the convention in this document, inverse megameters (Mm^{-1}). Traditionally, for visibility-protection applications, the most sensitive portion of the spectrum for human vision (550 nm) has been used to characterize light extinction and its components.



Source: Malm (1999, 025037).

Figure 9-1. Important factors involved in seeing a scenic vista are outlined. Image-forming information from an object is reduced (scattered and absorbed) as it passes through the atmosphere to the human observer. Air light is also added to the sight path by scattering processes. Sunlight, light from clouds, and ground-reflected light all impinge on and scatter from particulates located in the sight path. Some of this scattered light remains in the sight path, and at times it can become so bright that the image essentially disappears. A final important factor in seeing and appreciating a scenic vista are the characteristics of the human observer.

A parametric analysis has shown that a constant fractional change in light extinction results in a similar perceptual change regardless of certain baseline conditions (Pitchford et al., 1990, 156871). From this assessment, the deciview haze index, which is a log transformation of light extinction, similar in many ways to the decibel index for acoustic measurements, was developed (Pitchford and Malm, 1994, 044922). A one deciview (1dv) change is about a 10% change in light extinction, which is a small change that is detectable for sensitive viewing situations. The haze index in deciview units is an appropriate metric for expressing the extent of haze changes where the perceptibility of the change is an issue. The RHR has adopted the deciview haze index as the metric for tracking long-term haze trends of visibility-protected federal lands (U.S. EPA, 2001, 157068). Light extinction and its components are more useful metrics for characterizing the apportionment of haze to its pollutant components due to the approximately linear relationship between pollutant species concentrations and their contributions to light extinction.

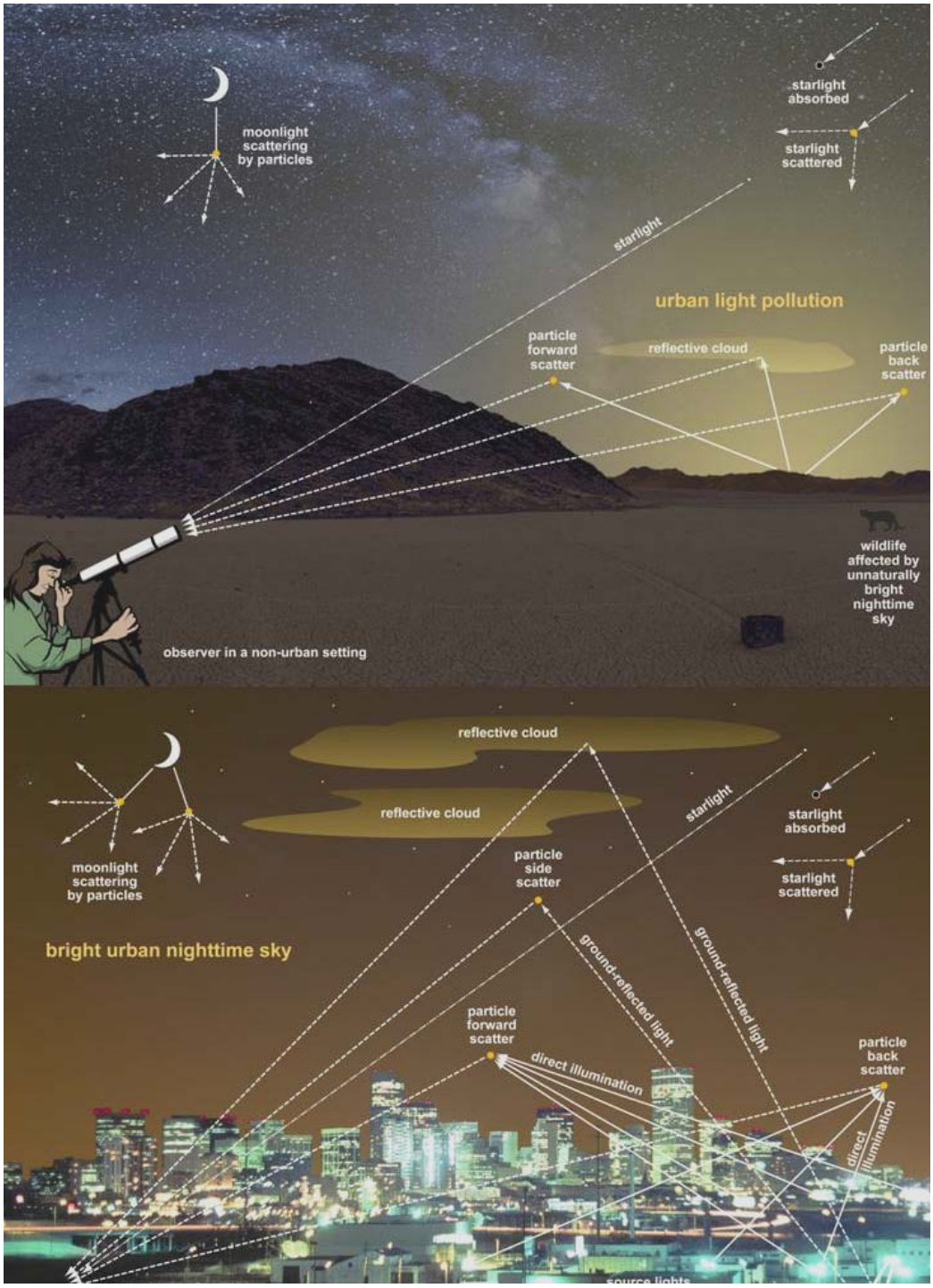


Figure 9-2. Schematic of remote-area (top) and urban (bottom) nighttime sky visibility showing the effects of PM and light pollution.

Daytime visibility has dominated the attention of those who have studied the visibility effects of air pollution, though nighttime visibility is also known to be affected by air pollution. Stargazing is a popular human activity in urban and remote settings. The reduction in visibility of the night sky is primarily dependent on the addition of light into the sight path, the brightness of the night sky, and the reduction in contrast of stars against the background (see the schematic in Figure 9-2). These are

controlled by the addition of PM, which enhances scattering, and the addition of anthropogenic sources of light. Scattering of anthropogenic light contributes to the "skyglow" within and over populated areas, adding to the total sky brightness. The visual result is a reduction of the number of visible stars and the disappearance of diffuse or subtle phenomena such as the Milky Way. The extinction of starlight is a secondary and minor effect also caused by increased scattering and absorption. Anthropogenic light sources include artificial outdoor lighting, which varies dramatically across space. Natural sources include the Moon, planets, and stars that have a predictable rhythm across time.

The nighttime visual environment has some important differences to note. Light sources and ambient conditions are typically five to seven orders of magnitude dimmer at night than in sunlight. Moonlight, like sunlight, introduces light throughout an observer's sight path at a constant angle. On the other hand, dim starlight emanates from all over the celestial hemisphere while artificial lights are concentrated in cities and illuminate the atmosphere from below. Sight paths are often inclined upward at night as targets may be nearby terrain features or celestial phenomena. Extinction behaves the same at night as during the day, lowering the contrast of scenes through scattering and absorption; nevertheless the different light sources will yield variable changes in visibility as compared to what has been established for the daytime scenario. Little research has been conducted on nighttime visibility. Even if the air quality-visibility interactions are shown to be similar between day and night settings, the human psychophysical response at night is expected to differ. Though recent advances in the ability to instrument and quantify nighttime scenes (Duriscoe et al., 2007, 156411) have been made and can be utilized to evaluate nocturnal visibility, the state of the science is not yet comparable to that associated with daytime visibility impairment. The remainder of this document focuses exclusively on daytime visibility.

9.2.2.1. Non-PM Visibility Effects

Light extinction due to the gaseous components of the atmosphere is relatively well understood and well estimated for any atmospheric conditions. Absorption of visible light by gases in the atmosphere is primarily by NO_2, and can be directly and accurately estimated from NO_2 concentrations by multiplying by the absorption efficiency. Scattering by gases is described by the Rayleigh scattering theory.

NO_2 absorbs more light in the short wavelength blue portion of the spectrum than at longer wavelengths. For this reason a plume or layer of NO_2 removes more of the blue light from the scene viewed through the layer giving a yellow or brown appearance to the layer or plume. This filtering of blue light by NO_2 can deepen the brown appearance of hazes over urban areas, although it is not the sole cause of such discoloration (U.S. EPA, 1993, 017649). The photopic-weighted absorption efficiency at the 550 nm wavelength is incorporated into the revised version of the algorithm for estimating light extinction from aerosol data that is used for implementing the RHR (Pitchford et al., 2007, 098066). However, NO_2 is not routinely measured at any of the monitoring sites representing visibility protected areas where its impacts are assumed to be inconsequential compared to those of PM. At background concentrations NO_2 absorption is generally less than five percent of the light scattering by clean air (Rayleigh scattering), making it imperceptible. Plume visibility models are available to assess both achromatic contrast and discoloration associated with NO_2 light absorption, for point source emissions (Latimer and Ireson, 1980, 035723; Seigneur et al., 1984, 156965).

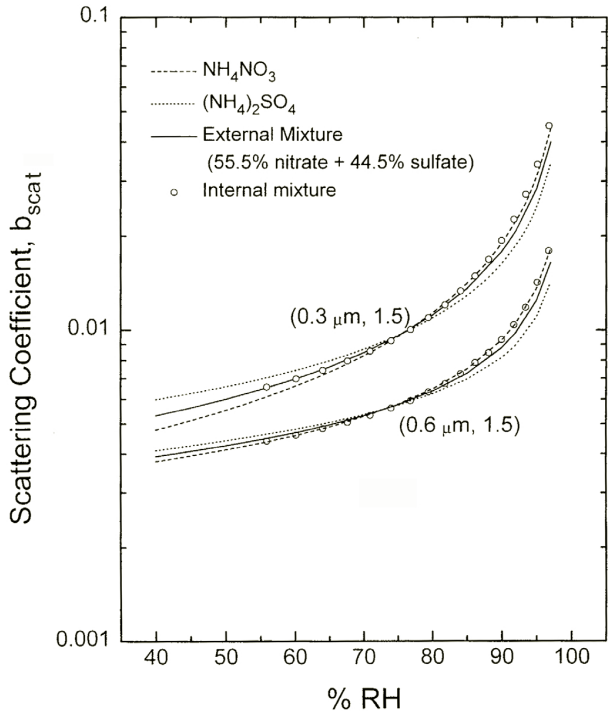
9.2.2.2. PM Visibility Effects

Particle light extinction is more complex than that caused by gaseous components. PM is responsible for most visibility impairment except under near-pristine conditions, where Rayleigh scattering is the largest contributor to light extinction or in plumes of combustion sources that are well-controlled for particulate emissions (e.g., coal-fired power plants with bag houses), where light absorption by NO_2 may dominate the light extinction.

Light-absorbing carbon (e.g., DE soot and smoke) and some crustal minerals are the only commonly occurring airborne particle components that absorb light. All particles scatter light, and generally particle light scattering is the largest of the four light extinction components. While a larger particle scatters more light than a similar shaped smaller particle of the same composition, the light scattered per unit of mass concentration (i.e., mass scattering efficiency in units of $Mm^{-1}/[\mu g/m^3]$ which reduces to m^2/g) is greatest for particles with diameters from ~0.3-1.0 μm. If

the index of refraction, particle shape and concentration as a function of particle size are well characterized, Mie theory can be used to accurately calculate the light scattering and absorption by those particles. However, it is rare that these particle properties are known, so assumptions are used in place of missing information to develop a simplified calculation scheme that provides an estimate of the particle light extinction from available data sets.

Particles composed of water soluble inorganic salts (i.e., ammoniated sulfate, ammonium nitrate, sodium chloride, etc.) are hygroscopic in that they absorb water as a function of relative humidity to form a liquid solution droplet. Aside from the chemical consequences of this water growth, the droplets become larger when relative humidity increases, resulting in increased light scattering. Hence, the same PM dry concentration produces more haze. Figure 9-3 shows the effect of water growth as a function of relative humidity on light scattering for two size distributions of ammonium nitrate and ammonium sulfate particles as well as for internal and external mixtures (i.e., mixed within the same particle and in separate particles, respectively) of the two components. This figure illustrates a number of important points. The water growth effect is substantial with an increase in light scattering by about a factor of 10 between 40% and 97% relative humidity for the same dry particle concentrations. The amount of scattering is significantly dependent on the dry particle size distribution. However the growth curves for ammonium sulfate, ammonium nitrate and mixtures of the two particle components are similar at any of the dry particle size distributions. Water growth curves are also available for sodium chloride, the major component in sea salt, which is an important PM component at coastal locations.



Source: Reprinted with Permission of the American Geophysical Union from Tang (1996, 157042).

Figure 9-3. Effect of relative humidity on light scattering by mixtures of ammonium nitrate and ammonium sulfate.

Using Mie theory, the scattering and absorption of any wavelength of light by a particle of known size and index of refraction (a function of the wavelength of light) can be calculated (Van de Hulst, 1981, 191972). Particle density is used to convert the particle light extinction to its mass extinction efficiency (i.e., the ratio of particle light extinction to its mass). To expand the calculations from one particle at a time to the multitude of particles in ambient aerosol, information

about the aerosol size and composition distributions are needed. Aerosol mixture refers to how the major components that make up the particles are mixed. Methods have been developed to treat simple mixture models ranging from external mixtures where the various components are assumed to be in separate particles, to multi-component mixtures where individual particles contain several components (Ouimette and Flagan, 1982, 025047). The latter includes internally mixed particles where two or more components are mixed within the particles, and layered aerosol with a core of one component covered by a shell of another component.

The Mie theory solution for an external mixture can be simplified to a linear relationship where the light extinction is the sum of the mass concentration of each species multiplied by its specific mass extinction efficiency (Ouimette and Flagan, 1982, 025047). This formulation promotes the concept of apportioning the light extinction among the various PM species. For internally mixed aerosol, the light extinction response to adding or removing mass of any component to the aerosol is dependent on how such changes would affect the particle size, density and index of refraction distribution of the aerosol. However, a number of investigators have shown that the differences among the calculated light extinction values using external and various internal mixture assumptions are generally less than about 10% (Lowenthal et al., 1995, 045134; Ramsey, 1966, 013946; Sloane, 1983, 025039; Sloane, 1984, 025040; Sloane, 1986, 045954; Sloane and Wolff, 1985, 045953; Wolff, 1985, 044680). This provides a basis to accept the apportionment of light extinction to the PM components calculated using an external mixture assumption as a meaningful surrogate for their contributions.

Ambient aerosols are usually a complex and unknown combination of both internal and external mixtures of the particle components. Despite these complexities, PM light scattering can be accurately calculated for any relative humidity if the chemical composition as a function of dry particle size is known (Hand et al., 2002, 190367; Malm and Pitchford, 1997, 002519). However, most routinely available ambient monitoring programs do not include data with sufficient detail to make such calculations. The IMPROVE network with its greater than 150 remote area monitoring sites (DeBell, 2006, 156388) and the CSN (Jayanty, 2003, 156605) with its greater than 150 urban area monitoring sites collect 24-h duration fine particle samples ($PM_{2.5}$) that are analyzed for the major PM components including SO_4^{2-}, nitrate, and carbonaceous particulate. CSN also analyzes for ammonium ion, but does not monitor coarse mass ($PM_{10-2.5}$), while IMPROVE measures coarse mass but does not analyze for ammonium ion. Neither data set has sufficient size resolution to make Mie theory calculations of light extinction, nor does either program routinely monitor NO_2 concentrations, which would be required to calculate its contribution to light extinction by absorption.

A simple algorithm similar in form to the linear equation that results from Mie theory applied with an external mixture assumption is frequently used to estimate light extinction from the concentrations of the major components. The concentration of each of the major aerosol components is multiplied by a dry extinction efficiency value and for the hygroscopic components (e.g., ammoniated sulfate and ammonium nitrate) an additional multiplicative term to account for the water growth to estimate that components contribution to light extinction. Both the dry extinction efficiency and water growth terms are developed by some combination of empirical assessment and theoretical calculation using typical particle size distributions associated with each of the major aerosol components, and they are evaluated by comparing the algorithm estimates of light extinction with coincident optical measurements. Summing the contribution of each component gives the estimate of total light extinction. The most commonly used of these is referred to as the IMPROVE algorithm because it was developed specifically to use the IMPROVE aerosol monitoring data and was evaluated using IMPROVE optical measurements at the subset of sites that make those measurements (Malm et al., 1994, 044920). The formula for the traditional IMPROVE algorithm is shown below.

$$
\begin{aligned}
b_{ext} \approx\ & 3 \times f(RH) \times [Sulfate] \\
& + 3 \times f(RH) \times [Nitrate] \\
& + 4 \times [Organic\ Mass] \\
& + 10 \times [Elemental\ Carbon] \\
& + 1 \times [Fine\ Soil] \\
& + 0.6 \times [Coarse\ Mass] \\
& + 10
\end{aligned}
$$

Equation 9-1

Source: DeBell (2006, 156388)

Light extinction (b_{ext}) is in units of Mm^{-1}, the mass concentrations of the components indicated in brackets are in $\mu g/m^3$, and *f(RH)* is the unitless water growth term that depends on relative humidity. The dry extinction efficiency for particulate organic mass is larger than those for particulate SO_4^{2-} and nitrate principally because the density of the dry inorganic compounds is higher than that assumed for the PM organic mass components. Since IMPROVE does not include ammonium ion monitoring, the assumption is made that all SO_4^{2-} is fully neutralized ammonium sulfate and all nitrate is assumed to be ammonium nitrate. Though often reasonable, neither assumption is always true (see Section 9.2.3.1). In the eastern U.S. during the summer there is insufficient ammonia in the atmosphere to neutralize the SO_4^{2-} fully. Fine particle nitrates can include sodium or calcium nitrate, which are the fine particle fraction of generally much coarser particles due to nitric acid interactions with sea salt at near-coastal areas (sodium nitrate) or nitric acid interactions with calcium carbonate in crustal aerosol (calcium nitrate). Despite the simplicity of the algorithm, it performs reasonably well and permits the contributions to light extinction from each of the major components (including the water associated with the SO_4^{2-} and nitrate compounds) to be separately approximated.

The *f(RH)* terms inflate the particulate SO_4^{2-} and nitrate light scattering for high relative humidity conditions. For relative humidity below 40% the *f(RH)* value is 1, but it increases to 2 at ~66%, 3 at ~83%, 4 at ~90%, 5 at ~93% and 6 at ~95% relative humidity. The result is that both particulate SO_4^{2-} and nitrate are more efficient per unit mass than any other aerosol component for relative humidity above ~85% where its total light extinction efficiency exceeds the $10 m^2/g$ associated with EC. Based on this algorithm, particulate SO_4^{2-} and nitrate are estimated to have comparable light extinction efficiencies (i.e., the same dry extinction efficiency and *f(RH)* water growth terms), so on a per unit mass concentration basis at any specific relative humidity they are treated as equally effective contributors to visibility effects. The strong relationship demonstrated between dry light scattering and fine PM mass concentration or ambient light extinction and fine PM mass concentration under low relative humidity conditions noted by a number of investigators (Charlson et al., 1968, 095355; Chow et al., 2002, 037784; Chow et al., 2002, 036166; McMurry, 2000, 081517; Samuels et al., 1973, 070601; Waggoner and Weiss, 1980, 070152; Waggoner et al., 1981, 095453) is reasonable based on this algorithm when the PM fractional composition is either relatively constant or varies most among PM components with similar dry extinction efficiency values (e.g., SO_4^{2-}, nitrate and organic mass efficiencies).

9.2.2.3. Direct Optical Measurements

Light extinction and its components (i.e., scattering and absorption by particles and gases) can be determined directly by optical measurements using commercially available instruments (Trijonis et al., 1990, 157058). Though these measurements are all wavelength dependent, the convention for visibility monitoring purposes is to make measurement at or near 550 nm, which is the wavelength of maximum eye response. Direct PM light extinction, scattering and absorption measurements offer a number of advantages compared to estimates using an algorithm applied to PM speciation data. The direct optical measurements are considered more accurate because they do not depend on the assumed particle characteristics (e.g., size, shape, density, component mixture, etc.) thought to be associated with the major PM species. Also the optical measurements are made with high time resolution (e.g., minutes to hourly) compared with the filter composition based estimates that are

typically 24-h duration, allowing the former to better characterize sub-daily temporal patterns which can help in identifying influential source categories and characterize atmospheric phenomenon. The higher time resolution attainable with direct light extinction measurements are also more commensurate than the 24-h light extinction estimates from PM samples with the short exposure time associated with perceived visibility effects.

Path-averaged light extinction can be determined by long-path transmissometers that monitors the intensity of light that has traversed a known distance from a known initial intensity light source. Transmission (i.e., the ratio of the final to the initial light intensity) is the natural logarithm of the product of the path-averaged light extinction and the distance the light has traversed. Transmissometer path-length establishes the useful range of light extinction over which the measurements can be accurately measured, with path-lengths of 10 km or more required for pristine conditions and <1 km more appropriate for hazier situations or to measure the visibility impacts associated with fogs or precipitation events. The National Park Service (NPS) operated long-path transmissometers at up to 25 locations from 1986 through 2004 (DeBell, 2006, 156388), but have more recently discontinued their use at all but one remote area location due to the cost of maintenance and the difficulties of performing calibration. Transmissometers are currently in routine service at five urban areas.

A number of instruments measure the light scattered by particles and gases from a source of known intensity. These include forward scattering, back scattering, polar, and integrating nephelometers. Of these the integrating nephelometers with its high sensitivity and sample control options has been more widely used for air quality-related visibility and PM monitoring purposes, while the robust design of the open air forward scattering instruments have seen extensive use by the National Weather Service (NWS) Automated Surface Observing System (ASOS) for characterizing visibility principally for transportation safety purposes (NOAA, 1998). The potential utility of the ASOS visibility network at about 900 locations for air quality monitoring has been established, but the lack of resolution in the reported data is a serious impediment to this use of the data (Richards et al., 1996, 190476).

Integrating nephelometers draw air into a sample chamber, making it possible to modify the sample either by changing its humidity or controlling the particle size range that is measured. This feature makes it possible to use sample-controlled nephelometers to investigate the effects of ambient PM size and water growth characteristic on light scattering (Covert et al., 1972, 072055; Malm and Day, 2001, 190431; Rood et al., 1987, 046397). For instance the coarse particle contribution to light scattering can be estimated using a nephelometer that alternately samples through a 2.5 μm size selective inlet and a 10 μm size selective inlet. This separation by size may be useful in that it would allow correction of the underestimated light scattering of larger particles due to nephelometer angular truncation errors (Anderson and Ogren, 1998, 156213). For routine monitoring, integrating nephelometers are typically either used to measure the PM component of light scattering when operated at ambient relative humidity or to measure dry PM light scattering as a high-time resolution surrogate for PM mass concentration when operated with a heater or other sample air drier. Integrating nephelometers operated at ambient conditions by the IMPROVE program have replaced the long-path transmissometer as the principal optical measurement at about 30 locations (DeBell, 2006, 156388).

PM light absorption can also be inferred from measured changes in the light transmitted through a filter used to sample the PM compared to an identical clean filter (Bond et al., 1999, 156281). Such measurements can be made subsequent to sampling (Campbell et al., 1995, 190171) or continuously during sampling by using specifically designed sampler (Hansen et al., 1982, 190368; Hansen et al., 1984, 002396). All of the filter-based methods require adjustments to the optical measurements to account for filter and sampled particle light scattering effects associated with particles concentrated on and within the matrix of the filters (Bond et al., 1999, 156281). Often PM light absorption measurements are used to infer BC concentration by assuming it is the dominant PM contributor to light absorption with a near constant absorption efficiency (Allen et al., 1999, 048923; Babich et al., 2000, 156239). In fact commercially available aethalometers incorporate an absorption efficiency value so they can directly report BC concentrations. Like nephelometers, commercially available aethalometers can be obtained with either single or multiple-wavelength measurement capabilities, where the multi-wavelength data can be used to better characterize the PM. More recently these have been used to distinguish BC that absorbs light strongly over the full visible light spectrum (e.g., DE) from brown carbon that absorbs appreciably more at shorter wavelengths than at long wavelengths (e.g., WS) (Andreae and Gelencsér, 2006, 156215).

Other approaches to measure light absorption include a photoacoustic instrument that measures the heating associated with absorbed light by suspended PM (Arnott et al., 1999, 020650; Moosmuller et al., 1998, 020657), as well as by the difference between light extinction and light scattering measurements (Bond et al., 1999, 156281).

9.2.2.4. Value of Good Visual Air Quality

The term visual air quality (VAQ) is used here to refer to the visibility effects caused solely by air quality conditions. For example, it excludes the reduced visibility caused by fog. Two broadly different approaches have traditionally been used to define and quantify the value of good VAQ. One approach assesses the monetary value associated with visibility changes; the other assesses the psychological value of visual air quality. With respect to the latter, reduced VAQ is considered an environmental stressor (Campbell, 1983, 190172) that is associated with heightened amounts of anxiety, tension, anger, fatigue, depression, and feelings of helplessness (Evans et al., 1987, 190347; Zeidner and Shechter, 1988, 189973). Though the relationship between impaired VAQ and mental health is poorly understood, there are greater emergency calls associated with psychiatric disturbances during periods with reduced VAQ (Rotton and Frey, 1982, 190477). Studies have shown that reduced VAQ affects people's behavior, including reductions in outdoor activities, and increased hostility and aggressive behavior (Cunningham, 1979, 191974; Evans et al., 1982, 190521; Jones and Bogat, 1978, 190396; Rotton et al., 1979, 190478).

The value of VAQ (both monetary and non-monetary) has been investigated in two broadly different settings, non-recreational or urban settings and recreational settings, such as the NPs and wilderness areas where visibility is protected by the RHR (Trijonis et al., 1990, 157058). In urban settings, public surveys have shown that greater than 80% of the participants are aware of poor VAQ conditions (Cohen et al., 1986, 190182), though attitudes towards poor VAQ have been shown to vary by socio-economic status, health, and length of residence in the urban setting (Barker, 1976, 072137). The economic importance of urban visibility has been examined by a number of studies designed to quantify the benefits (or willingness to pay) associated with potential improvements in urban visibility. Urban visibility valuation research prior to 1997 was summarized in Chestnut and Dennis (1997, 014525), and was also described in the 2004 PM AQCD (U.S. EPA, 2004, 056905) and the 2005 PM Staff Paper (U.S. EPA, 2005, 090209). These reviews summarize 34 estimates (based on different cities or model specifications) from six different studies. Since the mid 1990s, however, only one new valuation study of urban visibility has been published (Beron et al., 2001, 156270) which is summarized below (Section 9.2.4.6).

In recreational settings, experience based demand models have been developed using on-site and mail-in surveys to judge the relative importance to NP visitors of various park attributes including good VAQ, to assess visitor awareness of VAQ conditions, and to explore possible relationships between VAQ and visitor satisfaction (Ross et al., 1985, 044287; Ross et al., 1987, 037420). At the three western and two eastern NPs where this survey was conducted, visitors rated the attribute identified as "clean, clear air" among the most important features of the parks. A random sample of 1,800 visitors at one of the parks (Grand Canyon) showed that visitor awareness of VAQ impacts increased as measured visibility conditions decreased, and that overall park enjoyment and satisfaction decreased with reduced VAQ. Grand Canyon visitors when asked to indicate how they would budget their time (e.g., between visiting an archaeological site or a view lookout point) indicated that they would to be willing to significantly alter their behavior to experience views under improved VAQ (Malm et al., 1984, 044292).

9.2.3. Monitoring and Assessment

Monitoring and the assessment of monitoring data serve a number of goals with regard to the visibility effects of PM, including improving the understanding of the physio/chemical/optical properties of the aerosol, characterizing spatial and temporal air quality patterns, and assessing the causes (i.e., pollution sources and atmospheric processes) that are responsible for visibility impairment. Information generated by special studies employing sophisticated instrumentation are typically needed to advance the understanding of aerosol properties, while characterizing trends is the product of analyzing routine monitoring data. Whereas, assessing the causes of haze usually involves a weight-of-evidence approach applied to special study and/or routine monitoring data sets

plus the use of air quality simulation modeling. This section summarizes recently available information that is based on monitoring data.

9.2.3.1. Aerosol Properties

Particle size is the most influential physical property of aerosols with respect to their dry light extinction efficiency. Chemical composition by size is used to ascertain density (needed to convert aerodynamic to physical size and to determine particle mass as a function of size) and to identify the water growth characteristics of the aerosol (needed to calculate the particle size, density and index of refraction at ambient RH). To characterize aerosol properties of interest for visibility effects, field monitoring programs typically include particle size distribution monitoring, high size resolution particle sampling with subsequent compositional analysis, and optical monitoring. These generate data that permit optical closure assessments where the light scattering and/or light extinction estimates from the aerosol data are compared to corresponding optical data. Since component contributions to visibility are generally assessed by applying the IMPROVE or some similar algorithm to measured or modeled aerosol concentration data, this section will include recent investigations that evaluate or address various assumptions inherent in the use of these simple algorithms.

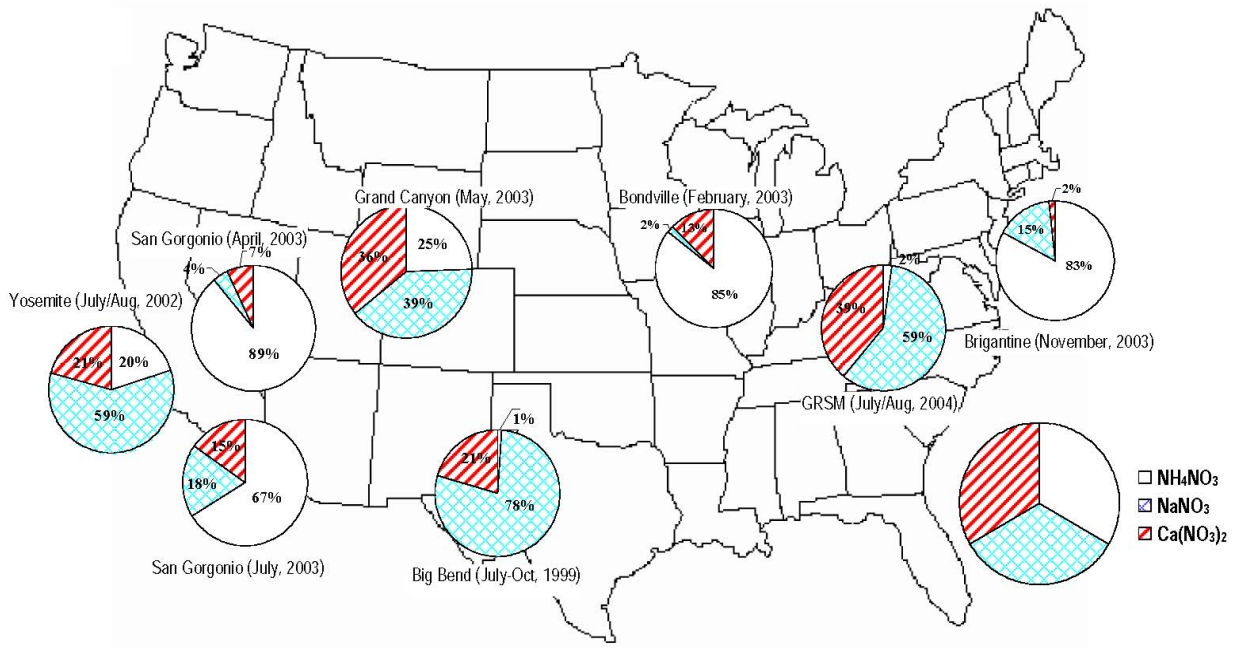
One component of the Big Bend Regional Aerosol and Visibility Observational (BRAVO) Study, conducted at Big Bend NP, TX in the summer and fall of 1999, entailed use of detailed measurements of aerosol chemical composition, size distribution, water growth, and optical properties to characterize the aerosol and assess the relationship between aerosol physical, chemical and optical properties (Malm et al., 2003, 190434; Schichtel et al., 2004, 179902). Fine ammoniated sulfate during the BRAVO Study was about half the fine particle mass concentration and was shown to be responsible for about 35% of the light extinction. Rayleigh scattering was the second largest contributor at about 25%, followed by coarse particle (about 18%), and organic compounds (about 13%). There was little fine particle nitrate (less than 5% of the mass concentration) and most of it is apparently in the form of sodium nitrate and two thirds of it was found in the coarse mode where it comprises about 8% of the coarse particle mass concentration. Both the composition of the nitrate and the fact of much of it being in the coarse size mode (2.5 μm >D>10 μm) are inconsistent with the implied assumptions of the IMPROVE algorithm.

A year-long special study of coarse particle speciation was conducted at nine IMPROVE remote area monitoring sites during 2003-2004 to provide additional information about the geographic and seasonal variations in coarse particle composition (Malm et al., 2007, 156730). The same sampling and analytical methodologies procedures were used for the PM_{10} samples as are routinely used on the IMPROVE $PM_{2.5}$ samples. The IMPROVE coarse particle speciation study did not include ammonium analysis, so SO_4^{2-} and nitrate ions were assumed to be ammonium sulfate and ammonium nitrate. As expected crustal minerals were the largest contributors to coarse mass overall (about 60%), though at Mt. Rainier the fraction of coarse PM that was organic exceeded the crustal mineral by nearly two to one (i.e., 59.2% compared to 33.5%) On average across sites the organic particulate contributed significantly at about one quarter of the coarse mass, while ammonium nitrate was the third largest contributor to coarse mass (about 8%). Sea salt was negligible overall but high at the one coastal site (i.e., 12% at Brigantine, NJ). The two California sites, San Gorgonio and Sequoia, had the highest coarse nitrate concentrations, 0.74 $\mu g/m^3$ and 0.69 $\mu g/m^3$, and high fine nitrates concentrations on average, 2.66 $\mu g/m^3$ and 2.14 $\mu g/m^3$, respectively. Brigantine, a coastal site in New Jersey, had the highest fraction of total nitrate in the coarse size range (36%). The authors speculate that Brigantine's particulate nitrate is likely sodium nitrate, the result of nitric acid reactions with sodium chloride. The nine-site average fraction of total nitrate in the coarse size range is 26%. By contrast, coarse SO_4^{2-} concentrations are small with only about ~1% of the total SO_4^{2-} in the coarse fraction.

Routine IMPROVE monitoring data include the mass concentration, but not the composition of the coarse PM fraction, so the algorithm used to estimate light extinction does not include any provision for varied coarse PM composition as shown in this study. This study shows that about 10% of the coarse mass across the nine monitoring sites is composed of hygroscopic materials (i.e., ammonium sulfate, ammonium nitrate and sea salt), which during high humidity conditions will scatter more light than estimated by the current algorithm (e.g., ~20% bias at ~90% relative humidity). However, at coastal sites such as the Brigantine, NJ, IMPROVE site where the combined concentration of the inorganic salts (i.e., sea salt, nitrate and SO_4^{2-}) constitute a significant fraction

(~24% on average) of the coarse mass concentration, the IMPROVE algorithm underestimation of light extinction by coarse PM can be significant for high relative humidity conditions (~60% at ~90% relative humidity). The resulting underestimation of total light extinction can be much smaller since fine particle light extinction generally exceeds that contributed by coarse particles. Another issue with regard to estimating light extinction from coarse PM concentration when the composition is not crustal minerals, as has been assumed, has to do with the lower average density of the coarse mode particles that results in greater particle numbers and/or larger particles and therefore a greater light extinction efficiency (Malm and Hand, 2007, 155962).

Special studies with more complete, higher time resolution and size resolved particulate inorganic ion species chemistry and precursor gases were conducted at seven of the nine sites with IMPROVE coarse particle speciation monitoring (Lee et al., 2008, 156686). This work confirmed the presence of sodium and calcium nitrate (referred to as mineral nitrate) primarily in the coarse particle size range in addition to fine particle ammonium nitrate where low temperatures, high humidity and excess ammonium (beyond that required to neutralize the particulate SO_4^{2-}) favored particle phase equilibrium. Figure 9-4 is a map showing the locations and sample times and estimated composition of the total particulate nitrate for the seven locations for this special study. Sites with a high fraction of ammonium nitrate (e.g., San Gorgonio, Bondville, and Brigantine) have the highest nitrate contributions to total mass concentration and haze, whereas sites with high mineral nitrates tend to have low total nitrate contributions. This work shows that the common assumption that particulate nitrate is in the fine particle size range and consists principally of ammonium nitrate is not necessarily true.



Source: Reprinted with Permission of Atmospheric Environment from Lee et al. (2008, 156686)

Figure 9-4. Estimated fractions of total particulate nitrate during each field campaign comprised of ammonium nitrate, reacted sea salt nitrate (shown as $NaNO_3$), and reacted soil dust nitrate (shown as $Ca(NO_3)_2$).

Extinction efficiencies for individual particle species can be theoretically calculated from sized-resolved aerosol measurements and can be inferred using multiple linear regression applied to aerosol composition and light extinction measurement data. In a recent publication, Hand and Malm (2007, 155825) reviewed the literature since 1990 in which aerosol mass scattering efficiency values were calculated or inferred. From these they have compiled normalized dry scattering efficiency

values for the individual species. Based on 93 separate determinations including marine, remote continental and urban areas data sets, the average dry mass scattering efficiency for ammonium sulfate is 2.5 ± 0.6 m^2/g. Average values tended to be somewhat lower for the marine aerosol (~2 m^2/g) than for remote continental (~2.7 m^2/g) and urban (2.6 m^2/g) areas, and values also tended to be lower for fairly clean arid locations compared with more humid polluted areas.

Based on 48 separate determinations including remote area and urban area data sets, the average dry mass scattering efficiency for ammonium nitrate is 2.7 ± 0.5 m^2/g (Hand and Malm, 2007, 155825). Average values were higher in remote locations (2.8 ± 0.5 m^2/g) compared to urban locations (2.2 ± 0.5 m^2/g) though this might be accounted for by the predominate use of multiple linear regression for the remote areas, which can be biased high, compared to the use of theoretical calculations for the urban data sets.

Organic fine PM extinction efficiency of 3.9 ± 1.5 m^2/g is based on 58 separate determinations, though much higher values (~6 m^2/g) resulted for locations influenced by industrial and biomass combustion sources (Hand and Malm, 2007, 155825). These organic fine PM extinction efficiency values were adjusted to use a consistent ratio of organic mass to OC (OC) of 1.8 for each determination of the mass concentration. This value is generally associated with aged organic PM, while for more freshly emitted PM, such as in an urban environment, a smaller ratio (e.g., 1.4) would be more appropriate. This could explain the discrepancy between two approaches used to estimate the organic PM light extinction efficiency for Phoenix (Hand and Malm, 2006, 156517), which resulted in a significantly lower value where a site specific regression method was used compared to the value obtained from a method optimized for remote-area monitoring (2.47 m^2/g compared to 3.71 m^2/g). However in Fresno both the mass balance and light scattering balance was improved by using a ratio of 1.8 instead of 1.4 to estimate the organic compound mass (Watson and Chow, 2007, 157127). Another possible or partial factor with respect to urban light extinction efficiency for organic PM may be that the size distribution of freshly emitted organic PM in urban areas extends significantly into the ultra-fine particle size range (Demerjian and Mohnen, 2008, 156392) that is less efficient per mass concentration at light scattering than the generally larger-sized aged organic PM such as from a distant forest fire as was measured at the Baltimore Supersite.

Hand and Malm (2007, 155825) also reviewed and made recommendations for extinction efficiencies for the other PM components including mixed coarse mode (1.0 ± 0.9 m^2/g based on 51 determinations) and fine mode dust or soil (3.3 ± 0.6 m^2/g based on 23 determinations, but recommending 1.0 m^2/g for use with data from realistic collection efficiency samplers) and fine sea salt (4.5 ± 0.9 m^2/g based on 25 determinations, but recommending 1.0 m^2/g to 1.3 m^2/g for use with data from realistic collection efficiency samplers). This work did not address light absorption efficiency of EC, CB, or crustal PM.

The Hand and Malm (2007, 155825) average dry mass light scattering efficiency values are generally consistent with the values for the IMPROVE algorithm (as shown in Equation 9-1). However the adoption of the IMPROVE algorithm by EPA for calculating the haze metric used to track trends and assess the nominal pace of progress for the RHR (U.S. EPA, 2001, 157068) resulted in much greater scrutiny of its performance in estimating extinction (Lowenthal and Kumar, 2003, 156712; Malm, 1999, 025037; Malm and Hand, 2007, 155962; Ryan et al., 2005, 156934). Among the issues raised is that the algorithm tended to underestimate the light extinction for the haziest conditions and overestimate light extinction for the clearest conditions in regions such as the southeastern U.S., though it generally worked well in the arid western U.S. Furthermore, they showed the lack of mass or light scattering closure at coastal sites due to sea salt that was not accounted for by the IMPROVE algorithm. These assessments used mass concentration and light extinction closure and regression analysis methods to infer that the dry extinction efficiency for the major fine particle components would need to vary in order to avoid the biased estimates of light extinction at the extremes. Theoretical calculations of SO_4^{2-} dry extinction efficiencies for 41 days of size-resolved chemical composition data for Big Bend, TX as part of the BRAVO Study produced a range of results from ~2.4 m^2/g to ~4.1 m^2/g, with the larger dry extinction efficiency values tending to be associated with higher ammonium sulfate mass concentration and narrower size distributions (Schichtel et al., 2004, 179902).

In response to the technical concerns raised about the performance of the IMPROVE algorithm, a revised algorithm was developed (Pitchford et al., 2007, 098066). The revised version of the algorithm differs from the original algorithm by: including a fine sea salt term related to the measured chloride ion concentration; increasing by about 30% the mass concentration of the organic aerosol component by changing the ratio of organic compound mass to OC mass from 1.4 to 1.8;

using site elevation dependent Rayleigh scattering in place of 10 Mm^{-1} that had been used at every site; adding a NO_2 light absorption term; and employing a split component model for the secondary particulate components (i.e., SO_4^{2-}, nitrate and organic species) with new water growth terms to better estimate their extinction at the high and low extremes of the range. The revised algorithm is displayed below in Equation 9-2.

$$
\begin{aligned}
b_{ext} \approx\ & 2.2 \times f_s(RH) \times [Small\ Sulfate] + 4.8 \times f_L(RH) \times [Large\ Sulfate] \\
& + 2.4 \times f_s(RH) \times [Small\ Nitrate] + 5.1 \times f_L(RH) \times [Large\ Nitrate] \\
& + 2.8 \times [Small\ Organic\ Mass] + 6.1 \times [Large\ Organic\ Mass] \\
& + 10 \times [Elemental\ Carbon] \\
& + 1 \times [Fine\ Soil] \\
& + 1.7 \times f_{ss}(RH) \times [Sea\ Salt] \\
& + 0.6 \times [Coarse\ Mass] \\
& + Rayleigh\ Scattering\ (Site\ Specific) \\
& + 0.33 \times [NO_2\ (ppb)]
\end{aligned}
$$

Equation 9-2

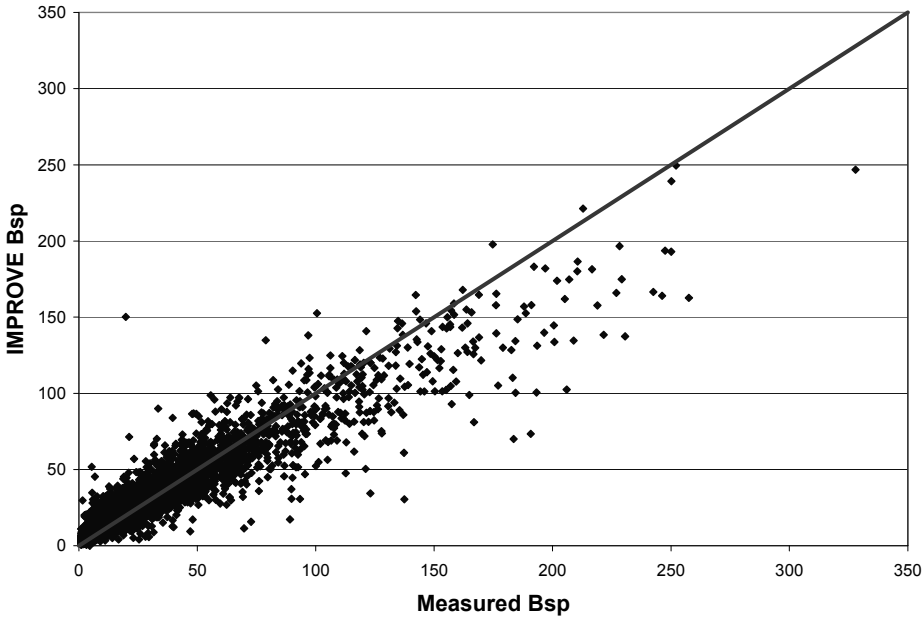
Source: Reprinted with Permission of the Air & Wast Management Association from Pitchford et al. (2007, 098066)

Small and large SO_4^{2-}, nitrate and organic mass are used to refer to the splitting of the concentrations of each of those three species into two size distributions. This approach accounts for increased light extinction efficiency with mass by using a simple mixing model that assume that each of these three components are comprised of an external mixture of small and large particle size modes. Conceptually, the large mode particles represent aged or cloud-processed aerosol, while the small mode particles represent relatively newly generated particles from the gas phase precursors. The former are more likely to be associated with high concentrations while the latter are likely to be at relatively low concentration.

The geometric mean diameter and standard deviations assumed for these two size modes are 0.5 μm and 1.5 for the large mode particles and 0.2 μm and 2.2 for the small mode particles. Mie theory applied to these size distributions for the three species results in dry extinction efficiencies for the small and large mode ammonium sulfate (2.2 m^2/g and 4.8 m^2/g), ammonium nitrate (2.4 m^2/g and 5.1 m^2/g) and organic mass (2.8 m^2/g and 6.1 m^2/g). Water growth terms specifically derived for the small and large size distribution using the upper branch of the hygroscopic growth curves for ammonium sulfate are applied to both the SO_4^{2-} and nitrate PM. No water growth is assumed for organic PM.

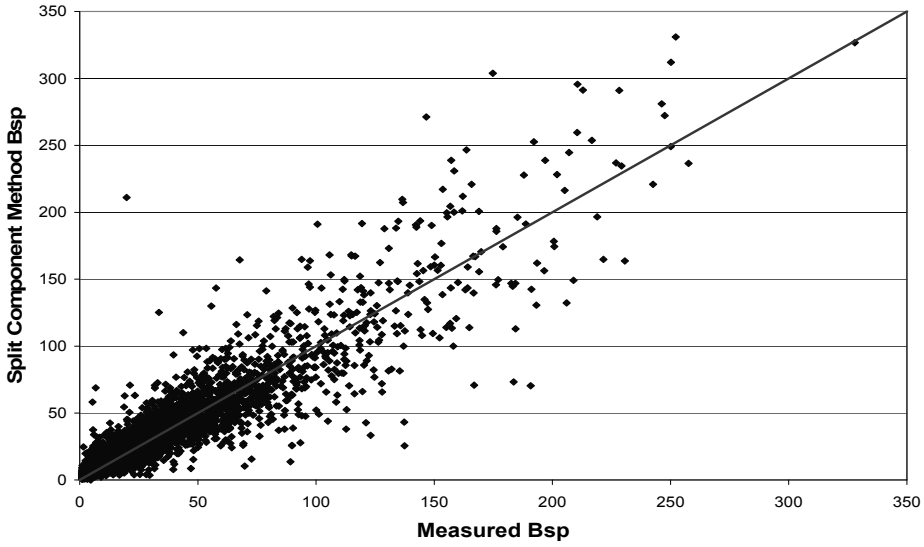
A simple empirically developed apportionment approach that was evaluated by testing the new algorithms estimated light scattering at the 21 IMPROVE sites that have nephelometer-measured light scattering data. For each sample, the fraction of the fine particle component (SO_4^{2-}, nitrate, or organic mass) that is assigned to the large mode is calculated by dividing the total concentration of the component by 20 $\mu g/m^3$ (e.g., if the total fine particle nitrate concentration is 4 $\mu g/m^3$, the large mode concentration is 1/5 of 4 $\mu g/m^3$ or 0.8 $\mu g/m^3$, leaving 3.2 $\mu g/m^3$ in the small mode). If the total concentration of a component exceeds 20 $\mu g/m^3$, all of it is assumed to be in the large mode.

Figure 9-5 and Figure 9-6 are scatterplots of the estimated versus measured light scattering for the two algorithms. The revised algorithm has noticeably reduced bias at the upper and lower extremes. However, the new algorithm estimates have somewhat reduced precision (i.e., the points are more broadly scattered). States have adopted the new algorithm for the technical assessments that support their RHR State Implementation Plans, but the revised algorithm was too recently developed to be incorporated into any of the peer-reviewed technical literature reported on below. In general the differences resulting from use of the original versus the revised IMPROVE algorithm in identifying best and worst haze conditions and the apportionment of the various PM components are small with exception of coastal locations where sea salt may be a significant contributor.



Source: Reprinted with Permission of the Air & Waste Management Associaiton from Pitchford, et al. (2007, 098066)

Figure 9-5. A scatter plot of the original IMPROVE algorithm estimated particle light scattering versus measured particle light scattering.



Source: Reprinted with Permission of the Air & Waste Management Associaiton from Pitchford, et al. (2007, 098066).

Figure 9-6. Scatter plot of the revised algorithm estimates of light scattering versus measured light scattering.

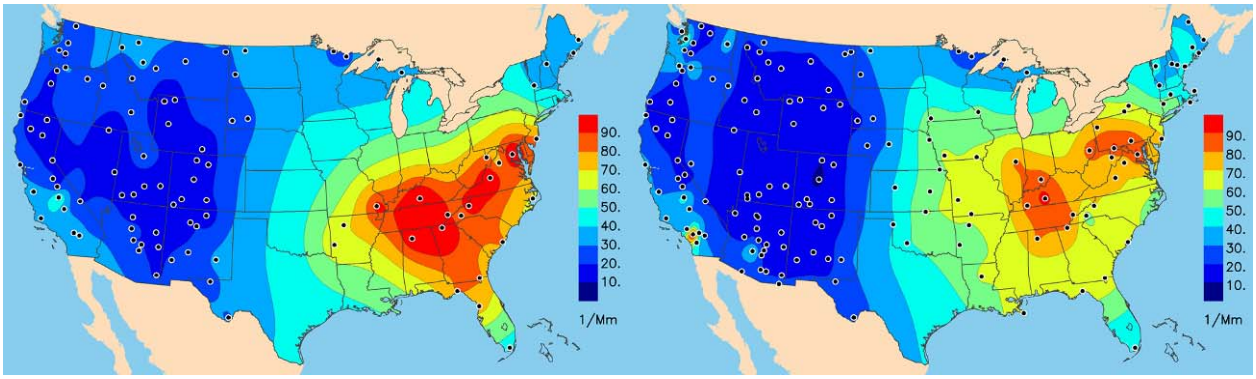
9.2.3.2. Spatial Patterns

The IMPROVE network is the basis for much of what is known about particulate species spatial and temporal patterns for remote areas of the U.S. Though IMPROVE includes some urban monitoring sites, most of what is known about urban particle speciation trends is based on the EPA Speciation Trend Network (STN) and other similarly operated state particle speciation sites jointly referred to as the Chemical Speciation Network (CSN) (Jayanty, 2003, 156605). The number of IMPROVE network sites has increased considerably beginning in 2000, first to increase its ability to generate data representative of the 156 visibility-protected NPs and wilderness areas, then later as the states in the central U.S. requested additional remote-area monitoring to better understand their contributions to regional haze. The expansion of the network into the central U.S. significantly improved the understanding of spatial trends in a region of the country that had little speciation monitoring. Except as otherwise noted most of the information in this section was from the IMPROVE Report IV (DeBell, 2006, 156388) and displays of data that are readily generated using the Visibility Information Exchange Web Site (VIEWS). VIEWS, the ambient monitoring data system, is one of several websites (as described in Table 9-1) sponsored by the Regional Planning Organizations (RPO) that documents substantial, though often otherwise unpublished, technical information generated to support implementation of the RHR.

Figure 9-7 shows maps of remote area light extinction estimates from PM speciation data for two years selected to demonstrate the additional information available due to the expansion of the IMPROVE network into the central U.S. The locations of monitoring sites supplying the data shown as color contours are shown as dot on the maps. Users of such contour maps are usually cautioned that the contours are only there to guide the eye to sites with similar measurements and that nothing should be implied about spatial patterns where there are no monitoring sites. Certainly these plots give proof to the wisdom of such warnings. Prior to 2001 there were no IMPROVE or any other remote-area aerosol speciation monitoring sites in the central states between northern Minnesota and Michigan to the north and Arkansas and Kentucky to the south. The lack of monitoring over such a large region in the center of the country hid the presence of high average regional haze over the midwestern U.S. Smaller scale differences are seen in the rest of the country and some of those are due to interannual variations as well as to better spatial resolution made possible by a more dense monitoring network.

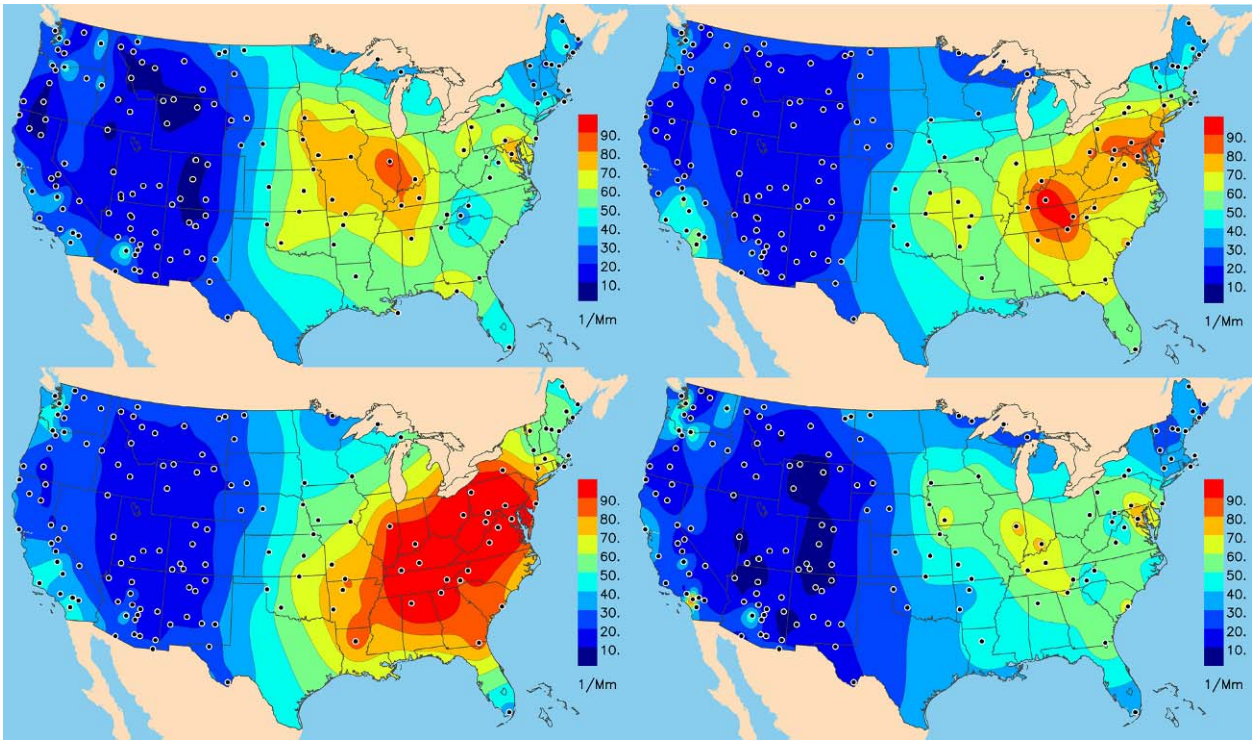
Table 9-1. Regional Planning Organization websites with visibility characterization and source attribution assessment information.

Type of Information	Name and Web Address	RPO	Information Content and Comments
RPO Home Pages	Western Regional Air Partnership http://www.wrapair.org/	WRAP	Organizational structure, plans, projects, reports and links to other sites with additional information. MANE-VU works in close cooperation with Northeast States for Coordinated Air Use Management (NESCAUM) and Mid-Atlantic Regional Air Management Association (MARAMA) to develop the technical information for RHR in the Northeast. All three web sites contain unique technical support information.
	Central Regional Air Planning Association http://www.cenrap.org/	CENRAP	
	Midwest Regional Planning Organization http://64.27.125.175/mrpo.html	MRPO	
	Visibility Improvement State and Tribal Association of the Southeast http://www.vistas-sesarm.org/	VISTAS	
	Mid-Atlantic/Northeast Visibility Union http://www.manevu.org/ http://www.nescaum.org/topics/regional-haze http://www.marama.org/visibility/	MANE-VU NESCAUM MARAMA	
Visibility - Air Quality Monitoring Data	Visibility Information Exchange Web Site http://vista.cira.colostate.edu/views/	All RPOs	All IMPROVE and most other PM speciation data, RHR compatible derived parameters, and user-friendly tools to summarize and display data.
Emission Inventory Data	Emissions Data Management System http://www.wrapedms.org/default_login.asp	WRAP	WRAP emission inventory data warehouse and tools that provides a consistent approach to regional emissions tracking
Monitoring Data Assessment	Causes of Haze Assessment http://www.coha.dri.edu/	WRAP CENRAP	Monitoring site-specific descriptive characterizations and maps, seasonal and trends analysis, air flow analysis, & receptor modeling.
Visibility Modeling	U. of California-Riverside Modeling Center http://pah.cert.ucr.edu/aqm/308/ http://pah.cert.ucr.edu/aqm/cenrap/index.shtml http://pah.cert.ucr.edu/vistas/	WRAP CENRAP VISTAS	Descriptions of input data, performance, and results of regional scale modeling (CMAQ & CAMx) & source attribution for base and future year regional haze.
Integrated Information to Support RHR SIP Preparations	Technical Support System http://vista.cira.colostate.edu/tss/	WRAP	Provides access and common formats to display and summarize emissions inventory information, monitoring data/ assessment and regional haze modeling result to aid state and tribal analyst prepare RHR implementation plans.



Source: VIEWS (http://vista.cira.colostate.edu/views/)

Figure 9-7. IMPROVE network PM species estimated light extinction for 2000 (left) and for 2004 (right).



Source: VIEWS (http://vista.cira.colostate.edu/views/)

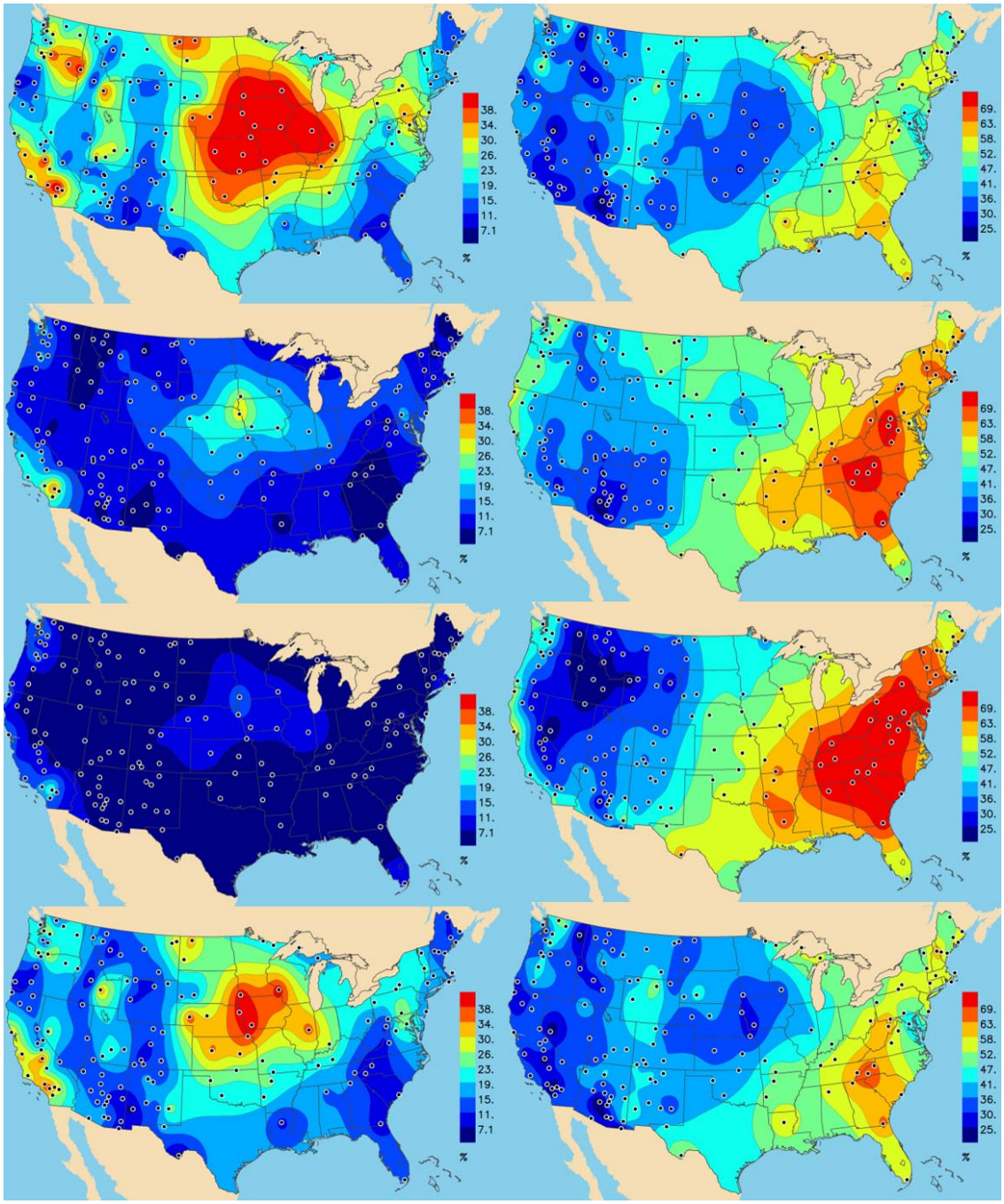
Figure 9-8. Mean estimated light extinction from PM speciation measurements for the first (top left), second (top right), third (bottom left), and fourth (bottom right) calendar quarters of 2004.

Figure 9-8 shows the seasonal pattern of PM species estimated light extinction using maps of mean values for each of the calendar quarter for 2004. The first quarter has the highest region of haze centered in the midwestern U.S.; the warmer second and third quarters have the region of highest haze over the Ohio River Valley; and the fourth quarter is a composite with high haze in both

the Midwest and Ohio River Valley. Smaller regions of haze show up in the Columbia River Valley (border between Washington and Oregon) in the colder first and fourth quarters and in Southern California in the warmer second and third quarters.

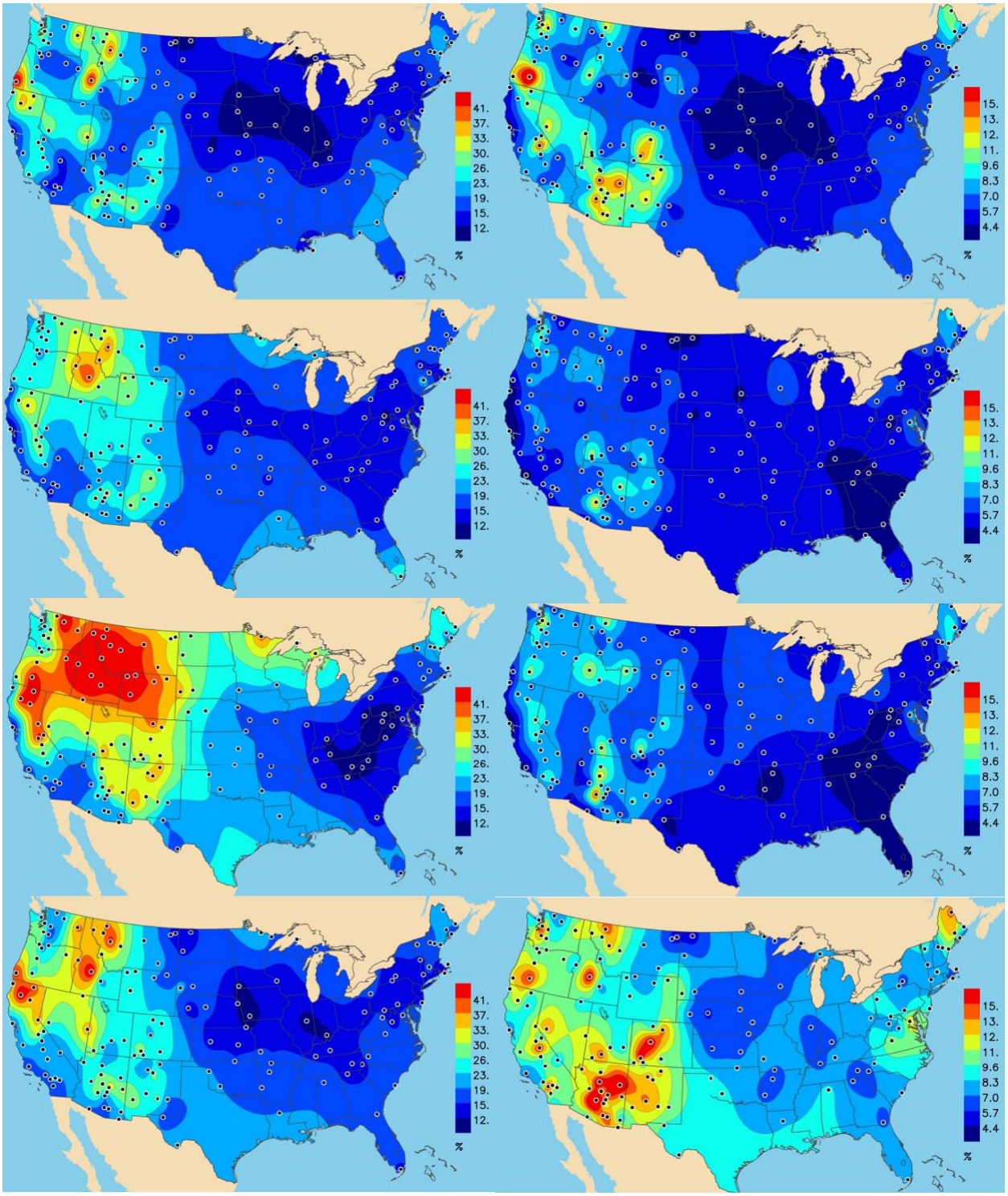
The IMPROVE algorithm permits each PM component contribution to light extinction to be separately estimated. Figure 9-9, Figure 9-10, and Figure 9-11 display the seasonal variation of the percent contribution to aerosol light extinction by the various component estimates. Figure 9-9 shows the contributions by SO_4^{2-} and nitrate particulate including the haze enhancement caused by the absorbed water in humid conditions. As shown in Figure 9-9, a large regional pattern of high contribution to haze by nitrate PM is centered in the Midwest, and during the cooler months the nitrate PM is the dominant cause of haze in the region responsible for a third to a half of the particulate light extinction. Midwestern particulate nitrate is responsible for the regional pattern of the highest haze conditions shifting from the Ohio River Valley during summer to the Midwest in the winter as shown in Figure 9-8. Particulate nitrate is also a significant contributor to particulate light extinction year-around in parts of California, where it generally contributes 20%-40%. The Pacific Northwest, parts of Idaho and Utah experience large contributions to particulate light extinction by nitrates during the colder seasons, with contributions of 20%-30%. Figure 9-9 also shows that particulate SO_4^{2-} is the predominate contributor in the eastern U.S., where it contributes 40% or more on average and during the summer months up to three quarters of the particulate light extinction over much of the East. In the western U.S. particulate SO_4^{2-} generally contribute 20-50% of the particle light extinction. Regions of the lowest fractional contributions by particulate SO_4^{2-} and nitrate for any calendar quarter are generally in the western U.S.

Figure 9-10 shows the contributions to haze by the carbonaceous PM components (i.e., organic mass and EC). They show broadly similar patterns with the greatest contributions in the western U.S. especially during the warmer months of the year. For the most part this spatial pattern results from the dominant contributions to haze by SO_4^{2-} and nitrate PM in the eastern half of the U.S., leaving relatively little for other component contributions. The fractional contribution to haze by organic PM is generally two to five times that of EC. In absolute terms, both carbonaceous components tend to have two to three times higher concentrations in the eastern U.S. than in the non-coastal western states.



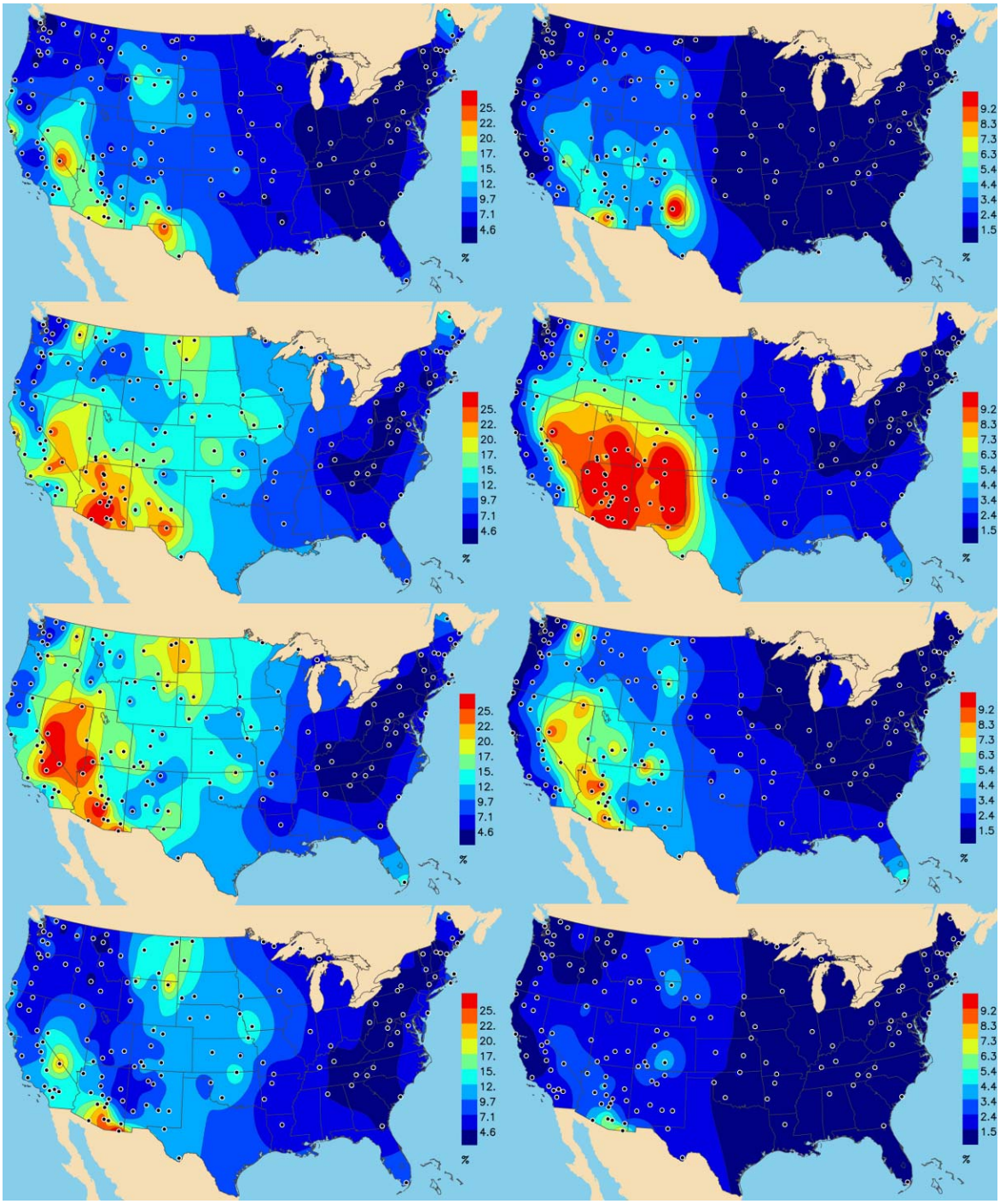
Source: VIEWS (http://vista.cira.colostate.edu/views/)

Figure 9-9. Percent contributions of ammonium nitrate (left column) and ammonium sulfate (right column) to particulate light extinction for each calendar quarter of 2004 (first through fourth quarter arranged from top to bottom). Note that the contour intervals are not the same for the two species contributions.



Source: VIEWS (http://vista.cira.colostate.edu/views/)

Figure 9-10. Percent contributions of organic mass (left column) and EC (right column) to particulate light extinction for each calendar quarter of 2004 (first through fourth quarter arranged from top to bottom). Note that the contour intervals are not the same for the two species contributions.



Source: VIEWS (http://vista.cira.colostate.edu/views/)

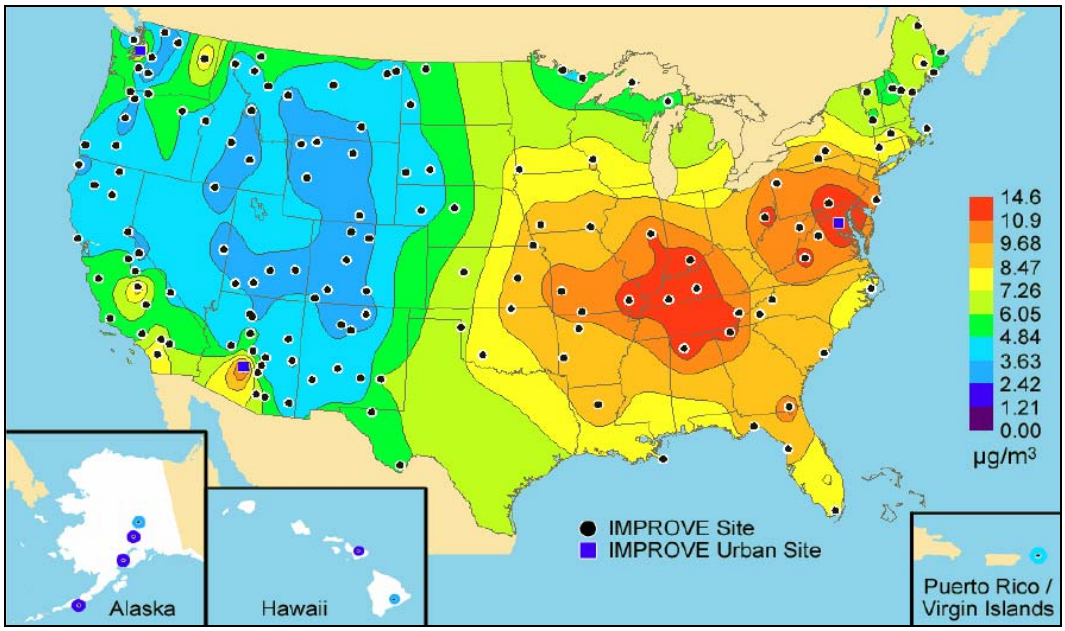
Figure 9-11. Percent contributions of coarse mass (left column) and fine soil (right column) to particulate light extinction for each calendar quarter of 2004 (first through fourth quarter arranged from top to bottom). Note that the contour intervals are not the same for the two species contributions.

Figure 9-11 shows the contributions to haze by coarse mass and fine soil components. As with the carbonaceous components, these crustal dominated components have a similar spatial pattern with regions of highest contribution to haze in the western U.S., and just as for the carbonaceous PM, the explanation for low contributions in the eastern U.S. is the dominant contributions to haze by SO_4^{2-} and nitrate PM leaving relatively little for other components. The crustal components contribute more to haze in the arid regions of the west including the southwestern deserts. In absolute terms, coarse mass concentrations are as high in the rural areas of the center of the country (including Oklahoma, Arkansas, Kansas, Missouri, and Iowa) as they are in the Desert Southwest. Typically coarse mass contributions to haze exceed those of fine mass by a factor of 2-4.

9.2.3.3. Urban and Regional Patterns

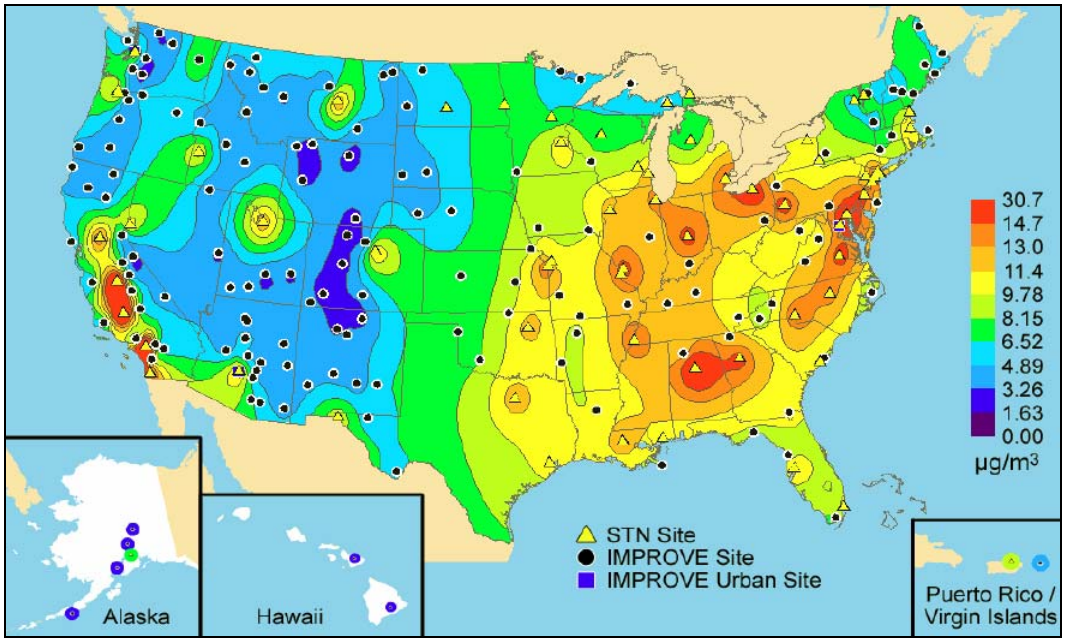
Using a combination of IMPROVE and CSN data, it is possible to compare urban $PM_{2.5}$ concentrations and composition to corresponding remote-area regional values. These are shown as paired color contours maps for IMPROVE and IMPROVE plus CSN (see Figure 9-12 through Figure 9-23). The degree of comparability of the data from these 2 networks was assessed by an analysis of two years of co-located IMPROVE and CSN data from 6 urban areas. The CSN organic mass data were adjusted for a positive sampling artifact prior to inclusion in this assessment, in a fashion similar to that used for the IMPROVE data set (pages 29-30, DeBell, 2006, 156388). Note that the contour scales are different between the two maps for each component pair of maps so that each contains as much information as possible using ten concentration contours. To assess the degree to which urban areas have higher PM component concentrations compared to regional background note how many contour intervals surround the urban monitoring sites. The U.S. EPA (2004, 190219) used the pairing of IMPROVE and CSN monitoring sites at 13 selected urban areas to separate local and regional contributions of three major $PM_{2.5}$ components as shown in Figure 9-24.

In Figure 9-12 and Figure 9-13, urban $PM_{2.5}$ concentrations are systematically higher than those in the surrounding non-urban regions. The urban excess is generally much higher in the western U.S. than in the East (e.g., there are five contour intervals separating Salt Lake City from its remote regional area compared to only two for Indianapolis). This implies that eastern and western urban $PM_{2.5}$ concentrations and resulting visibility are less different than the eastern and western regional concentrations and visibility.



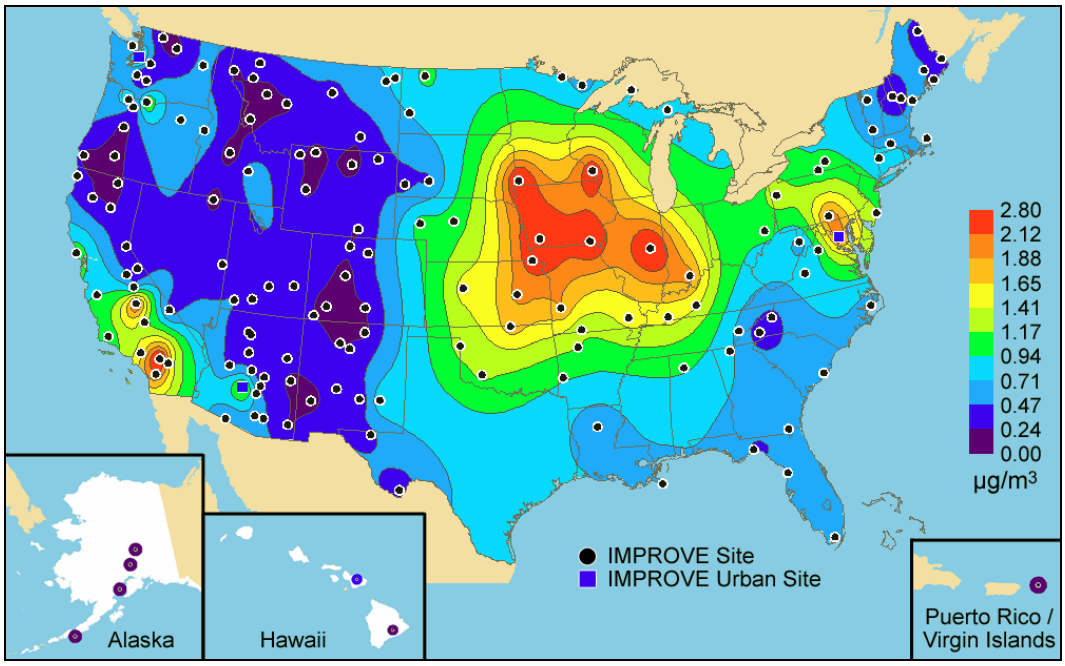
Source: Debell (2006, 156388).

Figure 9-12. IMPROVE Mean $PM_{2.5}$ mass concentration determined by summing the major components for the 2000-2004.



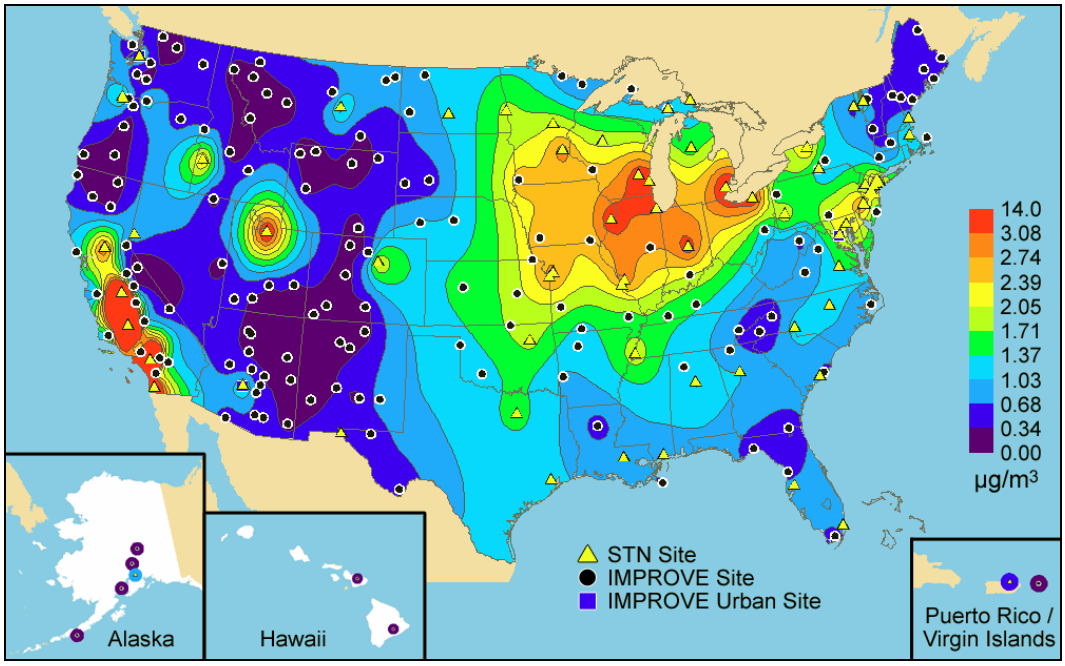
Source: Debell (2006, 156388).

Figure 9-13. IMPROVE and CSN (STN) mean $PM_{2.5}$ mass concentration determined by summing the major components for 2000-2004.



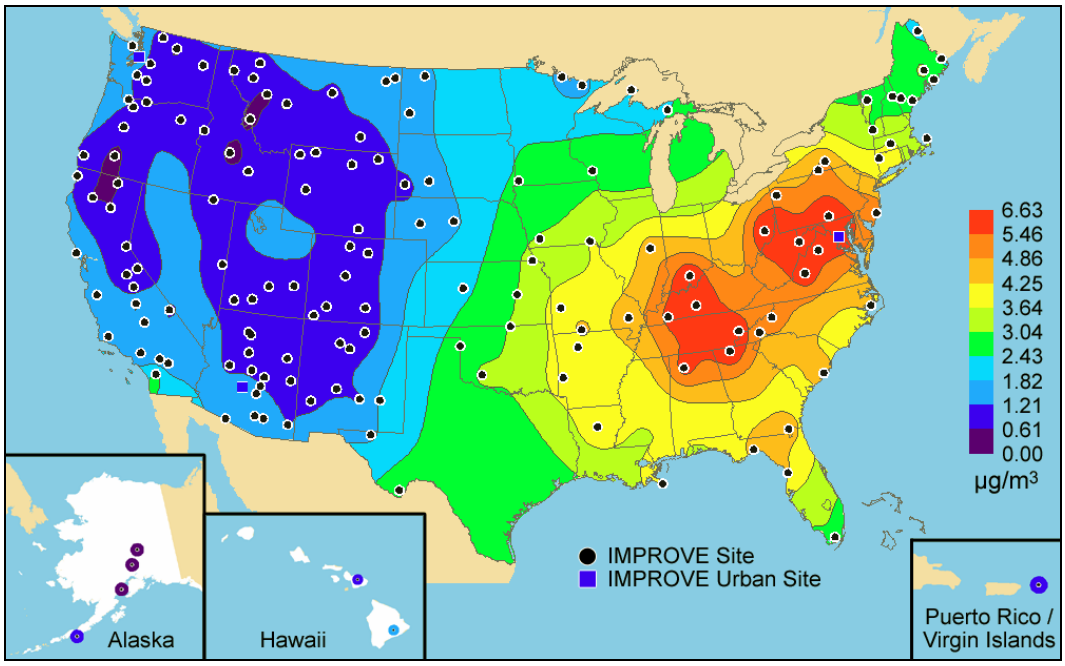
Source: Debell (2006, 156388).

Figure 9-14. IMPROVE mean ammonium nitrate concentrations for 2000-2004.



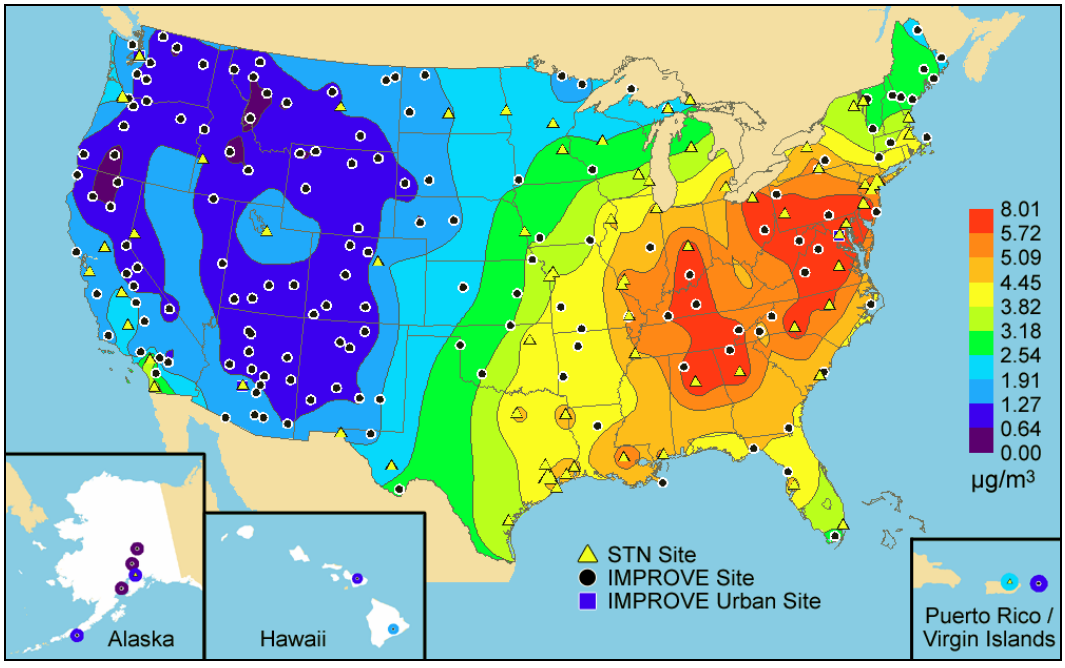
Source: Debell (2006, 156388).

Figure 9-15. IMPROVE and CSN (STN) mean ammonium nitrate concentrations for 2000-2004.



Source: Debell (2006, 156388).

Figure 9-16. IMPROVE mean ammonium sulfate concentrations for 2000-2004.



Source: Debell (2006, 156388).

Figure 9-17. IMPROVE and CSN (STN) mean ammonium sulfate concentrations for 2000-2004.

Figure 9-14, Figure 9-15, and Figure 9-24 show the $PM_{2.5}$ nitrate in remote and urban areas. Here the western states have urban particulate nitrate concentrations that far exceed twice the remote

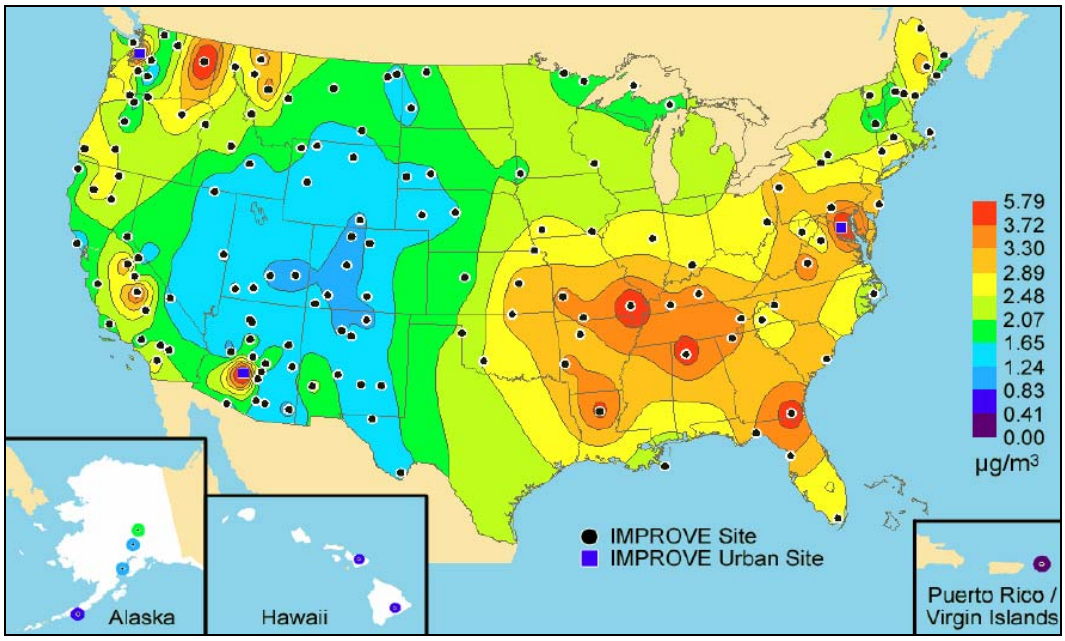
area regional concentrations. For the Central Valley of California and Los Angeles areas, the urban excess of ammonium nitrate exceeds regional concentrations by 2 $\mu g/m^3$ to 12 $\mu g/m^3$. In the region of the Midwest nitrate bulge, the urban concentrations were less than twice the regional concentrations for an annual urban excess of about 1 $\mu g/m^3$. Northeast and southeast of the Midwest nitrate bulge, annual urban particulate nitrate concentrations are several tenths to about 1 $\mu g/m^3$ above the remote area regional concentrations, with warmer southern locations tending to have the smaller concentrations of both regional and urban excess particulate nitrate.

As shown in Figure 9-16, Figure 9-17, and Figure 9-24, annual-averaged urban particulate SO_4^{2-} concentrations are generally not much higher than the regional values, with urban excess generally of less than about 0.5 $\mu g/m^3$. The exceptions apparent by comparing Figure 9-16 and Figure 9-17 are in Texas and Louisiana where urban excess particulate SO_4^{2-} are >1 $\mu g/m^3$, perhaps caused by local emissions (e.g., from oil refineries). Urban contributions are a larger fraction of the total particulate SO_4^{2-} concentrations in the western U.S. because the regional concentrations are much lower than in the East. The modest additional particulate SO_4^{2-} concentrations associated with urban areas suggests that most particulate SO_4^{2-} is regionally distributed, and that IMPROVE and CSN monitoring sites can be used together to enhance the ability to delineate particulate SO_4^{2-} spatial distributions. For example, note that the additional data from urban sites shown in Figure 9-17 extends north and south of the distribution of the high particulate SO_4^{2-} loading shown in Figure 9-16 over Tennessee and Kentucky, as well as the high loadings over southern Pennsylvania, eastern West Virginia and northern Virginia. (The color-contour suggested dip in concentrations between the two eastern particulate SO_4^{2-} high concentrations regions may not exist in the atmosphere, but this cannot be verified without speciation monitoring sites in southern Ohio, the border of Kentucky and West Virginia and western Virginia.)

Urban and remote area carbonaceous $PM_{2.5}$ are displayed in Figure 9-18 and Figure 9-19 (organic mass), Figure 9-20 and Figure 9-21 (EC), and Figure 9-24 (total carbon = organic + EC concentration). Just as with particulate nitrate, both organic mass and EC concentrations are more than twice the remote-area background concentrations for western urban monitoring locations. One of the more interesting pairing of sites is for the Virgin Islands compared to the urban site at San Juan, Puerto Rico (see the map cutout Figure 9-18 through Figure 9-21). The San Juan urban excess OC is moderate, while the EC value is among the most extreme inferred in this manner. For eastern urban areas, approximately half the total carbon is local while the other half is regional. In eastern urban areas, carbonaceous and SO_4^{2-} particulate are the two major components of $PM_{2.5}$, with roughly equal contributions, and account for over 80% of the mass concentration. Edgerton et al. (2004, 156413) showed that carbonaceous $PM_{2.5}$ is responsible for most of the urban excess above regional concentrations at four urban/rural paired Southeastern Aerosol Research and Characterization (SEARCH) monitoring sites in the southeastern U.S. However, the higher overall light extinction efficiency for SO_4^{2-} resulting from its hydrophilicity gives it ~ 2:1 dominance in responsibility for eastern urban light extinction.

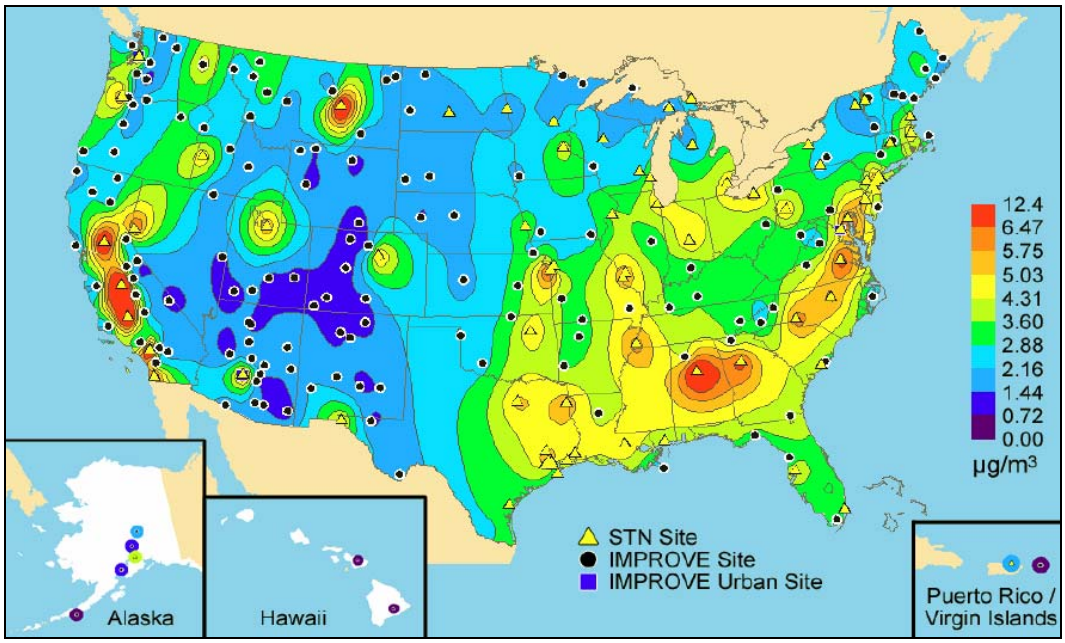
Urban and remote area soil $PM_{2.5}$ concentrations are displayed in Figure 9-22 and Figure 9-23. Urban fine soil concentrations are at most a few tenths of a $\mu g/m^3$ higher than the regional background concentrations and in some regions they are much less. Just as with carbonaceous $PM_{2.5}$, the Virgin Island, San Juan, Puerto Rico pair are interesting for fine soil. In this case, both of these island monitoring sites have high concentrations of fine soil, which is caused by the influence of the trans-Atlantic transport path of dust from Africa (Prospero, 1996, 156889).

No urban-remote pair of coarse mass concentration maps is available because CSN does not monitor coarse mass. In Malm et al. (2004, 156728) a map of annual mean coarse mass concentration is shown for 2003 which includes the values for IMPROVE urban sites, including two in the western U.S. with much more coarse mass than the nearby remote areas monitoring sites (i.e., ~24 $\mu g/m^3$ compared to ~9 $\mu g/m^3$ for Phoenix, AZ, and ~6 $\mu g/m^3$ compared to ~2 $\mu g/m^3$ for Puget Sound, WA) and one eastern IMPROVE site at Washington, DC with less coarse mass than the surrounding remote area values (~2 $\mu g/m^3$ compared to ~4 $\mu g/m^3$).



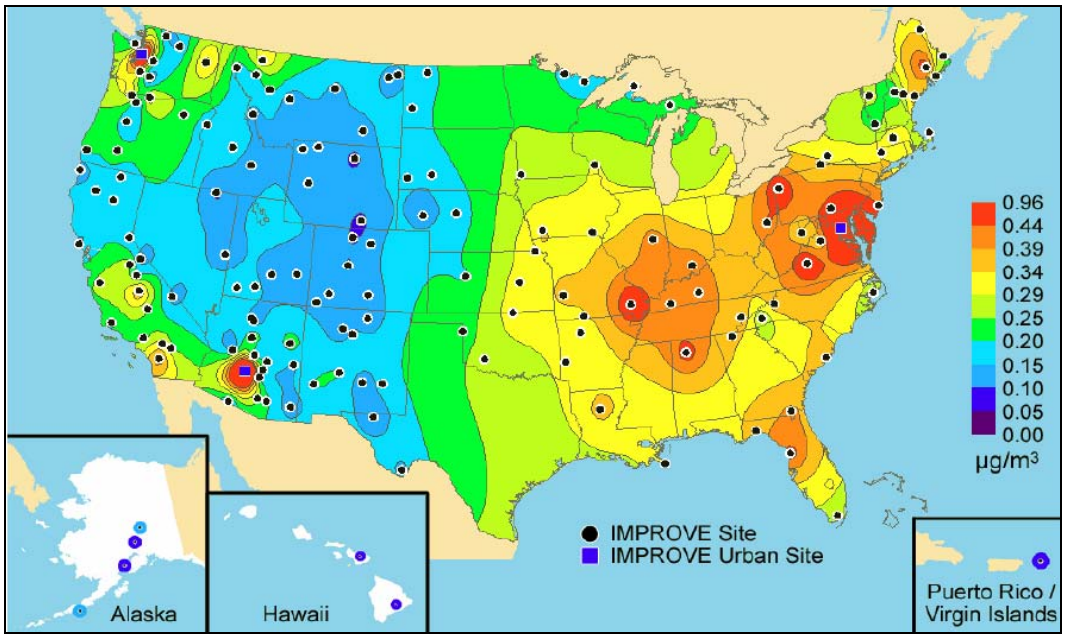
Source: Debell (2006, 156388).

Figure 9-18. IMPROVE monitored mean organic mass concentrations for 2000-2004.



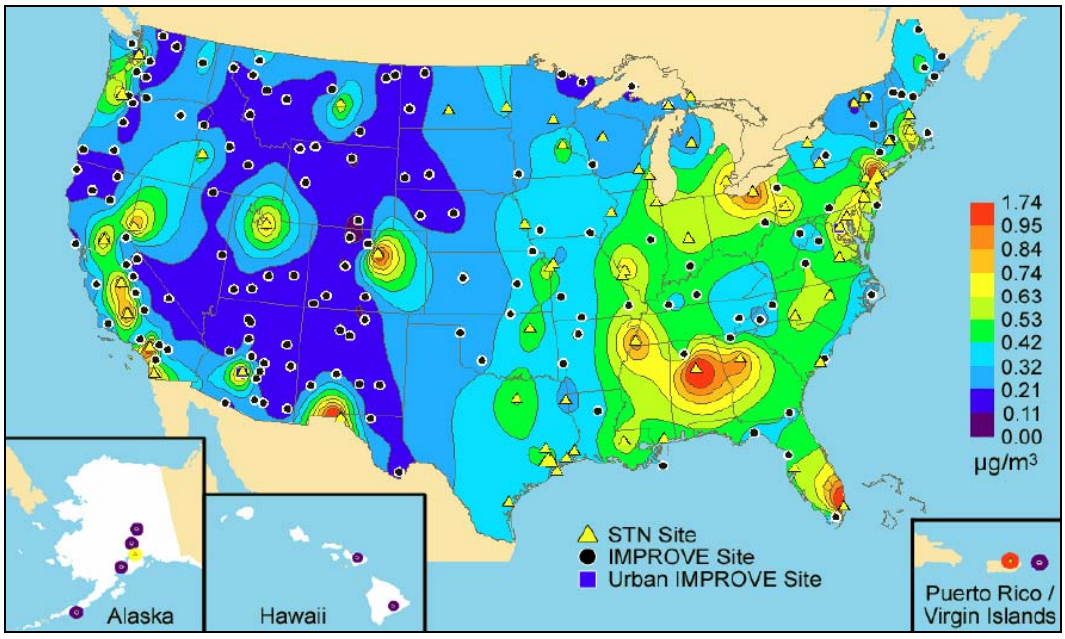
Source: Debell (2006, 156388).

Figure 9-19. IMPROVE and CSN (STN) mean organic mass concentrations for 2000-2004.



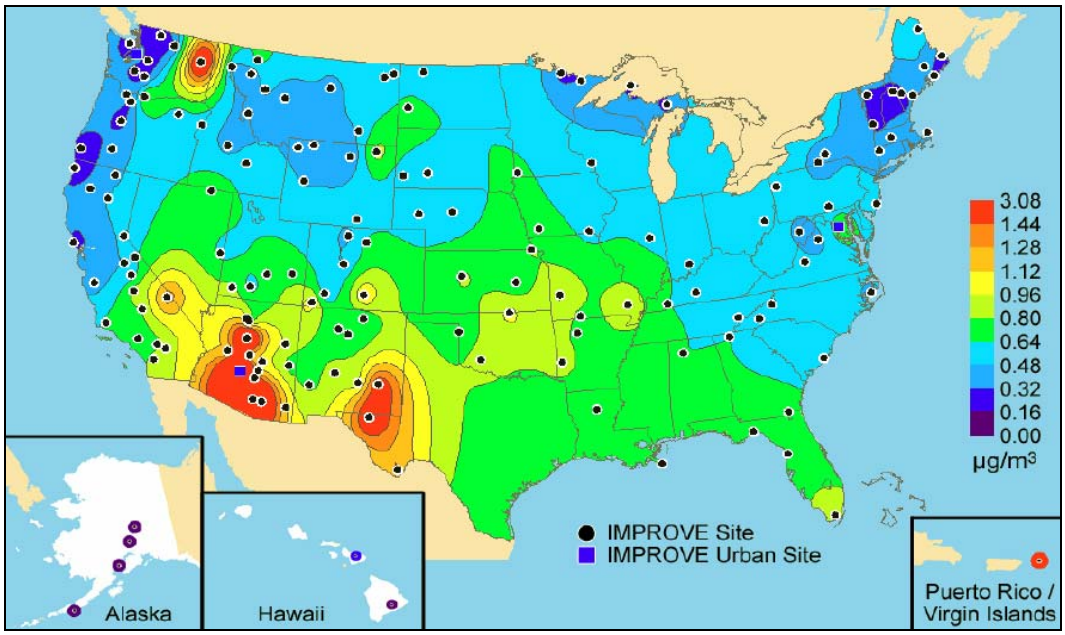
Source: Debell (2006, 156388).

Figure 9-20. IMPROVE mean EC concentrations for 2000-2004.



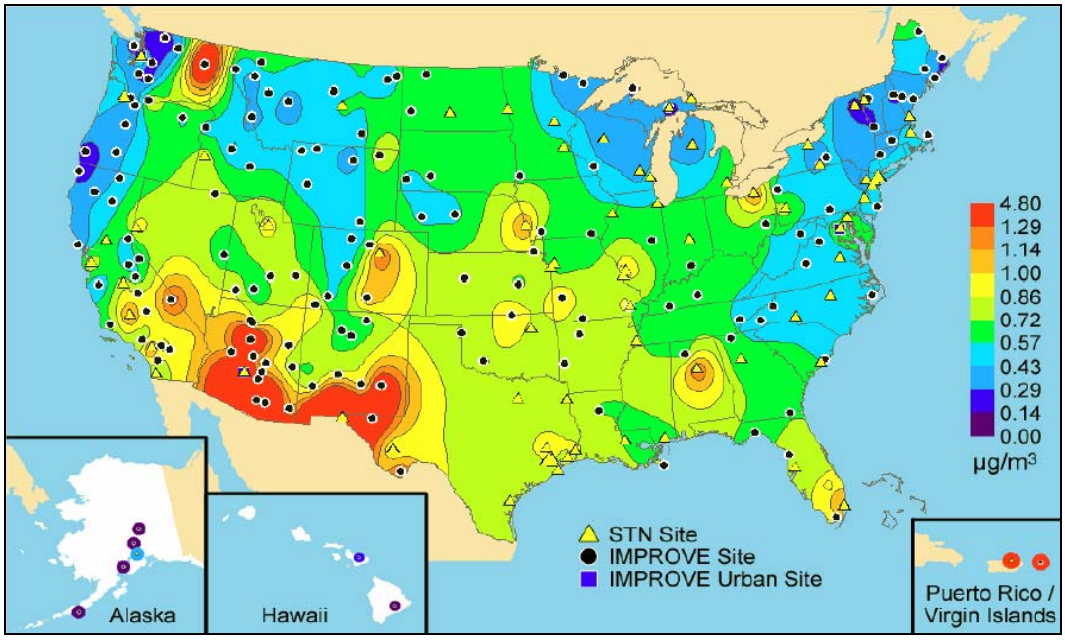
Source: Debell (2006, 156388).

Figure 9-21. IMPROVE and CSN (STN) mean EC concentrations for 2000-2004.



Source: Debell (2006, 156388).

Figure 9-22. IMPROVE mean fine soil concentrations for 2000-2004.



Source: Debell (2006, 156388).

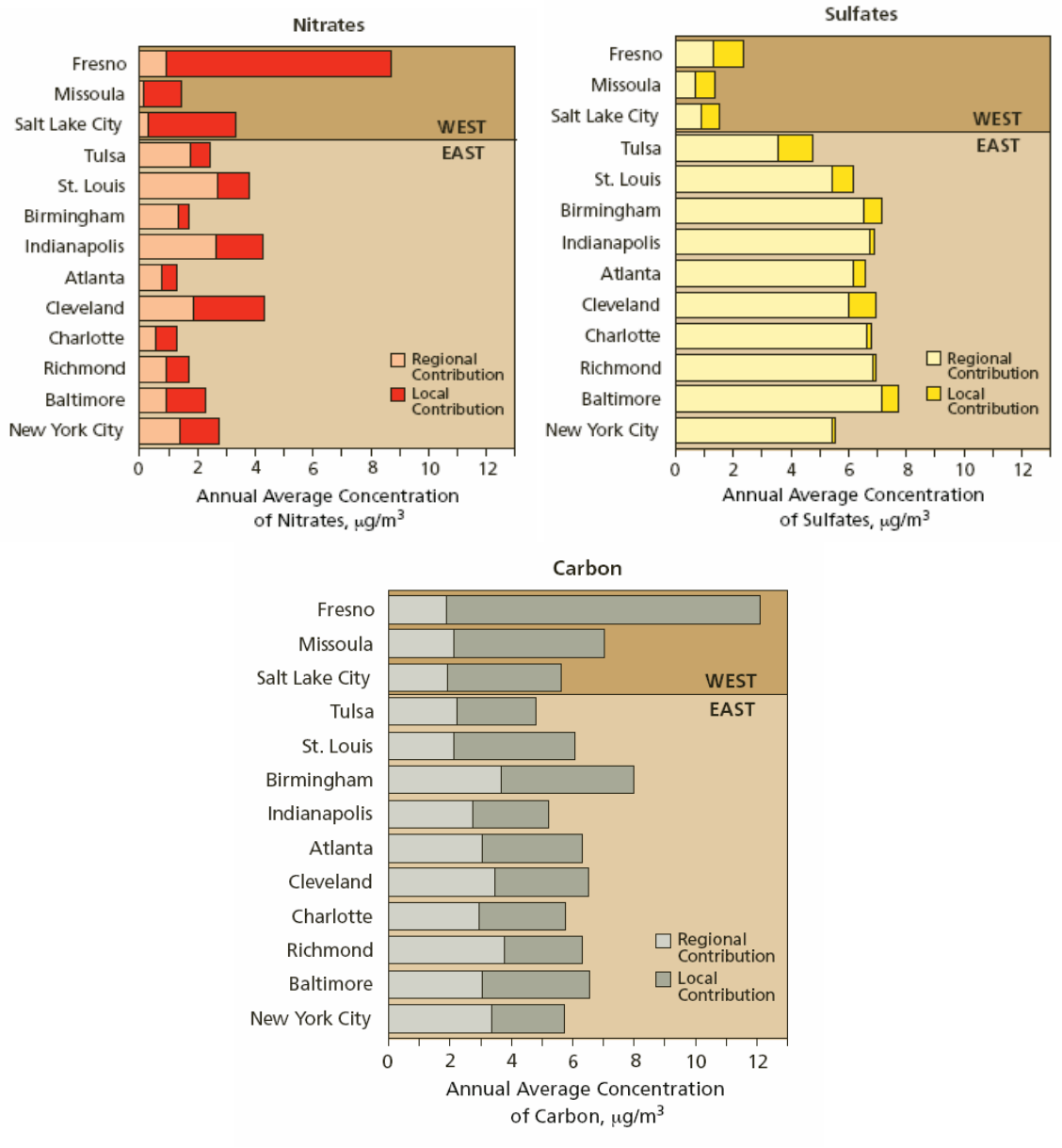
Figure 9-23. IMPROVE and CSN (STN) fine soil concentrations, 2000-2004.

Figure 9-25 shows the remote area coarse mass concentrations as measured by the IMPROVE network. The pattern of high coarse mass concentrations from Oklahoma to Iowa is comparable to the high concentrations in the desert southwest, though as shown in Figure 9-11 it contributes a

smaller relative share of the light extinction because of the higher contributions to haze by particulate nitrate and sulfate in this agricultural region of the country. Comparing Figure 9-22 and Figure 9-25 shows that the coarse mass and fine soil concentration patterns are similar for the desert southwest but there is a much lower fine soil to coarse mass concentration ratio for the agricultural center of the country, suggesting a regional difference in the size distribution of the coarse mass, perhaps due to differences in suspendable soil materials.

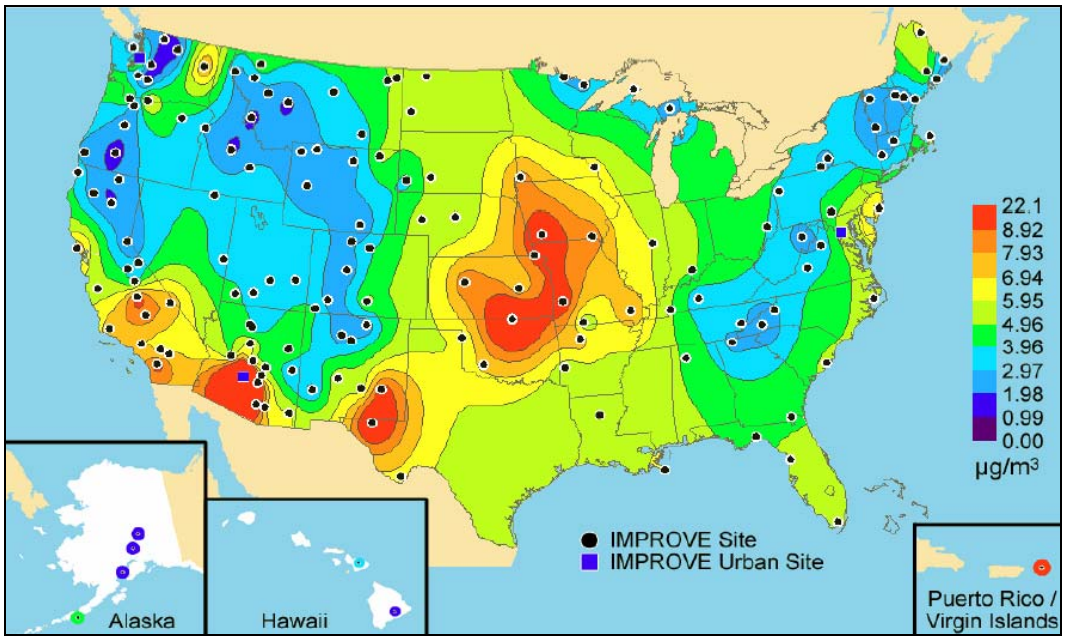
9.2.3.4. Temporal Trends

Visibility trend analysis requires relatively long data records to avoid having meteorologically driven interannual variability obscure more meaningful emissions-driven air quality trends. A requirement for long-term data limits the number of monitoring sites useful for trend analysis. Maps that show haze trends for IMPROVE sites for the 10-year period 1995-2004 for the mean of the 20% best and the 20% worst haze days where sites are required to have a minimum of 6 complete years of data during the 10-year period are shown in Figure 9-26 and Figure 9-27, respectively. The best haze days have improving haze at most sites (32 of 47), no trend at several sites (10 of 47) and degrading visibility at just one site (Great Sand Dunes, CO). The worst haze days have improving haze conditions at several sites (13 of 47), no trend at most sites (30 of 47), and degrading visibility at a few western sites (4 of 47).



Source: U.S. EPA (2004, 190219)

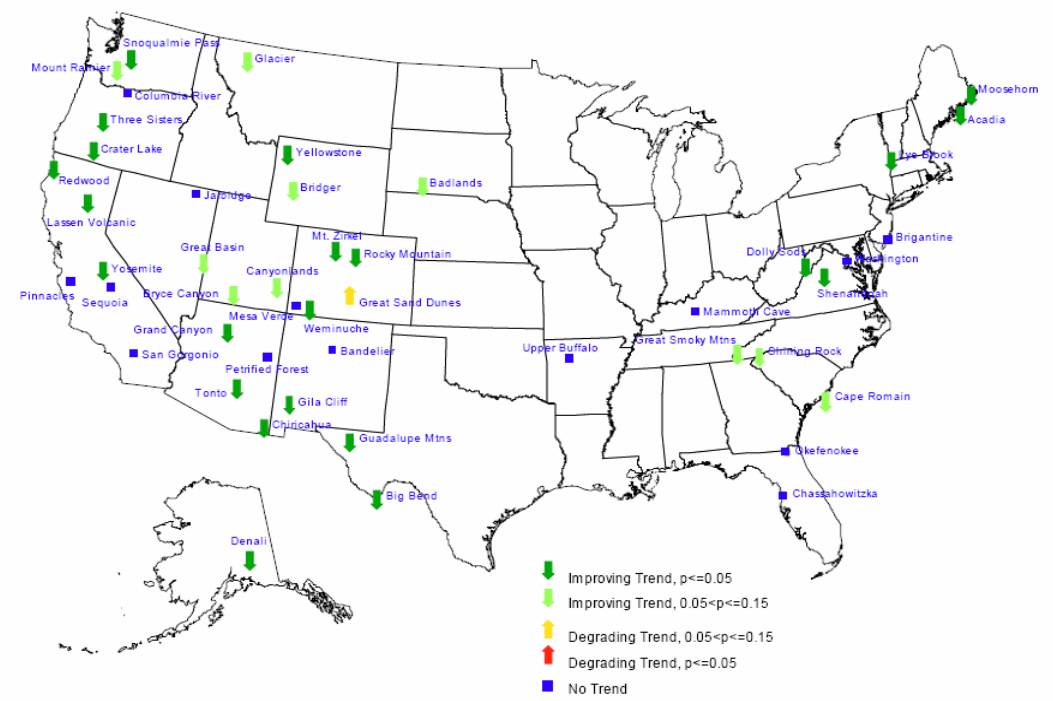
Figure 9-24. Regional and local contributions to annual average $PM_{2.5}$ by particulate SO_4^{2-}, nitrate and total carbon (i.e., organic plus EC) for select urban areas based on paired IMPROVE and CSN monitoring sites.



Source: Debell (2006, 156388).

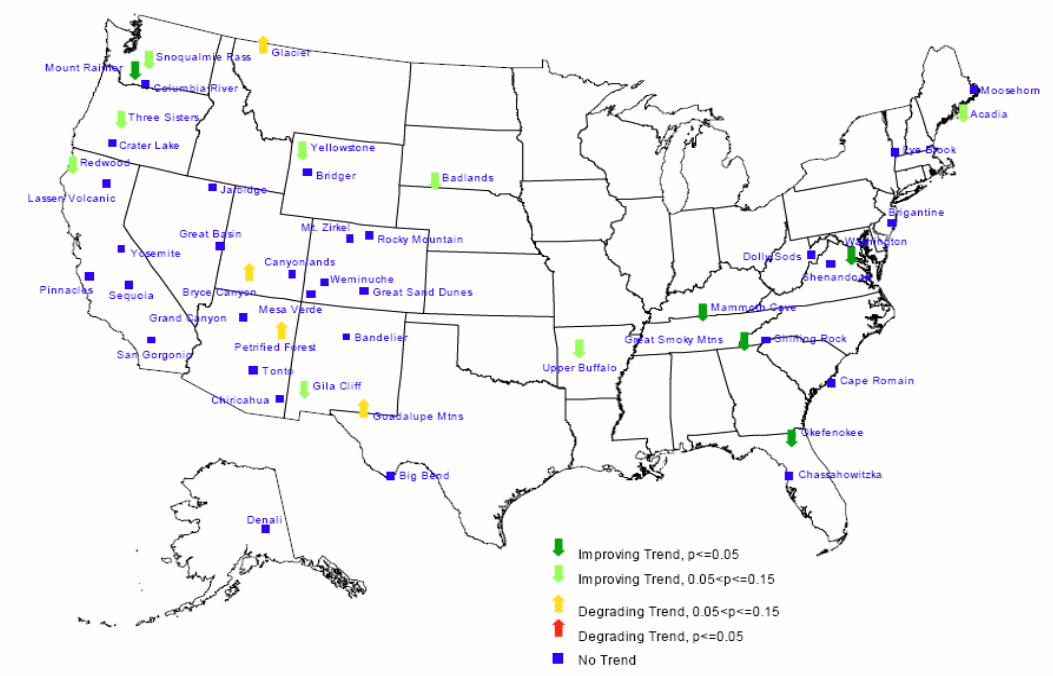
Figure 9-25. IMPROVE mean coarse mass concentrations for 2000-2004.

Eight-, ten-, and sixteen-year trends analysis conducted for the Western Regional Air Partnership (WRAP) as part of the Causes of Haze Assessment (http://www.wrapair.or) show that improving trends for the 20% best haze days for the sites in the western U.S. generally correspond to improving trends for all of the major components with the exception of particulate nitrate. Trends assessment for the worst haze days at western sites show consistent reductions in particulate SO_4^{2-}, but otherwise have mixed increasing and decreasing haze component trends, many of which are not statistically significant. Substantial interannual and shorter term spatial and temporal wildfire activity variations have been shown to have a significant impact on the variability of haze in the western U.S. (Park et al., 2006, 190469; Spracklen et al., 2007, 190485). Edgerton et al. (2004, 156413) showed a decreasing trend in $PM_{2.5}$ of about 18% (corresponding to 1 µg/m^3 to 2 µg/m^3) for 4 urban-rural paired SEARCH sites in the Southeastern U.S. corresponding to similar reductions in SO_4^{2-} and carbonaceous particulate.



Source: Debell (2006, 156388)

Figure 9-26. Ten-year (1995-2004) haze trends for the mean of the 20% best annual haze conditions.



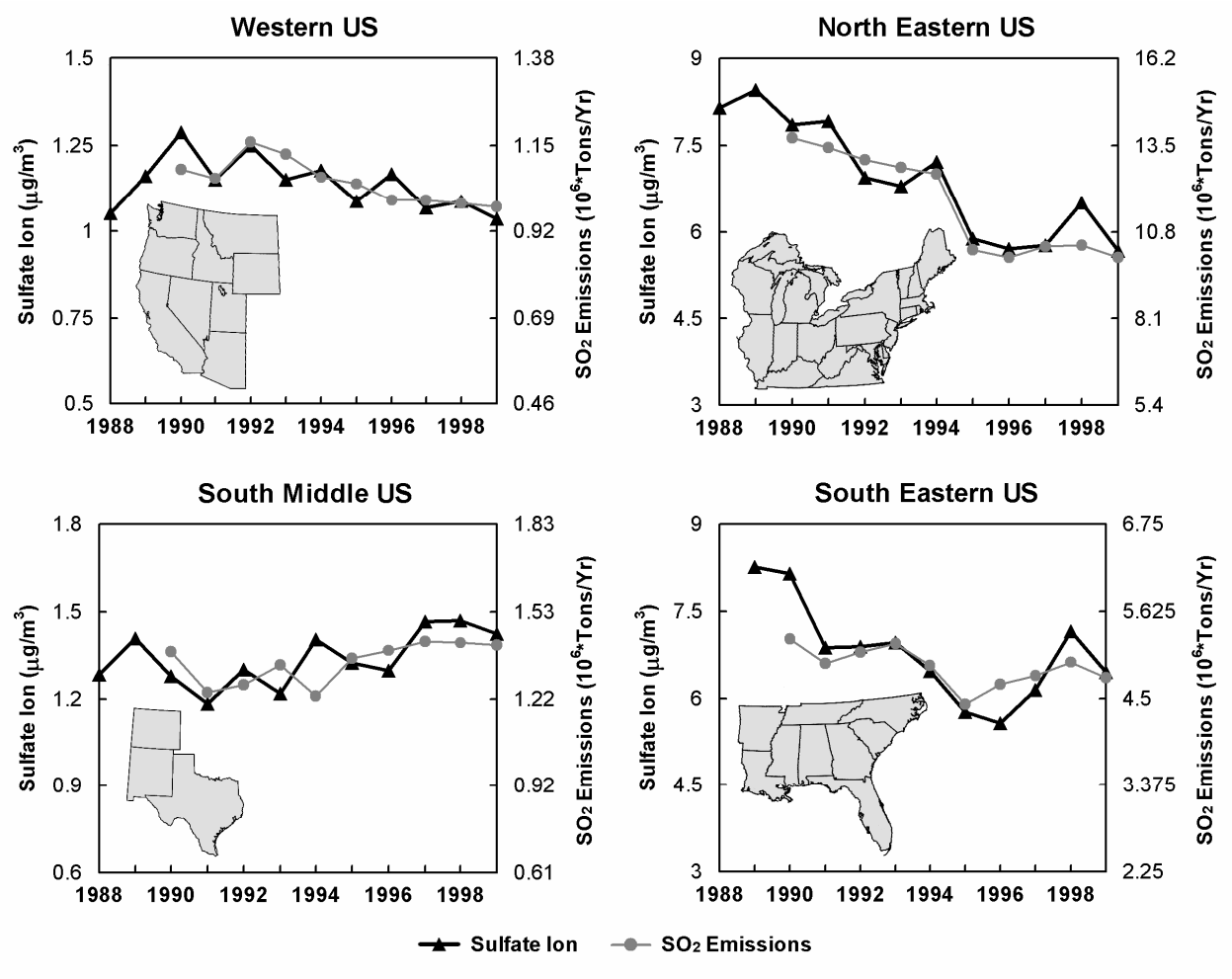
Source: Debell (2006, 156388)

Figure 9-27. Ten-year (1995-2004) haze trends for the mean of the 20% worst annual haze conditions.

Malm et al. (2002, 156727) conducted 10-year (1988-1998) trends analyses on the combination of IMPROVE and CASTNET (Clean Air Status and Trends Network) (Baumgardner et al., 1999, 011308) particulate SO_4^{2-} concentration datasets, which were shown to produce comparable SO_4^{2-} concentrations at 23 co-located monitoring sites. Figure 9-28 shows time plots of 80th percentile particulate SO_4^{2-} concentrations and annual average SO_2 emissions from the National Emissions Trends (U.S. EPA, 2000, 012211) database for four regions of the U.S. Note that the concentration and emissions scales on the plots are each a factor of three, so that an equal percentage change in particulate SO_4^{2-} and SO_2 emissions slope in any plot will have the same trend line slope. Each plot shows a strong correspondence between 80th percentile particulate SO_4^{2-} and SO_2 emissions trends. The western U.S. had steadily declining trends in both, for an overall decrease of about 15%. The northeastern U.S. had a decrease of about 27% over the 10-year period with the largest 1-year decrease of about 20% between 1994 and 1995 as a result of the Phase I implementation of the Acid Rain Program. The southwestern U.S. (Texas, New Mexico and Colorado) had about a 15% increase in particulate SO_4^{2-} and SO_2 emissions over the 10-year period. The southeastern U.S. had a declining trend for the early 1990s followed by an increasing trend for the later half of the decade, with a net decrease over the decade of less than 10%. Others have shown similar decreasing particulate SO_4^{2-} concentration trends and a correspondence in trends between SO_2 emissions and particulate SO_4^{2-} concentration by region (Holland et al., 1999, 092051; U.S. EPA, 2004, 056905).

Holland et al. (1999, 092051) developed and compared NO_X emissions trends from 1989 to 1995 to corresponding trends in total nitrogen concentration (defined as particulate nitrate plus gaseous nitric acid) for the eastern U.S. (states between Louisiana to Minnesota and further east) based on data from 34 rural CASTNet dry deposition monitoring sites. They found a decrease in nitrogen median values of about 8% associated with a decrease of 5.4% in non-biogenic NO_X emissions. Trends in haze associated with particulate SO_4^{2-} and nitrate concentrations should correspond fairly well with trends in their concentration due to the simple relationship between concentration and light extinction at any relative humidity. However, nitrogen as defined in the Holland et al. (1999, 092051) trend analysis includes the nitrogen from particulate nitrate and gaseous nitric acid, but nitric acid does not contribute to light extinction. For situations with limited

atmospheric ammonia or elevated temperatures, trends in nitrogen may be principally in nitric acid with no net change in nitrate light extinction. Alternately with abundant ammonia and low temperatures the trend in nitrogen may be principally in particulate nitrate and the nitrate component of haze.



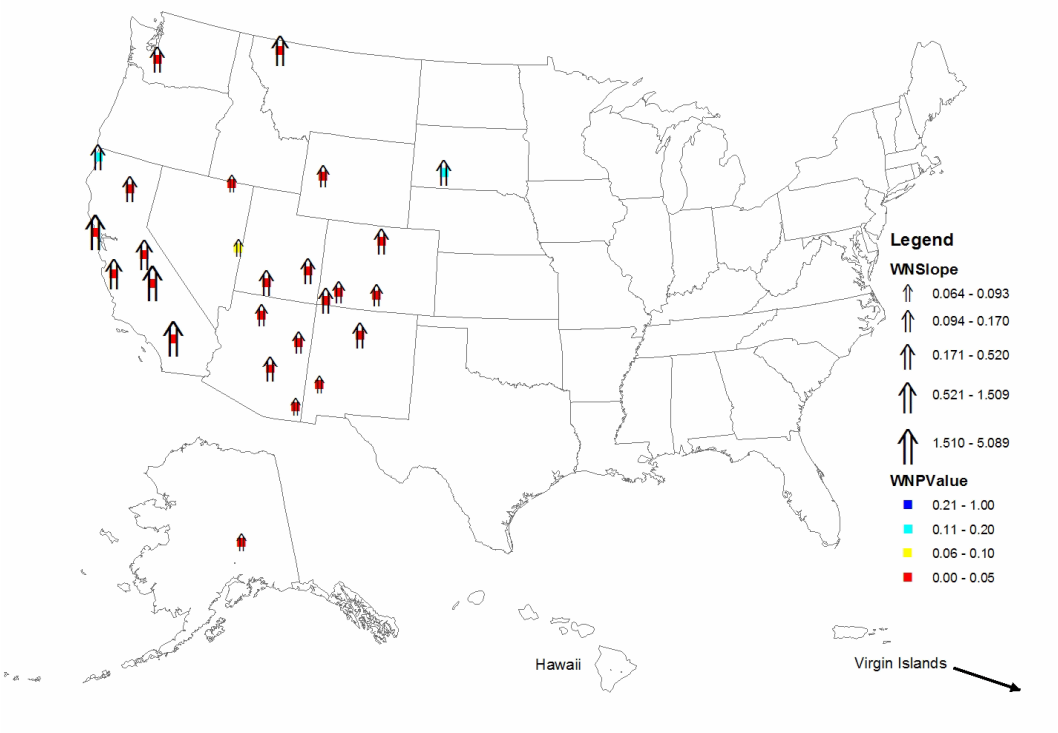
Source: Reprinted with Permission of the American Geophysical Union from Malm et al. (2002, 156727).

Figure 9-28. Ten-year trends in the 80th percentile particulate SO_4^{2-} concentration based on IMPROVE and CASTNet monitoring and net SO_2 emissions from the National Emissions Trends (NET) data base by region of the U.S.

Ten-year trends (1994-2003) of particulate nitrate contribution to light extinction during the 20% worst haze conditions conducted as part of the Causes of Haze Assessment (see the link in Table 9-1) are shown in Figure 9-29. This indicates that haze from particulate nitrates is increasing across the western U.S. at a rate of several Mm^{-1} per year in parts of California and at a rate of several tenths of an Mm^{-1} across the Four-Corners states. A similar particulate nitrate trends map (not shown here) for the 20% best haze conditions that is available at the same web site shows decreasing particulate nitrate contribution to light extinction at nearly all of the western monitoring sites. While statistically significant, these trends for both the 20% worst and 20% best haze periods are influenced by an unexplained nationwide period of depressed nitrate concentrations measured by the IMPROVE network during a 4-yr period from the winter of 1996-1997 through the winter of 2000-2001. Extensive examinations of plausible monitoring methodological explanations have failed

to offer any evidence that the data are invalid (McDade, 2004, 192075), but no satisfactory atmospheric or emissions-related explanation has been offered to account for this 4-yr depression of nitrate. Similar analyses of particulate nitrate haze trends are not available for the rest of the country.

Maps of remote-area 8-, 10-, and 16-yr trends for carbonaceous and crustal PM species based on IMPROVE monitoring are available for the western U.S. conducted as part of the Causes of Haze Assessment. Generally these show a broad range of results (i.e., a mixture of statistically significant upward or downward trends and insignificant trends often with neighboring sites having opposing trends) that vary considerably depending on the number of years selected (i.e., 8, 10, or 16) and whether trends are for the best, worst, or middle of the haze distribution data. The scatter in these results is undoubtedly due to the high interannual variability and varying locations of wildfire and wind-suspended dust emissions that dominate the remote-area concentrations of the carbonaceous and crustal PM species in the western U.S.



Source: http://www.coha.dri.edu/

Figure 9-29. Map of 10-yr trends (1994-2003) in haze by particulate nitrate contribution to haze for the worst 20% annual haze periods. The orientation, size and color of the arrows indicate the direction, magnitude and statistical level of significance of the trends. These consistent upward trends may be a misleading result due to an unexplained sampling issue (see text for additional information).

9.2.3.5. Causes of Haze

In order to attribute haze to emissions from individual sources, source types, or source regions, generally, any of a number of receptor and air quality simulation modeling approaches are applied. When using multiple approaches, the results of each are reconciled using a weight-of-evidence methodology. Commonly this methodology has been applied to the extensive datasets generated by special studies designed to estimate source-receptor relationships for a few receptor locations or for individual emission sources (Pitchford et al., 1999, 156873; Pitchford et al., 2005, 156874; Schichtel

et al., 2005, 156957). More recently the Regional Planning Organizations (RPOs) have sponsored extensive regional haze source attribution assessments using weight-of-evidence methodologies to reconcile attribution results for virtually all of the remote-area IMPROVE sites to support the development of State Implementation Plans for the RHR. Additionally, a number of recent urban special studies, including those sponsored by EPA PM Supersites program (Solomon and Hopke, 2008, 156997), have addressed the causes of and sources contributing to urban excess PM concentrations above region concentrations. Attribution results uncertainties are generally larger than those of the measurements upon which they are based because they also include model uncertainties and assumptions, as well as issues of representativeness (e.g., How well does the data used in the analysis represent the typical emissions, air quality and meteorological conditions of interest?). As such it is advisable to treat the attribution results reported below as semi-quantitative.

The relative importance of the PM species that contribute to haze varies by region of the U.S. and time of year as shown in Figure 9-9, Figure 9-10, and Figure 9-11, above. Generally haze in the western half of the U.S. is not dominated by any one or two PM species. In the eastern half of the U.S., SO_4^{2-}, especially during summer, and nitrate during the winter in the Midwest are the dominant haze species. As described above, urban haze can be viewed as a composite of the regional and local contributions where local contributions seem to be dominated by carbonaceous and, to a lesser extent, nitrate and crustal PM components. There have been far fewer urban investigations that explicitly consider visibility impacts, though there are numerous studies of urban PM source attribution. The order of discussion below on the cause of haze is by region beginning in the western U.S. and proceeding to the east, analogous to dominant air flow patterns across the lower 48 states and will include information from urban studies along side those of remote-area haze investigations.

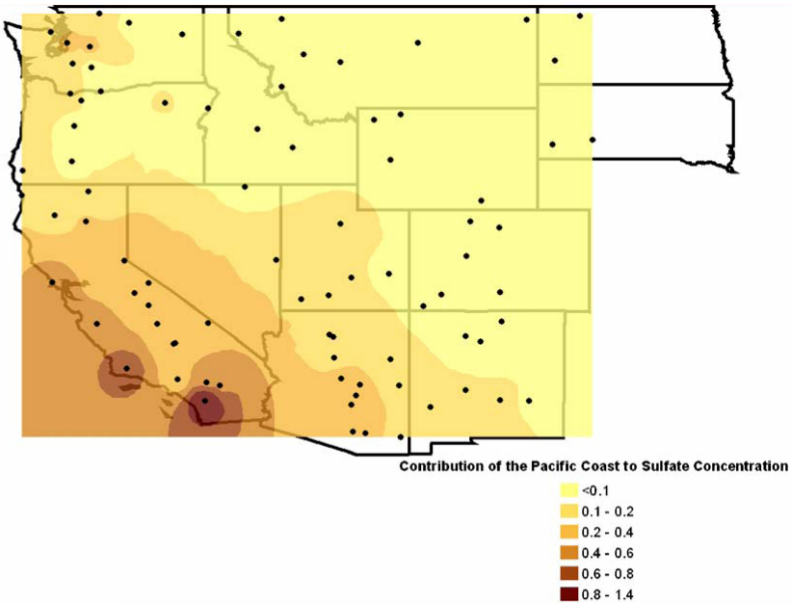
Based on modeling of an episode (September 23-25, 1996) in the California South Coast Air Basin (SCAB) and another episode (January 4-6, 1996) in the San Joaquin Valley (SJV) by Ying and Kleeman (2006, 098359), about 80% of the particulate SO_4^{2-} for both regions is from upwind sources (i.e., likely from offshore sources including marine shipping, long-range transport and natural marine sources), with most of the remaining is associated with diesel and high-sulfur fuel combustion. Kleeman et al. (1999, 011286), using a combination of measurements and modeling, showed that the upwind particulate SO_4^{2-} source region for the SCAB was over the Pacific Ocean (confirmed by measurements on Santa Catalina Island) and that these particles subsequently grew with accumulation of additional secondary aerosol material, principally ammonium nitrate as they traversed the SCAB. The majority of the nitric acid that forms particulate nitrate in the SCAB is from diesel and gasoline combustion (~63%), while much of the ammonia is from agricultural sources (~40%), catalyst equipped gasoline combustion (~16%), and upwind sources (~18%). The majority of the OC found in SCAB was attributed in this study to primary emissions by transportation-related sources, including diesel (~13%) and gasoline (~44%) engines and paved road dust (~12%). At the Fullerton site in the middle of the SCAB the concentration of locally generated organics is roughly double that of the locally generated nitrates (~5.6 $\mu g/m^3$ compared to ~2.4 $\mu g/m^3$), while at Riverside on the east edge of the SCAB and near the large agricultural sources of ammonia emissions, the particulate nitrate concentrations are nearly double that of organic PM (~17 $\mu g/m^3$ compared to ~10 $\mu g/m^3$).

Ying and Kleeman (2006, 098359) showed that during the winter 1996 episode in the SJV most of the nitric acid that forms particulate nitrate is from upwind sources (~57%) with diesel and gasoline combustion contributing most of the rest (30%), while much of the ammonia is from upwind sources (~39%) and a combination of area, soil and fertilizer sources (~52%). In an assessment of PM particle size and composition in the SJV during the winter of 2000-2001, Herner et al. (2006, 135981) showed that fresh emissions of carbonaceous PM from combustion sources in urban locations (Sacramento, Modesto, and Bakersfield, CA) move quickly from ultrafine particle size (i.e., diameter ~0.1 μm) to accumulation mode by condensation with accumulation mode (i.e., diameter ~0.5 μm) particles, and that secondary nitrate particle formation occurs preferentially on the surface of hydrated ammonium sulfate particles during the afternoon when gas-phase nitric acid is at peak photo-chemical production from NO_X. Given the abundance of ammonia emissions and low ambient temperatures, particulate nitrate production in this way is only limited by the availability of nitric acid. Due to the cool winter conditions there was little SOA production during this study. Sea salt was shown to dominate the larger coarse particle mode during on-shore wind at the background coastal monitoring site at Bodega Bay, north of San Francisco, CA.

Using a regression analysis to find the dependence of particulate SO_4^{2-} concentration measured over a 3-year period (2000-2002) at 84 western IMPROVE monitoring sites on the

modeled transport trajectories to the sites for each sample period, Xu et al. (2006, 102706) were able to infer the source regions that supplied particulate SO_4^{2-} in the western U.S. Among the source regions included in this analysis was the near coastal Pacific Ocean (i.e., a 300-km zone off the coast of California, Oregon, and Washington). Up to half of the particulate SO_4^{2-} measured at Southern California monitoring sites was associated with this source region. As shown in Figure 9-30 the zone of impact from this source region included large regions of California, Arizona, and Nevada. The authors made the case that high sulfur content fuel used in marine shipping and port emissions may be largely responsible. As a result, the WRAP RPO emissions inventory was modified to include marine shipping and a Pacific Offshore source region was added to source attribution by air quality simulation modeling.

The SO_4^{2-} attribution results of the WRAP air quality modeling (results available on the Technical Support System (TSS) website, see Table 9-1 for the web-link) credit the Pacific offshore source region with somewhat smaller contributions than those from the trajectory regression work by Xu et al. (2006, 102706) with concentrations at the peak impact site in California that are about 45% compared to 50% by regressions and even greater differences for more distant monitoring sites. Based on the modeling attribution the Pacific offshore source region was responsible for 10-20% of the nitrate measured in Southern California.



Source: Reprinted with Permission of Atmospheric Environment from Xu et al. (2006, 102706).

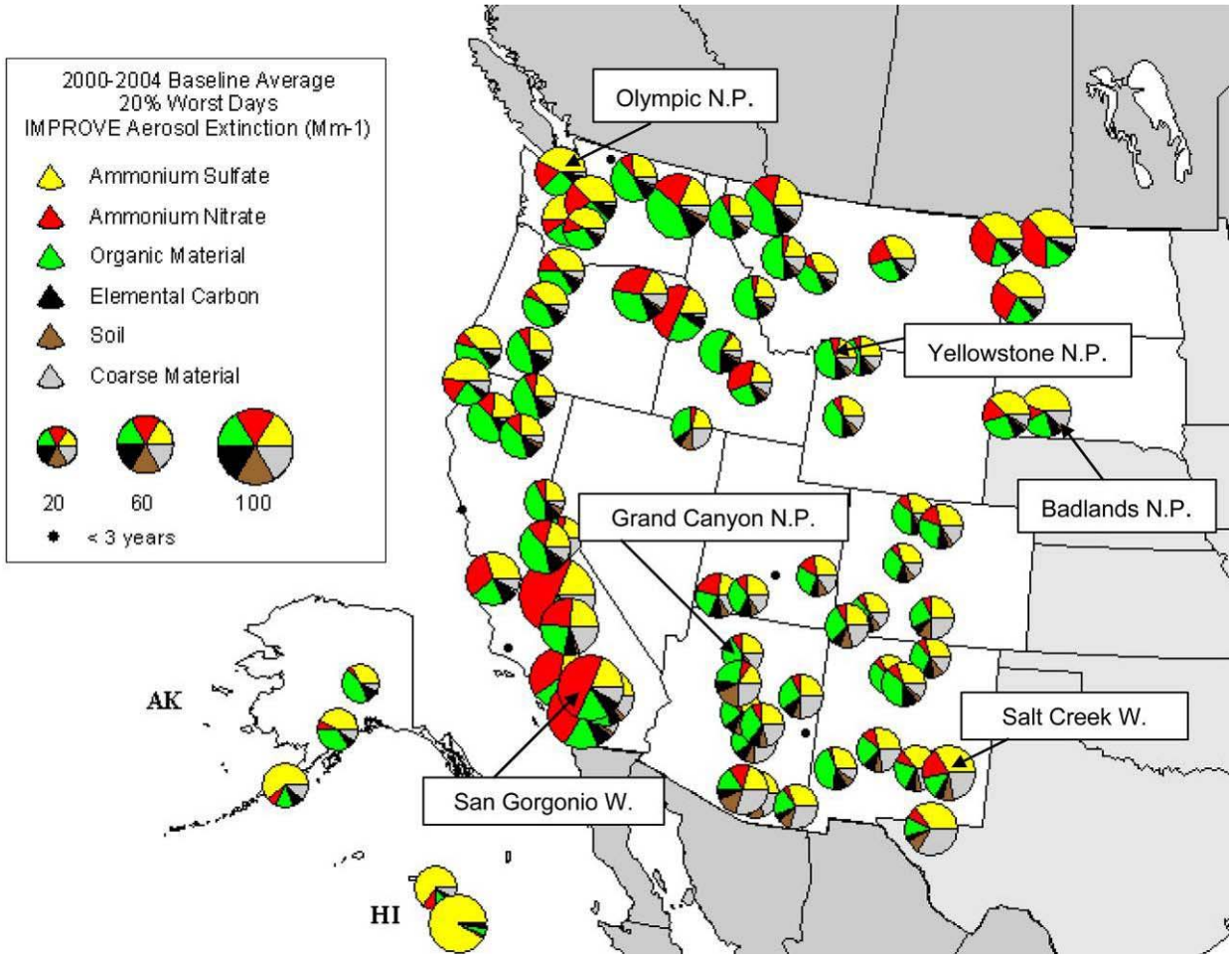
Figure 9-30. Contributions of the Pacific Coast area to the ammonium sulfate (μg/m^3) at 84 remote-area monitoring sites in western U.S. based on trajectory regression for all sample periods from 2000-2002 (dots denote locations of the IMPROVE aerosol monitoring sites).

A coordinated effort by federal, state, and county air quality organizations to determine the causes of haze in the Columbia River Gorge (a deep and narrow gap in the Cascade Mountains on the Washington/Oregon border) through extensive multiyear measurements and high spatial resolution air quality modeling of typical episodes demonstrated the multitude of emission sources that contribute to its impairment (Pitchford et al., 2007, 098066). During the summer, gorge winds are generally from the west and relatively dry. More than half of the haze during a typical summer episode is from a combination of international and other distant sources (~22% at the western end of the gorge) plus regional natural sources including wildfire and secondary organic PM from biogenic emissions (~39% at the eastern end of the gorge). The Portland/Vancouver metropolitan area was responsible for a significant amount of the haze during the summer (~20% on in the western end of

the gorge), while sources within the gorge were responsible for a moderate amount of haze (~6% and ~9% at the western and eastern ends of the gorge). The wind is much more often from the east during the winter. The highest haze conditions in the gorge are during the winter and are associated with fog conditions that rapidly convert precursor gaseous emissions of NO_X and SO_2 from local and regional combustion sources and NH_4 from local and regional agricultural activities to secondary nitrate and SO_4^{2-} PM that persist as a post-fog intense haze. Contributions by these sources east of the gorge contribute ~57% of the haze on the eastern end of the gorge, with half of the nitrate and SO_4^{2-} particulate from electric utility emissions and most of the rest from transportation sources. Other sources contributing during the winter haze at the eastern end of the gorge are from sources outside the modeling domain (i.e., most of Washington and Oregon) and within the gorge (~23% and ~10%, respectively).

An assessment of concurrent measurements at the nearby Mt. Hood IMPROVE monitoring site (45 km south of the Columbia River at 1,531 m ASL) shows that Columbia River Gorge haze conditions and especially the wintertime high nitrate/SO_4^{2-} contributions to haze are not typical of the generally higher elevation remote areas of the region (Pitchford et al., 2007, 098066). However Gorge-like high wintertime nitrate and SO_4^{2-} are found at the Hells Canyon IMPROVE site, which is similarly situated in a narrow canyon of the Snake River almost 400 km east of the Gorge (from the VIEWS web site, see Table 9-1), implying that there may be a substantial vertical concentration gradient during winter in this complex terrain.

Several example monitoring locations distributed across the northern and southern portions of the western U.S. have been selected to illustrate the attribution results from the WRAP-sponsored attribution analysis tools that estimate the relative responsibility for haze of the various PM species by source region and source type. The selected sites include Olympic NP, WA; Yellowstone NP, WY; and Badlands NP, SD across the north, and San Gorgonio Wilderness (W), CA; Grand Canyon NP, AZ and Salt Creek W, NM across the south as shown in Figure 9-31.



Source: http://vista.cira.colostate.edu/airdata/linkbrowser/LinkBrowserNormal.aspx

Figure 9-31. Shows the IMPROVE monitoring sites in the WRAP region with at least three years of valid data and identifies the six sites selected to demonstrate the apportionment tools. Pie diagrams show the composition for the mean of the 20% worst haze conditions and the mean light extinction (Mm^{-1}) by the size of the circle (see figure key).

WRAP-sponsored CMAQ modeling for 2002 used virtual tracers of SO_2 and NO_X emissions that tracked the source region and category through the transport and transformation processes to particulate SO_4^{2-} and nitrate. This was used to produce pie diagrams of particulate SO_4^{2-} and nitrate attribution results by source region for each of these sites as shown in Figure 9-32 (produced using the TSS, see Table 9-1). Based on these sites, over half of the particulate SO_4^{2-} in remote areas of the Pacific coastal states is from outside of the U.S. (Pacific offshore and outside of the domain). The outside of the domain values were derived by simulating the fate of the boundary condition concentrations, which for the WRAP air quality modeling were obtained using output from the GEOS-CHEM global air quality model (Fiore et al., 2003, 047805). The SO_4^{2-} fraction from the region labeled outside of domain was approximately uniform throughout the western U.S. with site-to-site variation in the fraction caused mostly by variations in total SO_4^{2-} concentration. The more northerly sites have impacts from Canadian emissions, while the southern sites have impacts from Mexican emissions. Half of the Salt Creek, New Mexico SO_4^{2-} is from the domestic source emissions further to the east, which also contribute about 20% to Badlands particulate SO_4^{2-} concentrations. A breakout of the emission sources from within the WRAP region by source type (not shown) has most of the emissions from point sources, with the combination of motor vehicle,

area and wildfire emissions contributing from a few percent at the furthest eastern sites to about half at San Gorgonio.

By comparison, the particulate nitrate is much more from domestic regional emission sources, with ~60-80% being from emissions within the WRAP region. For the west coast sites about 25% of the nitrate is from a combination of Pacific offshore emissions (i.e., marine shipping) and outside domain regions. Canadian emissions are responsible for about 10-30% of the particulate nitrate for the three northern sites, but Mexican emissions do not contribute appreciably to particulate nitrate for the three southern sites. Motor vehicles are the largest contributing NO_X source category responsible for particulate nitrate for these six WRAP sites, with a combination of point, area and wildfire source categories also contributing from about 10-50% of the WRAP regional emissions.

WRAP only used the virtual tracer approach to investigate source locations and categories for SO_2 and NO_X emissions. A different type of virtual tracer modeling tool was used to track the various OC compounds and sort them into three groups for 2002. The first group labeled primary organics includes all of the organics that are emitted directly as PM from any source type and location. The second group labeled anthropogenic secondary organics is PM produced in the atmosphere by aromatic VOCs. The third category labeled biogenic secondary organics is PM produced in the atmosphere by biogenic VOCs. Organic PM in the biogenic secondary category includes those that would functionally be considered man-made emissions (e.g., those from agricultural crops and urban landscapes), though in most remote areas of the west these man-made VOC emissions are small compared to those of the natural biogenic sources. Figure 9-33, Figure 9-34, and Figure 9-35 show the monthly averaged apportionment of organic PM for the 6 selected monitoring locations.

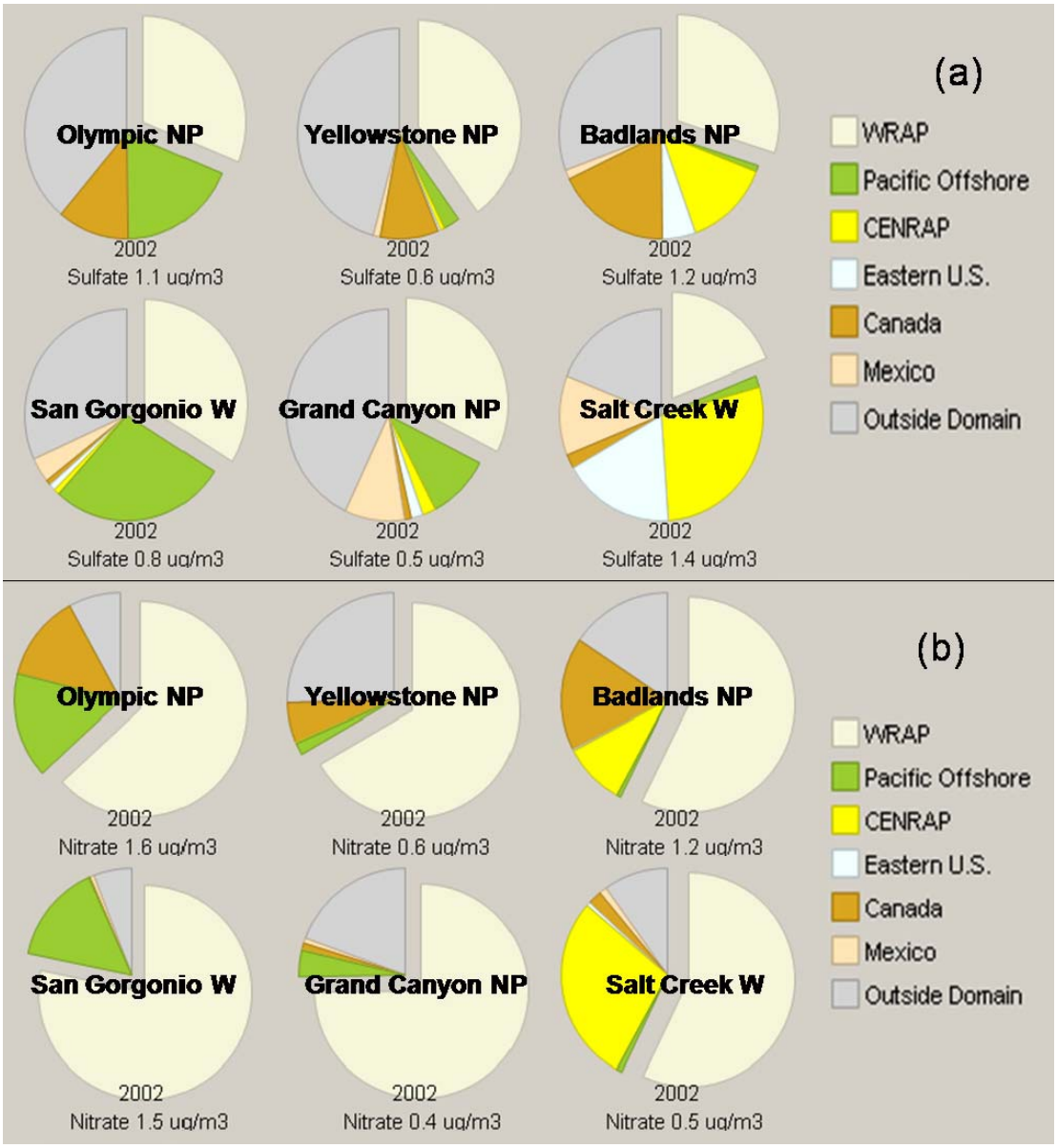
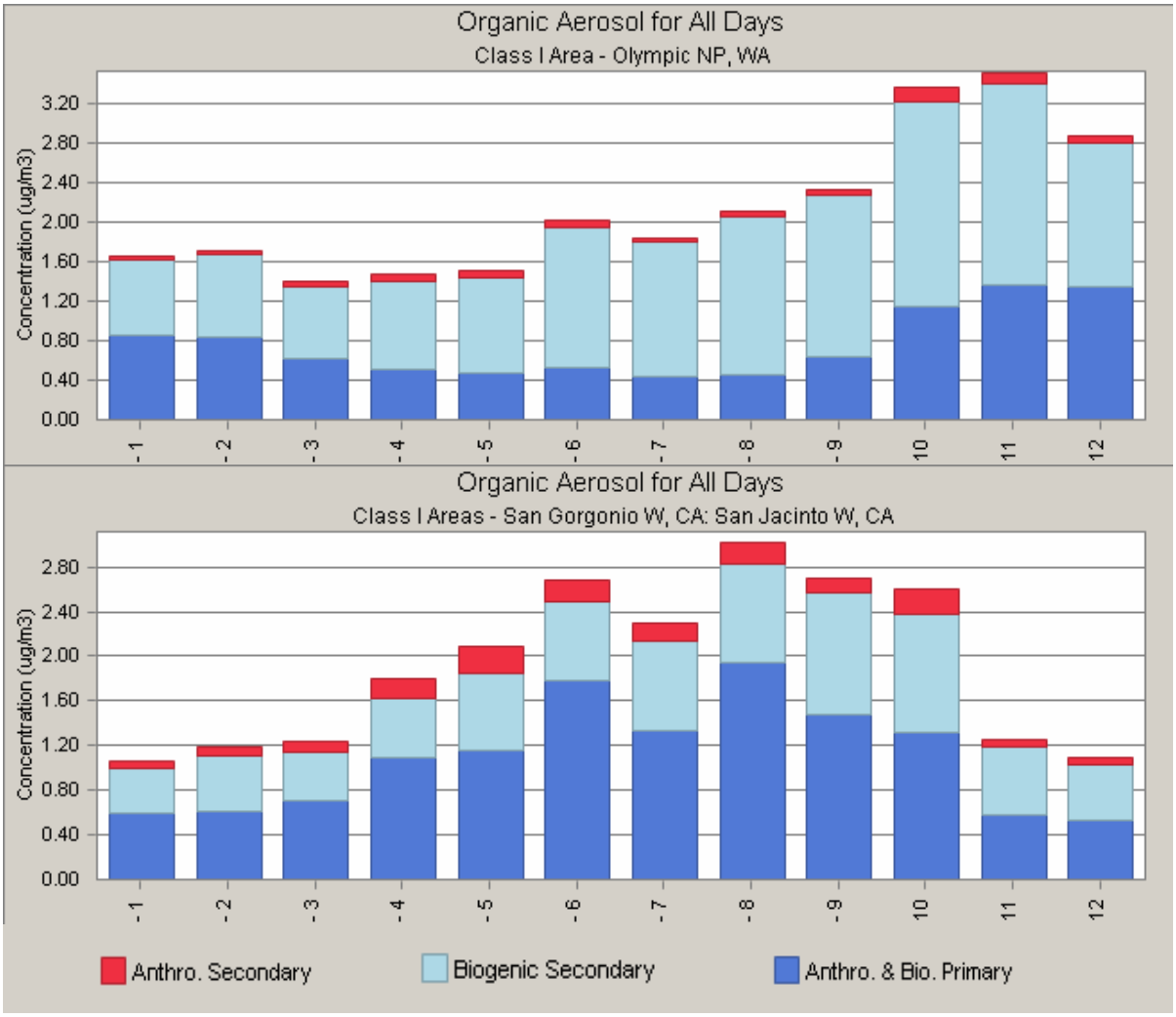


Figure 9-32. **Particulate SO_4^{2-} (a) and nitrate (b) source attribution by region using CAMx modeling for six western remote area monitoring sites : top left to right Olympic NP, WA; Yellowstone NP, WY; Badlands NP, SD; bottom left to right San Gorgonio W, CA; Grand Canyon NP, AZ; and Salt Creek W, NM. WRAP includes ND, SD, WY, CO, NM and all states further west. CENRAP includes all states east of WRAP and west of the Mississippi River including MN. Eastern U.S. includes all states east of CENRAP. The Pacific Offshore extends 300km to the west of CA, OR, and WA. Outside Domain refers to the modeling domain, which extend hundreds of kilometers into the Pacific and Atlantic Oceans and from Hudson Bay Canada to just north of Mexico City. This figure was assembled from site-specific diagrams produced on the TSS web site (see Table 9-1) for 2002.**

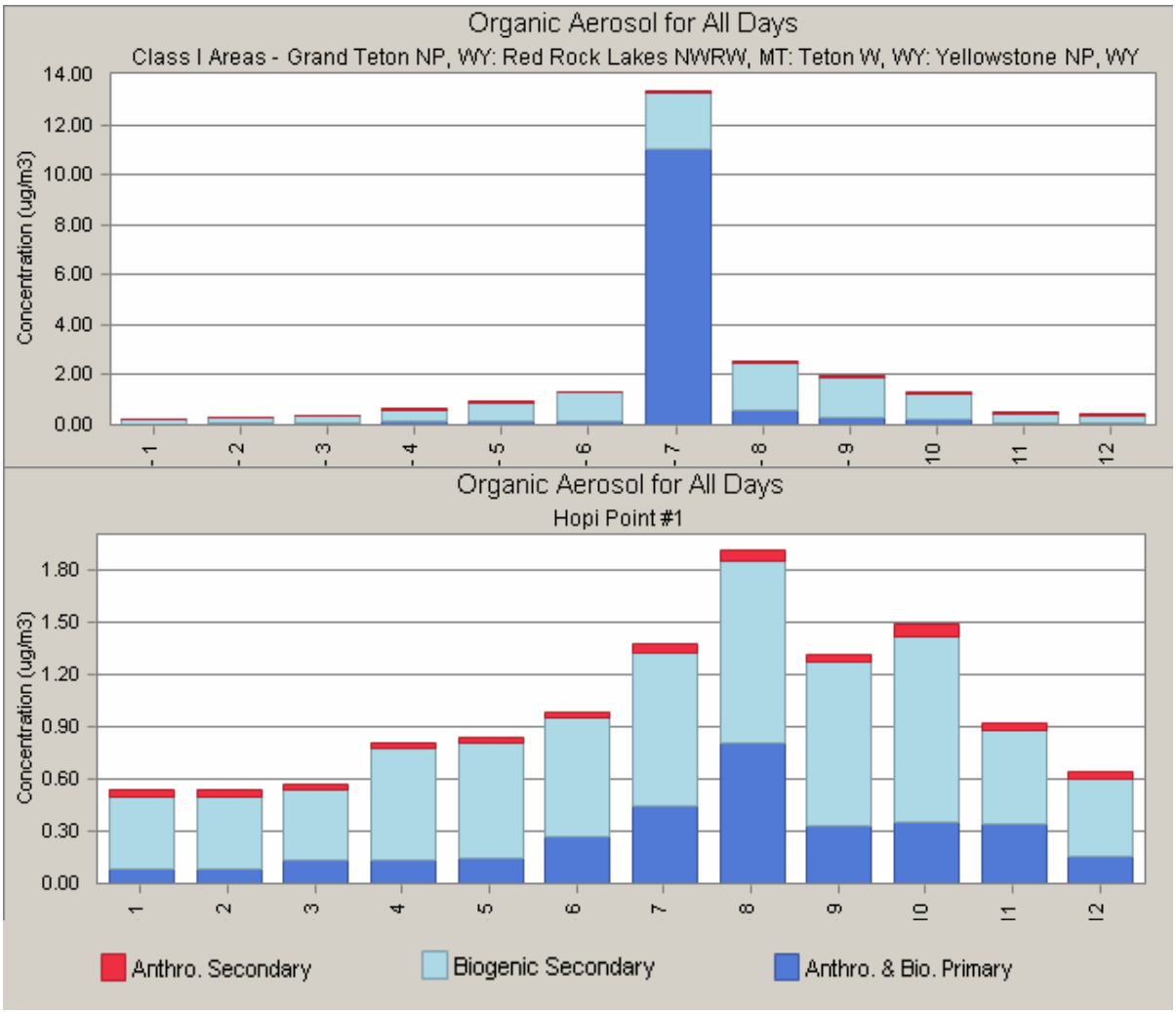


Source: From the TSS website, see Table 9-1.

Figure 9-33. Monthly averaged model predicted organic mass concentration apportioned into primary PM and anthropogenic and biogenic secondary PM categories for the Olympic NP (top) and San Gorgonio W (bottom) monitoring sites.

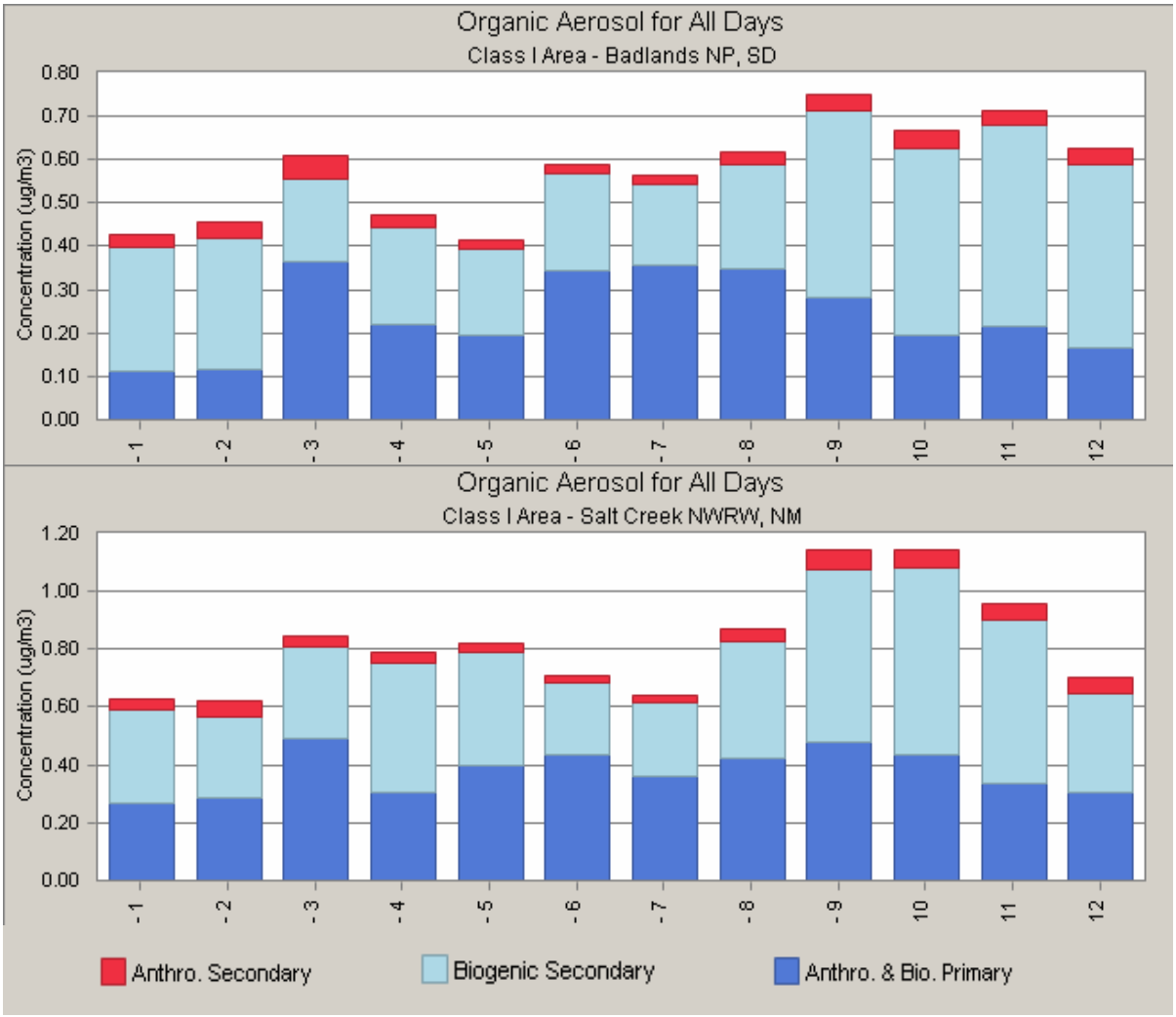
Based on the modeling results for these six sites and confirmed by measurements (see, e.g., Figure 9-10), a west-to-east decreasing gradient of organic mass exists with annual concentrations from ~2 μg/m^3 for the coastal state sites to ~1 μg/m^3 for the intermountain west sites, to <1 μg/m^3 for the sites just east of the Rocky Mountains, discounting the large fire impacts for July at Yellowstone NP which raised its annual mean to ~2 μg/m^3. At all of these remote-area sites anthropogenic secondary PM is estimated to be a small fraction of the organic mass, with the largest fractional contribution at the San Gorgonio monitoring site immediately downwind of the major Southern California urban areas, yet having <10% of the monthly mean organic mass from anthropogenic secondary PM. Of the six selected monitoring sites, San Gorgonio has the highest fraction of the organic PM from primary emissions (~57%), followed by Yellowstone (~55%), then the two eastern-most sites (Badlands ~42% and Salt Creek 41%), and with Grand Canyon and Olympic NPs the lowest fraction by primary emissions (~37%). Yellowstone NP would have had the lowest fraction of organic PM by primary emissions had it not been for the month of July (the 11-mo mean was 29%) when wild fire smoke contributed. Results from recent chamber and field studies, and modeling would seem to call into question apportionment of primary and secondary carbon done by traditional air quality model simulations of OC, as described above, due to the combined effects of

extensive evaporation of semivolatile primary emissions when diluted and to photochemical reactions of low volatility gas phase species that substantially increases the amount of secondary organic PM (Robinson et al., 2007, 156053).



Source: From the TSS website, see Table 9-1.

Figure 9-34. Monthly averaged model predicted organic mass concentration apportioned into primary PM and anthropogenic and biogenic secondary PM categories for the Yellowstone NP (top) and Grand Canyon (Hopi Point) (bottom) monitoring sites.



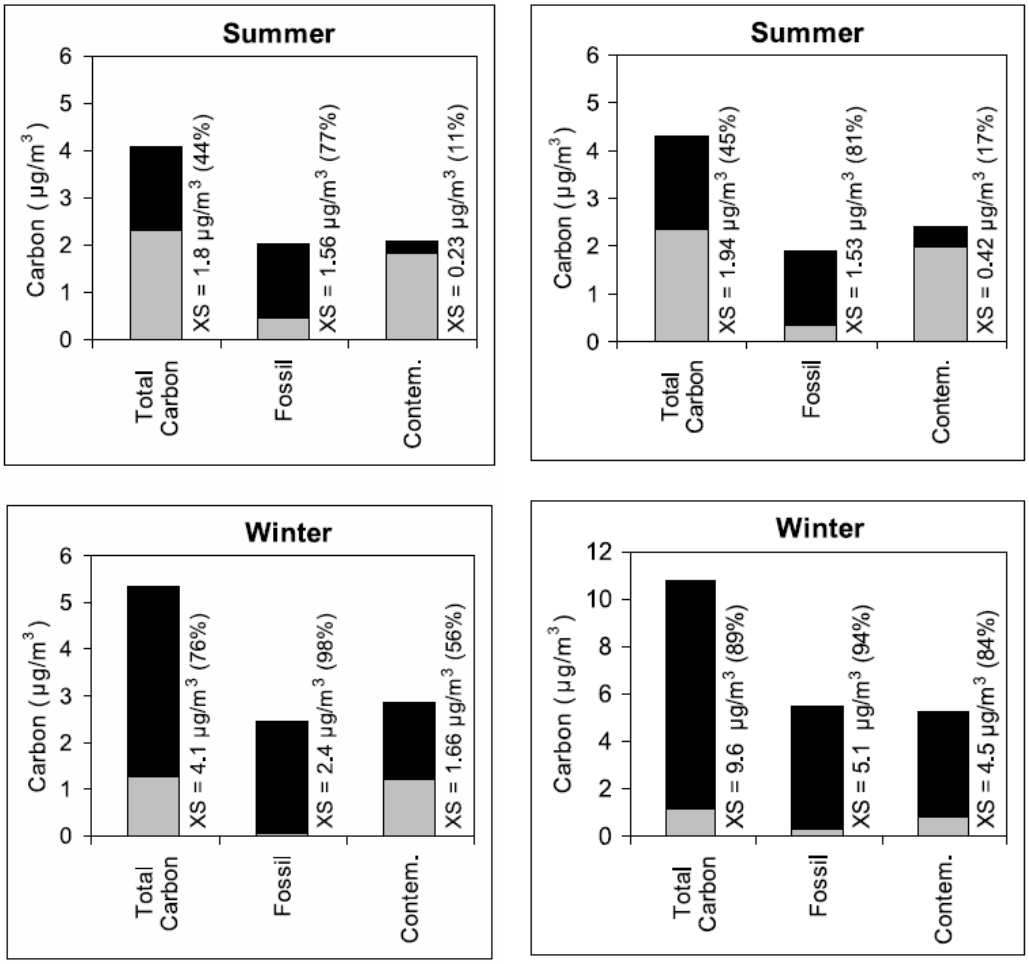
Source: From the TSS website, see Table 9-1.

Figure 9-35. Monthly averaged model predicted organic mass concentration apportioned into primary PM and anthropogenic and biogenic secondary PM categories for the Badland NP (top) and Salt Creek W (bottom) monitoring sites.

Radiocarbon (^{14}C) dating techniques were used to group ambient PM carbon into fossil and contemporary source categories at 12 IMPROVE monitoring sites across the U.S., 8 of which are in the WRAP region (Schichtel et al., 2008, 156958). Results of this work showed that contemporary carbon accounts for about half the carbon in urban areas, 70-97% in near-urban areas (i.e., San Gorgonio) and 82-100% in remote areas. Comparing these radiocarbon dating results with the WRAP virtual tracer modeling results for organic aerosol (above), and presuming that the modeled anthropogenic secondary organic is fossil carbon and the biogenic secondary is contemporary carbon, suggests that a large fraction of the model-determined regional primary organic PM is from contemporary carbon sources (e.g., smoke from wildfires).

Schichtel et al. (2008, 156958) compared radiocarbon measurements at two sets of urban/rural paired sites in the west (Mount Rainer/Seattle, and Tonto/Phoenix). Figure 9-36 shows that most of total carbon urban excess (i.e., urban site concentration minus the regional site concentration) in the summer is from fossil carbon sources (87% and 79%, respectively), while in the winter there is a surprisingly high fraction of the urban excess at both sites that is from contemporary carbon sources (41% and 47%, respectively). This implies that urban, and therefore anthropogenic, activities

generate almost as much $PM_{2.5}$ carbon from contemporary sources (e.g., residential wood combustion) as from the fossil sources during the winter for these two western urban areas.



Source: Reprinted with Permission of the American Geophysical Union from Schichtel et al. (2008, 156958).

Figure 9-36. Comparison of carbon concentrations between Seattle (Puget Sound site) and Mt. Rainer (left) and between Phoenix and Tonto (right) showing the background site concentration (gray) and the urban excess concentration (black) for total, fossil and contemporary carbon during the summer and winter studies.

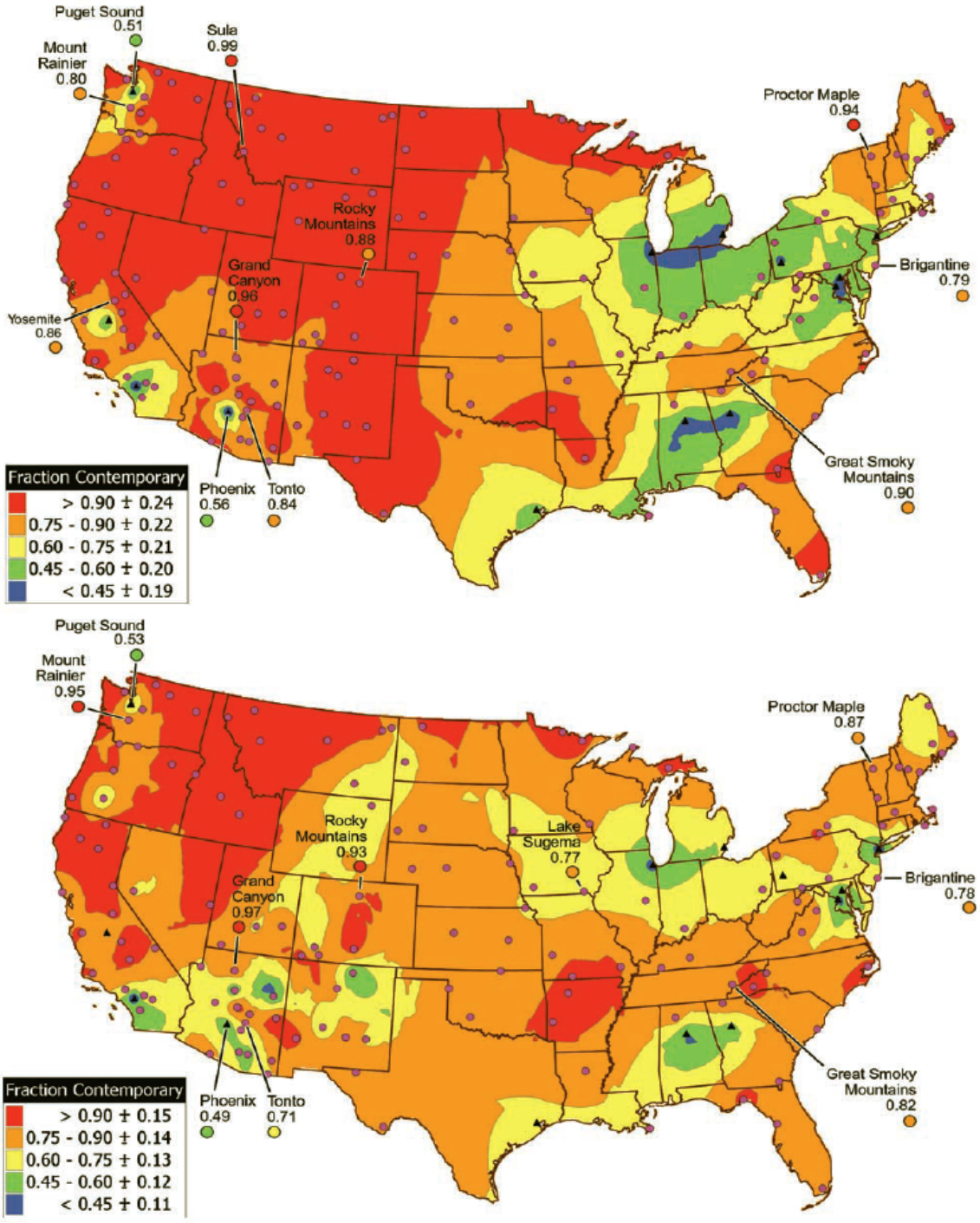
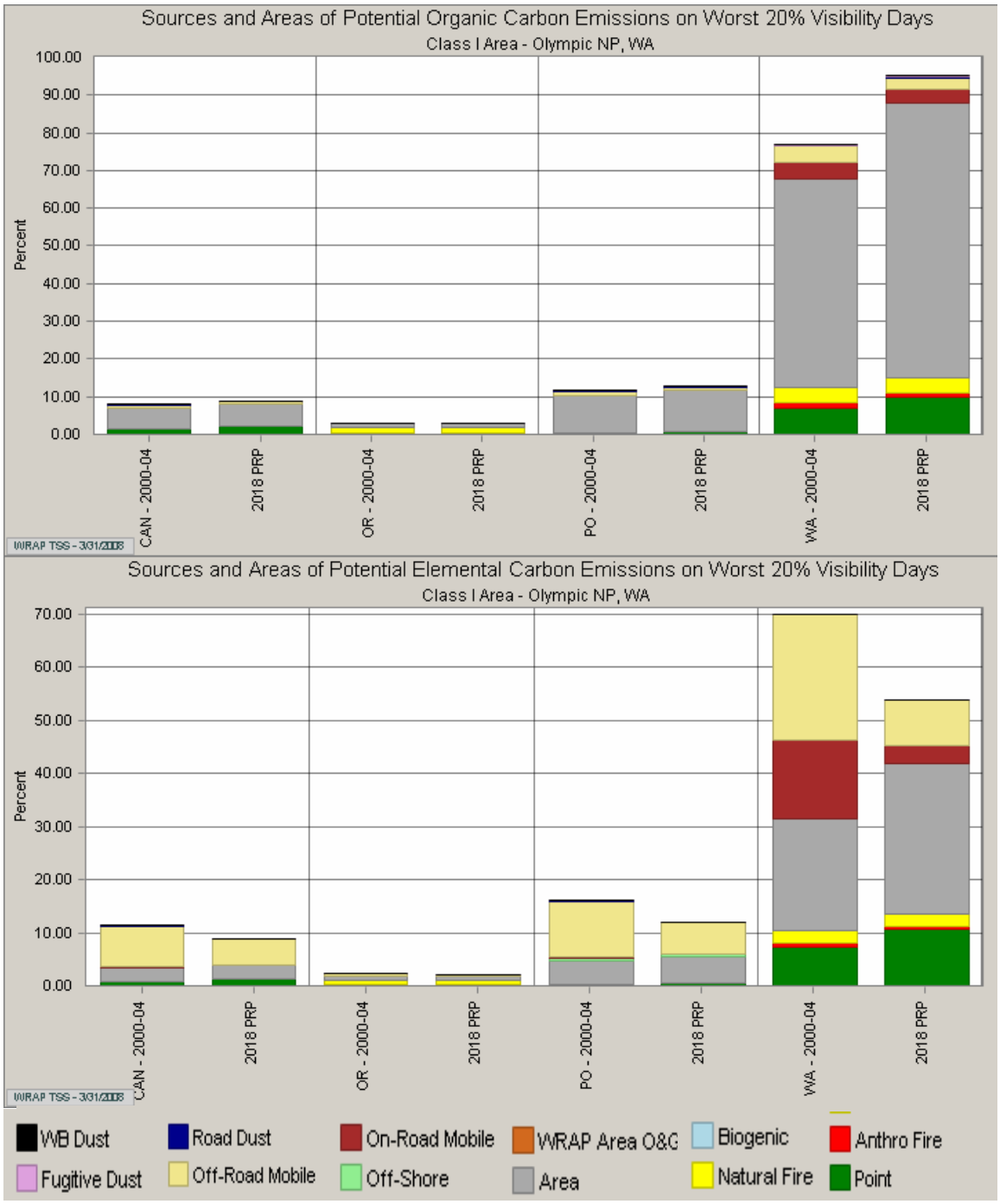


Figure 9-37. Average contemporary fraction of $PM_{2.5}$ carbon for the summer (top) and winter (bottom), estimated from IMPROVE monitoring data (June 2004-February 2006) based on EC/TC ratios. The contemporary values from radiocarbon dating for the 12 monitoring sites are indicated in by colored circles with the site names. Color contours are shown to aid in showing sites with similar values. Site locations are indicated by circles for remote area sites and triangles for urban sites.

Contemporary carbon estimates for all of the IMPROVE network monitoring sites for data from two summer seasons (June, July and August, 2004/2005) and two winter seasons (December, 2004/2005, January and February, 2005/2006) were calculated from the measured EC to total carbon (EC/TC) ratios using the 12-site empirical relationship between radiocarbon determined contemporary carbon fraction and IMPROVE measured EC/TC ratio (Schichtel et al., 2008, 156958). The results are displayed in color contour maps in Figure 9-37, which also shows the radiocarbon determined contemporary carbon for the 12 sites. The lowest contemporary carbon estimates (<60%) in both seasons are for urban areas. In the rural West, most of the sites have over 90% of their PM carbon from contemporary carbon sources during the summer and from 60% to over 90% during the winter. In the rural East, most of the sites have 45-90% of their PM carbon from contemporary carbon sources during the summer and from 60% to over 90% in the winter.

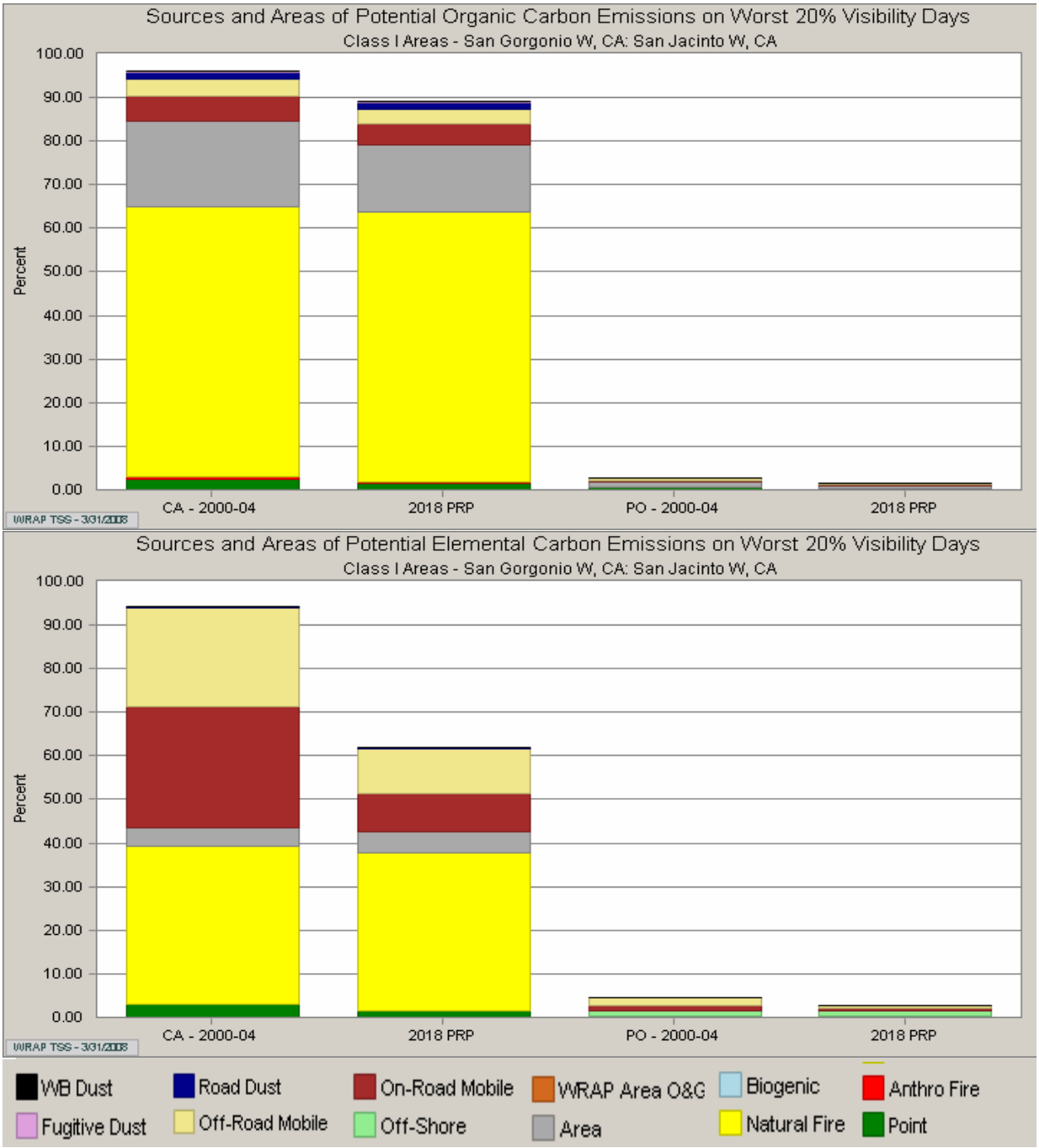
Schichtel et al. (2008, 156958) showed a strong relationship between the site-averaged EC/TC ratios and the site-averaged fraction of fossil carbon separately for the summer and winter data sets (i.e., R^2 of 0.71 and 0.87, respectively). Using regression analysis they estimated that the summer and winter EC/TC ratios associated with purely fossil carbon were 0.35 ± 0.039 and 0.46 ± 0.028, respectively, and for purely contemporary carbon the EC/TC ratios were 0.12 ± 0.011 and 0.19 ± 0.0095. These ratios are shown to be consistent with corresponding ratios from the literature for source testing primary fossil and contemporary combustion sources respectively. They are also shown to be consistent with the 90 percentile value of the EC/TC ratio from the urban IMPROVE monitoring sites (0.41 and 0.44 for summer and winter) and the 10th percentile values of the EC/TC ratio for remote areas IMPROVE monitoring sites (0.07 and 0.16 for summer and winter), which they argue are dominated by fossil and contemporary carbon, respectively.

The largest sources of contemporary carbon are primary emissions from biomass burning and SOA from biogenic precursor gases (e.g., terpenes from conifer forests). Schichtel et al. (2008, 156958) estimated the 12-site overall contribution by secondary organic PM to the summer contemporary carbon fraction as 36 ± 6.4% by assuming the EC/TC ratio for contemporary carbon during the winter represented the ratio of primary emissions only (i.e., no secondary organic PM formation in the winter) and that the EC/TC ratio for primary emissions is independent of seasons. This approach should provide a lower bound estimate of the secondary OC species. The same method applied to the fossil carbon fraction yielded an estimate of 23 ± 10% of the fossil carbon PM from secondary organic formation in the atmosphere during the summer. These estimates correspond to over 40% of the contemporary and over 35% of the fossil OC being from secondary PM formation.



Source: From the TSS website (see Table 9-1)

Figure 9-38. Results of the weighted emissions potential tool applied to primary OC emissions (top) and EC emissions (bottom) for the baseline and projected 2018 emissions inventories for Olympic NP. Only source regions (WRAP states and other regions) with the largest estimated contributions are shown (i.e., Canada, Oregon, Pacific Off-Shore, and Washington from left to right). The scale is normalized (i.e., unitless) one over distance weighted emissions multiplied by trajectory residence time.



Source: From the TSS website (see Table 9-1).

Figure 9-39. Results of the weighted emissions potential tool applied to primary OC emissions (top) and EC emissions (bottom) for the baseline and projected 2018 emissions inventories for San Gorgonio W. Only source regions (WRAP states and other regions) with the largest estimated contributions are shown (i.e., California and Pacific Off-Shore from left to right). The scale is normalized (i.e., unitless) one over distance weighted emissions multiplied by trajectory residence time.

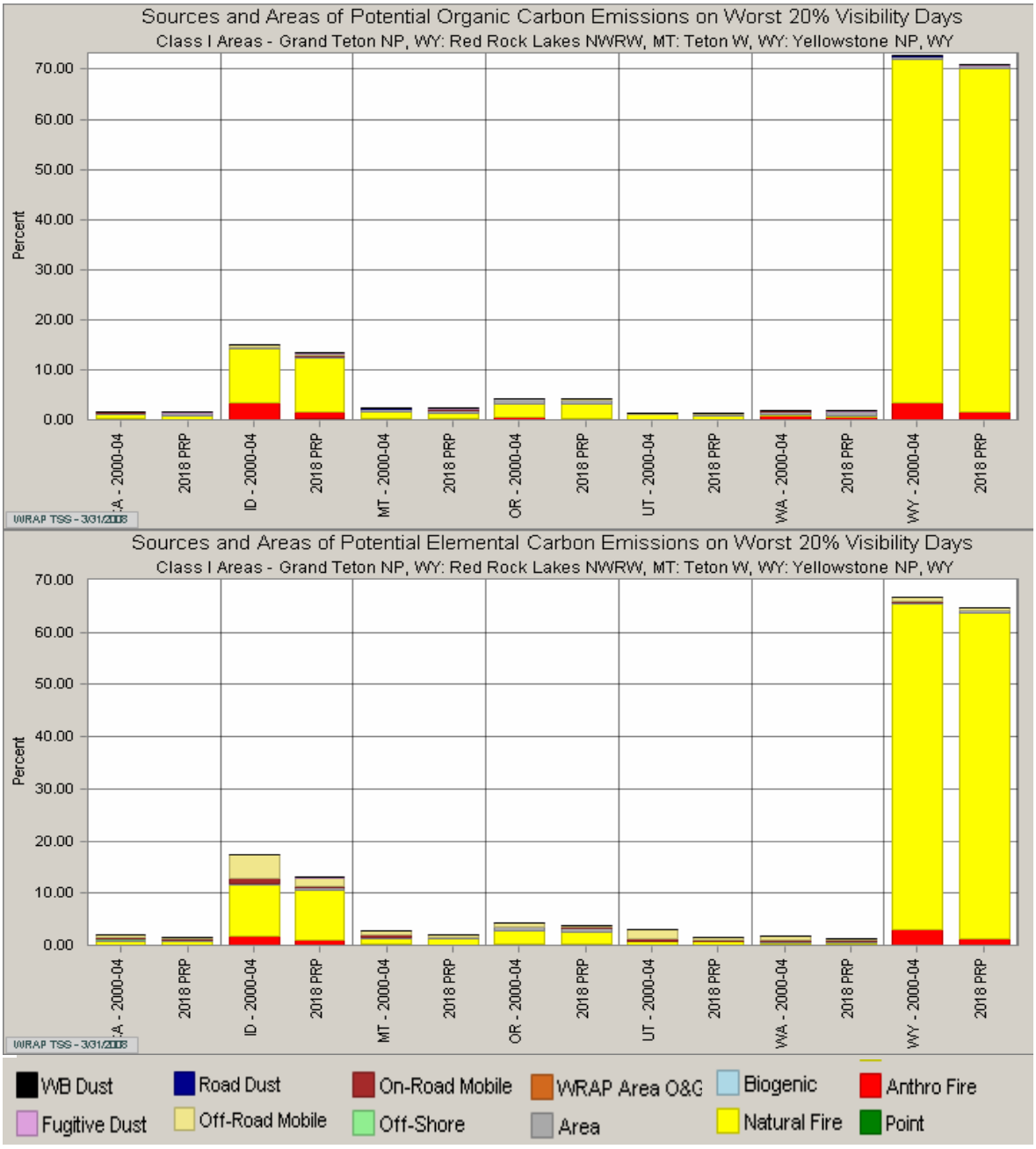
WRAP applied a weighted emissions potential analysis tool that combined gridded emissions data with back-trajectory analysis that simulated the transport pathway to the various monitoring sites to infer likely source region and emission categories for the 20% best and 20% worst haze conditions for each of the IMPROVE PM speciation monitoring locations in the West. Unlike the virtual tracer approach that uses a full regional air quality simulation model, this method does not explicitly account for chemistry or removal processes and it does not incorporate the sophisticated dispersion estimates (i.e., it uses one over distance weighting for dispersion), so it should be considered a screening tool that has been found to be helpful in identifying the likely sources contributing to haze. More information on this approach is available elsewhere (see the link to the TSS in Table 9-1). Primary OC and EC PM species results from the weighted emissions potential tool for the worst 20% haze days using the 2000-2004 base years' emissions and trajectories, and the same trajectories with 2018-projected emissions for each of the 6 selected western monitoring locations are shown in Source: From the TSS website (see Table 9-1)

Figure 9-38 through Figure 9-43.

For Olympic NP (Source: From the TSS website (see Table 9-1)

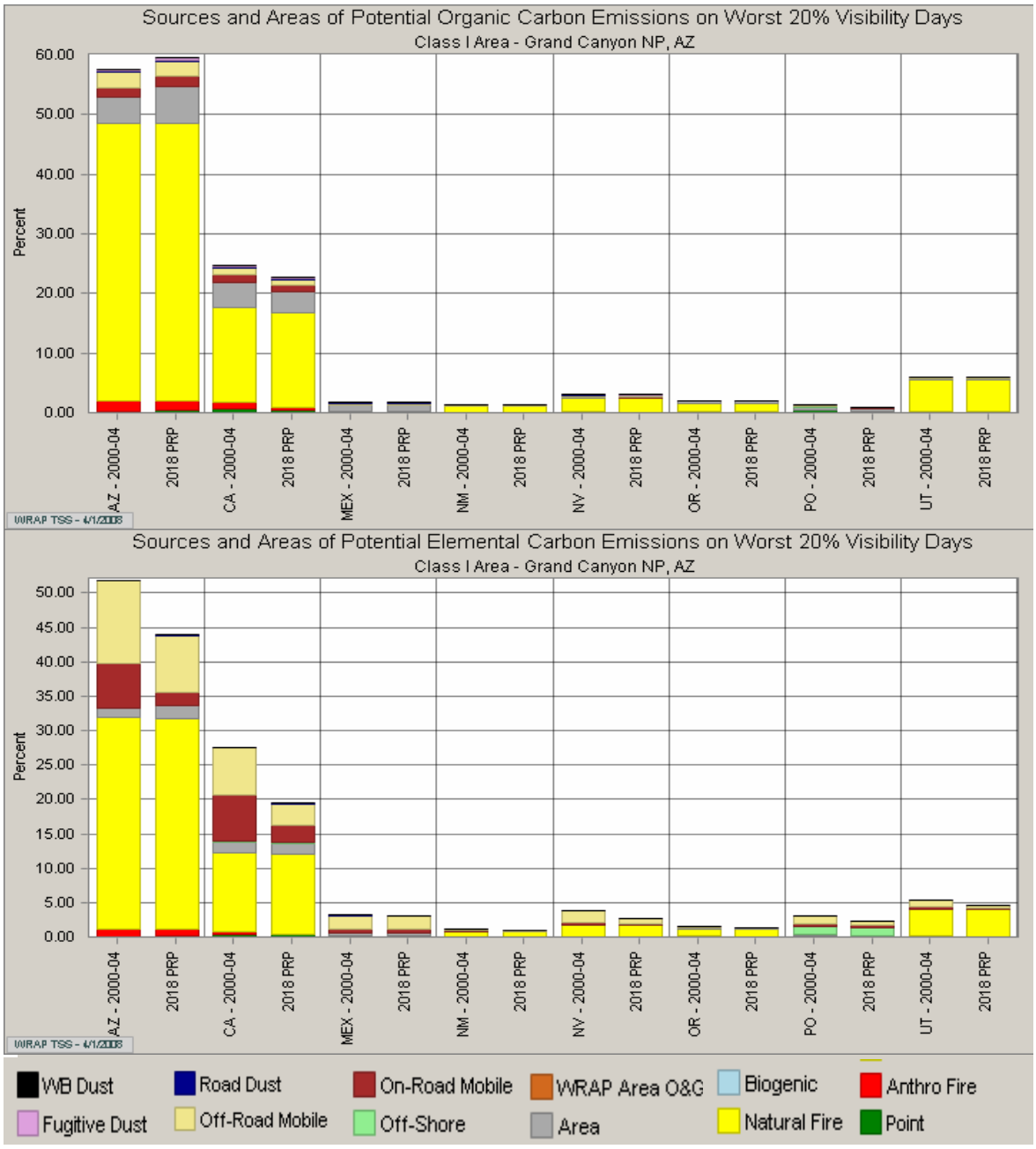
Figure 9-38), most of the primary OC as well as most of the EC PM is likely to be from the state of Washington during the worst haze days. This is because the multi-day trajectories that transport emissions on its worst days tend to be short (within 200 km based on maps available on TSS, see Table 9-1). Area sources, which include emissions from residential wood heating, watercraft, non-mobile urban and other sources too small to be labeled as point sources, are the big contributors to primary organic, while on- and off-road mobile emissions plus area sources are large contributors to the EC at Olympic NP. The 2018 projected growth in area sources and decrease in emissions of mobile source emissions is anticipated to increase the haze by primary OC while reducing the haze by EC at Olympic NP The same analysis applied to San Gorgonio (Figure 9-39), is similar in that the majority of the emissions with the potential to contribute to primary OC and EC PM is from the home state, California in this case. However, the likely importance of natural fire emissions for carbonaceous PM species sites is substantially greater at San Gorgonio W. than it was for Olympic NP.

The weighted emissions potential results applied to Yellowstone NP and Grand Canyon NP (Figure 9-40 and Figure 9-41) show the likely dominance of natural fire emissions in the intermountain western U.S. to primary OC and EC PM during worst haze conditions for these two locations. Numerous states have emissions that have the potential to contribute noticeably to these carbonaceous species, due to relatively long multi-day trajectories (500-1,000 km) on worst haze days, though for both sites the home state has the greatest potential based on this inverse distance weighting approach. On- and off-road mobile sources in Arizona and California have significant potential to contribute to Grand Canyon carbonaceous particles, especially EC concentrations, probably due to some of the trajectories being over the populated areas of these two states to the south and southwest of Grand Canyon.



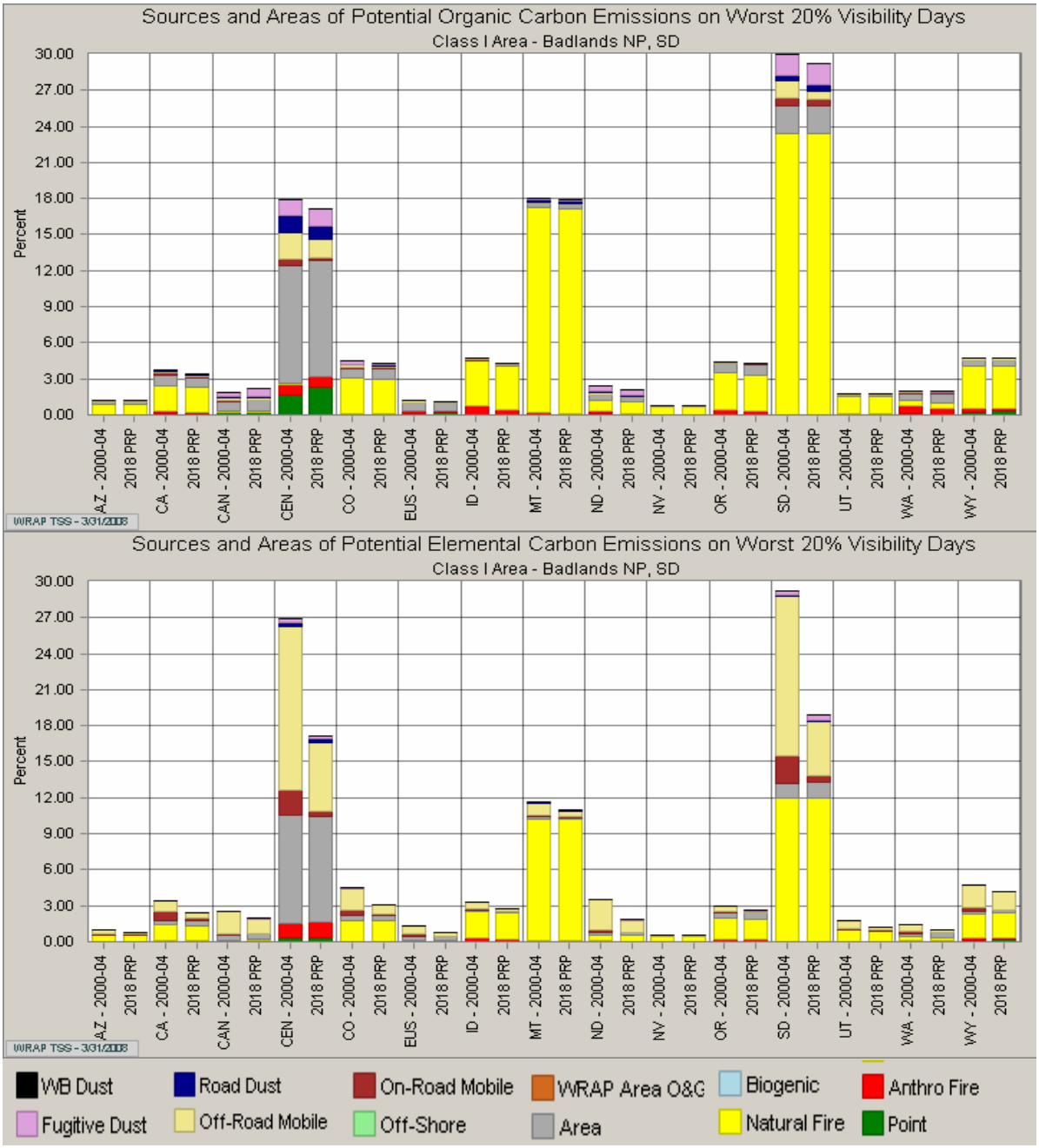
Source: From the TSS website (see Table 9-1).

Figure 9-40. Results of the weighted emissions potential tool applied to primary OC emissions (top) and EC emissions (bottom) for the baseline and projected 2018 emissions inventories for Yellowstone NP. Only source regions (WRAP states and other regions) with the largest estimated contributions are shown (i.e., California, Idaho, Montana, Oregon, Utah, Washington, and Wyoming from left to right). The scale is normalized (i.e., unitless) one over distance weighted emissions multiplied by trajectory residence time.



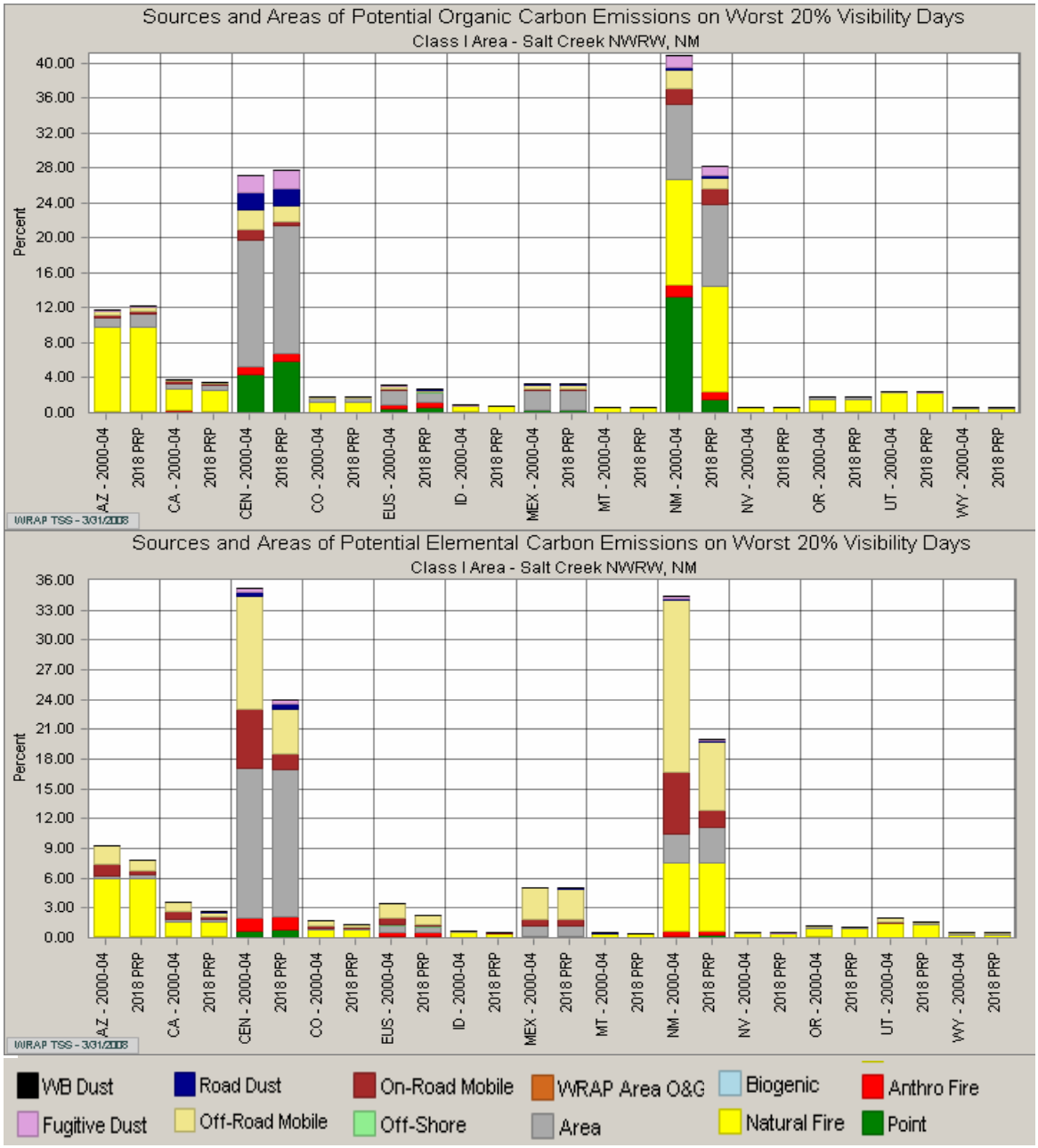
Source: From the TSS website (see Table 9-1).

Figure 9-41. Results of the weighted emissions potential tool applied to primary OC emissions (top) and EC emissions (bottom) for the baseline and projected 2018 emissions inventories for Grand Canyon NP. Only source regions (WRAP states and other regions) with the largest estimated contributions are shown (i.e., Arizona, California, Mexico, New Mexico, Nevada, Oregon, Pacific Off-shore and Utah from left to right). The scale is normalized (i.e., unitless) one over distance weighted emissions multiplied by trajectory residence time.



Source: From the TSS website (see Table 9-1).

Figure 9-42. Results of the weighted emissions potential tool applied to primary OC emissions (top) and EC emissions (bottom) for the baseline and projected 2018 emissions inventories for Badlands NP. Only source regions (WRAP states and other regions) with the largest estimated contributions are shown (i.e., Arizona, California, Canada, CenRAP, Colorado, eastern U.S., Idaho, Montana, North Dakota, Nevada, Oregon, South Dakota, Utah, Washington, and Wyoming from left to right). The scale is normalized (i.e., unitless) one over distance weighted emissions multiplied by trajectory residence time.



Source: From the TSS website (see Table 9-1).

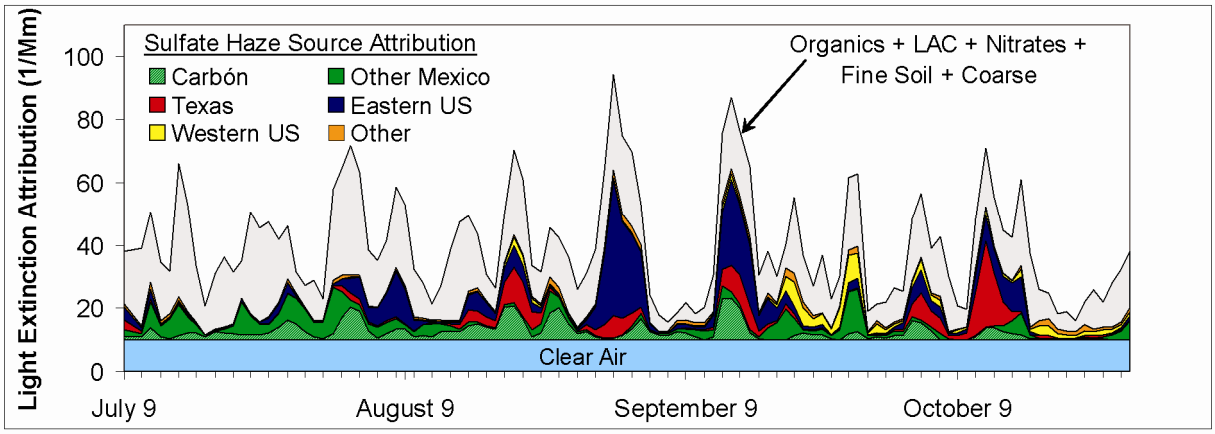
Figure 9-43. Results of the weighted emissions potential tool applied to primary OC emissions (top) and EC emissions (bottom) for the baseline and projected 2018 emissions inventories for Salt Creek W. Only source regions (WRAP states and other regions) with the largest estimated contributions are shown (i.e., Arizona, California, CenRAP, Colorado, eastern U.S., Idaho, Mexico, Montana, New Mexico, Nevada, Oregon, Utah, and Wyoming from left to right). The scale is normalized (i.e., unitless) one over distance weighted emissions multiplied by trajectory residence time.

For the most easterly of the selected WRAP sites, Badlands NP and Salt Creek, the weighted emissions potential results for primary OC and EC (Figure 9-42 and Figure 9-43) show potential contributions from a greater number of states and multi-state regions than for selected sites further to the west. This may be due in part to trajectories associated with worst haze conditions for these two sites being moderately long (~500 km) and in multiple directions. Natural fire emissions have the greatest potential to contribute to organic species PM at Badlands NP, but are less likely to be dominant at Salt Creek or at either site in its contribution to EC PM concentrations. The contributions by emissions from area and mobile sources from the home states and states to the east (Central States Regional Air Partnership states are labeled "CEN" in the figures) are potentially greater than by natural fire; this is especially true for contributions to EC PM.

WRAP applied the weighted emissions potential tool to assess likely source types and regions contributing to coarse mass concentrations. The results for the six selected monitoring sites (not shown) are as follows. Most dust at Olympic NP is likely to be from fugitive dust sources in Washington state, while at San Gorgonio it is likely more from road dust with smaller amounts from fugitive dust sources. The amount from wind-blown dust is small for both of these far westerly sites. Wind-blown dust is likely the largest source contributing to coarse mass at Grand Canyon NP, Badlands NP and Salt Creek W with most of it originating in the home-state for those sites. The weighted emissions potential results for coarse mass at Yellowstone are different from those of the other five selected sites in that Idaho and Montana each have a higher potential to contribute to coarse mass on the worst haze days than the home state (Wyoming), and that wind-blown and road dust both contribute substantially as does fugitive dust and natural fire.

In another WRAP-sponsored effort to better understand the causes of remote area haze in the western U.S., each of the worst haze days for all western IMPROVE monitoring sites where dust (defined as the sum of coarse mass and fine soil PM) was the largest contributor to light extinction was separately assessed to categorize the most likely dust source (Kavouras et al., 2007, 156630; Kavouras et al., 2009, 191976) and the Causes of Haze Website – see Table 9-1). Elemental composition was used to assess the likelihood that the dust was associated with long-range transport from Asia. A regression analysis at each site between dust concentrations and coincident local wind speed was used to generate site-specific estimates of local windblown dust for each sample period. Finally, back trajectory analysis combined with maps constructed of wind erosion potential (i.e., developed by combining soil types and land cover classifications) are used in a manner similar to the weighted emissions potential analysis to identify the likelihood of regionally transported wind-blown dust as the source. These assessments were conducted on each of the 610 so-called "worst dust haze days" at 70 monitoring sites for data from 2001-2003 to classify each day by its likely contributions from Asian dust, local windblown dust, upwind transport and undetermined. The undetermined category includes those sample periods that failed to be classified into one of the other three source categories suggesting that mechanically suspended dust activities (e.g., unpaved road dust, agricultural, construction and mining activities) may be responsible.

Of the 610 "worst dust haze days" at the 70 WRAP monitoring sites, 55 sample periods are classified as Asian dust influenced, almost exclusively in the spring; 201 sample period are classified as local windblown dust, mostly in the spring but some in all seasons; 240 sample periods are classified as upwind transported dust, with a broader seasonal distribution centered on summer and few instances during winter; and 114 are in the undetermined category with most in summer and least in winter. Most dust days occurred in the deserts of Arizona, New Mexico, Colorado, western Texas and southern California, and these were dominated by local and regionally transported wind-blown dust (e.g., 84% for Salt Creek W). Asian dust caused only a few of the worst dust days during the 3-year assessment period, though it is an important source (i.e., 10-40% of the worst dust days) for sites in the more northern regions of the West with greater vegetative land-cover where local and regionally transported wind-blown dust was infrequent. The frequency of worst dust events classified as undetermined was greatest for sites in the vicinity of large urban and agricultural areas such as those in California and southern Arizona.



Source: Reprinted with Permission of the Air & Waste Management Associaiton from Pitchford et al. (2005, 156874)

Figure 9-44. BRAVO study haze contributions for Big Bend NP, TX during a 4-mo period in 1999. Shown are impacts by various particulate SO_4^{2-} sources, as well as the total light extinction (black line) and Rayleigh or clear air light scattering.

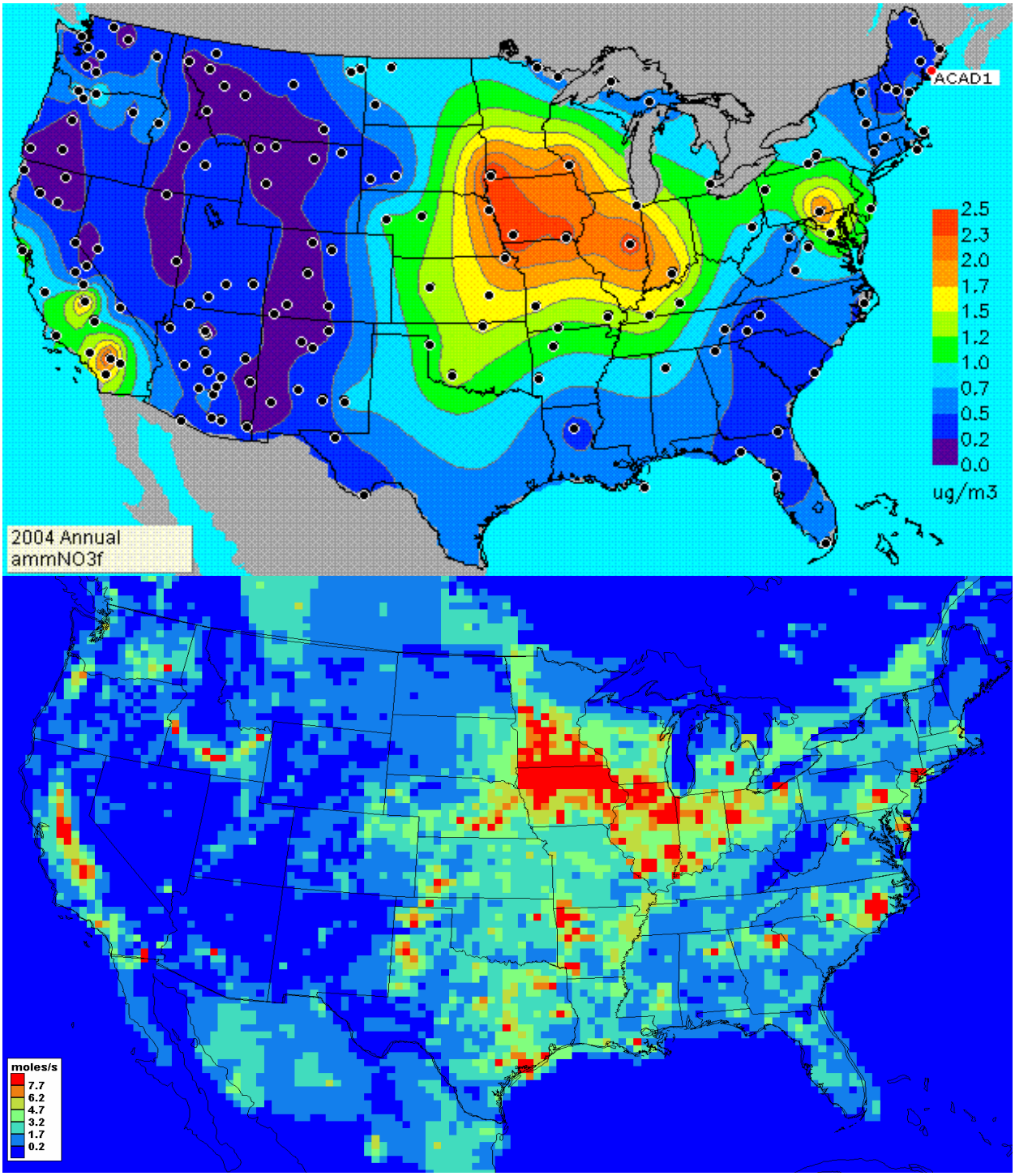


Figure 9-45. Maps of spatial patterns for average annual particulate nitrate measurements (top), and for ammonia emissions for April 2002 from the WRAP emissions inventory (bottom).

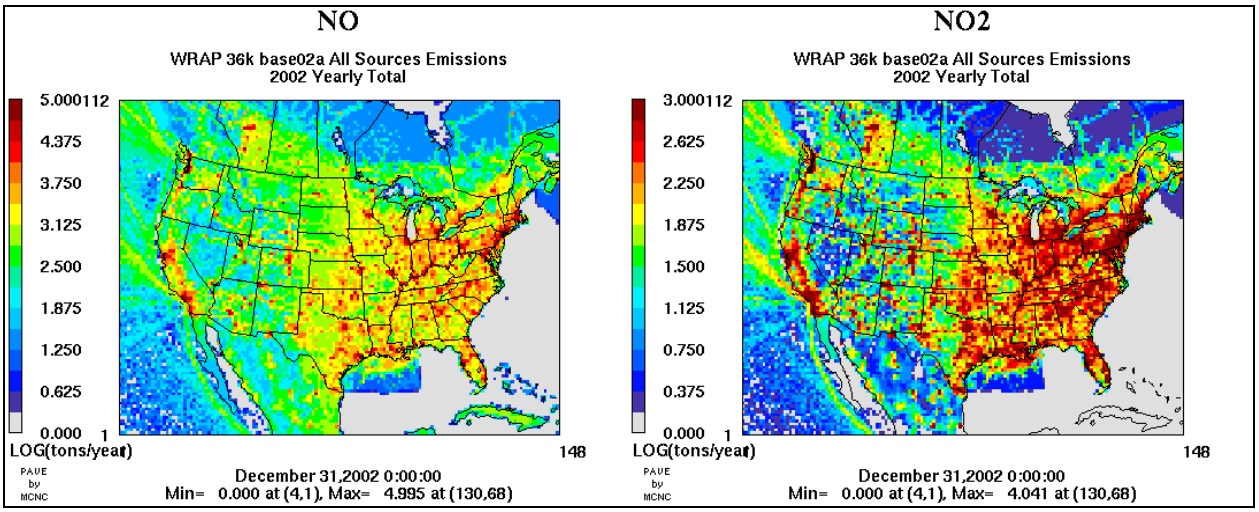


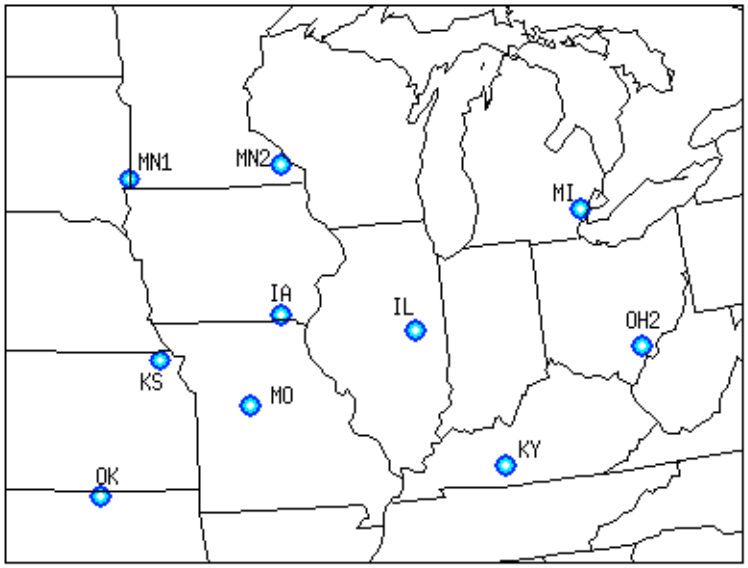
Figure 9-46. Maps of spatial patterns of annual NO (left) and NO_2 (right) emissions for 2002 from the WRAP emissions inventory.

Source attribution of the particulate SO_4^{2-} contribution to haze at Big Bend NP, TX was a primary motivation for the BRAVO study. Schichtel et al. (2005, 156957) showed that during the four-month field monitoring study (July-October 1999), SO_2 emissions sources in the U.S. and Mexico were responsible for ~55% and ~38% of the particulate SO_4^{2-}, respectively. Among U.S. source regions, Texas was responsible for ~16%, eastern U.S. ~30%, and the western U.S. ~9%. A large coal fired power plant, the Carbón facility in Mexico, just south of Eagle Pass, TX, was responsible for ~19%, making it the largest single contributor. Pitchford et al. (2005, 156874) put these results into the context of other component contributions to regional haze, plus seasonal and longer-term variations in haze by particulate components. Figure 9-44 shows the temporal variation of the contributions by the various SO_2 emissions source regions plus the Carbón facility during the BRAVO study period. The largest particulate SO_4^{2-} peak haze periods are dominated by infrequent large contribution by emission sources in TX and the eastern U.S., while Mexican sources including the Carbón facility are more frequent contributors to haze, but at generally lower light extinction values. Particulate nitrate contributions to haze at Big Bend NP are among the lowest measured in the U.S. (~3% of light extinction on average and for worst haze episodes).

Nitrate concentrations are a significant contributor to light extinction further to the north of Texas in the center of the country. While SO_4^{2-} can be in particulate form though not fully neutralized by ammonia, nitric acid from NO_X emissions requires neutralization by ammonium to become particulate ammonium nitrate. One way to explore the causes of the Midwest nitrate bulge is to compare its spatial distribution with the spatial distributions of NO_X and ammonia emissions. Figure 9-45 shows a map of the annual average particulate nitrate concentrations (top) with a map of ammonia emissions directly below it. Animal agriculture is responsible for most of the ammonia emissions in the Midwest. The striking similarity between the ambient particulate nitrate concentration and the ammonia emissions spatial patterns with regional maximum centered on Iowa is in contrast to the NO_X (i.e., NO + NO_2) emissions spatial patterns, shown in Figure 9-46. NO_X emissions are high over a broad region of the country associated with the larger population densities and greater numbers of fossil fuel electric generation plant generally to the east of the Midwest nitrate bulge. While both ammonia and nitric acid are needed to form particulate ammonium nitrate, the maps suggest the Midwest nitrate bulge is due primarily to the abundance of free ammonia (i.e., the amount beyond what is required to neutralize the acidic particulate SO_4^{2-}). By contrast, the region to the east of the Midwest nitrate bulge should have plenty of nitric acid given the higher emissions of NO_X, but apparently has a deficiency of free ammonia. The few eastern monitoring sites with locally high particulate nitrate (near southeastern PA) are located within a small region of high density animal agriculture that shows up as a high ammonia emissions region in Figure 9-45. Note that California's South Coast and Central Valley have both high ammonia and high NO_X emissions, explaining the high particulate nitrate contribution to haze there.

To better understand the role of ammonia in the formation of the Midwest nitrate bulge, the Midwest RPO and Central States Regional Air Partnership deployed a measurement program from late 2003 through early 2005 at 10 locations (9 rural and 1 urban) in the region (see Figure 9-47) to monitor particulate SO_4^{2-}, nitrate, and ammonium ions, plus the precursor gases sulfur dioxide, nitric acid, and ammonia (Kenski et al., 2004, 192078; Sweet et al., 2005, 180038). These data have been used as input for thermodynamic equilibrium modeling to assess the changes in PM concentrations that would result from changes to precursor concentrations (Blanchard and Tanenbaum, 2006, 190005; Blanchard et al., 2007, 098659). Blanchard and Tanenbaum (2006, 190005) and Blanchard et al. (2007, 098659) conclude that the current conditions at nine of the ten sites are near the point of transition between the precursor species (nitric acid and ammonia) that limits the formation of particulate nitrate. If excess ammonia increases, either by greater ammonia emissions or by anticipated decreases in SO_2 emissions, then nitric acid concentration would need to be reduced (via lower NO_X emissions) in order to reduce the particulate nitrate concentration.

Given the comparability of particulate SO_4^{2-} and nitrate with regard to their light extinction efficiencies, their visibility impacts are proportional to the sum of their mass concentrations. A reduction in SO_4^{2-} caused by SO_2 emission reductions would reduce the particulate SO_4^{2-} concentration, though according to the thermodynamic equilibrium modeling for these sites the particulate nitrate concentration will be increased somewhat. However, the total particulate SO_4^{2-} plus nitrate concentration would be reduced so visibility impacts would be decreased. At current ammonium concentrations the predicted response of changes to SO_4^{2-} and nitric acid concentrations (i.e., SO_2 and NO_X emissions changes) are similar in respect to the resulting magnitude of changes to the total particulate SO_4^{2-} plus nitrate concentrations. At all but two sites the total particulate SO_4^{2-} plus nitrate concentrations would decrease if either ammonia or nitric acid where reduced.

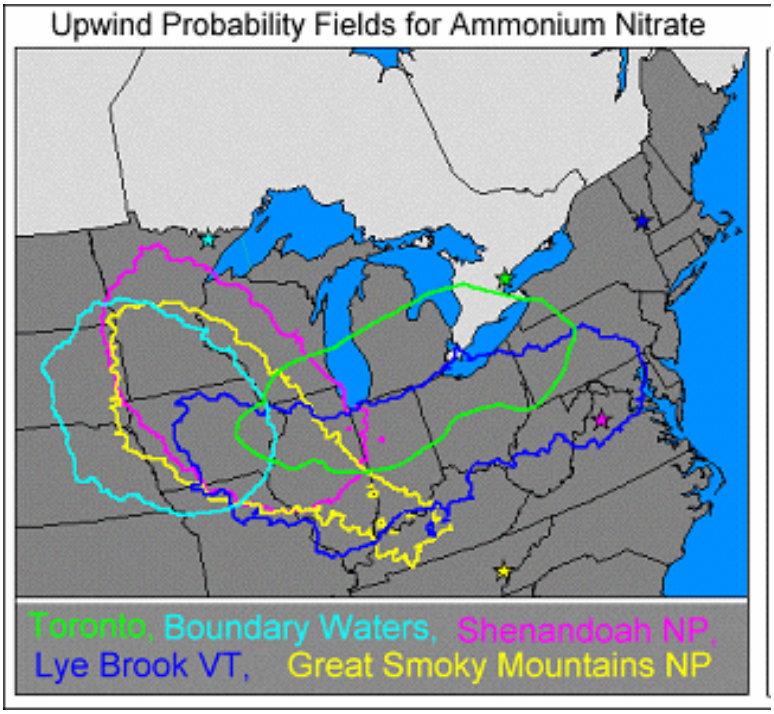


Source: Kenski et al. (2004, 192078)

Figure 9-47. Midwest ammonia monitoring network.

A further degree of complications in understanding the response of particulate nitrate to changes in precursor concentrations results from the temperature and humidity dependence of the partition between particulate ammonium nitrate and the disassociated gaseous nitric acid and ammonia. This dependence causes seasonal and even diurnal differences in the expected responses of particulate nitrate concentrations to changes in precursor concentrations. As expected, during the colder times of the year the total particulate concentrations are more sensitive to changes in ammonia and nitric acid concentrations than during the warmer seasons when SO_4^{2-} concentrations are greater.

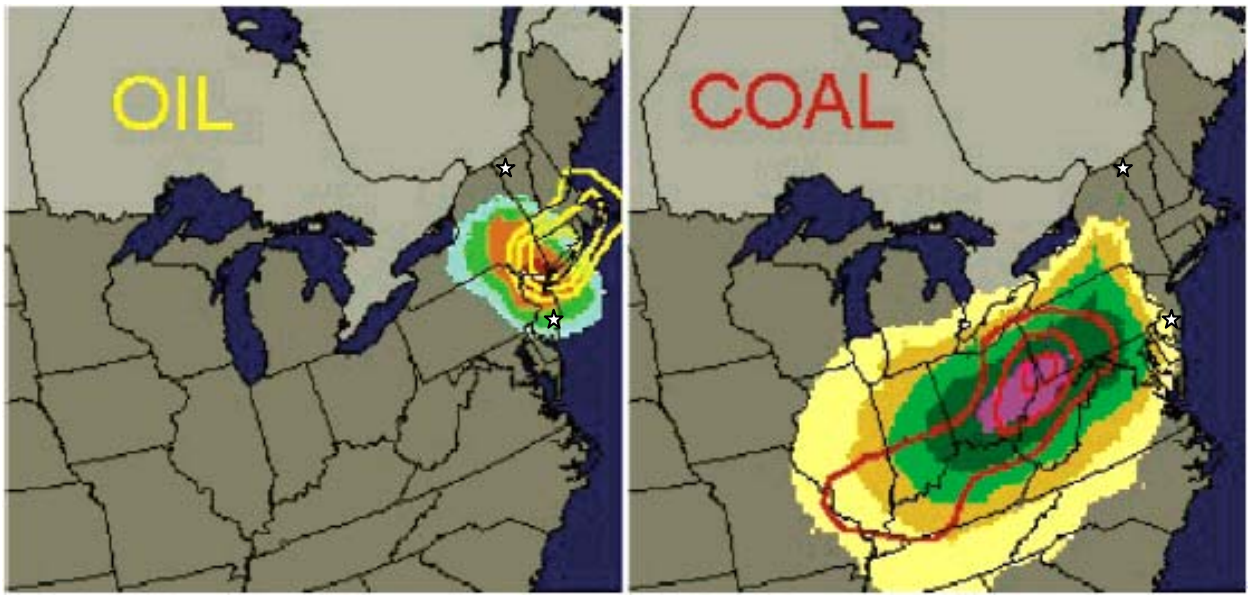
As shown in Figure 9-48, results of an air transport assessment to identify emission source areas associated with high particulate nitrate at five monitoring locations in the East (four remote-area sites and Toronto, Canada) implicate the high ammonia emissions region of the Midwest as a common source region (Canada-US Air Quality Committee, 2004, 190519). This assessment does not preclude local sources of the precursor gases responsible for particulate ammonium nitrate, but does suggest that long-range transport of particulate nitrate or ammonia from the high emissions region of the Midwest is also contributing to eastern nitrate episodes.



Source: Canada-U.S. Air Committee (2004, 190519).

Figure 9-48. Upwind transport probability fields associated with high particulate nitrate concentrations measured at Toronto, Canada; Boundary Water Canoe Area, MN; Shenandoah NP, VA; Lye Brook, VT; and Great Smoky Mountains NP, TN.

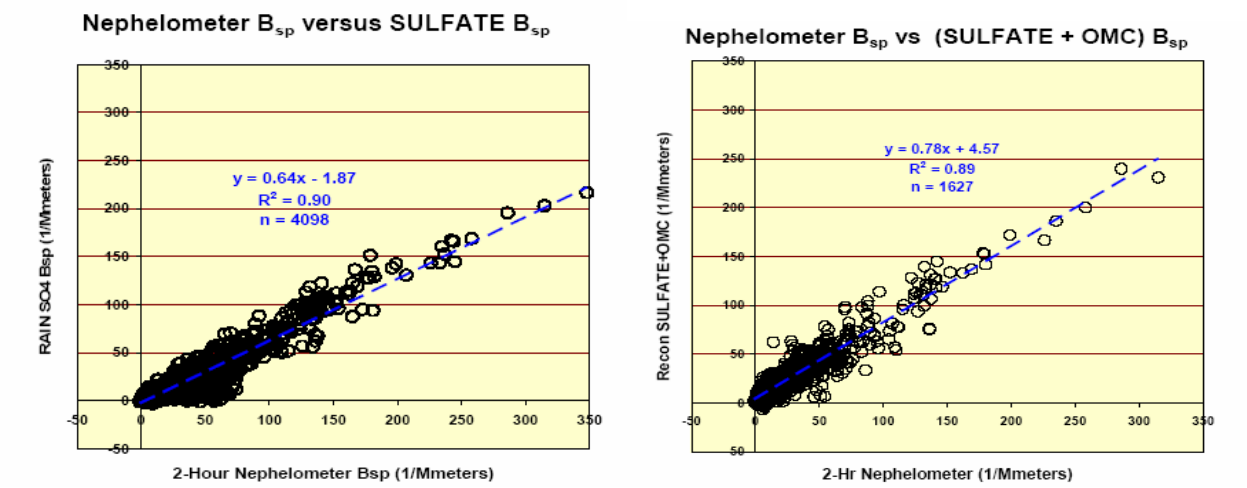
In a similar air transport assessment for measurements at Underhill, VT and at Brigantine, NJ, Hopke et al. (2005, 156567) identified separate regions associated with particulate SO_4^{2-} accompanied by trace particulate components associated with coal burning (e.g., Se) and accompanied by trace particulate components associated with oil burning (e.g., V). As shown in Figure 9-49, the coal-burning related particulate SO_4^{2-} for these two monitoring sites is associated with long-range transport from the Ohio River Valley, while oil-burning related particulate SO_4^{2-} is from more nearby emissions in the high population region of coastal New York, New Jersey, Massachusetts, and Connecticut.



Source: Reprinted with Permission of Environmental Science and Technology from Hopke, et al. (2005, 156567).

Figure 9-49. Trajectory probability fields for periods with high particulate SO_4^{2-} measured at Underhill, VT and Brigantine, NJ (shown as white stars) associated with oil-burning trace components (left) and with coal-burning trace components (right). Shown for comparison are the interpolated SO_2 emissions areal density contours for oil combustion sources (emissions times 10) and coal combustion sources, displayed as yellow and red contour lines, respectively.

The Regional Aerosol Intensive Network (RAIN) was established by MANE-VU to generate enhanced continuous visibility, plus fine particle mass and composition monitoring data at a string of three monitoring locations along the transport path from the Ohio River Valley to coastal Maine (NESCAUM, 2006, 156802). The dominant role of particulate SO_4^{2-} in the northeast is well demonstrated by a scatter plot of RAIN data that shows the relationship between particulate SO_4^{2-} extinction, calculated using the IMPROVE algorithm plotted against directly measured particle light scattering for hourly data over a 8-mo period, beginning in July 2004 at the Acadia NP, ME monitoring site (see Figure 9-50). Particulate SO_4^{2-} explains 90% of the variance in particulate light scattering even though it is responsible for only about 64% of the total light extinction (annual averaged value from the VIEWS web site). Adding the contribution by the second-largest regional contributor to light extinction, particulate OC with about 14%, does not improve the variance explained, but does increase the slope to 0.78. The noticeable difference between these two plots is that the particulate SO_4^{2-} alone underestimates light scattering during low haze periods (points on the plot are below the regression line for light scattering <70 Mm^{-1}), while the agreement is improved with the addition of particulate OC contributions to haze (regression slope is nearer to one and reduced bias for low haze periods). This implies that particulate SO_4^{2-} and any other co-varying PM species are largely responsible for the highly impacted periods, while OC and other co-varying PM species contribute more during the less extreme haze periods. Particulate nitrate contribution to light extinction at Acadia is about 10% on average.

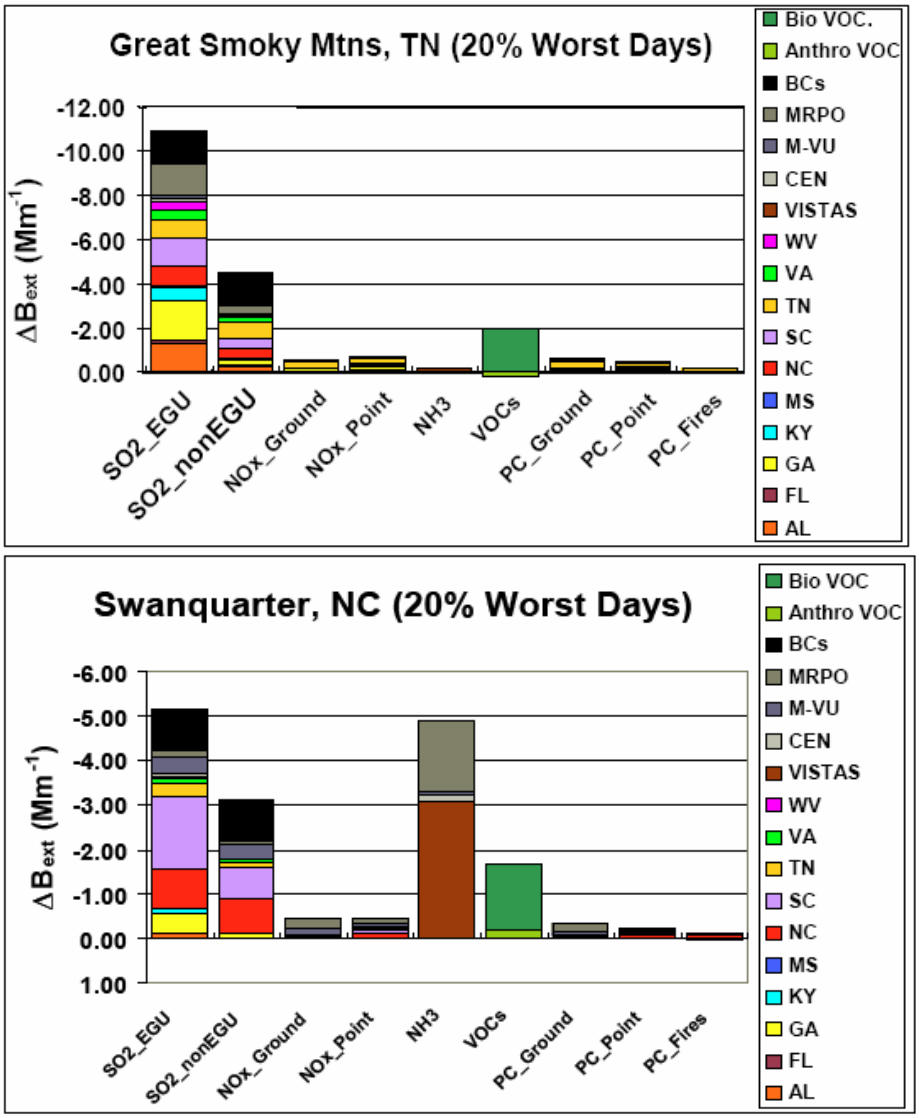


Source: RAIN Preliminary Data Analysis Report (NESCAUM, 2006, 156802)

Figure 9-50. Scatter plots of particulate SO_4^{2-} (left) and particulate SO_4^{2-} and organic mass (right) versus nephelometer measured particle light scattering for Acadia NP, ME.

Particulate nitrate concentrations are considerably lower in the SO_4^{2-}-dominated warmer southeastern U.S. than in the Northeast and upper Midwest. Blanchard et al. (2007, 098659) conducted thermodynamic equilibrium modeling on data from the eight SEARCH monitoring sites and found that total particulate nitrate plus SO_4^{2-} is much more responsive to changes in SO_2 concentrations than to changes in nitric acid concentrations, which in turn is more responsive than changes in ammonia concentrations.

The VISTAS RPO commissioned an emissions sensitivity study using CMAQ modeling on winter and summer 2009 emissions projected from the 2002 emissions inventory (NCDENR, 2007, 156798). Figure 9-51 contains bar plots for two North Carolina Class I areas that indicate projected changes in light extinction for the worst haze day due to 30% emissions reductions by particulate species, source types and location across the Southeastern states modeling domain (i.e., as far west as Texas, as far north as Pennsylvania, as far south as the Florida Keys, and as far east as ~300 km from the North Carolina coast). Great Smoky Mountains in the southern Appalachian Mountains has the greatest sensitivity to changes by SO_2 emissions from electrical generation units (EGU) and to a lesser extent other SO_2 emission sources in the region. Reductions of NO_X emissions from ground or point sources are not nearly as effective as SO_2 reductions in reducing the light extinction at Great Smoky Mountains. This is due principally to the worst days at Great Smoky Mountains occurring during the summer, when temperatures are too high to support high particulate nitrate concentrations. For the same reason, ammonia emission reductions are also ineffective. Swanquarter W, NC is a coastal location where some of the worst haze days are during the winter and include contributions from particulate ammonium nitrate. Both SO_2 and ammonia emissions reductions would be effective at reducing worst haze days at the Swanquarter W, though NO_X emissions are not as effective presumably because the atmosphere is ammonia-limited for particulate nitrate production.



Source: NCDENR (2007, 156798).

Figure 9-51. CMAQ air quality modeling projections of visibility responses on the 20% worst haze days at Great Smoky Mountains NP, NC (top) and Swanquarter W, NC (bottom) to 30% reductions. This is from a projected 2009 emission inventory of visibility-reducing pollutants by source category and geographic areas.

9.2.4. Urban Visibility Valuation and Preference

The Clean Air Act §302(h) defines public welfare to include the effects of air pollution on "…visibility, … and personal comfort and wellbeing." Though good visibility conditions in Class I (e.g., NPs) and wilderness areas have long been recognized as important to the public welfare (see discussions in EPA (2004, 056905; 2005, 090209) and Chestnut and Dennis (1997, 014525), visibility conditions in urban areas also contribute to the public welfare. Although visibility impairment may be caused by either natural or manmade conditions (or both), it is only impairment that occurs as a result of air pollution (either alone or in combination with water vapor or other atmospheric conditions) that can be mitigated by regulations such as the RHR (40 CFR 51.300 through 309) or the Secondary NAAQS. The term visual air quality (VAQ) is used here to refer to

the visibility effects caused solely by air quality conditions, so for example it excludes the reduced visibility caused by fog. Visibly poor air quality causes people to be concerned about substantive health risks, but degraded VAQ adversely affects people in additional ways. These include the aesthetic and wellbeing benefits of better visibility, improved road and air safety, and enhanced recreation in activities like hiking and bicycling. Because the human health impacts of air pollution are assessed under the Primary NAAQS, it is necessary to separate out these non-health components associated with the visibility condition produced by a given amount of air pollution when assessing the need for additional regulation to protect the public welfare effect of visibility under the Secondary NAAQS. The degree to which previous human preference and valuation studies for VAQ have adequately made this distinction and separation is an important issue in applying results from available studies in a Secondary NAAQS (or benefits estimation for any policy affecting VAQ) context. The remainder of this discussion is focused on those aesthetic and wellbeing qualities associated with a given VAQ in urban areas.

The term "urban visibility" is used to refer to VAQ throughout a city or metropolitan area. Urban visibility includes the VAQ conditions in all locations that people experience in their daily lives, including scenes such as residential streets and neighborhood parks, commercial and industrial areas, highway and commuting corridors, central downtown areas, and views from elevated locations providing a broad overlook of the metropolitan area. Thus urban visibility includes VAQ conditions in major cities and smaller towns and encompasses all the VAQ an individual resident sees on a regular basis. Visibility conditions in urban and suburban locations are therefore distinct from visibility in rural or wilderness settings such as the Class 1 areas defined by the Clean Air Act, which include NPs and similar natural settings.

Visibility has direct significance to people's enjoyment of daily activities and their overall wellbeing. Visibility conditions can be described both as an aesthetic quality as well as a scientifically measurable set of atmospheric conditions. Due to the subjective nature of aesthetics, people's preferences with respect to visibility are difficult to express or quantify, but people have expressed in many different ways that they enjoy and value a clear view. A number of social science studies have been undertaken to link perceived urban visibility to an array of effects reflecting the overall desire for good VAQ, and the benefits of improving currently degraded VAQ. This wide range of diverse studies have identified types of benefits of good VAQ.

For example, psychological research has demonstrated that people are emotionally affected by low VAQ such that their overall sense of wellbeing is diminished (e.g., Bickerstaff and Walker, 2001, 156271). Researchers have also shown that perception of pollution is correlated with stress, annoyance, and symptoms of depression (Evans and Jacobs, 1982, 179899; Jacobs et al., 1984, 156596; Mace et al., 2004, 180255). Sociological research has demonstrated that VAQ is deeply intertwined with a "sense of place," effecting people's sense of the desirability of a neighborhood quite apart from the actual physical conditions of the area (e.g., ABT, 2002, 156186; Day, 2007, 156386; Elliot et al., 1999, 010716; Howel et al., 2002, 156571). Public policy research finds that people think it is important to protect visibility, and accept the concept of setting standards to protect visibility (e.g., ABT, 2001, 156185; BBC Research & Consulting, 2002, 156258; Ely et al., 1991, 056599; Pryor, 1996, 056598). Finally, economic valuation research has measured the amount of money that people are willing to pay to protect or improve both urban visibility (e.g., summary review in Beron et al., 2001, 156270; Chestnut and Dennis, 1997, 014525) and natural locations such as NPs and other locations defined by the Clean Air Act as Class I visibility area (e.g., summary review in Chestnut and Dennis, 1997, 014525).

Urban visibility has been examined in two types of studies directly relevant to the NAAQS review process: urban visibility preference studies and urban visibility valuation studies. The purpose of the remainder of this section is to review preference studies in four urban areas, as well as one new urban visibility valuation study not previously discussed in previous EPA Criteria Documents or OAQPS Staff Papers.

Both types of studies are designed to evaluate individuals' desire (or demand) for good VAQ where they live, using different metrics to evaluate demand. Urban visibility preference studies examine individuals' demand by investigating what amount of visibility degradation is unacceptable while economic studies examine demand by investigating how much one would be willing to pay to improve visibility.

9.2.4.1. Urban Visibility Preference Studies

One group of urban visibility research projects focused on identifying preferences for urban VAQ without necessarily estimating the economic value of improving visibility. This group of preference studies used a common focus group method to estimate the visibility impairment conditions that respondents described as "acceptable." The specific definition of acceptable was largely left to each individual respondent, allowing each to identify their own preferences.

There are three completed studies that used this method, and two pilot studies that provided additional information (Table 9-2). The completed studies were conducted in Denver, Colorado (Ely et al., 1991, 056599), two cities in British Columbia, Canada (Pryor, 1996, 056598), and Phoenix, Arizona (BBC Research & Consulting, 2002, 156258). The additional studies were conducted in Washington, DC (ABT, 2001, 156185; Smith and Howell, 2009, 198803).

Each study collected information in a focus group setting, presenting slides depicting various visibility conditions. All four studies used photographs of a single scene from the study's city; each photo included images of the broad downtown area and spreading out to the hills or mountains composing the scene's backdrop. The maximum sight distance under good conditions varied by city, ranging from 8 km in Washington, DC to mountains hundreds of kilometers away in Denver. Multiple photos of the same scene were used to present approximately 20 different visibility impairment conditions. The Denver and British Columbia studies used actual photographs taken in the same location to depict various visibility conditions. The Phoenix and Washington, DC studies used photographs prepared using the WinHaze software from Air Resource Specialists (ARS). WinHaze is a computer-imaging software program that simulates visual air quality differences of various scenes, allowing the user to "degrade" an original near-pristine visibility condition photograph to create a photograph of each desired VAQ condition.

A common characteristic of the three visibility preference studies was that each was conducted in the West where distant mountains were shown in the photograph used to elicit local participant responses about visibility. Among other issues, the Washington D.C. pilot study was the first step in a process to expand the results to other regions where typical scenes may have different sensitivity to perceived visibility changes in PM air quality and where participants may have different acceptable visibility preference values.

The range of median preference values for an acceptable amount of visibility degradation from the 4 urban areas was approximately 19-33 dv. Measured in terms of visual range (VR), these median acceptable values were between approximately 59 and 20 km.

Table 9-2. Summary of urban visibility preference studies.

	Denver, CO	Phoenix, AZ	2 British Columbia cities	Washington, DC (2001)	Washington, DC (2009)
Report Date	**1991**	**2003**	**1996**	**2001**	**2009**
Duration of session		45 min	50 min	2 h	
Compensation	None (civic groups)	$50	None (class room exercise)	$50	None
# focus group sessions	17	27 total at 6 locations, Including 3 in Spanish	4	1	3 tests
# participants	214	385	180	9	64
Age range	Adults	18-65+	University students	27-58	Adults
Annual or seasonal	Wintertime	Annual	Summertime	Annual	Annual
# total scenes presented	Single scene of downtown with mountains in background	Single scene of downtown and mountains, 42 km maximum distance	Single scene from each city	Single scene of DC Mall and downtown, 8 km maximum sight	Single scene of DC Mall and downtown, 8 km maximum sight
# of total visibility conditions presented	20 conditions (+ 5 duplicates)	21 conditions (+ 4 duplicates)	20 conditions (10 each from each city)	20 conditions (+ 5 duplicates)	22 conditions

	Denver, CO	Phoenix, AZ	2 British Columbia cities	Washington, DC (2001)	Washington, DC (2009)
Source of slides	Actual photos taken between 9am and 3pm	WinHaze	Actual photos taken at 1 p.m. or 4 p.m.	WinHaze	WinHaze
Medium of presentation	Slide projection	Slide projection	Slide projection	Slide projection	Slide projection
Ranking scale used	7 point scale	7 point scale	7 point scale	7 point scale	7 point scale
Visibility range presented	11 to 40 dv	15 to 35 dv	13-25 dv (Chilliwack) 13.5-31.5 dv (Abbotsford)	9-38 dv	9-45 dv
Health issue directions	Ignore potential health impacts; visibility only	Judge solely on visibility, do not consider health	Judge solely on visibility, do not consider health	Health never mentioned, "Focus only on visibility"	Health never mentioned, "Focus only on visibility"
Key questions asked	a) Rank VAQ (1-7 scale)	a) Rank VAQ (1-7 scale)	a) Rank VAQ (1-7 scale)	a) Rank VAQ (1-7 scale)	a) Rank VAQ (1-7 scale)
	b) Is each slide "acceptable"	b) Is each slide "acceptable"	b) Is each slide "acceptable"	b) Is each slide "acceptable"	b) Is each slide "acceptable"
	c) "How much haze is too much?"	c) How many days a year would this picture be "acceptable"		c) if this hazy, how many hs would it be acceptable (3 slides only)	
				d) valuation question	
Mean dv found "acceptable"	20.3 dv	23-25 dv	~23 dv(Chilliwack), ~19 dv(Abbotsford)	~20 dv (range 20-25)	~30 dv

9.2.4.2. Denver, Colorado Urban Visibility Preference Study

The Denver urban visibility preference study (Ely et al., 1991, 056599) was conducted on behalf of the Colorado Department of Public Health and Environment (CDPHE). The study conducted a series of focus group sessions with 17 civic and community groups in which a total of 214 individuals were asked to rate slides. The slides depicted varying values of VAQ for a well-known Denver vista, including a broad view of downtown Denver with the mountains to the west composing the scene's background. The participants were instructed to base their judgments on three factors:

1. The standard was for an urban area, not a pristine NP area where the standards might be more strict;
2. The value of an urban visibility standard violation should be set at a VAQ value considered to be unreasonable, objectionable, and unacceptable visually; and
3. Judgments of standards violations should be based on visibility only, not on health effects.

Participants were shown 25 randomly ordered slides of actual photographs. The visibility conditions presented in the slides ranged from 11-40 dv, approximating the 10th-90th percentile of wintertime visibility conditions in Denver. The participants rated the 25 slides based on a scale of 1 (poor) to 7 (excellent), with 5 duplicates included. They were then asked to judge whether the slide would violate what they would consider to be an appropriate urban visibility standard (i.e., whether the amount of impairment was "acceptable" or "unacceptable"). The individual's judgment of a slide's VAQ and whether the slide violated a visibility standard were highly correlated (Pearson correlation coefficient >80%), as were the VAQ ratings and the yes/no "acceptable" response. The participant's median response was that a visibility condition of 20.3 dv (extinction coefficient $b_{ext} = 76Mm^{-1}$, or VR ~51 km) was judged as "acceptable." The CDPHE subsequently established a Denver visibility standard at this value (defined as $b_{ext} = 76Mm^{-1}$), based on the median 50% acceptability findings from the study.

9.2.4.3. Phoenix, Arizona Urban Visibility Preference Study

The Phoenix urban visibility preference study (BBC Research & Consulting, 2002, 156258) was conducted on behalf of the Arizona Department of Environmental Quality. The Phoenix study patterned its focus group survey process after the Denver study. The study included 385 participants in 27 separate focus group sessions. Participants were recruited using random digit dialing to obtain a sample group designed to be demographically representative of the larger Phoenix population. Focus group sessions were held at six neighborhood locations throughout the metropolitan area to improve the participation rate. Three sessions were held in Spanish in one region of the city with a large Hispanic population (25%), although the final overall participation of native Spanish speakers (18%) in the study was modestly below the targeted value. Participants received $50 as an inducement to participate.

Participants were shown a series of 25 images of the same vista of downtown Phoenix, with South Mountain in the background at a distance of about 40 km. Photographic slides of the images were developed using WinHaze. The visibility impairment conditions ranged from 15-35 dv (the extinction coefficient, b_{ext}, range was approximately 45 Mm^{-1} to 330 Mm^{-1}, or a visual range of 87-12 km). Participants first individually rated the randomly shown slides on a VAQ scale of 1 (unacceptable) to 7 (excellent). Participants were instructed to rate the photographs solely on visibility, and to not base their decisions on either health concerns or what it would cost to have better visibility. Next, the participants individually rated the randomly ordered slides as "acceptable" or "unacceptable," defined as whether the visibility in the slide is unreasonable or objectionable. Better visibility conditions (15 dv and 20 dv) were judged "acceptable" by 90% of all participants. At 24 dv nearly half of all participants thought the VAQ was "unacceptable," with almost three-quarters judging 26 dv as unacceptable.

The Phoenix urban visibility study formed the basis of the decision of the Phoenix Visibility Index Oversight Committee for a visibility index for the Phoenix Metropolitan Area (Arizona DEQ, 2000, 019164). The Phoenix Visibility Index establishes an indexed system with 5 categories of visibility conditions, ranging from "Excellent" (14 dv or less) to "Very Poor" (29 dv or greater). The "Good" range is 15-20 dv. The environmental goal of the Phoenix urban visibility program is to achieve continued progress through 2018 by moving the number of days in lower quality categories into better quality categories.

9.2.4.4. British Columbia, Canada Urban Visibility Preference Study

The British Columbia urban visibility preference study (Pryor, 1996, 056598) was conducted on behalf of the Ministry of Environment. The study conducted focus group sessions that were also developed following the methods used in the Denver study. Participants were students at the University of British Columbia, who participated in one of four focus group sessions with between 7 and 95 participants. A total of 180 respondents completed surveys (29 did not complete the survey).

Participants in the study were shown slides of two suburban locations in British Columbia: Chilliwack and Abbotsford. Using the same general protocol as the Denver study, Pryor found that responses from this study found the acceptable level of visibility was 23 dv in Chilliwack and 19 dv in Abbotsford. Pryor (1996, 056598) discusses some possible reasons for the variation in standard visibility judgments between the two locations. Factors discussed include the relative complexity of the scenes, potential bias of the sample population (only University students participated), and the different amounts of development at each location. Abbotsford (population 130,000) is an ethnically diverse suburb adjacent to the Vancouver Metro area, while Chilliwack (population 70,000) is an agricultural community 100 km east Vancouver in the Frazier Valley.

The British Columbia urban visibility preference study is being considered by the B.C. Ministry of the Environment as a part of establishing urban and wilderness visibility goals in British Columbia.

9.2.4.5. Washington, DC Urban Visibility Preference Studies

The Washington, DC urban visibility pilot study (ABT, 2001, 156185) was conducted on behalf of the EPA, and was designed to be a pilot focus group study, an initial developmental trial run of a larger study. The intent of the pilot study was to study both focus group method design and potential survey questions. Due to funding limitations, only a single focus group session was held,

consisting of one extended session with nine participants. No further urban visibility focus group sessions were held in Washington, DC.

Due to the small number of participants, it is not possible to make statistical inferences about the opinions of the general population. The study does, however, provide additional useful information about urban visibility studies, potentially helping to both better understand previous studies as well as design future studies.

The study also adopted the general Denver study method, modifying it as appropriate to be applicable in an eastern urban setting which has substantially different visibility conditions than any of the three western locations of the other preference studies. Washington's (and the entire East) visibility is typically substantially worse than western cities, and has different characteristics. Washington's visibility impairment is primarily a uniform whitish haze dominated by sulfates, relative humidity values are higher, the low lying terrain provides substantially shorter maximum sight distances, and many residents are not well informed that anthropogenic emissions impair visibility on hazy days.

The Washington focus group session included questions on valuation, as well as on preferences. The focus group was asked to state its preferences measured in an increase in the general cost of living for certain increments of improvement in visibility on a typical summer day. A general cost of living approach is one payment vehicle approach that can be used in willingness to pay studies, especially for environmental issues arising from multiple diverse emission sources (e.g., transportation, electricity generation, industry, etc.) making a specific price increase potentially misleading.

The first part of the focus group session was designed to be an hour long, and was comparable to the focus group sessions in the Denver and Phoenix studies. A single scene was used; a panoramic shot of the Potomac River, Washington mall and downtown Washington, DC. In the first part of the session people were asked to rate the VAQ of 25 photographs (prepared using WinHaze, and projected on a large screen), judge the acceptability of visibility condition in each slide, and answer the valuation questions. The second half of the session, however, was a moderated discussion session about the format and content of the first phase of the session. In this moderated discussion, participants were asked about their understanding of each question asked in the first half of the session. Particular issues in designing a focus group session were also explored. Important participant comments included:

1. Participants had been asked how they reacted to the initial direction to base their answers only on visibility, but health was never explicitly mentioned by the focus group moderator. Participants strongly agreed with the decision to not mention that health effects are associated with visibility impairment. They understood the directions as meaning they should ignore health issues, and said their answers would have been different if they included health as well as visibility in their judgments.
2. Differentiating between haze and weather conditions was difficult. Weather was not discussed in the focus group session, and the photographs were WinHaze altered photos with identical weather conditions. Participants mentioned they were still confused about the role of weather and humidity in the different visibility conditions presented in the photos.
3. Questions about how many hours an impairment level would be acceptable were confusing. Most participants were normally indoors during most of the day, so questions about duration of outdoor conditions were difficult to answer.
4. Participants strongly agreed that not mentioning the purpose of the study, or the sponsor, until the very end (after all the questions were answered) was viewed as very important. Most felt this information would have influenced their answers.

The Smith and Howell (2009, 198803) study recreated the same WinHaze images used in the 2001 Washington, DC urban visibility preference study, and followed a shortened version of the same question protocol as the 2001 study. The WinHaze images were presented to a total of 64 participants who were all employees of CRA International, Inc. (Smith and Howell also are CRA International employees).

The stated purpose of the Smith and Howell (2009, 198803) study was to explore the robustness of the 2001 pilot study results. To investigate this issue, Smith and Howell (2009, 198803) conducted three different tests concerning urban visibility preferences. Each participant was involved with only one test. Test 1 was designed to replicate the 2001 study. Test 2 reduced the

upper end of the range of VAQ by eliminating the 11 images used in Test 1 with a VAQ above 27.1 dv. Test 3 increased the upper end of the range of VAQ by including two new images of worse VAQ; the two new images had a VAQ of 42 dv and 45 dv. Smith and Howell (2009, 198803) concluded that changing the range of VAQ presented to the participants affects the responses about whether a particular VAQ is acceptable.

9.2.4.6. Urban Visibility Valuation Studies

The one recent urban visibility benefit assessment not included in earlier reviews is "The Benefits of Visibility Improvement: New Evidence from the Los Angeles Metropolitan Area" (Beron et al., 2001, 156270). Rather than a contingent valuation method (CVM) technique used in the majority of other urban visibility valuation studies, Beron et al. (2001, 156270) used a housing market hedonic technique. The housing hedonic methods were used in previous urban visibility studies by Murdoch and Thayer (1988, 156788) and Trijonis et al. (1985, 078468). A housing market hedonic study views a housing unit as composed of a bundle of attributes, and uses housing sale price data from a large number of units in a metropolitan area to estimate the value of each component. Hedonic pricing has been used to estimate economic values for environmental effects that have a direct effect on housing market values. It relies on the measurement of differentials in property values under various environmental quality conditions including air pollution, visibility and other environmental amenities such as access to nearby beaches and parks, as well as by physical attributes of the house and attributes of the neighborhood.

Beron et al. (2001, 156270) obtained data on approximately 840,000 owner-occupied, single family housing sales between 1980 and 1995 from the California South Coast Air Basin (composed of Los Angeles and Orange Counties, and the portions of Riverside and San Bernardino Counties in the greater metropolitan area). The real estate data included information on the sale price of the house, 13 housing attributes (square footage, number of bathrooms, etc.), 9 neighborhood attributes (percent poverty, school quality, FBI crime index, etc.), and three air pollution variables: ozone, particulates (measured by total suspended particulates, or TSP), and visibility. Visibility was measured as the annual average of visual range, measured in miles, and was obtained from seven airports within the study region. The visibility range was from 12.4 miles (Los Angeles International Airport, 1991) to 31.9 miles (Palm Springs Airport, 1995). Ozone data (39 monitors) and TSP data (40 monitors) were obtained from the South Coast Air Quality Management District. Annual mean values for each year were calculated for ozone and TSP.

Beron et al. (2001, 156270) presented results for a hypothetical basin-wide 20% visibility improvement, or an increase from 15.3 to 18.4 miles, which is equivalent to approximately 27.6 dv to 25.8 dv. The initial results reflect the change in the purchase price of a house associated with this difference in VAQ, which can be interpreted as a present value of a stream of annual values over the lifetime of the house. The authors therefore selected a time horizon (30 yrs) and an interest rate (8%) to calculate an annual per household benefit per dv ranging from $484 to $1,756. The Beron results are higher than the CVM-based values summarized in Chestnut and Dennis (1997, 014525), which ranged from $12 to $132 per dv. It should be noted that the $132 CVM values cited by Chestnut and Dennis (1997, 014525) is from a study in the Los Angeles area (Brookshire, 1979, 156298). The Beron et al. (2001, 156270) results are also higher than the Trijonis et al. (1990, 157058) hedonic study in the Los Angeles area, which had a range of $134 to $360 per dv per year. All values reported here are in terms of 1994 prices.

A critical question for all urban visibility valuation studies is the extent to which the estimated values strictly reflect preferences for visibility, and do not include a component of preferences for reducing health risk from air pollution. The ability to isolate the value of visibility from within the collection of intertwined benefits from visual air quality, which is inherently multi-attributed, is a challenge for all visibility valuation studies. Each study attempts to isolate visibility from other effect categories, but different studies take different approaches.

Beron et al. (2001, 156270) include two measures of air pollution directly related to health effects in their housing market hedonic study, ozone and particulates (using TSP as the metric for particulates), as well as visibility. They argue that the presence of the two health-related pollution conditions results in an estimated hedonic demand function for visibility that successfully separates the health component of demand for overall air quality from the visibility component. An alternative interpretation is that the estimated visibility function still includes a component of health risk because the housing market data does not support completely isolating the demand for visibility (due

to correlated variables, omitted variables, measurement error, model specification error, etc.) from demand for health risk reductions measured by the two health related air quality metrics.

A key issue in interpreting the Beron et al. (2001, 156270) results is whether the objective measures of air quality characteristics (e.g., visibility, PM concentrations, etc.) capture people's perceptions of the different aspects of air quality in a given location. To the extent the people simultaneously use what they see regarding VAQ as an indicator of the overall air quality including potential health risks, then including all the measures in the equation is not necessarily sufficient to isolate one effect from the other.

9.2.5. Summary of Effects on Visibility

Visibility impairment is caused by light scattering and absorption by suspended particles and gases. NO_2 is the only commonly occurring atmospheric pollutant gas that absorbs visible spectrum radiation, though in most situations the amount of light absorption by NO_2 is overwhelmed by the higher amounts of particulate light extinction (i.e., the combination of scattering and absorption) usually accompanying high NO_2 concentrations. Light scattering by gases in a pollutant-free atmosphere provides a limit to visibility in pristine conditions and is the largest contributor to the total light extinction during the least visibility-impaired periods in remote regions of the western U.S. There is strong and consistent evidence that PM is the overwhelming source of visibility impairment in both urban and remote areas. EC and some crustal minerals are the only commonly occurring airborne particle components that absorb light. All particles scatter light, and generally light scattering by particles is the largest of the four light extinction components. Although a larger particle scatters more light than a similarly shaped smaller particle of the same composition, the light scattered per unit of mass is greatest for particles with diameters from approximately 0.3-1.0 μm.

For studies where detailed data on particle composition by size data are available, accurate calculations of light extinction can be made. However, routinely available PM speciation data can be used to make reasonable estimates of light extinction using relatively simple algorithms that multiply the concentrations of each of the major PM species by its dry extinction efficiency and by a water growth term that accounts for particle size change as a function of relative humidity for hygroscopic species (e.g., SO_4^{2-}, nitrate, and sea salt). This permits the visibility impairment associated with each of the major PM components to be separately approximated from PM speciation monitoring data. There are six major PM components: $PM_{2.5}$ SO_4^{2-} usually assumed to be ammonium sulfate, $PM_{2.5}$ nitrate usually assumed to be ammonium nitrate, $PM_{2.5}$ OC, $PM_{2.5}$ EC, $PM_{2.5}$ crustal material (referred to as fine soil), and $PM_{10-2.5}$ or coarse mass.

Direct optical measurement of light extinction measured by transmissometer, or by combining the PM light scattering measured by integrating nephelometers with the PM light absorption measured by an aethalometer offer a number of advantages compared to algorithm estimates of light extinction based on PM composition and relative humidity data. The direct measurements are not subject to the uncertainties associated with assumed scattering and absorption efficiencies used in the PM algorithm approach. The direct measurements have higher time resolution (i.e., minutes to hours), which is more commensurate with the visibility effects compared with calculated light extinction using routinely available PM speciation data (i.e., 24-h duration).

Particulate SO_4^{2-} and nitrate are produced in the atmosphere from gaseous precursors, making them secondary PM species. They both have comparable light extinction efficiencies (haze impacts per unit mass concentration) at any relative humidity value, their light scattering per unit mass concentration increases with increasing relative humidity, and at sufficiently high humidity values (RH>85%) they are the most efficient particulate species contributing to haze. Particulate SO_4^{2-} is the dominant source of regional haze in the eastern U.S. (>50% of the particulate light extinction) and an important contributor to haze elsewhere in the country (>20% of particulate light extinction).

Particulate nitrate is a minor component of remote-area regional haze in the non-California western and eastern U.S., but an important contributor in much of California and in the upper Midwestern U.S. especially during winter when it is the dominant contributor to particulate light extinction. While both nitric acid (a reaction product of NO_X emissions) and ammonia are needed to form ammonium nitrate, the apparent reason for the Midwest nitrate bulge (i.e., region of high winter PM nitrate) is an abundance of atmospheric ammonia in this region principally from agricultural emissions. There is evidence that transport from the Midwest nitrate bulge region is responsible for some of the ammonium nitrate episodes experienced in downwind regions far to the east. Urban particulate nitrate concentrations are significantly elevated above surrounding remote-area

background concentrations with the largest urban contributions in the western U.S. Particulate ammonium nitrate concentrations in California and the Midwestern nitrate bulge region are an order of magnitude greater than estimated natural ammonium nitrate concentrations. Thermodynamic and air quality simulation modeling show that particulate nitrate concentrations are sensitive to changes in either NO_X emissions (from a combination of mobile and point sources) or ammonia emissions (principally from agricultural sources), with the responsiveness of particulate nitrate to emissions changes depending on the relative abundance of ammonia and nitric acid in the atmosphere.

EC and OC have the highest dry extinction efficiencies of the major PM species and are responsible for a large fraction of the haze especially in the Northwestern U.S., though absolute concentrations are as high in the eastern U.S. Both are a product of incomplete combustion of fuels, including those used in internal combustion processes (gasoline and diesel emissions) and open biomass burning (smoke from wild and prescribed fire). OC PM species are also produced by atmospheric transformation of precursor gaseous emissions. Smoke plume impacts from large wildfires dominate many of the worst haze periods in the western U.S. Carbonaceous PM is generally the largest component of urban excess $PM_{2.5}$ (i.e., the difference between urban and regional background concentration). Western urban areas have more than twice the average concentrations of carbonaceous PM than remote areas sites in the same region. In eastern urban areas, $PM_{2.5}$ is dominated by about equal concentrations of carbonaceous and SO_4^{2-} components, though the usually high relative humidity in the East causes the hydrated SO_4^{2-} particles to be responsible for about twice as much of the urban haze as that caused by the carbonaceous PM.

Radiocarbon dating of carbonaceous PM from twelve sites (eight in the West, two of which are urban) showed that about half of the urban area carbonaceous PM is from contemporary as opposed to fossil sources, while in remote areas the fraction that is contemporary ranges from 82-100%. Summer urban excess carbonaceous PM is dominated by fossil carbon for the two western urban areas (Phoenix, AZ and Seattle, WA), but nearly half of the winter urban excess for these two urban areas are from contemporary carbon sources (e.g., residential wood combustion). An empirical relationship between the radiocarbon analysis results and the more widely measured EC and OC data set was used to estimate the fraction of contemporary carbon at about 150 monitoring locations nationwide. The highest fraction of contemporary carbon is for the western remote areas sites during the summer (>90% contemporary) and the least was for eastern urban areas during the summer (<45% contemporary). Winter tended to have less extreme fractions of contemporary carbon for both remote and urban areas. A lower bound estimate of 40% of the contemporary and 35% of the fossil carbon is from secondary conversion of gaseous precursor during the summer at the twelve radiocarbon monitoring sites, suggesting that primary carbonaceous PM whether from fossil or contemporary sources represent less than two thirds of the total carbonaceous PM.

$PM_{2.5}$ crustal material (referred to as fine soil) and coarse mass (i.e., PM_{10} minus $PM_{2.5}$) are significant contributors to haze for remote areas sites in the arid Southwestern U.S. where they contribute a quarter to a third of the haze, with coarse mass usually contributing twice that of fine soil. Coarse mass concentrations are as high in the Central Great Plains as in the Southwestern deserts though there are no corresponding high concentrations of fine soil as in the Southwest. Also, the relative contribution to haze by the high coarse mass in the Great Plains is much smaller because of the generally higher haze values caused by the high concentrations of SO_4^{2-} and nitrate PM in that region.

A comprehensive assessment of the 610 worst haze sample periods over a 3-yr period in the western U.S. where dust is the major contributor categorized each site/sampler period into four causal groups: Asian dust, local windblown dust, transported regional windblown dust, and undetermined dust (i.e., not in one of the three other groups). Most dust days occurred at sites in Arizona, New Mexico, Colorado, western Texas, and southern California, and these were dominated by local and regionally transported wind-blown dust. Asian dust caused only a few of the worst dust days during the 3-year assessment period, though it is an important source of dust for the more northerly regions of the West (responsible for 10-40% of their worst dust periods) where there is rarely any windblown dust probably due to the greater ground cover. The frequency of worst dust events classified as undetermined was greatest for sites in the vicinity of large urban and agricultural areas such as those in California and Southern Arizona.

Visibility has direct significance to people's enjoyment of daily activities and their overall sense of wellbeing. For example, psychological research has demonstrated that people are emotionally affected by poor VAQ such that their overall sense of wellbeing is diminished. Urban visibility has been examined in two types of studies directly relevant to the NAAQS review process:

urban visibility preference studies and urban visibility valuation studies. Both types of studies are designed to evaluate individuals' desire for good VAQ where they live, using different metrics. Urban visibility preference studies examine individuals' preferences by investigating the amount of visibility degradation considered unacceptable, while economic studies examine the value an individual places on improving VAQ by eliciting how much the individual would be willing to pay for different amounts of VAQ improvement.

There are three urban visibility preference studies and two additional pilot studies that have been conducted to date that provide useful information on individuals' preferences for good VAQ in the urban setting. The completed studies were conducted in Denver, Colorado (Ely et al., 1991, 056599), two cities in British Columbia, Canada (Pryor, 1996, 056598) and Phoenix, AZ (BBC Research & Consulting, 2002, 156258). The additional studies were conducted in Washington, DC (ABT, 2001, 156185; Smith and Howell, 2009, 198803). The range of median preference values for an acceptable amount of visibility degradation from the 4 urban areas was approximately 19-33 dv. Measured in terms of visual range (VR), these median acceptable values were between approximately 59 and 20 km.

The economic importance of urban visibility has been examined by a number of studies designed to quantify the benefits (or willingness to pay) associated with potential improvements in urban visibility. Urban visibility valuation research prior to 1997 was summarized in Chestnut and Dennis (1997, 014525), and was also described in the 2004 PM AQCD (U.S. EPA, 2004, 056905) and the 2005 PM Staff Paper (U.S. EPA, 2005, 090209). Since the mid-1990s, little new information has become available regarding urban visibility valuation.

Collectively, the evidence is sufficient to conclude **that a causal relationship exists between PM and visibility impairment.**

9.3. Effects on Climate

While most of this ISA is restricted to consideration of the emissions, transport and transformation, resulting concentrations, and effects from PM in the U.S., because the effects endpoint here is climate, a larger spatial domain is needed. However, this assessment is not intended to be comprehensive even as a survey of the enormous range and volume of science related to climate effects from PM; rather, particular attention has been paid to data relevant to the U.S.

The two principal sources for material in this section are Chapter 2, "Changes in Atmospheric Constituents and in Radiative Forcing," (Forster et al., 2007, 092936) in the comprehensive Working Group I report in the Fourth Assessment Report (AR4) from the Intergovernmental Panel on Climate Change (IPCC), Climate Change 2007: The Physical Science Basis (IPCC, 2007, 092765), hereafter IPCC AR4; and the U.S. Climate Change Science Program Synthesis and Assessment Product 2.3, "Atmospheric Aerosol Properties and Climate Impacts," by Chin et al. (2009, 192130), hereafter CCSP SAP2.3. The EPA is a constituent agency member of the U.S. federated CCSP along with NOAA and NASA, which led production of CCSP SAP2.3 incorporating significant sections from EPA data and reports related particularly to U.S. emissions and measurements. Sections from each of these recent comprehensive reports are included here in their entirety or as emended as noted where they represent the most thorough summary of the climate effects of aerosols. (In the sections included from IPCC AR4 and CCSP SAP2.3, 'aerosols' is more frequently used than "PM" and that word is retained.)

9.3.1. The Climate Effects of Aerosols

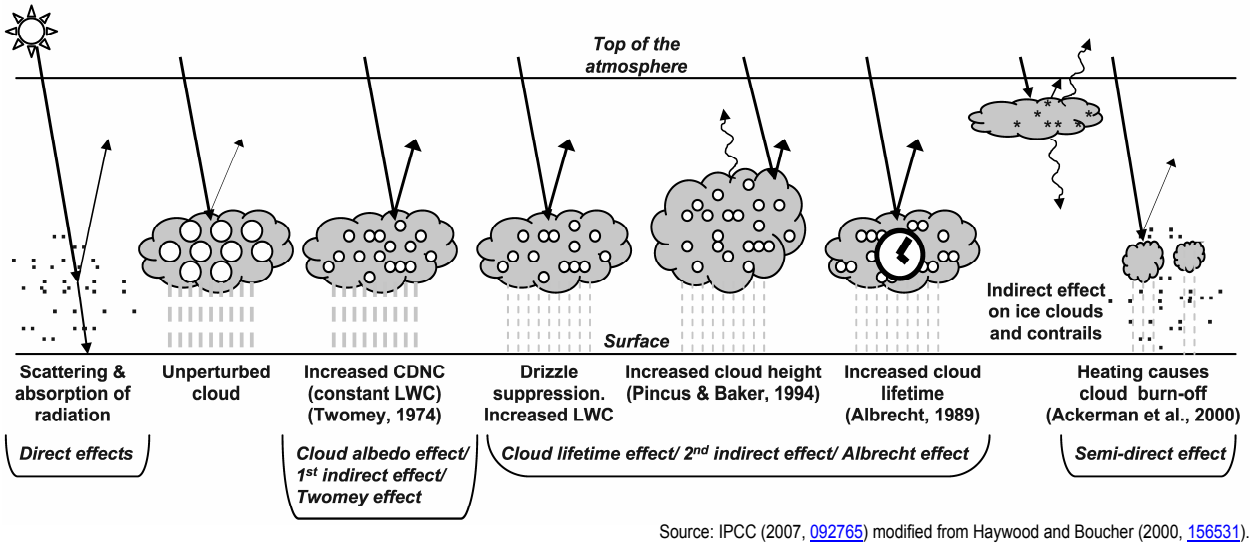
Section 9.3.1 comes directly from CCSP SAP2.3 Chapter 1 Section 1.2, with section, table, and figure numbers changed to be internally consistent with this ISA.

> Aerosols exert a variety of impacts on the environment. Aerosols (sometimes referred to particulate matter or "PM," especially in air quality applications), when concentrated near the surface, have long been recognized as affecting pulmonary function and other aspects of human health. Sulfate and nitrate aerosols play a role in acidifying the surface downwind of gaseous sulfur and odd nitrogen sources. Particles deposited far downwind might fertilize iron-poor waters in remote oceans, and Saharan dust reaching the Amazon Basin is thought to contribute nutrients to the rainforest soil.

Aerosols also interact strongly with solar and terrestrial radiation in several ways. Figure 9-52 offers a schematic overview. First, they scatter and absorb sunlight (Charlson and Pilat, 1969, 190025; McCormick and Ludwig, 1967, 190528; Mitchell, 1971, 190546); these are described as "direct effects" on shortwave (solar) radiation. Second, aerosols act as sites at which water vapor can accumulate during cloud droplet formation, serving as cloud condensation nuclei or CCN. Any change in number concentration or hygroscopic properties of such particles has the potential to modify the physical and radiative properties of clouds, altering cloud brightness (Twomey, 1977, 190533) and the likelihood and intensity with which a cloud will precipitate (e.g., Albrecht, 1989, 045783; Gunn and Phillips, 1957, 190595; Liou and Ou, 1989, 190407).

Collectively changes in cloud processes due to anthropogenic aerosols are referred to as aerosol indirect effects. Finally, absorption of solar radiation by particles is thought to contribute to a reduction in cloudiness, a phenomenon referred to as the semi-direct effect. This occurs because absorbing aerosol warms the atmosphere, which changes the atmospheric stability, and reduces surface flux.

The primary direct effect of aerosols is a brightening of the planet when viewed from space, as much of Earth's surface is dark ocean, and most aerosols scatter more than 90% of the visible light reaching them. The primary indirect effects of aerosols on clouds include an increase in cloud brightness, change in precipitation and possibly an increase in lifetime; thus the overall net impact of aerosols is an enhancement of Earth's reflectance (shortwave albedo). This reduces the sunlight reaching Earth's surface, producing a net climatic cooling, as well as a redistribution of the radiant and latent heat energy deposited in the atmosphere. These effects can alter atmospheric circulation and the water cycle, including precipitation patterns, on a variety of length and time scales (e.g., Ramanathan et al., 2001, 042681; Zhang et al., 2006, 190933).



Source: IPCC (2007, 092765) modified from Haywood and Boucher (2000, 156531).

Figure 9-52. Aerosol radiative forcing. Airborne particles can affect the heat balance of the atmosphere, directly, by scattering and absorbing sunlight, and indirectly, by altering cloud brightness and possibly lifetime. Here small black dots represent aerosols, circles represent cloud droplets, and straight lines represent short-wave radiation, and wavy lines, long-wave radiation. LWC is liquid water content, and CDNC is cloud droplet number concentration. Confidence in the magnitudes of these effects varies considerably (see Chapter 3). Although the overall effect of aerosols is a net cooling at the surface, the heterogeneity of particle spatial distribution, emission history, and properties, as well as differences in surface reflectance, mean that the magnitude and even the sign of aerosol effects vary immensely with location, season and sometimes inter-annually. The human-induced component of these effects is sometimes called "climate forcing."

Several variables are used to quantify the impact aerosols have on Earth's energy balance; these are helpful in describing current understanding, and in assessing possible future steps.

For the purposes of this report, aerosol radiative forcing (RF) is defined as the net energy flux (downwelling minus upwelling) difference between an initial and a perturbed aerosol loading state, at a specified level in the atmosphere. (Other quantities, such as solar radiation,

are assumed to be the same for both states.) This difference is defined such that a negative aerosol forcing implies that the change in aerosols relative to the initial state exerts a cooling influence, whereas a positive forcing would mean the change in aerosols exerts a warming influence.

There are a number of subtleties associated with this definition:

(1) The initial state against which aerosol forcing is assessed must be specified. For direct aerosol radiative forcing, it is sometimes taken as the complete absence of aerosols. IPCC AR4 (2001, 156587) uses as the initial state their estimate of aerosol loading in 1750. That year is taken as the approximate beginning of the era when humans exerted accelerated influence on the environment.

(2) A distinction must be made between aerosol RF and the anthropogenic contribution to aerosol RF. Much effort has been made to distinguishing these contributions by modeling and with the help of space-based, airborne, and surface-based remote sensing, as well as in situ measurements. These efforts are described in subsequent chapters (of the CCSP SAP2.3).

(3) In general, aerosol RF and anthropogenic aerosol RF include energy associated with both the shortwave (solar) and the long-wave (primarily planetary thermal infrared) components of Earth's radiation budget. However, the solar component typically dominates, so in this document, these terms are used to refer to the solar component only, unless specified otherwise. The wavelength separation between the short- and long-wave components is usually set at around three or four micrometers.

(4) The IPCC AR4 (2007, 092765) defines radiative forcing as the net downward minus upward irradiance at the tropopause due to an external driver of climate change. This definition excludes stratospheric contributions to the overall forcing. Under typical conditions, most aerosols are located within the troposphere, so aerosol forcing at TOA and at the tropopause are expected to be very similar. Major volcanic eruptions or conflagrations can alter this picture regionally, and even globally.

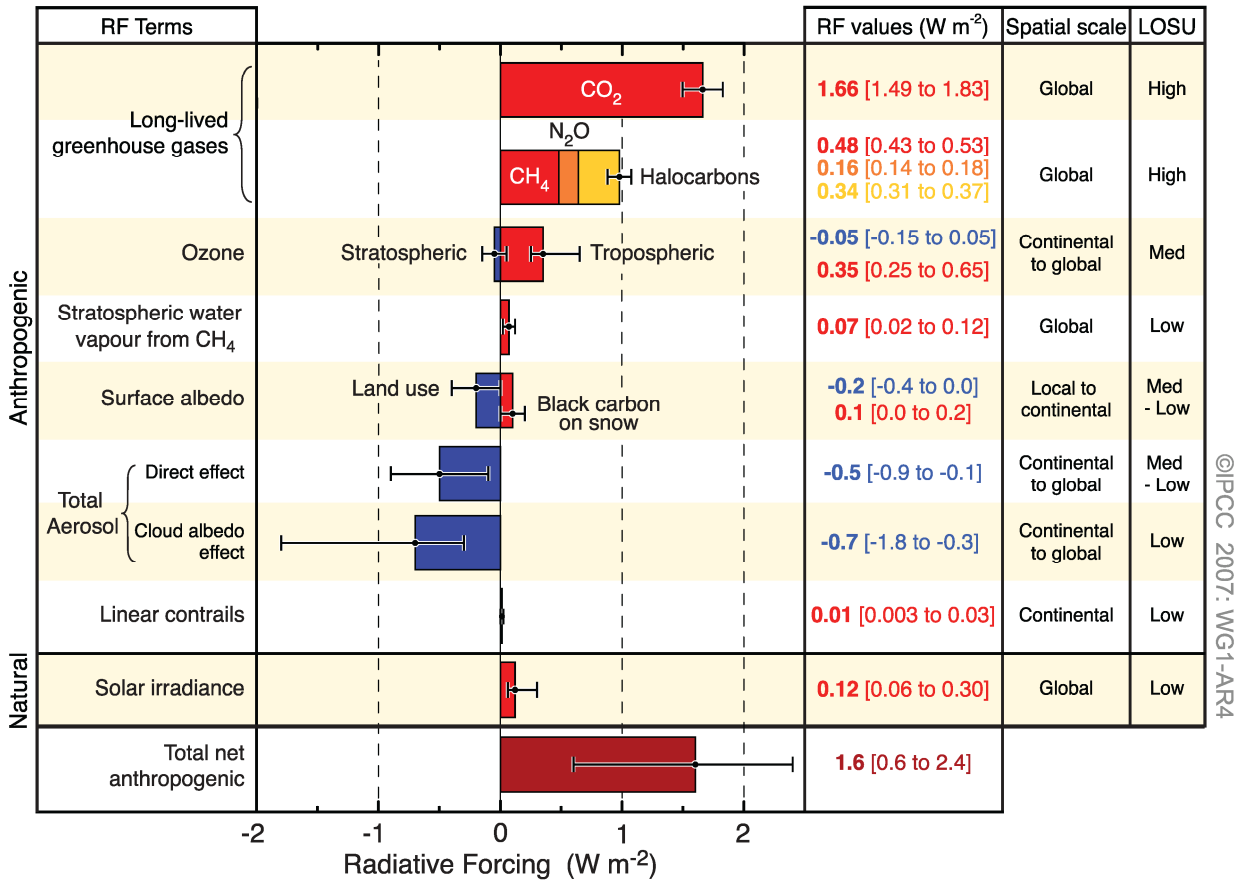
(5) Aerosol radiative forcing can be evaluated at the surface, within the atmosphere, or at top-of-atmosphere (TOA). In this document, unless specified otherwise, aerosol radiative forcing is assessed at TOA.

(6) As discussed subsequently, aerosol radiative forcing can be greater at the surface than at TOA if the aerosols absorb solar radiation. TOA forcing affects the radiation budget of the planet. Differences between TOA forcing and surface forcing represent heating within the atmosphere that can affect vertical stability, circulation on many scales, cloud formation, and precipitation, all of which are climate effects of aerosols. In this document, unless specified otherwise, these additional climate effects are not included in aerosol radiative forcing.)

(7) Aerosol direct radiative forcing can be evaluated under cloud-free conditions or under natural conditions, sometimes termed "all-sky" conditions, which include clouds. Cloud-free direct aerosol forcing is more easily and more accurately calculated; it is generally greater than all-sky forcing because clouds can mask the aerosol contribution to the scattered light. Indirect forcing, of course, must be evaluated for cloudy or all-sky conditions. In this document, unless specified otherwise, aerosol radiative forcing is assessed for all-sky conditions.

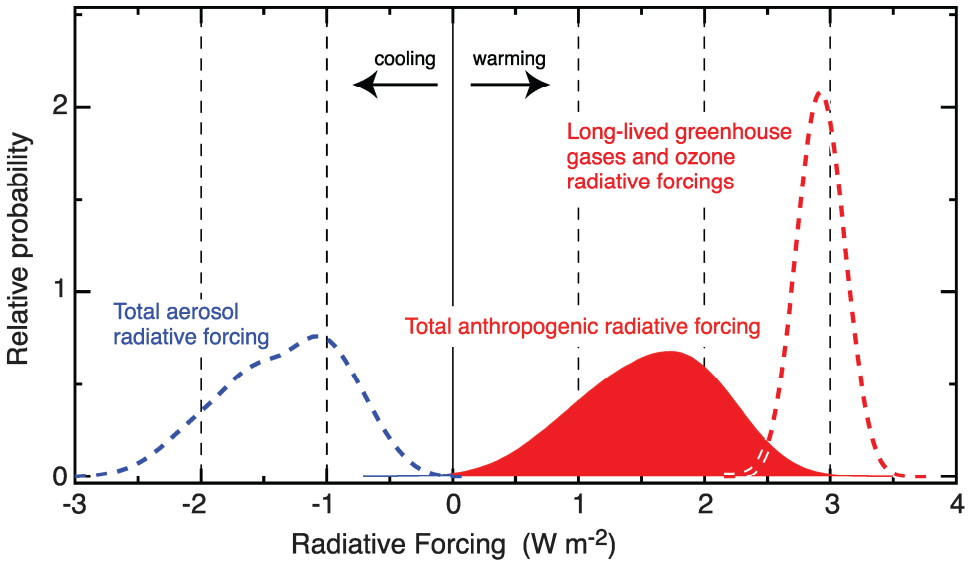
(8) Aerosol radiative forcing can be evaluated instantaneously, daily (24 h) averaged, or assessed over some other time period. Many measurements, such as those from polar-orbiting satellites, provide instantaneous values, whereas models usually consider aerosol RF as a daily average quantity. In this document, unless specified otherwise, daily averaged aerosol radiative forcing is reported.

(9) Another subtlety is the distinction between a "forcing" and a "feedback." As different parts of the climate system interact, it is often unclear which elements are "causes" of climate change (forcings among them), which are responses to these causes, and which might be some of each. So, for example, the concept of aerosol effects on clouds is complicated by the impact clouds have on aerosols; the aggregate is often called aerosol-cloud interactions. This distinction sometimes matters, as it is more natural to attribute responsibility for causes than for responses. However, practical environmental considerations usually depend on the net result of all influences. In this report, "feedbacks" are taken as the consequences of changes in surface or atmospheric temperature, with the understanding that for some applications, the accounting may be done differently.



Source: IPCC (2007, 092765).

Figure 9-53. **Global average radiative forcing (RF) estimates and uncertainty ranges in 2005, relative to the pre-industrial climate. Anthropogenic CO_2, methane (CH_4), nitrous oxide (N_2O), ozone, and aerosols as well as the natural solar irradiance variations are included. Typical geographical extent of the forcing (spatial scale) and the assessed level of scientific understanding (LOSU) are also given. Forcing is expressed in units of watts per square meter (W/m^2). The total anthropogenic radiative forcing and its associated uncertainty are also given.**



Source: Adapted from IPCC (2007, 092765).

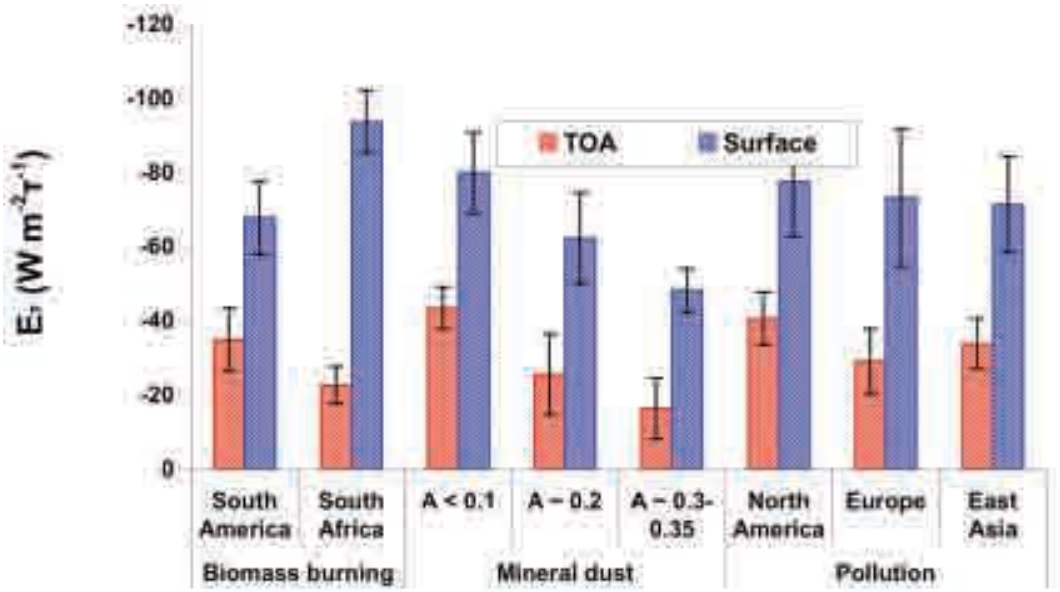
Figure 9-54. Probability distribution functions (PDFs) for anthropogenic aerosol and GHG RFs. Dashed red curve: RF of long-lived greenhouse gases plus ozone; dashed blue curve: RF of aerosols (direct and cloud albedo RF); red filled curve: combined anthropogenic RF. The RF range is at the 90% confidence interval.

In summary, aerosol radiative forcing, the fundamental quantity about which this report is written, must be qualified by specifying the initial and perturbed aerosol states for which the radiative flux difference is calculated, the altitude at which the quantity is assessed, the wavelength regime considered, the temporal averaging, the cloud conditions, and whether total or only human-induced contributions are considered. The definition given here, qualified as needed, is used throughout the report.

Although the possibility that aerosols affect climate was recognized more than 40 years ago, the measurements needed to establish the magnitude of such effects, or even whether specific aerosol types warm or cool the surface, were lacking. Satellite instruments capable of at least crudely monitoring aerosol amount globally were first deployed in the late 1970s. But scientific focus on this subject grew substantially in the 1990s (e.g., Charlson and Wigley, 1994, 189989; Charlson et al., 1991, 045793; 1992, 045794; Penner et al., 1992, 045825), in part because it was recognized that reproducing the observed temperature trends over the industrial period with climate models requires including net global cooling by aerosols in the calculation (IPCC, 1995, 190991; 1996, 190990), along with the warming influence of enhanced atmospheric greenhouse gas (GHG) concentrations – mainly carbon dioxide, methane, nitrous oxide, chlorofluorocarbons, and ozone.

Improved satellite instruments, ground- and ship-based surface monitoring, more sophisticated chemical transport and climate models, and field campaigns that brought all these elements together with aircraft remote sensing and in situ sampling for focused, coordinated study, began to fill in some of the knowledge gaps. By the Fourth IPCC Assessment Report, the scientific community consensus held that in global average, the sum of direct and indirect top-of-atmosphere (TOA) forcing by anthropogenic aerosols is negative (cooling) of about -1.3 W/m^2 (-2.2 to -0.5 W/m^2). This is significant compared to the positive forcing by anthropogenic GHGs (including ozone), about 2.9 ± 0.3 W/m^2 (IPCC, 2007, 092765). However, the spatial distribution of the gases and aerosols are very different, and they do not simply exert compensating influences on climate.

The IPCC aerosol forcing assessments are based largely on model calculations, constrained as much as possible by observations. At present, aerosol influences are not yet quantified adequately, according to Figure 9-53, as scientific understanding is designated as "Medium-Low" and "Low" for the direct and indirect climate forcing, respectively. The IPCC AR4 (2007, 092765) concluded that uncertainties associated with changes in Earth's radiation budget due to anthropogenic aerosols make the largest contribution to the overall uncertainty in radiative forcing of climate change among the factors assessed over the industrial period (Figure 9-54).



Source: Adapted with Permission of theAmerican Geophysical Union from from Zhou et al. (2005, 156183).

Figure 9-55. The clear-sky forcing efficiency Eτ, defined as the diurnally averaged aerosol direct radiative effect (W/m^2) per unit AOD at 550 nm, calculated at both TOA and the surface, for typical aerosol types over different geographical regions. The vertical black lines represent ± one standard deviation of Eτ for individual aerosol regimes and A is surface broadband albedo.

Although AOD, aerosol properties, aerosol vertical distribution, and surface reflectivity all contribute to aerosol radiative forcing, AOD usually varies on regional scales more than the other aerosol quantities involved. Forcing efficiency (Eτ), defined as a ratio of direct aerosol radiative forcing to AOD at 550 nm, reports the sensitivity of aerosol radiative forcing to AOD, and is useful for isolating the influences of particle properties and other factors from that of AOD. Eτ is expected to exhibit a range of values globally, because it is governed mainly by aerosol size distribution and chemical composition (which determine aerosol single-scattering albedo and phase function), surface reflectivity, and solar irradiance, each of which exhibits pronounced spatial and temporal variations. To assess aerosol RF, Eτ is multiplied by the ambient AOD.

Figure 9-55 shows a range of Eτ, derived from AERONET surface sun photometer network measurements of aerosol loading and particle properties, representing different aerosol and surface types, and geographic locations. It demonstrates how aerosol direct solar radiative forcing (with initial state taken as the absence of aerosol) is determined by a combination of aerosol and surface properties. For example, Eτ due to southern African biomass burning smoke is greater at the surface and smaller at TOA than South American smoke because the southern African smoke absorbs sunlight more strongly, and the magnitude of Eτ for mineral dust for several locations varies depending on the underlying surface reflectance. Figure 9-55 illustrates one further point, that the radiative forcing by aerosols on surface energy balance can be much greater than that at TOA. This is especially true when the particles have SSA substantially less than 1, which can create differences between surface and TOA forcing as large as a factor of five (e.g., Zhou et al., 2005, 156183).

Table 9-3. Top-of-atmosphere, cloud-free, instantaneous direct aerosol radiative forcing dependence on aerosol and surface properties. Here TWP, SGP, and NSA are the Tropical West Pacific island, Southern Great Plains, and North Slope Alaska observation stations maintained by the DOE ARM program, respectively. Instantaneous values are given at specific solar zenith angle. Upper and middle parts are from McComiskey et al. (2008, 190523). Representative, parameter-specific measurement uncertainty upper bounds for producing 1 W/m^2 instantaneous TOA forcing accuracy are given in the lower part, based on sensitivities at three sites from the middle part of the table.

Parameters	TWP	SGP	NSA
AEROSOL PROPERTIES (AOD, SSA, G), SOLAR ZENITH ANGLE (SZA), SURFACE ALBEDO (A), AND AEROSOL DIRECT RF AT TOA (F)			
AOD	0.05	0.1	0.05
SSA	0.97	0.95	0.95
g	0.8	0.6	0.7
A	0.05	0.1	0.9
SZA	30	45	70
F (W/m^2)	-2.2	-6.3	2.6
SENSITIVITY OF CLOUD-FREE, INSTANTANEOUS, TOA DIRECT AEROSOL RADIATIVE FORCING TO AEROSOL AND SURFACE PROPERTIES, W/M^2 PER UNIT CHANGE IN PROPERTY			
dFld(AOD)	-45	-64	51
dFld(SSA)	-11	-50	-60
dFldg	13	23	2
dFldA	8	24	6
REPRESENTATIVE MEASUREMENT UNCERTAINTY UPPER BOUNDS FOR PRODUCING 1 W/M^2 ACCURACY OF AEROSOL RF			
AOD	0.022	0.016	0.020
SSA	0.091	0.020	0.017
g	0.077	0.043	
A	0.125	0.042	0.167

Table 9-3 presents estimates of cloud-free, instantaneous, aerosol direct RF dependence on AOD, and on aerosol and surface properties, calculated for three sites maintained by the U.S. Department of Energy's Atmospheric Radiation Measurement (ARM) program, where surface and atmospheric conditions span a significant range of natural environments (McComiskey et al., 2008, 190523). Here aerosol RF is evaluated relative to an initial state that is the complete absence of aerosols. Note that aerosol direct RF dependence on individual parameters varies considerably, depending on the values of the other parameters, and in particular, that aerosol RF dependence on AOD actually changes sign, from net cooling to net warming, when aerosols reside over an exceedingly bright surface. Sensitivity values are given for snapshots at fixed solar zenith angles, relevant to measurements made, for example, by polar-orbiting satellites.

The lower portion of Table 9-3 presents upper bounds on instantaneous measurement uncertainty, assessed individually for each of AOD, SSA, g, and A, to produce a 1 W/m^2 top-of atmosphere, cloud-free aerosol RF accuracy. The values are derived from the upper portion of the table, and reflect the diversity of conditions captured by the three ARM sties. Aerosol RF sensitivity of 1 W/m^2 is used as an example; uncertainty upper bounds are obtained from the partial derivative for each parameter by neglecting the uncertainties for all other parameters. These estimates produce an instantaneous AOD measurement uncertainty upper bound between about 0.01 and 0.02, and SSA constrained to about 0.02 over surfaces as bright as or brighter than the ARM Southern Great Plains site, typical of mid-latitude, vegetated land. Other researchers, using independent data sets, have derived ranges of $E\tau$ and aerosol RF

sensitivity similar to those presented here, for a variety of conditions (Christopher and Jones, 2008, 189985; Yu et al., 2006, 156173; Zhou et al., 2005, 156183).

These uncertainty bounds provide a baseline against which current and expected near-future instantaneous measurement capabilities are assessed in Chapter 2 (of the CCSP SAP2.3). Model sensitivity is usually evaluated for larger-scale (even global) and longer-term averages. When instantaneous measured values from a randomly sampled population are averaged, the uncertainty component associated with random error diminishes as something like the inverse square root of the number of samples. As a result, the accuracy limits used for assessing more broadly averaged model results corresponding to those used for assessing instantaneous measurements would have to be tighter, as discussed in Chapter 4 (of the CCSP SAP2.3).

In summary, much of the challenge in quantifying aerosol influences arises from large spatial and temporal heterogeneity, caused by the wide variety of aerosol sources, sizes and compositions, the spatial non-uniformity and intermittency of these sources, the short atmospheric lifetime of most aerosols, and the spatially and temporally non-uniform chemical and microphysical processing that occurs in the atmosphere. In regions having high concentrations of anthropogenic aerosol, for example, aerosol forcing is much stronger than the global average, and can exceed the magnitude of GHG warming, locally reversing the sign of the net forcing. It is also important to recognize that the global-scale aerosol TOA forcing alone is not an adequate metric for climate change (NRC, 2005, 057409). Due to aerosol absorption, mainly by soot, smoke, and some desert dust particles, the aerosol direct radiative forcing at the surface can be much greater than the TOA forcing, and in addition, the radiative heating of the atmosphere by absorbing particles can change the atmospheric temperature structure, evolution, and possibly large-scale dynamical systems such as the monsoons (Kim et al., 2006, 190917; Lau et al., 2009, 190229). By realizing aerosol's climate significance and the challenge of charactering highly variable aerosol amount and properties, the U.S. Climate Change Research Initiative (CCRI) identified research on atmospheric concentrations and effects of aerosols specifically as a top priority (NRC, 2001, 053303).

9.3.2. Overview of Aerosol Measurement Capabilities

9.3.2.1. Satellite Remote Sensing

Section 9.3.2 with the exception of the final paragraph, comes directly from CCSP SAP2.3 Chapter 2, Section 2.2 with section, table, and figure numbers changed to be internally consistent with this ISA.

A measurement-based characterization of aerosols on a global scale can be realized only through satellite remote sensing, which is the only means of characterizing the large spatial and temporal heterogeneities of aerosol distributions. Monitoring aerosols from space has been performed for over two decades and is planned for the coming decade with enhanced capabilities (Forster et al., 2007, 092936; King et al., 1999, 190635; Lee et al., 2006, 190358; Mischenko et al., 2007, 190543). Table 9-4 summarizes major satellite measurements currently available for the tropospheric aerosol characterization and radiative forcing research.

Early aerosol monitoring from space relied on sensors that were designed for other purposes. The Advanced Very High Resolution Radiometer (AVHRR), intended as a cloud and surface monitoring instrument, provides radiance observations in the visible and near infrared wavelengths that are sensitive to aerosol properties over the ocean (Husar et al., 1997, 045900; Mishchenko et al., 1999, 190541). Originally intended for ozone monitoring, the ultraviolet (UV) channels used for the Total Ozone Mapping Spectrometer (TOMS) are sensitive to aerosol UV absorption with little surface interferences, even over land (Torres et al., 1998, 190503). This UV-technique makes TOMS suitable for monitoring biomass burning smoke and dust, though with limited sensitivity near the surface (Herman et al., 1997, 048393) and for retrieving aerosol single-scattering albedo from space (Torres et al., 2005, 190507). (A new sensor, the Ozone Monitoring Instrument (OMI) aboard Aura, has improved on such UV-technique advantages, providing higher spatial resolution and more spectral channels; see (Veihelmann et al., 2007, 190627). Such historical sensors have provided multi-decadal climatology of aerosol optical depth that has significantly advanced the understanding of aerosol distributions and long-term variability (e.g.,Geogdzhayev et al., 2002, 190574; Massie et al., 2004, 190492; Mishchenko and Geogdzhayev, 2007, 190545; Mishchenko et al., 2007, 190542; Torres et al., 2002, 190505; Zhao et al., 2008, 190935).

Over the past decade, satellite aerosol retrievals have become increasingly sophisticated. Now, satellites measure the angular dependence of radiance and polarization at multiple wavelengths from UV through the infrared (IR) at fine spatial resolution. From these observations, retrieved aerosol products include not only optical depth at one wavelength, but also spectral optical depth and some information about particle size over both ocean and land, as well as more direct measurements of polarization and phase function. In addition, cloud screening is much more robust than before and onboard calibration is now widely available.

Examples of such new and enhanced sensors include the MODerate resolution Imaging Spectroradiometer (MODIS, see Box 2.1 of CCSP SAP2.3), the Multi-angle Imaging SpectroRadiometer (MISR, see Box 2.2 of CCSP SAP2.3), Polarization and Directionality of the Earth's Reflectance (POLDER, see Box 2.3 of CCSP SAP2.3), and OMI, among others. The accuracy for AOD measurement from these sensors is about 0.05 or 20% of AOD (Kahn et al., 2005, 190966; Remer et al., 2005, 190221) and somewhat better over dark water, but that for aerosol microphysical properties, which is useful for distinguishing aerosol air mass types, is generally low. The Clouds and the Earth's Radiant Energy System (CERES, see Box 2.4 of CCSP SAP2.3) measures broadband solar and terrestrial radiances. The CERES radiation measurements in combination with satellite retrievals of aerosol optical depth can be used to determine aerosol direct radiative forcing.

Table 9-4. Summary of major satellite measurements currently available for the tropospheric aerosol characterization and radiative forcing research.

Category	Properties	Sensor/platform	Parameters	Spatial coverage	Temporal coverage
Column-integrated	Loading	AVHRR/NOAA-series	Optical depth	~daily coverage of global ocean	1981-present
		TOMS/Nimbus, ADEOSI, EP		~daily coverage of global land and ocean	1979-2001
		POLDER-1,2, PARASOL			1997-present
		MODIS/Terra, Aqua			2000-present (Terra) 2002-present (Aqua)
		MISR/Terra		~weekly coverage of global land and ocean, including bright desert and nadir sun-glint	2000-present
		OMI/Aura		~daily coverage of global land and ocean	2005-present
	Size, shape	AVHRR/NOAA-series	Ångström exponent	Global ocean	1981-present
		POLDER-1,2, PARASOL	Fine-mode fraction, Ångström exponent, non-spherical fraction	Global land and ocean	1997-present
		MODIS/Terra, Aqua	Fine-mode fraction	Global land and ocean (better quality over ocean)	2000-present (Terra) 2002-present (Aqua)
			Ångström exponent		
			Effective radium	Global ocean	
			Asymmetry factor		
		MISR/Terra	Ångström exponent, small, medium large fractions, non-spherical fractions	Global land and ocean	2000-present
	Absorption	TOMS/Nimbus, ADEOSI, EP	Absorbing aerosol index, single-scattering albedo, absorbing optical depth	Global land and ocean	1979-2001
		OMI/Aura			2005-present
		MISR/Terra	Single-scattering albedo (2-4 bins)		2000-present
Vertical-resolved	Loading, size, and shape	GLAS/ICESat	Extinction/backscatter	Global land and ocean, 16-day repeating cycle, single-nadir measurement	2003-present (~3 mo/yr)
		CALIOP/CALIPSO	Extinction/backscatter, color ratio, depolarization ratio		2006-present

Complementary to these passive sensors, active remote sensing from space is also now possible and ongoing (see Box 2.5 of CCSP SAP2.3). Both the Geoscience Laser Altimeter System (GLAS) and the Cloud and Aerosol Lidar with Orthogonal Polarization (CALIOP) are collecting essential information about aerosol vertical distributions. Furthermore, the constellation of six afternoon-overpass spacecrafts (as illustrated in Figure 9-60), the so-called A-Train (Stephens et al., 2002, 190412) makes it possible for the first time to conduct near simultaneous (within 15 minutes) measurements of aerosols, clouds, and radiative fluxes in multiple dimensions with sensors in complementary capabilities.

The improved accuracy of aerosol products (mainly AOD) from these new-generation sensors, together with improvements in characterizing the earth's surface and clouds, can help reduce the uncertainties associated with estimating the aerosol direct radiative forcing (Yu et al., 2006, 156173); and references therein). The retrieved aerosol microphysical properties, such as size, absorption, and non-spherical fraction can help distinguish anthropogenic aerosols from natural aerosols and hence help assess the anthropogenic component of aerosol direct radiative forcing (Bellouin et al., 2005, 155684; Christopher et al., 2006, 155729; Kaufman et al., 2005, 155891; Yu et al., 2006, 156173). However, to infer aerosol number concentrations and examine indirect aerosol radiative effects from space, significant efforts are needed to measure aerosol size distribution with much improved accuracy, characterize aerosol type, account for impacts of water uptake on aerosol optical depth, and determine the fraction of aerosols that is at the level of the clouds (Kapustin et al., 2006, 190961; Rosenfeld, 2006, 190233). In addition, satellite remote sensing is not sensitive to particles much smaller than 0.1 micrometer in diameter, which comprise of a significant fraction of those that serve as cloud condensation nuclei.

Finally, algorithms are being developed to retrieve aerosol absorption or SSA from satellite observations (e.g., Kaufman et al., 2002, 190955; Torres et al., 2005, 190507). The NASA Glory mission, scheduled to launch in 2009 and to be added to the A-Train, will deploy a multi-angle, multispectral polarimeter to determine the global distribution of aerosol and clouds. It will also be able to infer microphysical property information, from which aerosol type (e.g., marine, dust, pollution, etc.) can be inferred for improving quantification of the aerosol direct and indirect forcing on climate (Mischenko et al., 2007, 190543).

In summary, major advances have been made in both passive and active aerosol remote sensing from space in the past decade, providing better coverage, spatial resolution, retrieved AOD accuracy, and particle property information. However, AOD accuracy is still much poorer than that from surface-based sun photometers (0.01-0.02), even over vegetated land and dark water where retrievals are most reliable. Although there is some hope of approaching this level of uncertainty with a new generation of satellite instruments, the satellite retrievals entail additional sensitivities to aerosol and surface scattering properties. It seems unlikely that satellite remote sensing could exceed the sun photometer accuracy without introducing some as-yet-unspecified new technology. Spacebased lidars are for the first time providing global constraints on aerosol vertical distribution, and multi-angle imaging is supplementing this with maps of plume injection height in aerosol source regions. Major advances have also been made during the past decade in distinguishing aerosol types from space, and the data are now useful for validating aerosol transport model simulations of aerosol air mass type distributions and transports, particularly over dark water. But particle size, shape, and especially SSA information has large uncertainty; improvements will be needed to better distinguish anthropogenic from natural aerosols using space-based retrievals. The particle microphysical property detail required to assess aerosol radiative forcing will come largely from targeted in situ and surface remote sensing measurements, at least for the near-future, although estimates of measurement-based aerosol RF can be made from judicious use of the satellite data with relaxed requirements for characterizing aerosol microphysical properties.

MODerate resolution Imaging Spectroradiometer

MODIS performs near global daily observations of atmospheric aerosols. Seven of 36 channels (between 0.47 and 2.13 μm) are used to retrieve aerosol properties over cloud and surface-screened areas (Li et al., 2004, 190386; Martins et al., 2002, 190470). Over vegetated land, MODIS retrieves aerosol optical depth at three visible channels with high accuracy of $\pm 0.05 \pm 0.2\tau$ (Chu et al., 2002, 190001; Kaufman and Fraser, 1997, 190958; Levy et al., 2007, 190379; Remer et al., 2005, 190221). Most recently a deep blue algorithm (Hsu et al., 2004, 190622) has been implemented to retrieve aerosols over bright deserts on an operational basis, with an estimated accuracy of 20-30%. Because of the greater simplicity of the ocean surface, MODIS has the unique capability of retrieving not only aerosol optical depth with greater accuracy, i.e., $\pm 0.03 \pm 0.05\tau$ (Remer et al., 2002, 190218; 2005, 190221; Remer et al., 2008, 190224; Tanré et al., 1997, 190452), but also quantitative aerosol size parameters (e.g., effective radius, fine-mode fraction of AOD) (Kaufman et al., 2002, 190956; Kleidman et al., 2005, 190175; Remer et al., 2005, 190221). The fine-mode fraction has been used as a tool for separating anthropogenic aerosol from natural ones and estimating the anthropogenic aerosol direct climate forcing (Kaufman et al., 2005, 155891). Figure 9-56 shows composites of MODIS AOD and fine-mode fraction that illustrate seasonal and geographical variations of aerosol types. Clearly seen from the figure is heavy pollution over East Asia in both months, biomass burning smoke over South Africa, South America, and Southeast Asia in August,

heavy dust storms over North Atlantic in both months and over Arabian Sea in August, and a mixture of dust and pollution plume swept across North Pacific in April.

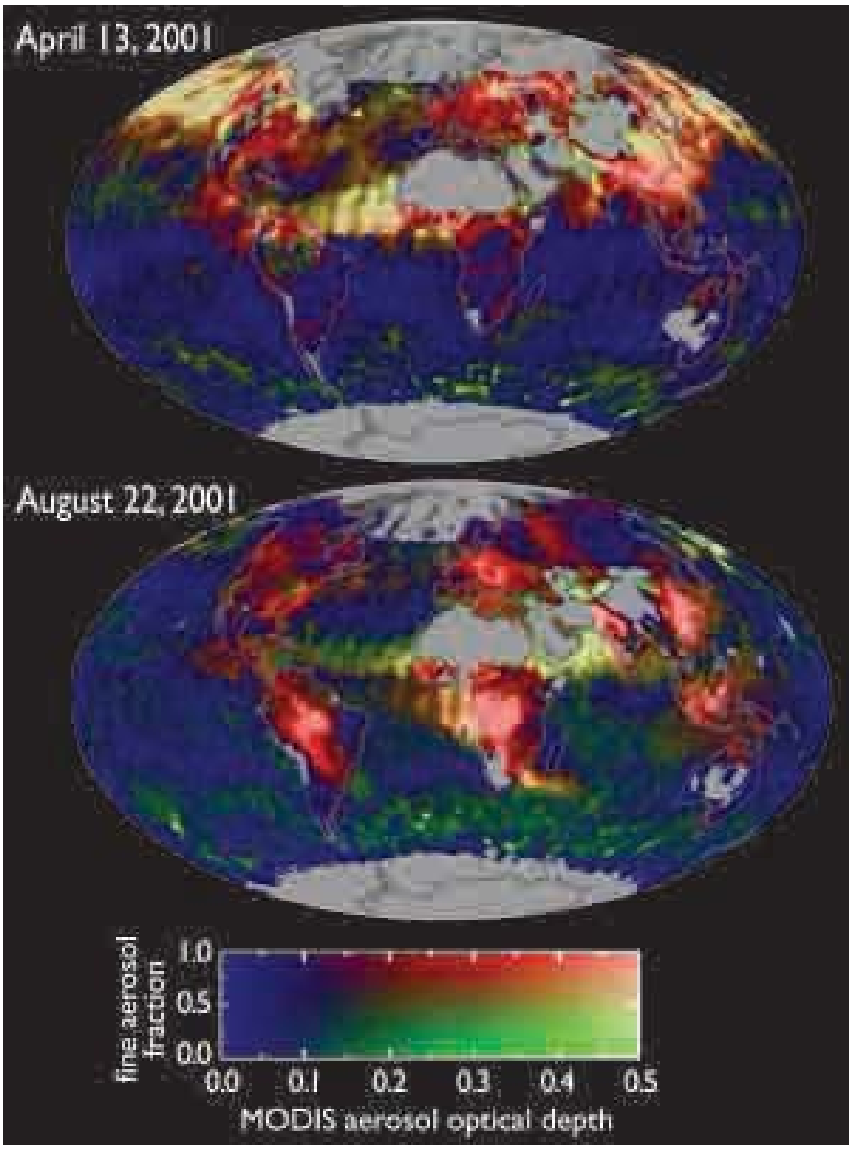
Multi-Angle Imaging SpectroRadiometer

MISR, aboard the sun-synchronous, polar orbiting satellite Terra, measures upwelling solar radiance in four visible-near-IR spectral bands and at nine view angles spread out in the forward and aft directions along the flight path (Diner et al., 2002, 189967). It acquires global coverage about once per week. A wide range of along-track view angles makes it feasible to more accurately evaluate the surface contribution to the TOA radiances and hence retrieve aerosols over both ocean and land surfaces, including bright desert and sunglint regions (Diner et al., 1998, 189962; Kahn et al., 2005, 190966; Martonchik et al., 1998, 190472; 2002, 190490). MISR AODs are within 20% or ± 0.05 of coincident AERONET measurements (Abdou et al., 2005, 190028; Kahn et al., 2005, 189961). The MISR multi-angle data also sample scattering angles ranging from about 60° to 160° in midlatitudes, yielding information about particle size (Chen et al., 2008, 189984; Kahn et al., 1998, 190970; 2001, 190969; 2005, 190966) and shape (Kalashnikova and Kahn, 2006, 190962). The aggregate of aerosol microphysical properties can be used to assess aerosol airmass type, a more robust characterization of MISR-retrieved particle property information than individual attributes. MISR also retrieves plume height in the vicinity of wildfire, volcano, and mineral dust aerosol sources, where the plumes have discernable spatial contrast in the multi-angle imagery (Kahn et al., 2007, 190964). Figure 9-57 is an example that illustrates MISR's ability to characterize the load, optical properties, and stereo height of near-source fire plumes.

POLarization and Directionality of the Earth's Reflectance

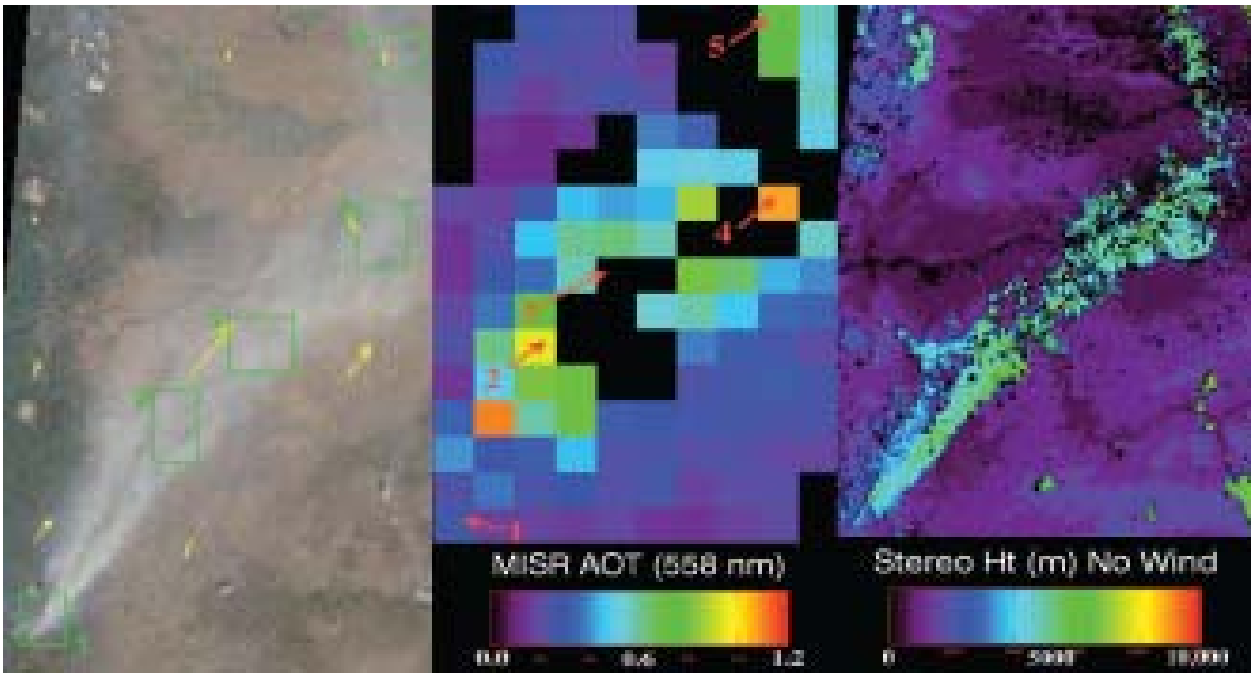
POLDER is a unique aerosol sensor that consists of wide field-of-view imaging spectro-radiometer capable of measuring multi-spectral, multi-directional, and polarized radiances (Deuzé et al., 2001, 192013). The observed radiances can be exploited to better separate the atmospheric contribution from the surface contribution over both land and ocean. POLDER -1 and -2 flew onboard the ADEOS (Advanced Earth Observing Satellite) from November 1996 to June 1997 and April to October of 2003, respectively. A similar POLDER instrument flies on the PARASOL satellite that was launched in December 2004.

Figure 9-58 shows global horizontal patterns of AOD and Ångström exponent over the oceans derived from the POLDER instrument for June 1997. The oceanic AOD map (Figure 9-58a) reveals near-coastal plumes of high AOD, which decrease with distance from the coast. This pattern arises from aerosol emissions from the continents, followed by atmospheric dispersion, transformation, and removal in the downwind direction. In large-scale flow fields, such as the trade winds, these continental plumes persist over several thousand kilometers. The Ångström exponent shown in Figure 9-58 exhibits a very different pattern from that of the aerosol optical depth; specifically, it exhibits high values downwind of industrialized regions and regions of biomass burning, indicative of small particles arising from direct emissions from combustion sources and/or gas-to-particle conversion, and low values associated with large particles in plumes of soil dust from deserts and in sea salt aerosols.



Source: Adapted from (Chin et al., 2007, 190062); original figure from Yoram Kaufman and Reto Stöckli.

Figure 9-56. A composite of MODIS/Terra observed aerosol optical depth (at 550 nm, green light near the peak of human vision) and fine-mode fraction that shows spatial and seasonal variations of aerosol types. Industrial pollution and biomass burning aerosols are predominately small particles (shown as red), whereas mineral dust and sea salt consist primarily of large particles (shown as green). Bright red and bright green indicate heavy pollution and dust plumes, respectively.

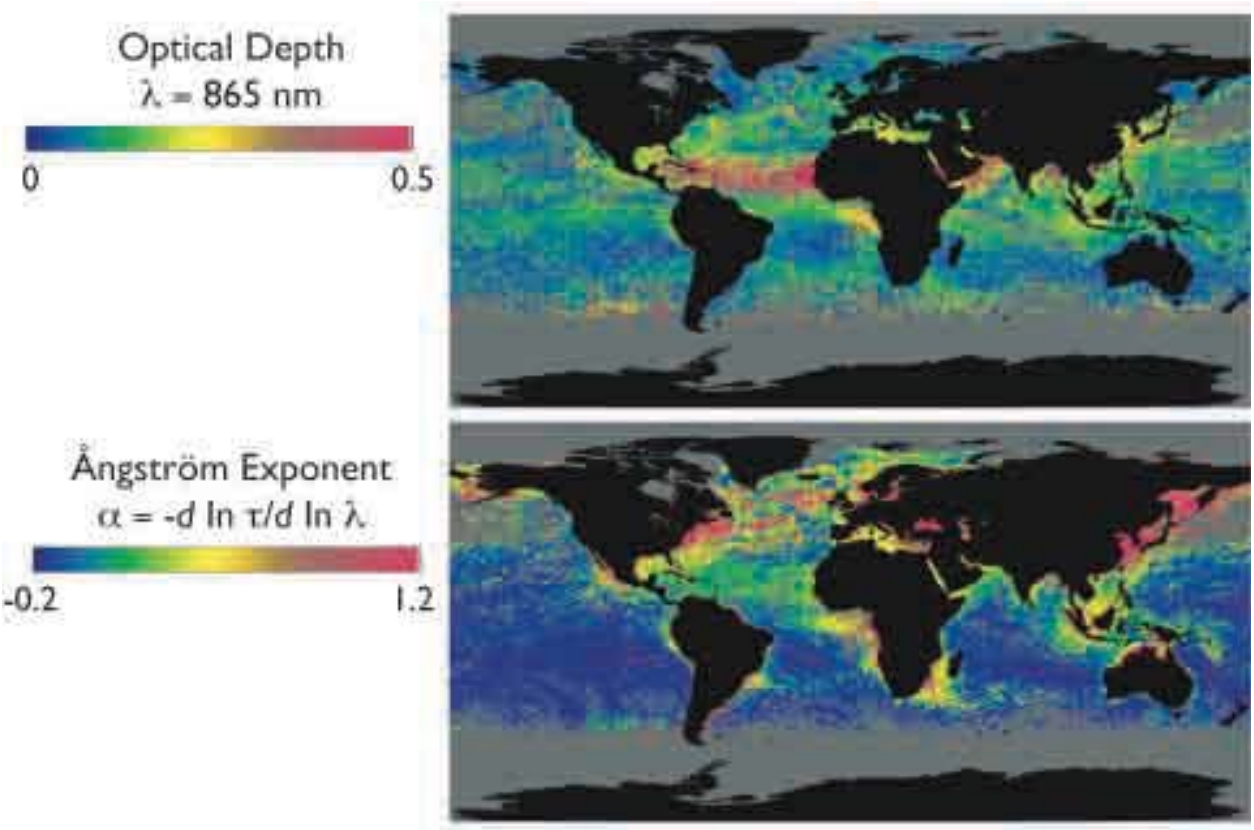


Source: Reprinted with Permission of theAmerican Geophysical Union from Kahn et al. (2007, 190964).

Figure 9-57. Oregon fire on September 4, 2003, as observed by MISR: (a) MISR nadir view of the fire plume, with five patch locations numbered and wind-vectors superposed in yellow; (b) MISR aerosol optical depth at 558 nm; and (c) MISR stereo height without wind correction for the same region.

9.3.2.2. Focused Field Campaigns

Over the past two decades, numerous focused field campaigns have examined the physical, chemical, and optical properties and radiative forcing of aerosols in a variety of aerosol regimes around the world, as listed in Table 9-5. These campaigns, which have been designed with aerosol characterization as the main goal or as one of the major themes in more interdisciplinary studies, were conducted mainly over or downwind of known continental aerosol source regions, but in some instances in low-aerosol regimes, for contrast. During each of these comprehensive campaigns, aerosols were studied in great detail, using combinations of in situ and remote sensing observations of physical and chemical properties from various platforms (e.g., aircraft, ships, satellites, and ground-based stations) and numerical modeling. In spite of their relatively short duration, these field studies have acquired comprehensive data sets of regional aerosol properties that have been used to understand the properties and evolution of aerosols within the atmosphere and to improve the climatology of aerosol microphysical properties used in satellite retrieval algorithms and CTMs.



Source : Reproduced with permission of Laboratoire d'Optique Atmospherique (LOA), Lille, FR; Laboratoire des Sciences du Climat et de l'Environnement (LSCE), Gif sur Yvette, FR; Centre National d'etudes Spatiales (CNES), Toulouse, FR; and NAtional Space Development Agency (NASDA), Japan.

Figure 9-58. Global maps at 18 km resolution showing monthly average (a) AOD at 865 nm and (b) Ångström exponent of AOD over water surfaces only for June, 1997, derived from radiance measurements by the POLDER.

9.3.2.3. Ground-Based In Situ Measurement Networks

Major U.S.-operated surface in situ and remote sensing networks for tropospheric aerosol characterization and climate forcing research are listed in Table 9-6. These surface in situ stations provide information about long-term changes and trends in aerosol concentrations and properties, the influence of regional sources on aerosol properties, climatologies of aerosol radiative properties, and data for testing models and satellite aerosol retrievals. The NOAA Earth System Research Laboratory (ESRL) aerosol monitoring network consists of baseline, regional, and mobile stations. These near-surface measurements include submicrometer and sub-10 micrometer scattering and absorption coefficients from which the extinction coefficient and single-scattering albedo can be derived. Additional measurements include particle concentration and, at selected sites, CCN concentration, the hygroscopic growth factor, and chemical composition.

Several of the stations, which are located across North America and world-wide, are in regions where recent focused field campaigns have been conducted. The measurement protocols at the stations are similar to those used during the field campaigns. Hence, the station data are directly comparable to the field campaign data so that they provide a longer-term measure of mean aerosol properties and their variability, as well as a context for the shorter-duration measurements of the field campaigns.

The Interagency Monitoring of Protected Visual Environment (IMPROVE), which is operated by the NP Service Air Resources Division, has stations across the U.S. located within NPs (Malm et al., 1994, 044920). Although the primary focus of the network is air pollution, the measurements are also relevant to climate forcing research. Measurements include fine and coarse mode ($PM_{2.5}$ and PM_{10}) aerosol mass concentration; concentrations of elements, sulfate, nitrate, organic carbon, and elemental carbon; and scattering coefficients.

In addition, to these U.S.-operated networks, there are other national and international surface networks that provide measurements of aerosol properties including, but not limited to, the World Meteorological Organization (WMO) Global Atmospheric Watch (GAW) network (http://www.wmo.int/pages/prog/arep/gaw/monitoring.html), the European Monitoring and Evaluation Programme (EMEP) (http://www.emep.int/), the Canadian Air and Precipitation Monitoring Network (CAPMoN) (http://www.msc-smc.ec.gc.ca/capmon/index_e.cfm), and the Acid Deposition Monitoring Network in East Asia (EANET) (http://www.eanet.cc/eanet.html).

Clouds and the Earth's Radiant Energy System

CERES measures broadband solar and terrestrial radiances at three channels with a large footprint (e.g., 20 km for CERES/Terra) (Wielicki et al., 1996, 190637). It is co-located with MODIS and MISR aboard Terra and with MODIS on Aqua. The observed radiances are converted to TOA irradiances or fluxes using the Angular Distribution Models (ADMs) that are functions of viewing angle, sun angle, and scene type (Loeb and Kato, 2002, 190432; Loeb et al., 2005, 190436; Zhang et al., 2005, 190929). Such estimates of TOA solar flux in clear-sky conditions can be compared to the expected flux for an aerosol-free atmosphere, in conjunction with measurements of aerosol optical depth from other sensors (e.g., MODIS and MISR) to derive the aerosol direct radiative forcing (Christopher et al., 2006, 155729; Loeb and Manalo-Smith, 2005, 190433; Patadia et al., 2008, 190558; Zhang and Christopher, 2003, 190928; Zhang et al., 2005, 190930). The derived instantaneous value is then scaled to obtain a daily average. A direct use of the coarse spatial resolution CERES measurements would exclude aerosol distributions in partly cloudy CERES scenes. Several approaches that incorporate coincident, high spatial and spectral resolution measurements (e.g., MODIS) have been employed to overcome this limitation (Loeb and Manalo-Smith, 2005, 190433; Zhang et al., 2005, 190930).

Active Remote Sensing of Aerosols

Following the success of a demonstration of lidar system aboard the U.S. Space Shuttle mission in 1994, i.e., Lidar In-space Technology Experiment (LITE) (Winker et al., 1996, 190914), the Geoscience Laser Altimeter System (GLAS) was launched in early 2003 to become the first polar orbiting satellite lidar. It provides global aerosol and cloud profiling for a one-month period out of every three-to-six months. It has been demonstrated that GLAS is capable of detecting and discriminating multiple layer clouds, atmospheric boundary layer aerosols, and elevated aerosol layers (e.g., Spinhirne et al., 2005, 190410). The Cloud-Aerosol Lidar and Infrared Pathfinder Satellite Observations (CALIPSO), launched on April 28, 2006, is carrying a lidar instrument (Cloud and Aerosol Lidar with Orthogonal Polarization - CALIOP) that has been collecting profiles of the attenuated backscatter at visible and near-infrared wavelengths along with polarized backscatter in the visible channel (Winker et al., 2003, 192017). CALIOP measurements have been used to derive the above-cloud fraction of aerosol extinction optical depth (Chand et al., 2008, 189974), one of the important factors determining aerosol direct radiative forcing in cloudy conditions. Figure 9-59 shows an event of trans-Atlantic transport of Saharan dust captured by CALIPSO. Flying in formation with the Aqua, AURA, POLDER, and CloudSat satellites, the vertically resolved information is expected to greatly improve passive aerosol and cloud retrievals as well as allow the retrieval of vertical distributions of aerosol extinction, fine- and coarse-mode separately (Huneeus and Boucher, 2007, 190624; Kaufman et al., 2003, 190954; Léon et al., 2003, 190366).

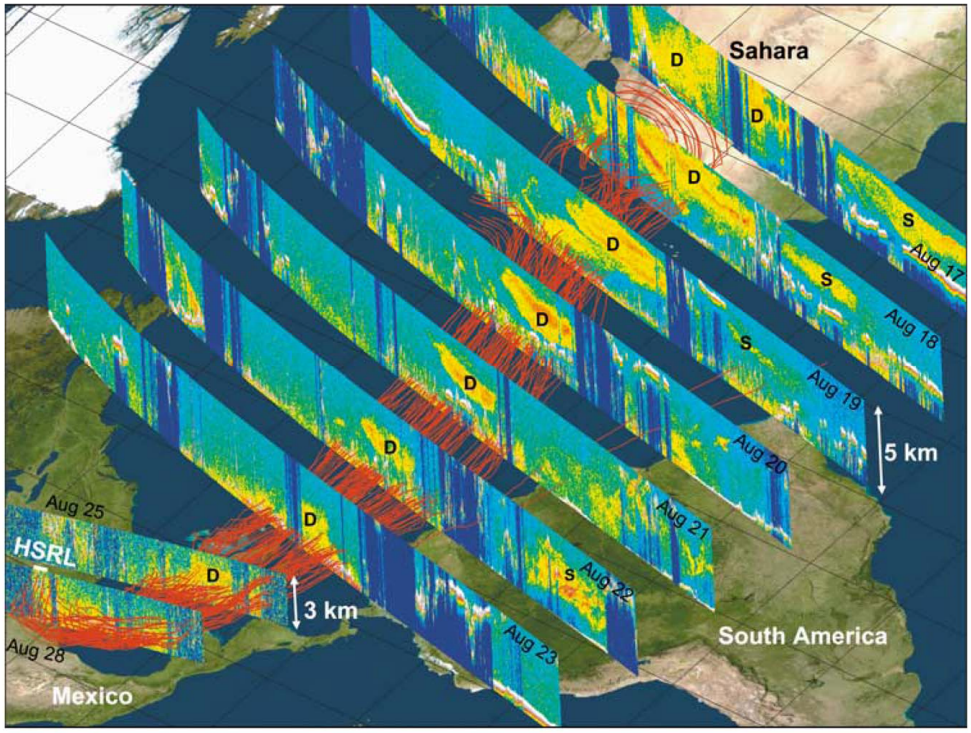


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Figure 9-59. A dust event that originated in the Sahara desert on 17 August 2007 and was transported to the Gulf of Mexico. Red lines represent back trajectories indicating the transport track of the dust event. Vertical images are 532 nm attenuated backscatter coefficients measured by CALIOP when passing over the dust transport track. The letter "D" designates the dust layer, and "S" represents smoke layers from biomass burning in Africa (17-19 August) and South America (22 August). The track of the high-spectral-resolution-lidar (HSRL) measurement is indicated by the white line superimposed on the 28 August CALIPSO image. The HSRL track is coincident with the track of the 28 August CALIPSO measurement off the coast of Texas between 28.75°N and 29.08°N.

9.3.2.4. In Situ Aerosol Profiling Programs

In addition to long-term ground based measurements, regular long-term aircraft in situ measurements recently have been implemented at several locations. These programs provide a statistically significant data set of the vertical distribution of aerosol properties to determine spatial and temporal variability through the vertical column and the influence of regional sources on that variability. In addition, the measurements provide data for satellite and model validation. As part of its long-term ground measurements, NOAA has conducted regular flights over Bondville, Illinois since 2006. Measurements include light scattering and absorption coefficients, the relative humidity dependence of light scattering, aerosol number concentration and size distribution, and chemical composition. The same measurements with the exception of number concentration, size distribution, and chemical composition were made by NOAA during regular overflights of DOE ARM's Southern Great Plains (SGP) site from 2000-2007 (Andrews et al., 2004, 190058) (http://www.esrl.noaa.gov/gmd/aero/net/index.html).

In summary of Sections 9.3.2.2, 9.3.2.3, and 9.3.2.4, in situ measurements of aerosol properties have greatly expanded over the past two decades as evidenced by the number of focused field campaigns in or downwind of aerosol source regions all over the globe, the continuation of existing and implementation of new sampling networks worldwide, and the implementation of regular aerosol profiling measurements from fixed locations. In addition, in situ measurement capabilities have undergone major advancements during this same time

period. These advancements include the ability to measure aerosol chemical composition as a function of size at a time resolution of seconds to minutes (e.g., Jayne et al., 2000, 190978), the development of instruments able to measure aerosol absorption and extinction coefficients at high sensitivity and time resolution and as a function of relative humidity (e.g., Baynard et al., 2007, 151669; Lack et al., 2006, 096032), and the deployment of these instruments across the globe on ships, at ground-based sites, and on aircraft. However, further advances are needed to make this newly developed instrumentation more affordable and turn-key so that it can be deployed more widely to characterize aerosol properties at a variety of sites worldwide.

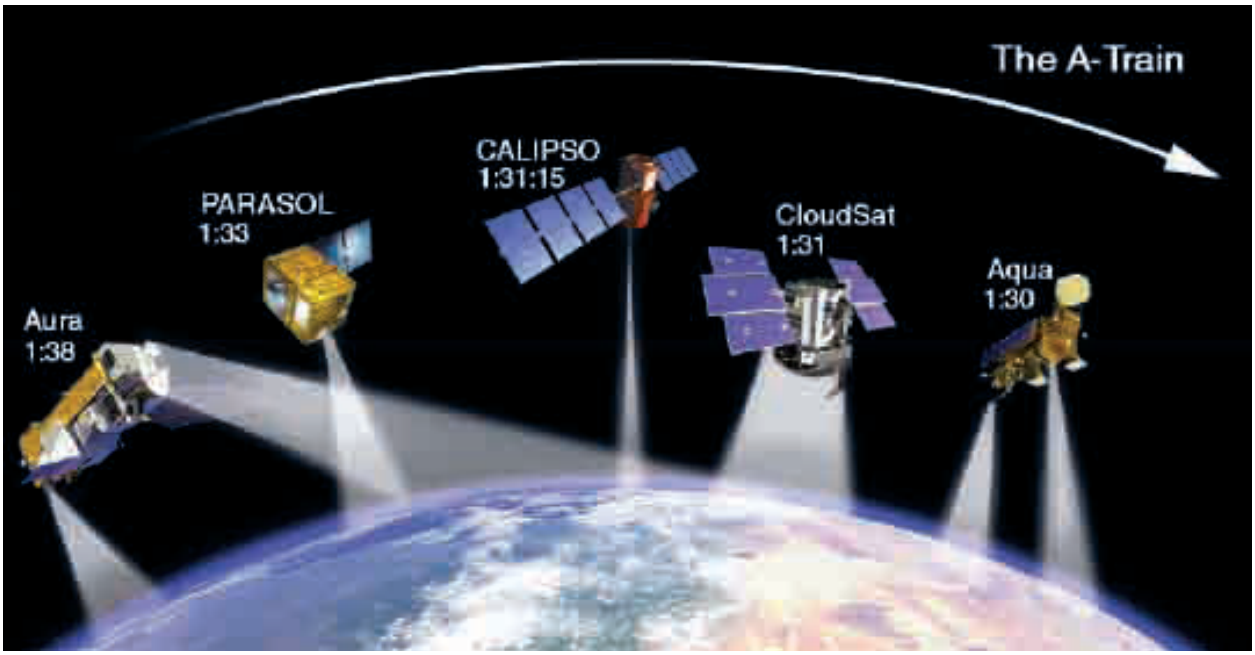


Figure 9-60. A constellation of five spacecraft that overfly the Equatorat about 1:30 p.m., the so-called A-Train, carries sensors having complementary capabilities, offering unprecedented opportunities to study aerosols from space in multiple dimensions.

Table 9-5. List of major intensive field experiments that are relevant to aerosol research in a variety of aerosol regimes around the globe conducted in the past two decades.

Aerosol Regimes	Intensive Field Experiments			Major References
	Name	Location	Time Period	
Anthropogenic aerosol and boreal forest from North America and West Europe	TARFOX	North Atlantic	July 1996	Russell et al. (1999, 190363)
	NEAQS	North Atlantic	July-August 2002	Quinn and Bates (2003, 049189)
	SCAR-A	North America	1993	Remer et al. (1997, 190216)
	CLAMS	East Coast of U.S.	July-August 2001	Smith et al. (2005, 190401)
	INTEX-NA, ICARTT	North America	Summer 2004	Fehsenfeld et al. (2006, 190531)
	DOE AIOP	Northern Oklahoma	May 2003	Ferrare et al. (2006, 190561)
	MILAGRO	Mexico City, Mexico	March 2006	Molina et al. (2008, 192019)
	TexAQS/GoMACCS	Texas and Gulf of Mexico	August-September 2006	Jiang et al. (2008, 156609); Lu et al. (2008, 190455)
	ARCTS	North-central Alaska to Greenland (Arctic haze)	March-April 2008	http://www.espo.nasa.gov/arctas/
	ARCTAS	Northern Canada (smoke)	June-July 2008	
	MINOS	Mediterranean region	July-August 2001	Lelieveld et al. (2002, 190361)
	LACE98	Lindberg, Germany	July-August 1998	Ansmann et al. (2002)
	Aerosols99	Atlantic	January-February 1999	Bates et al. (2001, 043385)
Brown haze in South Asia	INDOEX	Indian subcontinent and Indian Ocean	January-April 1998 & 1999	Ramanathan et al. (2001, 190196)
	ABC	South and East Asia	Ongoing	Ramanathan and Crutzen (2003, 190198)
Anthropogenic aerosol and desert dust mixture from East Asia	EAST-AIRE	China	March-April 2005	Li et al. (2007, 190392)
	INTEX-B	Northeastern Pacific	April 2006	Singh et al. (2008, 190394)
	ACE-Asia	East Asian and Northwest Pacific	April 2001	Huebert et al. (2003, 190623); Seinfeld et al. (2004, 190388)
	TRACE-P		March-April 2001	Jacob et al. (2003, 190987)
	PEM-West A & B	Western Pacific off East Asia	September-October 1991 February-March 1994	Hoell et al. (1996, 190607; 1997, 057373)
Biomass burning smoke in the tropics	BASE-A	Brazil	1989	Kaufman et al. (1992, 044557)
	SCAR-B	Brazil	August-September 1995	Kaufman et al. (1998, 089989)
	LBA-SMOCC	Amazon basin	September-November 2002	Andreae et al. (2004, 155658)
	SAFARI2000	South Africa and South Atlantic	August-September 2000	King et al. (2003, 094395)
	SAFARI92		September-October 1992	Lindesay et al. (1996, 190403)
	TRACE-ADABEX	South Atlantic	September-October 1992	Fishman et al. (1996, 190566)
	DABEX	West Africa	January-February 2006	Haywood et al. (2008, 190602)
Mineral dusts from North Africa and Arabian Peninsula	SAMUM	Southern Morocco	May-June 2006	Heintzenberg et al. (2008, 190605)
	SHADE	West coast of North Africa	September 2000	Tanrė et al. (2003, 190454)
	PRIDE	Puerto Rico	June-July 2000	Reid et al. (2003, 190213)
	UAE[2]	Arabian Peninsula	August-September 2004	Reid et al. (2008, 190214)
Remote oceanic aerosol	ACE-1	Southern Oceans	December 1995	Bates et al. ((1998, 190063) ; Quinn and Coffman (1998, 190918)

Source: Yu (2006, 156173)

Table 9-6. Summary of major U.S. surface in situ and remote sensing networks for the tropospheric aerosol characterization and radiative forcing research. All the reported quantities are column-integrated or column-effective, except as indicated.

	Surface Network	Measured/Derived Parameters				Spatial Coverage	Temporal Coverage
		Loading	Size, Shape	Absorption	Chemistry		
In situ	NOAA ESRL aerosol monitoring (http://www.esrl.noaa.gov/gmd/aero/)	Near-surface extinction coefficient, optical depth, CN/CNN number concentrations	Ångström exponent, hemispheric backscatter fraction, asymmetry factor, hygroscopic growth	Single-scattering albedo, absorption coefficient	Chemical composition in selected sites and periods	5 baseline stations, several regional stations, aircraft and mobile platforms	1976 onward
	NPS/EPA IMPROVE (http://vista.cira.colostate.edu/improve/)	Near-surface mass concentrations and derived extinction coefficients by species	Fine and coarse separately	Single-scattering albedo, absorption coefficient	Ions, ammonium SO_4^{2-}, ammonium nitrate organics, EC, fine soil	156 NPs and wilderness areas in the U.S.	1988 onward
Remote Sensing	NASA AERONET (http://aeronet.gsfc.nasa.gov)	Optical depth	Fine-mode fraction, Ångström exponents, asymmetry factor, phase function, non-spherical fraction	Single-scattering albedo, absorption optical depth, refractive indices	N/A	~200 sites over global land and islands	1993 onward
	DOE ARM (http://www.arm.gov)					6 sites and 1 mobile facility in N. America, Europe, and Asia	1989 onward
	NOAA SURFRAD (http://www.srrb.noaa.gov/surfrad/)		N/A	N/A	N/A	7 sites in the U.S.	1995 onward
	AERONET-MAN (http://aeronet.gsfc.nasa.gov/maritime_aerosol_network.html)					Global Ocean	2004-present periodically
	NASA MPLNET (http://mplnet.gsfc.nasa.gov/)	Vertical profiles of backscatter/ extinction coefficient	N/A	N/A	N/A	~30 sites in major continents, usually co-located with AERONET and ARM sites	2000 onward

Figure 9-61. Geographical coverage of active AERONET sites in 2006.

9.3.2.5. Ground-Based Remote Sensing Measurement Networks

The Aerosol Robotic Network (AERONET) program is a federated ground-based remote sensing network of well-calibrated sun photometers and radiometers (http://aeronet.gsfc.nasa.gov).

AERONET includes about 200 sites around the world, covering all major tropospheric aerosol regimes (Holben et al., 1998, 155848; 2001, 190618), as illustrated in Figure 9-61. Spectral measurements of sun and sky radiance are calibrated and screened for cloud-free conditions (Smirnov et al., 2000, 190397). AERONET stations provide direct, calibrated measurements of spectral AOD (normally at wavelengths of 440, 670, 870, and 1020 nm) with an accuracy of ± 0.015 (Eck et al., 1999, 190390). In addition, inversion-based retrievals of a variety of effective, column-mean properties have been developed, including aerosol single-scattering albedo, size distributions, fine-mode fraction, degree of non-sphericity, phase function, and asymmetry factor (Dubovik and King, 2000, 190197; Dubovik et al., 2000, 190177; Dubovik et al., 2002, 190202; O'Neill et al., 2003, 180187). The SSA can be retrieved with an accuracy of ± 0.03, but only for AOD >0.4 (Dubovik et al., 2002, 190202), which precludes much of the planet. These retrieved parameters have been validated or are undergoing validation by comparison to in situ measurements (e.g., Haywood et al., 2003, 190599; Leahy et al., 2007, 190232; Magi et al., 2005, 190468).

Recent developments associated with AERONET algorithms and data products include:

- simultaneous retrieval of aerosol and surface properties using combined AERONET and satellite measurements (Sinyuk et al., 2007, 190395) with surface reflectance taken into account (which significantly improves AERONET SSA retrieval accuracy) (Eck et al., 2008, 190409);
- the addition of ocean color and high frequency solar flux measurements; and
- the establishment of the Maritime Aerosol Network (MAN) component to monitor aerosols over the World oceans from ships of- opportunity (Smirnov et al., 2006, 190400).

Because of consistent calibration, cloud-screening, and retrieval methods, uniformly acquired and processed data are available from all stations, some of which have operated for over 10 years. These data constitute a high-quality, ground-based aerosol climatology and, as such, have been widely used for aerosol process studies as well as for evaluation and validation of model simulation and satellite remote sensing applications (e.g., Chin et al., 2002, 189996; Kahn et al., 2005, 190966; Remer et al., 2005, 190221; Yu et al., 2003, 156171; 2006, 156173). In addition, AERONET retrievals of aerosol size distribution and refractive indices have been used in algorithm development for satellite sensors (Levy et al., 2007, 190377; Remer et al., 2005, 190221). A set of aerosol optical properties provided by AERONET has been used to calculate the aerosol direct radiative forcing (Procopio et al., 2004, 190571; Zhou et al., 2005, 156183), which can be used to evaluate both satellite remote sensing measurements and model simulations.

AERONET measurements are complemented by other ground-based aerosol networks having less geographical or temporal coverage, such as the Atmospheric Radiation Measurement (ARM) network (Ackerman and Stokes, 2003, 192080), NOAA's national surface radiation budget network (SURFRAD) (Augustine et al., 2008, 189913) and other networks with multifilter rotating shadowband radiometer (MFRSR) (Harrison et al., 1994, 045805; Michalsky et al., 2001, 190537), and several lidar networks including:

- NASA Micro Pulse Lidar Network (MPLNET) (Welton et al., 2001, 157133; Welton et al., 2002, 190631);
- Regional East Atmospheric Lidar Mesonet (REALM) in North America (Hoff and McCann, 2002, 190612; Hoff et al., 2004, 190617);
- European Aerosol Research Lidar Network (EARLINET) (Matthias et al., 2004, 155971); and
- Asian Dust Network (AD-Net) (e.g., Murayama et al., 2001, 155992).

Obtaining accurate aerosol extinction profile observations is pivotal to improving aerosol radiative forcing and atmospheric response calculations. The values derived from these lidar networks with state-of-the-art techniques (Schmid et al., 2006, 190372) are helping to fill this need.

9.3.2.6. Synergy of Measurements and Model Simulations

Individual approaches discussed above have their own strengths and limitations, and are usually complementary. None of these approaches alone is adequate to characterize large spatial and temporal variations of aerosol physical and chemical properties and to address complex aerosol-climate interactions. The best strategy for characterizing aerosols and estimating their radiative forcing is to integrate measurements from different satellite sensors with complementary capabilities from in situ and surface based measurements. Similarly, while models are essential tools for estimating regional and global distributions and radiative forcing of aerosols at present as well as in the past and the future, observations are required to provide following, several synergistic approaches to studying aerosols and their radiative forcing are discussed.

Closure Experiments

During intensive field studies, multiple platforms and instruments are deployed to sample regional aerosol properties through a well-coordinated experimental design. Often, several independent methods are used to measure or derive a single aerosol property or radiative forcing. This combination of methods can be used to identify inconsistencies in the methods and to quantify uncertainties in measured, derived, and calculated aerosol properties and radiative forcings. This approach, often referred to as a closure experiment, has been widely employed on both individual measurement platforms (local closure) and in studies involving vertical measurements through the atmospheric column by one or more platforms (column closure) (Quinn et al., 1996, 192021; Russell et al., 1997, 190359).

Past closure studies have revealed that the best agreement between methods occurs for submicrometer, spherical particles such that different measures of aerosol optical properties and optical depth agree within 10-15% and often better (e.g., Clarke et al., 1996, 190003; Collins et al., 2000, 190059; Quinn et al., 2004, 190937; Schmid et al., 2000, 190369). Larger particle sizes (e.g., sea salt and dust) present inlet collection efficiency issues and non-spherical particles (e.g., dust) lead to differences in instrumental responses. In these cases, differences between methods for determining aerosol optical depth can be as great as 35% (Doherty et al., 2005, 190027; Wang et al., 2003, 157106). Closure studies on aerosol clear-sky DRF reveal uncertainties of about 25% for sulfate/carbonaceous aerosol and 60% for dust-containing aerosol (Bates et al., 2006, 189912). Future closure studies could integrate surface- and satellite-based radiometric measurements of AOD with in situ optical, microphysical, and aircraft radiometric measurements for a wide range of situations. There is also a need to maintain consistency in comparing results and expressing uncertainties (Bates et al., 2006, 189912).

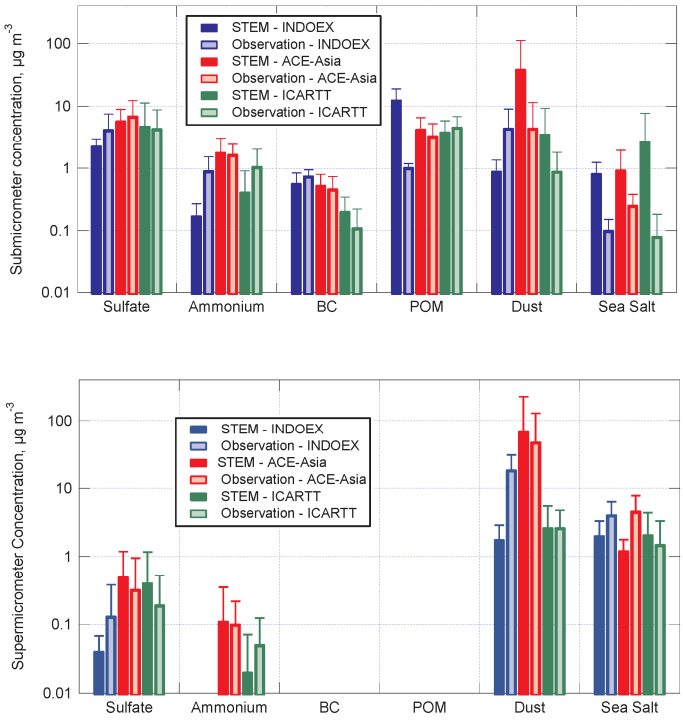
Constraining Models with In Situ Measurements

In situ measurements of aerosol chemical, microphysical, and optical properties with known accuracy, based in part on closure studies, can be used to constrain regional CTM simulations of aerosol direct forcing, as described by Bates et al. (2006, 189912). A key step in the approach is assigning empirically derived optical properties to the individual chemical components generated by the CTM for use in a Radiative Transfer Model (RTM). Specifically, regional data from focused, short-duration field programs can be segregated according to aerosol type (sea salt, dust, or sulfate/carbonaceous) based on measured chemical composition and particle size. Corresponding measured optical properties can be carried along in the sorting process so that they, too, are segregated by aerosol type. The empirically derived aerosol properties for individual aerosol types, including mass scattering efficiency, single-scattering albedo, and asymmetry factor, and their dependences on relative humidity, can be used in place of assumed values in CTMs. Short-term, focused measurements of aerosol properties (e.g., aerosol concentration and AOD) also can be used to evaluate CTM parameterizations on a regional basis, to suggest improvements to such uncertain model parameters, such as emission factors and scavenging coefficients (e.g., Koch et al., 2007, 190185). Improvements in these parameterizations using observations yield increasing confidence in simulations covering regions and periods where and when measurements are not available. To evaluate the aerosol

properties generated by CTMs on broader scales in space and time, satellite observations and long-term in situ measurements are required.

Improved Model Simulations with Satellite Measurements

Global measurements of aerosols from satellites (mainly AOD) with well-defined accuracies offer an opportunity to evaluate model simulations at large spatial and temporal scales. The satellite measurements can also be used to constrain aerosol model simulations and hence the assessment of aerosol DRF through data assimilation or objective analysis process (e.g., Collins et al., 2001, 189987; Liu et al., 2005, 190414; Yu et al., 2003, 156171; 2004, 190926; 2006, 156173; Zhang et al., 2008, 190932). Both satellite retrievals and model simulations have uncertainties. The goal of data integration is to minimize the discrepancies between them, and to form an optimal estimate of aerosol distributions by combining them, typically with weights inversely proportional to the square of the errors of individual descriptions. Such integration can fill gaps in satellite retrievals and generate global distributions of aerosols that are consistent with ground-based measurements (Collins et al., 2001, 189987; Liu et al., 2005, 190414; Yu et al., 2003, 156171; 2006, 156173). Recent efforts have also focused on retrieving global sources of aerosol from satellite observations using inverse modeling, which may be valuable for reducing large aerosol simulation uncertainties (Dubovik et al., 2007, 190211). Model refinements guided by model evaluation and integration practices with satellite retrievals can then be used to improve aerosol simulations of the pre- and post-satellite eras. Current measurement-based understanding of aerosol characterization and radiative forcing is assessed in Section 9.3.3 through intercomparisons of a variety of measurement-based estimates and model simulations published in literature. This is followed by a detailed discussion of major outstanding issues in Section 9.3.4.



Source: Bates et al. (2006, 189912).

Figure 9-62. Comparison of the mean concentration (μg/m^3) and standard deviation of the modeled (STEM) aerosol chemical components with shipboard measurements during INDOEX, ACE-Asia, and ICARTT.

Further complexity is added when attempting to relate surface $PM_{2.5}$ to aerosol optical depths. The main approach to derive surface $PM_{2.5}$ from satellite optical depths from MISR is based on the

use of model derived profiles to determine ratios of aerosol optical depth to surface $PM_{2.5}$ (Liu and Koutrakis, 2007, 187007; Liu et al., 2007, 098197; Van Donkelaar et al., 2006, 192108).

Van Donkelaar et al. (2006, 192108) derived r = 0.69 (MODIS) and 0.58 (MISR) with annual average ground based $PM_{2.5}$ across the U.S. and Canada. For comparison, r between AERONET total AOD and surface measurements was 0.71. On average, MODIS tended to overestimate surface $PM_{2.5}$ by ~5 $\mu g/m^3$, while MISR estimates were biased high by about 3 $\mu g/m^3$. Liu et al. (2007, 098197) and Liu and Koutrakis (2007, 187007) used MISR derived fractional AODs in their analysis and found improvement in the retrievals when fractional AODs were used instead of total AOD, allowing for better fits to the radiance data. They found that fractional AODs can explain 13-62% of the variability in $PM_{2.5}$ and its components in the eastern U.S. and 28-56% of the variability in the western U.S. The models tended to underpredict $PM_{2.5}$ by ~7-8% in both the East and West. The relative errors in surface $PM_{2.5}$ were estimated to be 30% in the East and 34% in the West. For AODs >0.15 (nominal continental background values), dust particles could be distinguished from other particles with an estimated error of 4%. Performance improves substantially over polluted urban areas because they have much larger AOD. For example, Gupta et al. (2006, 137694) derived a Pearson r between MODIS AOD and surface $PM_{2.5}$ of 0.96 for several urban areas around the world. The MODIS Aerosol Optical Depth (AOD)/ In-situ $PM_{2.5}$ correlation summary plot shown in Figure 9-63 below illustrates the correlation between AOD and surface $PM_{2.5}$ across the U.S. and parts of Canada. The correlation is based on coincident MODIS AOD pixels and 1-h $PM_{2.5}$ concentrations from the in-situ continuous surface monitors. The parameter plotted is the monitoring site-specific running correlation coefficient during the preceding 60 days (in color scale). The correlation coefficient has values between 1 (perfectly correlated) and -1 (perfectly anti-correlated). A value of zero indicates that the two measurements vary independently of each other.

The running time period of the correlation determination is given in the plot title, 20090704-20090901. The size of the point at each site indicates the number of coincidences between MODIS AOD pixels and the measured surface 1-h $PM_{2.5}$ concentrations for that period. Correlation significance generally increases with increasing number of coincidences. Higher correlations suggest the MODIS AOD pixel is reflective of in-situ surface $PM_{2.5}$ mass concentrations at the monitor location.

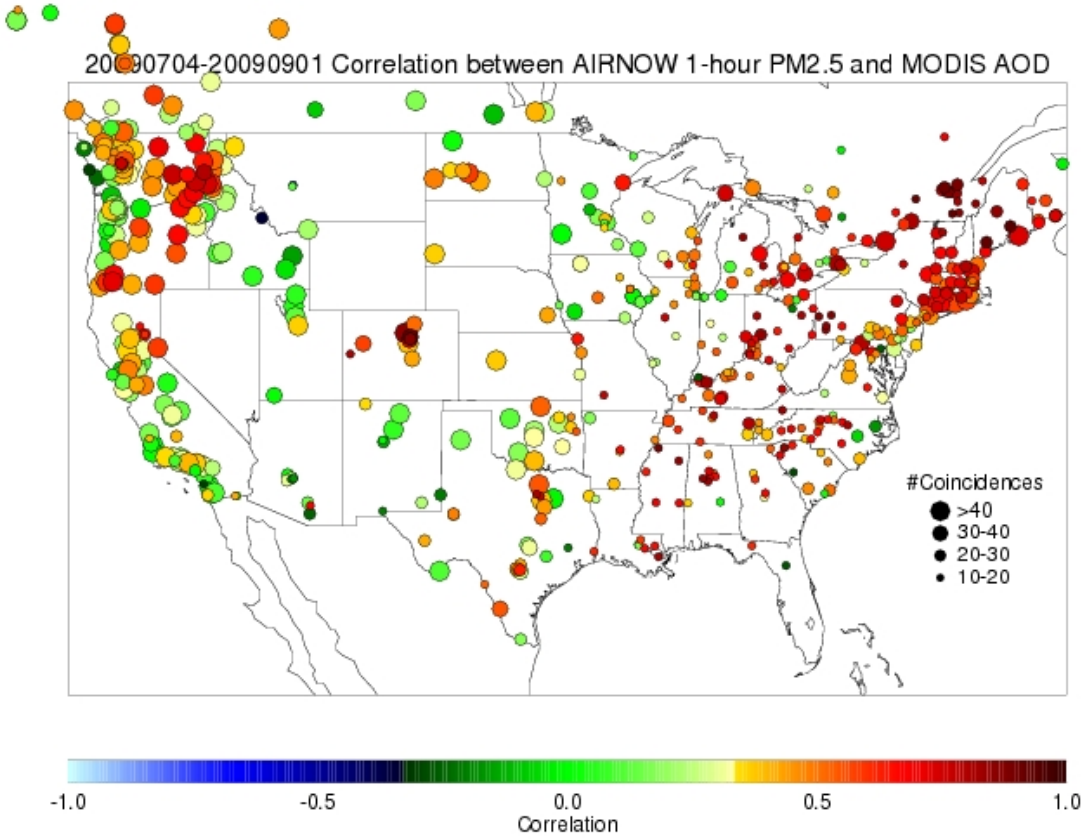


Figure 9-63. Correlations between one-hour $PM_{2.5}$ surface measurements in the U.S. and southern Canada reported to AIRNOW and MODIS satellite AOD values for the period between 4 July and 1 September 2009. Symbol size indicates number of coincident points at that location in that period; symbol color is indexed to degree of correlation from -1 (cooler) to +1 (warmer).

The data and image of the aerosol comparison shown in Figure 9-63 were taken from the multi-agency project, Infusing satellite Data into Environmental Air Quality Applications (IDEA), a partnership of NASA, NOAA, and EPA designed to improve air quality assessment, management, and prediction by infusing NASA satellite measurements into NOAA and EPA analyses for public benefit. IDEA is funded by these three agencies and managed by the University of Maryland Baltimore County and NOAA.

9.3.3. Assessments of Aerosol Characterization and Climate Forcing

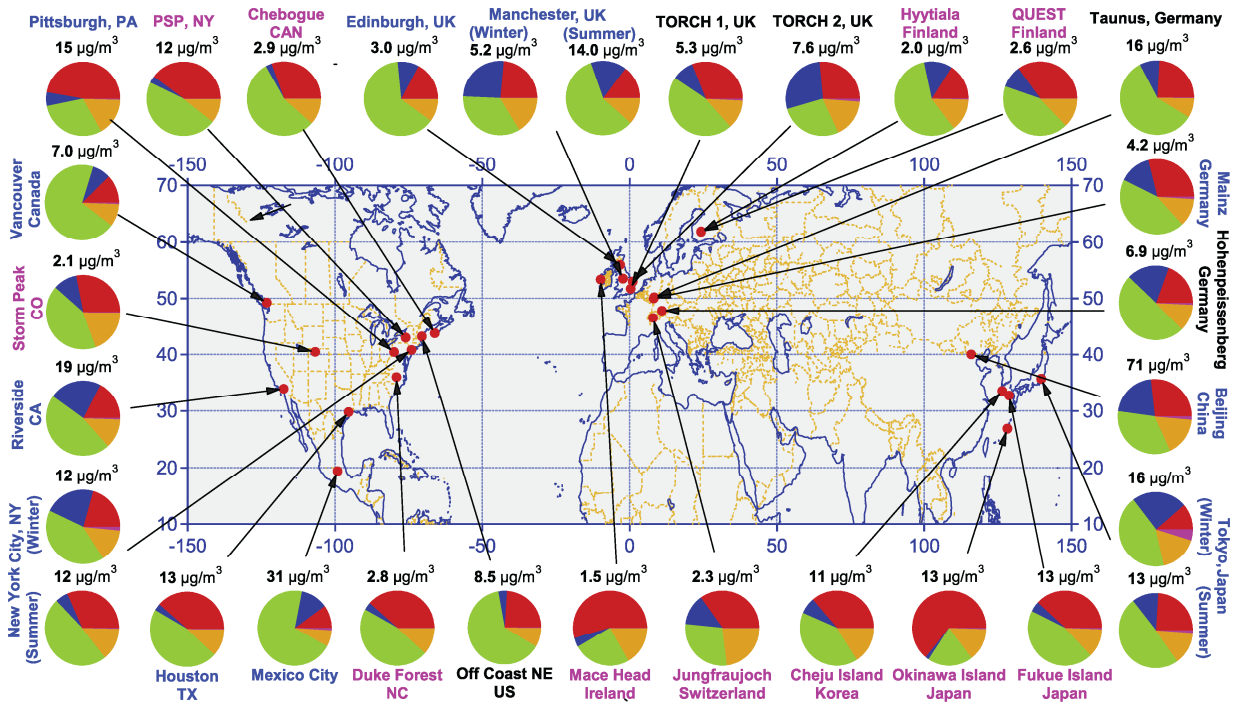
Sections 9.3.3 through 9.3.6 come directly from CCSP SAP2.3 Chapters 2, Section 2.3 through Chapter 3, Section 3.8, with section, table, and figure numbers changed to be internally consistent with this ISA.

This section focuses on the assessment of measurement-based aerosol characterization and its use in improving estimates of the direct radiative forcing on regional and global scales. In situ measurements provide highly accurate aerosol chemical, microphysical, and optical properties on a regional basis and for the particular time period of a given field campaign. Remote sensing from satellites and ground-based networks provide spatial and temporal coverage that intensive field campaigns lack. Both in situ measurements and remote sensing have been used to determine key parameters for estimating aerosol direct radiative forcing including aerosol single scattering albedo, asymmetry factor, optical depth remote sensing has also been providing simultaneous measurements of aerosol optical depth and radiative fluxes that can be combined to derive aerosol direct radiative forcing at the TOA with relaxed requirement for characterizing aerosol properties. Progress in using both satellite and surface-based measurements to study aerosol-cloud interactions and aerosol indirect forcing is also discussed.

9.3.3.1. The Use of Measured Aerosol Properties to Improve Models

The wide variety of aerosol data sets from intensive field campaigns provides a rigorous "testbed" for model simulations of aerosol properties and distributions and estimates of DRF. As described in Section 9.3.2.6, in situ measurements can be used to constrain regional CTM simulations of aerosol properties, DRF, anthropogenic component of DRF, and to evaluate CTM parameterizations. In addition, in situ measurements can be used to develop simplifying parameterizations for use by CTMs.

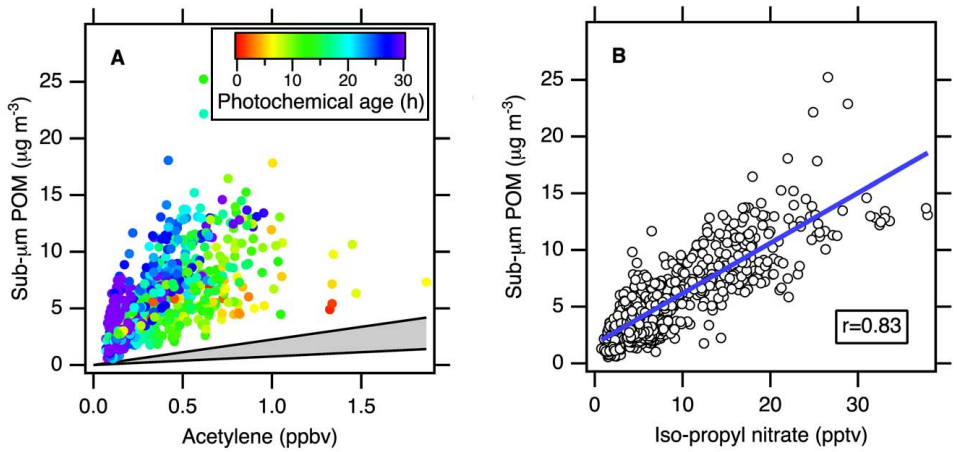
Several factors contribute to the uncertainty of CTM calculations of size-distributed aerosol composition including emissions, aerosol removal by wet deposition, processes involved in the formation of secondary aerosols and the chemical and microphysical evolution of aerosols, vertical transport, and meteorological fields including the timing and amount of precipitation, formation of clouds, and relative humidity. In situ measurements made during focused field campaigns provide a point of comparison for the CTM-generated aerosol distributions at the surface and at discrete points above the surface. Such comparisons are essential for identifying areas where the models need improvement.



Source: Data from Zhang et al. (2007, 189998).

Figure 9-64. Location of aerosol chemical composition measurements with aerosol mass spectrometers. Colors for the labels indicate the type of sampling location: urban areas (blue), <100 mi downwind of major cites (black), and rural/remote areas >100 miles downwind (pink). Pie charts show the average mass concentration and chemical composition: organics (green), SO_4^{2-} (red), nitrate (blue), ammonium (orange), and chloride (purple), of non-refractory PM_1.

Figure 9-62 shows a comparison of submicrometer and supermicrometer aerosol chemical components measured during INDOEX, ACEAsia, and ICARTT onboard a ship and the same values calculated with the STEM Model (e.g., Bates et al., 2004, 189958; Carmichael et al., 2002, 148319; Carmichael et al., 2003, 190042; Streets et al., 2006, 157019; Tang et al., 2003, 190441; Tang et al., 2004, 190445). To permit direct comparison of the measured and modeled values, the model was driven by analyzed meteorological data and sampled at the times and locations of the shipboard measurements every 30 min along the cruise track. The best agreement was found for submicrometer sulfate and BC. The agreement was best for sulfate; this is attributed to greater accuracy in emissions, chemical conversion, and removal for this component. Underestimation of dust and sea salt is most likely due to errors in model-calculated emissions. Large discrepancies between the modeled and measured values occurred for submicrometer particulate organic matter (POM) (INDOEX), and for particles in the supermicrometer size range such as dust (ACE-Asia), and sea salt (all regions). The model underestimated the total mass of the supermicrometer aerosol by about a factor of 3. POM makes up a large and variable fraction of aerosol mass throughout the anthropogenically influenced northern hemisphere, and yet models have severe problems in properly representing this type of aerosol. Much of this discrepancy follows from the models inability to represent the formation of secondary organic aerosols (SOA) from the precursor volatile organic compounds (VOC). Figure 9-64 shows a summary of the results from aerosol mass spectrometer measurements at 30 sites over North America, Europe, and Asia. Based on aircraft measurements of urban-influenced air over New England, de Gouw et al. (2005, 190020) found that POM was highly correlated with secondary anthropogenic gas phase species suggesting that the POM was derived from secondary anthropogenic sources and that the formation took one day or more.



Source: Data from de Guow et al. (2005, 190020).

Figure 9-65. Scatterplots of the submicrometer POM measured during NEAQS versus A) acetylene and B) iso-propyl nitrate. The colors of the data points in A) denote the photochemical age as determined by the ratios of compounds of known OH reactivity. The gray area in A) shows the range of ratios between submicrometer POM and acetylene observed by Kirchstetter et al. (1999, 010642) in tunnel studies.

Figure 9-65 shows scatterplots of submicrometer POM versus acetylene (a gas phase primary emitted VOC species) and isopropyl nitrate (a secondary gas phase organic species formed by atmospheric reactions). The increase in submicrometer POM with increasing photochemical age could not be explained by the removal of VOC alone, which are its traditionally recognized precursors. This result suggests that other species must have contributed and/or that the mechanism for POM formation is more efficient than assumed by models. Similar results were obtained from the 2006 MILAGRO field campaign conducted in Mexico City (Kleinman et al., 2008, 190074), and comparisons of GCM results with several long-term monitoring stations also showed that the model underestimated organic aerosol concentrations (Koch et al., 2007, 190185). Recent laboratory work suggests that isoprene may be a major SOA source missing from previous atmospheric models (Henze and Seinfeld, 2006, 190606; Kroll et al., 2006, 190195), but underestimating sources from certain economic sectors may also play a role (Koch et al., 2007, 190185). Models also have difficulty in representing the vertical distribution of organic aerosols, underpredicting their occurrence in the free troposphere (FT) (Heald et al., 2005, 190603). While organic aerosol presents models with some of their greatest challenges, even the distribution of well-characterized sulfate aerosol is not always estimated correctly in models (Shindell et al., 2008, 190391).

Comparisons of DRF and its anthropogenic component calculated with assumed optical properties and values constrained by in situ measurements can help identify areas of uncertainty in model parameterizations. In a study described by Bates et al. (2006, 189912), two different CTMs (MOZART and STEM) were used to calculate dry mass concentrations of the dominant aerosol species (sulfate, organic carbon, BC, sea salt, and dust).

In situ measurements were used to calculate the corresponding optical properties for each aerosol type for use in a radiative transfer model. Aerosol DRF and its anthropogenic component estimated using the empirically derived and a priori optical properties were then compared. The DRF and its anthropogenic component were calculated as the net downward solar flux difference between the model state with aerosol and of the model state with no aerosol. It was found that the constrained optical properties derived from measurements increased the calculated AOD (34 ± 8%), TOA DRF (32 ± 12%), and anthropogenic component of TOA DRF (37 ± 7%) relative to runs using the a priori values. These increases were due to larger values of the constrained mass extinction efficiencies relative to the a priori values. In addition, differences in AOD due to using the aerosol loadings from MOZART versus those from STEM were much greater than differences resulting from the a priori vs. constrained RTM runs. In situ observations also can be used to generate simplified parameterizations for CTMs and RTMs thereby lending an empirical foundation to uncertain parameters currently in use by models. CTMs generate concentration fields of individual aerosol chemical components that are then used as input to radiative transfer models (RTMs) for the calculation of DRF. Currently, these calculations are performed with a variety of simplifying assumptions concerning the RH dependence of light scattering by the aerosol.

Chemical components often are treated as externally mixed each with a unique RH dependence of light scattering. However, both model and measurement studies reveal that POM, internally mixed with water-soluble salts, can reduce the hygroscopic response of the aerosol, which decreases its water content and ability to scatter light at elevated relative humidity (e.g., Carrico et al., 2005, 190052; Saxena et al., 1995, 077273).

The complexity of the POM composition and its impact on aerosol optical properties requires the development of simplifying parameterizations that allow for the incorporation of information derived from field measurements into calculations of DRF (Quinn et al., 2005, 156033). Measurements made during INDOEX, ACE-Asia, and ICARTT revealed a substantial decrease in fσsp(RH) with increasing mass fraction of POM in the accumulation mode. Based on these data, a parameterization was developed that quantitatively describes the relationship between POM mass fraction and fσsp(RH) for accumulation mode sulfate-POM mixtures (Quinn et al., 2005, 156033). This simplified parameterization may be used as input to RTMs to derive values of fσsp(RH) based on CTM estimates of the POM mass fraction. Alternatively, the relationship may be used to assess values of fσsp(RH) currently being used in RTMs.

9.3.3.2. Intercomparisons of Satellite Measurements and Model Simulation of Aerosol Optical Depth

As aerosol DRF is highly dependent on the amount of aerosol present, it is of first-order importance to improve the spatial characterization of AOD on a global scale. This requires an evaluation of the various remote sensing AOD data sets and comparison with model-based AOD estimates. The latter comparison is particularly important if models are to be used in projections of future climate states that would result from assumed future emissions. Both remote sensing and model simulation have uncertainties and satellite-model integration is needed to obtain an optimum description of aerosol distribution.

Figure 9-65 shows an intercomparison of annual average AOD at 550 nm from two recent satellite aerosol sensors (MODIS and MISR), five model simulations (GOCART, GISS, SPRINTARS, LMDZ-LOA, LMDZ-INCA) and three satellite-model integrations (MO_GO, MI_GO, MO_MI_GO). These model-satellite integrations are conducted by using an optimum interpolation approach (Yu et al., 2003, 156171) to constrain GOCART simulated AOD with that from MODIS, MISR, or MODIS over ocean and MISR over land, denoted as MO_GO, MI_GO, and MO_MI_GO, respectively. MODIS values of AOD are from Terra Collection 4 retrievals and MISR AOD is based on early post launch retrievals. MODIS and MISR retrievals give a comparable average AOD on the global scale, with MISR greater than MODIS by 0.01~0.02 depending on the season. However, differences between MODIS and MISR are much larger when land and ocean are examined separately: AOD from MODIS is 0.02-0.07 higher over land but 0.03-0.04 lower over ocean than the AOD from MISR. Several major causes for the systematic MODIS-MISR differences have been identified, including instrument calibration and sampling differences, different assumptions about ocean surface boundary conditions made in the individual retrieval algorithms, missing particle property or mixture options in the look-up tables, and cloud screening (Kahn et al., 2007, 190963). The MODIS-MISR AOD differences are being reduced by continuous efforts on improving satellite retrieval algorithms and radiance calibration. The new MODIS aerosol retrieval algorithms in Collection 5 have resulted in a reduction of 0.07 for global land mean AOD (Levy et al., 2007, 190379), and improved radiance calibration for MISR removed ~40% of AOD bias over dark water scenes (Kahn et al., 2005, 190965).

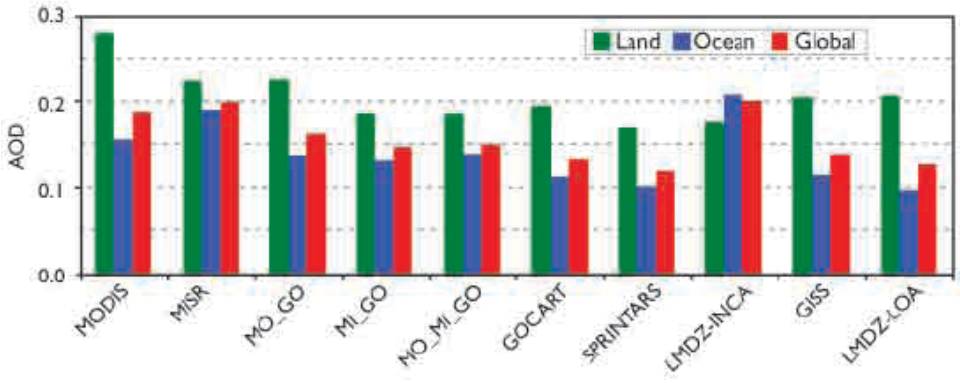
The annual and global average AOD from the five models is 0.19 ± 0.02 (mean ± standard deviation) over land and 0.13 ± 0.05 over ocean, respectively. Clearly, the model-based mean AOD is smaller than both MODIS- and MISR-derived values (except the GISS model). A similar conclusion has been drawn from more extensive comparisons involving more models and satellites (Kinne et al., 2006, 155903). On regional scales, satellite-model differences are much larger. These differences could be attributed in part to cloud contamination (Kaufman et al., 2005, 155891; Zhang et al., 2005, 190931) and 3D cloud effects in satellite retrievals (Kaufman et al., 2005, 155891; Wen et al., 2006, 179964) or to models missing important aerosol sources/sinks or physical processes (Koren et al., 2007, 190192). Integrated satellite-model products are generally in-between the satellite retrievals and the model simulations, and agree better with AERONET measurements (e.g., Yu et al., 2003, 156171). As in comparisons between models and in situ measurements (Bates et al., 2006, 189912), there appears to be a relationship between uncertainties in the representation of dust in models and the uncertainty in AOD, and its global distribution.

For example, the GISS model generates more dust than the other models (Figure 9-67), resulting in a closer agreement with MODIS and MISR in the global mean (Source: Data taken from Kinne et al. (2006, 155903)

Figure 9-66). However, the distribution of AOD between land and ocean is quite different from MODIS- and MISR-derived values.

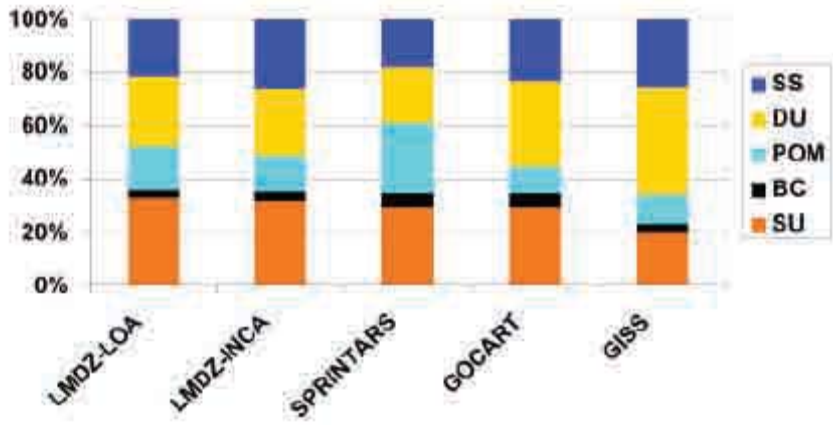
Figure 9-67 shows larger model differences in the simulated percentage contributions of individual components to the total aerosol optical depth on a global scale, and hence in the simulated aerosol single-scattering properties (e.g., single-scattering albedo, and phase function), as documented in Kinne et al. (2006, 155903). This, combined with the differences

in aerosol loading (as characterized by AOD) determines the model diversity in simulated aerosol direct radiative forcing, as discussed later. However, current satellite remote sensing capability is not sufficient to constrain model simulations of aerosol components.



Source: Data taken from Kinne et al. (2006, 155903)

Figure 9-66. Comparison of annual mean aerosol optical depth (AOD).



Source: Data taken from Kinne et al. (2006, 155903).

Figure 9-67. Percentage contributions of individual aerosol components. SU – sulfate, BC – BC, POM – particulate organic matter, DU – dust, SS – sea salt; to the total aerosol optical depth (at 550 nm) on a global scale simulated by the five models.

9.3.3.3. Satellite-Based Estimates of Aerosol Direct Radiative Forcing

Table 9-7 summarizes approaches to estimating the aerosol direct radiative forcing, including a brief description of methods, identifies major sources of uncertainty, and provides references. These estimates fall into three broad categories, namely (A) satellite-based, (B) satellite-model integrated, and (C) model-based. As satellite aerosol measurements are generally limited to cloud-free conditions, the discussion here focuses on assessments of clear-sky aerosol direct radiative forcing, a net (downwelling minus upwelling) solar flux difference between with aerosol (natural + anthropogenic) and in the absence of aerosol.

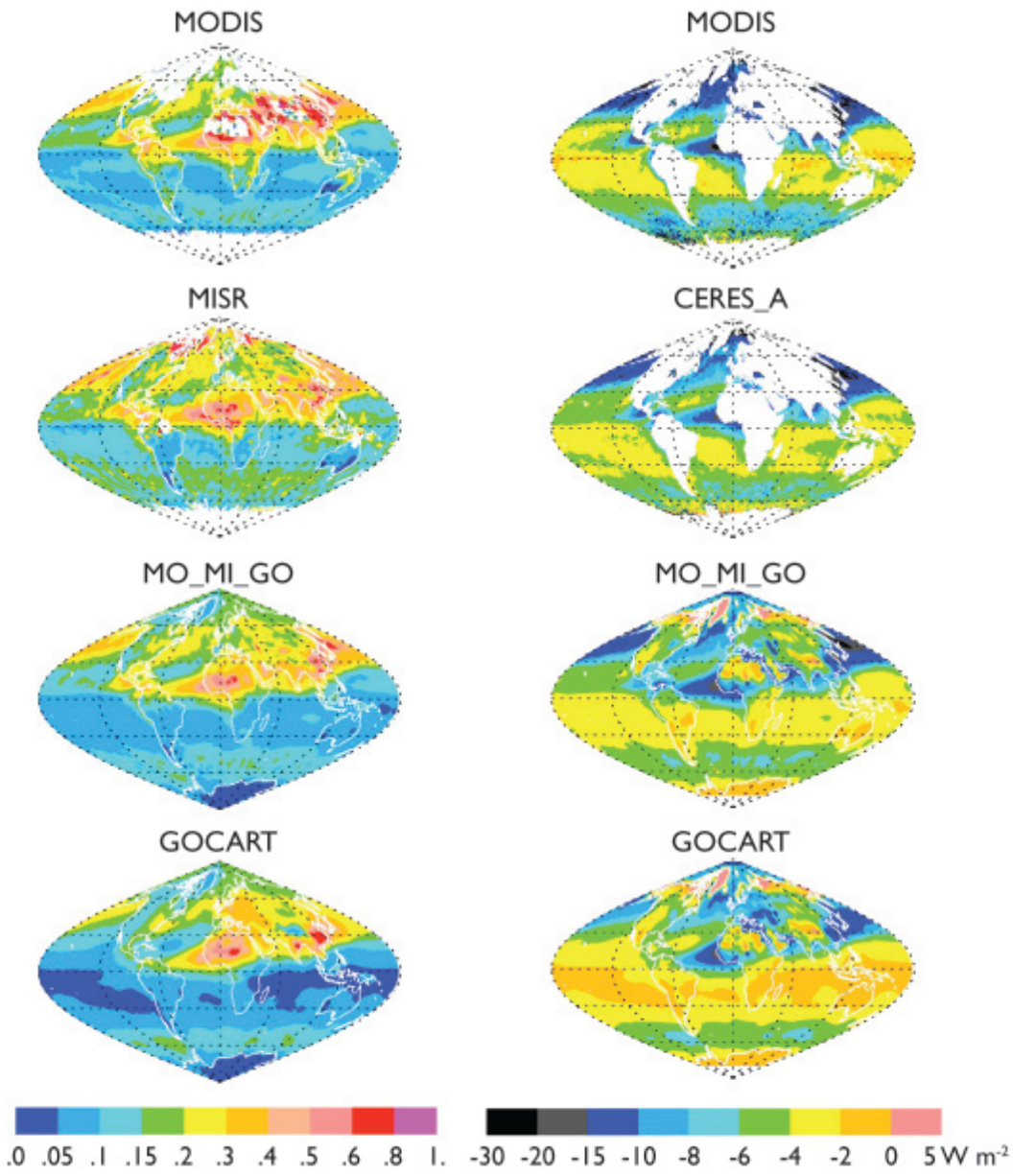
Global Distributions

Figure 9-68 shows global distributions of aerosol optical depth at 550 nm (left panel) and diurnally averaged clear-sky TOA DRF (right panel) for March-April-May (MAM) based on the different approaches. The DRF at the surface follows the same pattern as that at the TOA but is significantly larger in magnitude because of aerosol absorption. It appears that different approaches agree on large-scale patterns of aerosol optical depth and the direct radiative forcing. In this season, the aerosol impacts in the Northern Hemisphere are much larger than those in the Southern Hemisphere. Dust outbreaks and biomass burning elevate the optical depth to more than 0.3 over large parts of North Africa and the tropical Atlantic. In the tropical Atlantic, TOA cooling as large as -10 W/m^2 extends westward to Central America. In eastern China, the optical depth is as high as 0.6-0.8, resulting from the combined effects of industrial activities and biomass burning in the south, and dust outbreaks in the north. The Asian impacts also extend to the North Pacific, producing a TOA cooling of more than -10 W/m^2. Other areas having large aerosol impacts include Western Europe, midlatitude North Atlantic, and much of South Asia and the Indian Ocean. Over the "roaring forties" in the Southern Hemisphere, high winds generate a large amount of sea salt. Elevated optical depth, along with high solar zenith angle and hence large backscattering to space, results in a band of TOA cooling of more than -4 W/m^2. However, there is also some question as to whether thin cirrus (e.g., Zhang et al., 2005, 190931) and unaccounted-for whitecaps contribute to the apparent enhancement in AOD retrieved by satellite. Some differences exist between different approaches. For example, the early post-launch MISR retrieved optical depths over the southern hemisphere oceans are higher than MODIS retrievals and GOCART simulations. Over the "roaring forties," the MODIS derived TOA solar flux perturbations are larger than the estimates from other approaches.

Table 9-7. Summary of approaches to estimating the aerosol direct radiative forcing in three categories: (1) satellite retrievals; (2) satellite-model integrations; and (3) model simulations.

Category	Product	Brief Description	Identified Sources of Uncertainty	Major References
A Satellite retrievals	MODIS	Using MODIS retrievals of a linked set of AOD, ω_0, and phase function consistently in conjunction with a radiative transfer model (RTM) to calculate TOA fluxes that best match the observed radiances.	Radiance calibration, cloud-aerosol discrimination, instantaneous-to-diurnal scaling, RTM parameterizations	Remer and Kaufman (2006, 190222)
	MODIS_A	Splitting MODIS AOD over ocean into mineral dust, sea salt, and biomass-burning and pollution; using AERONET measurements to derive the size distribution and single-scattering albedo for individual components.	Satellite AOD and FMF retrievals, overestimate due to summing up the compositional direct forcing, use of a single AERONET site to characterize a large region	Bellouin et al. (2005, 155684)
	CERES_A	Using CERES fluxes in combination with standard MODIS aerosol.	Calibration of CERES radiances, large CERES footprint, satellite AOD retrieval, radiance-to-flux conversion (ADM), instantaneous-to-diurnal scaling, narrow-to-broadband conversion	Loeb and Manalo-Smith (2005, 190433); Loeb and Kato (2002, 190432)
	CERES_B	Using CERES fluxes in combination with NOAA NESDIS aerosol from MODIS radiances.		
	CERES_C	Using CERES fluxes in combination with MODIS (ocean) and MISR (non-desert land) aerosol with new angular models for aerosols.		Zhang et al. (2005, 086743; 2005, 157185); Zhang and Christopher (2003, 190928); Christopher et al. (2006, 155729); Patadia et al. (2008, 190558)
	POLDER	Using POLDER AOD in combination with prescribed aerosol models (similar to MODIS).	Similar to MODIS	Boucher and Tanré (2000, 190041); Bellouin et al. (2003, 189911)
B. Satellite-model integrations	MODIS_G	Using GOCART simulations to fill AOD gaps in satellite retrievals.	Propagation of uncertainties associated with both satellite retrievals and model simulations (but the model-satellite integration approach does result in improved AOD quality for MO_GO, and O_MI_GO)	*Aerosol single-scattering albedo and asymmetry factor are taken from GOCART simulations *Yu et al. (2003, 156171; 2004, 190926; 2006, 156173)
	MISR_G			
	MO_GO	Integration of MODIS and GOCART AOD.		
	MO_MI_GO	Integration of GOCART AOD with retrievals from MODIS (Ocean) and MISR (Land).		
	SeaWiFS	Using SeaWiFS AOD and assumed aerosol models.	Similar to MODIS_G and MISR_G, too weak aerosol absorption	Chou et al. (2002, 190008)
C. Model simulations	GOCART	Offline RT calculations using monthly avg aerosols with a time step of 30 min (without the presence of clouds).	Emissions, parameterizations of a variety of sub-grid aerosol processes (e.g., wet and dry deposition, cloud convection, aqueous-phase oxidation), assumptions on aerosol size, absorption, mixture, and humidification of particles, Meteorology fields, not fully evaluated surface albedo schemes, RT parameterizations	Chin et al. (2002, 189996); Yu et al. (2004, 190926)
	SPRINTARS	Online RT calculations every 3 hrs (cloud fraction = 0).		Takemura et al. (2002, 190438; 2005, 190439)
	GISS	Online model simulations and weighted by clear-sky fraction.		Koch and Hansen (2005, 190183); Koch et al. (2006, 190184)
	LMDZ-INCA	Online RT calculations every 2 hrs (cloud fraction = 0).		Balkanski et al. (2007, 189979); Schulz et al. (2006, 190381); Kinne et al. (2006, 155903)
	LMDZ-LOA	Online RT calculations every 2 hrs (cloud fraction = 0).		Reddy et al. (2005, 190207; 2005, 190208)

Source: Adapted from Yu et al. (2006, 156173).



Source: Yu et al. (2006, 156173)

Figure 9-68. **Geographical patterns of seasonally (MAM) averaged aerosol optical depth at 550 nm (left panel) and the diurnally averaged clear-sky aerosol direct radiative (solar spectrum) forcing (W/m^2) at the TOA (right panel) derived from satellite (Terra) retrievals. MODIS (Remer and Kaufman, 2006, 190222; Remer et al., 2005, 190221); MISR (Kahn et al., 2005, 190966); and CERES_A (Loeb and Manalo-Smith, 2005, 190433); GOCART simulations (Chin et al., 2002, 189996; Yu et al., 2004, 190926); and GOCART-MODIS-MISR integrations (MO_MI_GO) (Yu et al., 2006, 156173).**

Global Mean

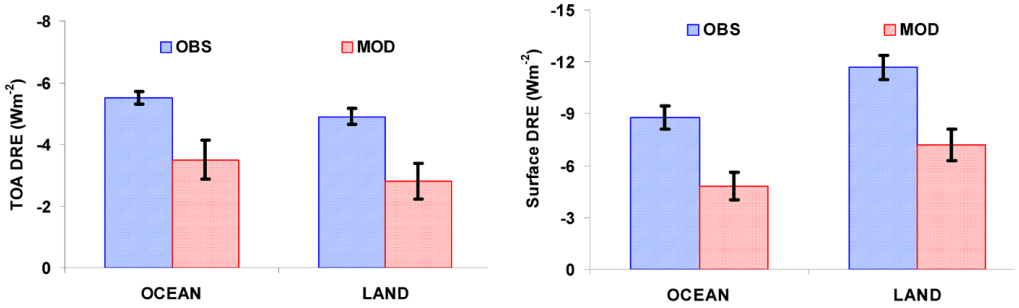
Figure 9-69 summarizes the measurement- and model-based estimates of clear-sky annual-averaged DRF at both the TOA and surface from 60°S to 60°N. Seasonal DRF values for individual estimates are summarized in Table 9-8 and Table 9-9 for ocean and land, respectively. Mean, median and standard error ε (ε=σ/(n-1)1/2), where σ is standard deviation and n is the number of methods) are calculated for measurement- and model-based estimates separately. Note that although the standard deviation or standard error reported here is not a fully rigorous measure of a true experimental uncertainty, it is indicative of the uncertainty because independent approaches with independent sources of errors are used (see Table 9-7; in the modeling community, this is called the "diversity;" see Section 9.3.6).

Ocean

For the TOA DRF, a majority of measurement-based and satellite-model integration-based estimates agree with each other within about 10%. On annual average, the measurement-based estimates give the DRF of -5.5 ± 0.2 W/m^2 (mean ± ε) at the TOA and -8.7 ± 0.7 W/m^2 at the surface. This suggests that the ocean surface cooling is about 60% larger than the cooling at the TOA. Model simulations give wide ranges of DRF estimates at both the TOA and surface. The ensemble of five models gives the annual average DRF (mean ± ε) of -3.2 ± 0.6 W/m^2 and -4.9 ± 0.8 W/m^2 at the TOA and surface, respectively. On average, the surface cooling is about 37% larger than the TOA cooling, smaller than the measurement-based estimate of surface and TOA difference of 60%. However, the 'measurement-based' estimate of surface DRF is actually a calculated value, using poorly constrained particle properties.

Land

It remains challenging to use satellite measurements alone for characterizing complex aerosol properties over land surfaces with high accuracy. As such, DRF estimates over land have to rely largely on model simulations and satellite-model integrations. On a global and annual average, the satellite-model integrated approaches derive a mean DRF of -4.9 W/m^2 at the TOA and -11.9 W/m^2 at the surface respectively. The surface cooling is more than a factor of 2 larger than the TOA cooling because of aerosol absorption. Note that the TOA DRF of -4.9 W/m^2 agrees quite well with the most recent satellite-based estimate of -5.1 ± 1.1 W/m^2 over non-desert land based on coincident measurements of MISR AOD and CERES solar flux (Patadia et al., 2008, 190558). For comparisons, an ensemble of five model simulations derives a DRF (mean ± ε) over land of -3.0 ± 0.6 W/m^2 at the TOA and -7.6 ± 0.9 W/m^2 at the surface, respectively. Seasonal variations of DRF over land, as derived from both measurements and models, are larger than those over ocean.



Source: Yu et al. (2006, 156173)

Figure 9-69. Summary of observation- and model-based (denoted as OBS and MOD, respectively) estimates of clear-sky, annual average DRF at the TOA and at the surface. The box and vertical bar represent median and standard error, respectively.

Table 9-8. Summary of seasonal and annual average clear-sky DRF (W/m^2) at the TOA and the surface (SFC) over global OCEAN derived with different methods and data.

Products	DJF		MAM		JJA		SON		ANN	
	TOA	**SFC**	**TOA**	**SFC**	**TOA**	**SFC**	**TOA**	**SFC**	**TOA**	**SFC**
MODIS	-5.9		-5.8		-6.0		-5.8		-5.9	
MODIX_A*	-6.0	-8.2	-6.4	-8.9	-6.5	-9.3	-6.4	-8.9	-6.4	-8.9
CERES_A	-5.3		-6.1		-5.4		-5.1		-5.5	
CERES_B	-3.8		-4.3		-3.5		-3.6		-3.8	
CERES_C	-5.3		-5.4		-5.2				-5.3	
MODIS_G	-5.5	-9.1	-5.7	-10.4	-6.0	-10.6	-5.5	-9.8	-5.7	-10.0
MISR_G**	-6.4	-10.3	-6.5	-11.4	-7.0	-11.9	-6.3	-10.9	-6.5	-11.1
MO_GO	-4.9	-7.8	-5.1	-9.3	-5.4	-9.4	-5.0	-8.7	-5.1	-8.8
MO_MI_GO	-4.9	-7.9	-5.1	-9.2	-5.5	-9.5	-5.0	-8.6	-5.1	-8.7
POLDER	-5.7		-5.7		-5.8		-5.6		-5.7 -5.2***	 -7.7***
SeaWiFS	-6.0	-6.6	-5.2	-5.8	-4.9	-5.6	-5.3	-5.7	-5.4	-5.9
Obs. Mean	-5.4	-8.3	-5.6	-9.2	-5.6	-9.4	-5.4	-8.8	-5.5	-8.7
Obs. Median	-5.5	-8.1	-5.7	-9.3	-5.5	-9.5	-5.4	-8.8	-5.5	-8.8
Obs. σ	0.72	1.26	0.64	1.89	0.91	2.10	0.79	1.74	0.70	1.65
Obs. ε	0.23	0.56	0.20	0.85	0.29	0.94	0.26	0.78	0.21	0.67
GOCART	-3.6	-5.7	-4.0	-7.2	-4.7	-8.0	-4.0	-6.8	-4.1	-6.9
SPRINTARS	-1.5	-2.5	-1.5	-2.5	-1.9	-3.3	-1.5	-2.5	-1.6	-2.7
GISS	-3.3	-4.1	-3.5	-4.6	-3.5	-4.9	-3.8	-5.4	-3.5	-4.8
LMDZ-INCA	-4.6	-5.6	-4.7	-5.9	-5.0	-6.3	-4.8	-5.5	-4.7	-5.8
LMDZ-LOA	-2.2	-4.1	-2.2	-3.7	-2.5	-4.4	-2.2	-4.1	-2.3	-4.1
Mod. Mean	-3.0	-4.4	-3.2	-4.8	-3.5	-5.4	-3.3	-4.9	-3.2	-4.9
Mod Median	-3.3	-41.	-3.5	-4.6	-3.5	-4.9	-3.8	-5.4	-3.5	-4.8
Mod. σ	1.21	1.32	1.31	1.84	1.35	1.82	1.36	1.63	1.28	1.60
Mod. ε	0.61	0.66	0.66	0.92	0.67	0.91	0.68	0.81	0.64	0.80
Mod./Obs.	.60	.51	.61	.50	.64	.52	.70	.61	.64	.55

* High bias may result from adding the DRF of individual components to derive the total DRF (Bellouin et al., 2005, 155684).

** High bias most likely results from an overall overestimate of 20% in early post-launch MISR optical depth retrievals (Kahn et al., 2005, 190966).

*** Bellouin et al. (2003, 189911) use AERONET retrieval of aerosol absorption as a constraint to the method in Boucher and Tanré (2000, 190041), deriving aerosol direct radiative forcing both at the TOA and the surface.

Sources of data: MODIS (Remer & Kaufman, 2006), MODIS_A (Bellouin et al., 2005, 155684), POLDER (Bellouin et al., 2003, 189911; Boucher and Tanré, 2000, 190041), CERES_A and CERES_B (Loeb and Manalo-Smith, 2005, 190433), CERES_C (Zhang et al., 2005, 190930), MODIS_G, MISR_G, MO_GO, MO_MI_GO (Yu et al., 2004, 190926; 2006, 156173), SeaWiFS (Chou et al., 2002, 190008), GOCART (Chin et al., 2002, 189996; Yu et al., 2004, 190926), SPRINTARS (Takemura et al., 2002, 190438), GISS (Koch and Hansen, 2005, 190183; Koch et al., 2006, 190184), LMDZ-INCA (Kinne et al., 2006, 155903; Schulz et al., 2006, 190381), LMDZ-LOA (Reddy et al., 2005, 190207; Reddy et al., 2005, 190208). Mean, median, standard deviation (σ), and standard error (ε) are calculated for observations (Obs) and model simulations (Mod) separately. The last row is the ratio of model median to observational median (taken from Yu et al., 2006, 156173).

Table 9-9. Summary of seasonal and annual average clear-sky DRF (W/m^2) at the TOA and the surface (SFC) over global LAND derived with different methods and data.

Products	DJF		MAM		JJA		SON		ANN	
	TOA	**SFC**	**TOA**	**SFC**	**TOA**	**SFC**	**TOA**	**SFC**	**TOA**	**SFC**
MODIS_G	-4.1	-9.1	-5.8	-14.9	-6.6	-17.4	-5.4	-12.8	-5.5	-13.5
MISR_G	-3.9	-8.7	-5.1	-13.0	-5.8	-14.6	-4.6	-10l.7	-4.9	-11.8
MO_GO	-3.5	-7.5	-5.1	-12.9	-5.8	-14.9	-4.8	-10.9	-4.8	-11.6
MO_MI_GO	-3.4	-7.4	-4.7	-11.8	-5.3	-13.5	-4.3	-9.7	-4.4	-10.6
Obs. Mean	-3.7	-8.2	-5.2	-13.2	-5.9	-15.1	-4.8	-11.0	-4.9	-11.9
Obs. Median	-3.7	-8.1	-5.1	-13.0	-5.8	-14.8	-4.7	-10.8	-4.9	-11.7
Obs. σ	0.33	0.85	0.46	1.29	0.54	1.65	0.46	1.29	0.45	1.20
Obs. ε	0.17	0.49	0.26	0.74	0.31	0.85	0.27	0.75	0.26	0.70
GOCART	02.9	-6.1	-4.4	-10.9	-4.8	-12.3	-4.3	-9.3	-4.1	-9.7
SPRINTARS	-1.4	-4.0	-1.5	-4.6	-2.0	-6.7	-1.7	-5.2	-1.7	-5.1
GISS	-1.6	-3.9	-3.2	-7.9	-3.6	-9.3	-2.5	-6.6	-2.8	-7.2
LMDZ-INCA	-3.0	-5.8	-4.0	-9.2	-6.0	-13.5	-4.3	-8.2	-4.3	-9.2
LMDZ-LOA	-1.3	-5.4	-1.8	-6.4	-2.7	-8.9	-2.1	-6.7	-2.0	-6.9
Mod. Mean	-2.0	-5.0	-3.0	-7.8	-3.8	-10.1	-3.0	-7.2	-3.0	-7.6
Mod Median	-1.6	-5.4	-3.2	-7.9	-3.6	-9.3	-2.5	-6.7	-2.8	-7.2
Mod. σ	0.84	1.03	1.29	2.44	1.61	2.74	1.24	1.58	1.19	1.86
Mod. ε	0.42	0.51	0.65	1.22	0.80	1.37	0.62	0.79	0.59	0.93
Mod./Obs.	0.43	0.67	0.63	0.61	0.62	0.62	0.53	0.62	0.58	0.62

Sources of data: MODIS_G, MISR_G, MO_GO, MO_MI_GO (Yu et al., 2004, 190926; 2006, 156173), GOCART (Chin et al., 2002, 189996; Yu et al., 2004, 190926), SPRINTARS (Takemura et al., 2002, 190438), GISS (Koch and Hansen, 2005, 190183; Koch et al., 2006, 190184), LMDZ-INCA (Balkanski et al., 2007, 189979; Kinne et al., 2006, 155903; Schulz et al., 2006, 190381), LMDZ-LOA (Reddy et al., 2005, 190207; Reddy et al., 2005, 190208). Mean, median, standard deviation (σ), and standard error (ε) are calculated for observations (Obs) and model simulations (Mod) separately. The last row is the ratio of model median to observational median. (Taken from Yu et al., 2006, 156173).

The above analyses show that, on a global average, the measurement-based estimates of DRF are 55-80% greater than the model-based estimates. The differences are even larger on regional scales. Such measurement-model differences are a combination of differences in aerosol amount (optical depth), single-scattering properties, surface albedo, and radiative transfer schemes (Yu et al., 2006, 156173). As discussed earlier, MODIS retrieved optical depths tend to be overestimated by about 10-15% due to the contamination of thin cirrus and clouds in general (Kaufman et al., 2005, 155891). Such overestimation of optical depth would result in a comparable overestimate of the aerosol direct radiative forcing. Other satellite AOD data may have similar contamination, which however has not yet been quantified. On the other hand, the observations may be measuring enhanced AOD and DRF due to processes not well represented in the models including humidification and enhancement of aerosols in the vicinity of clouds (Koren et al., 2007, 190192).

From the perspective of model simulations, uncertainties associated with parameterizations of various aerosol processes and meteorological fields, as documented under the AEROCOM and Global Modeling Initiative (GMI) frameworks (Kinne et al., 2006, 155903; Liu et al., 2007, 190427; Textor et al., 2006, 190456), contribute to the large measurement-model and model-model discrepancies. Factors determining the AOD should be major reasons for the DRF discrepancy and the constraint of model AOD with well evaluated and bias reduced satellite AOD through a data assimilation approach can reduce the DRF discrepancy significantly. Other factors (such as model parameterization of surface reflectance, and model-satellite differences in single-scattering albedo and asymmetry factor due to satellite sampling bias toward cloud-free conditions) should also contribute, as evidenced by the existence of a large discrepancy in the radiative efficiency (Yu et al., 2006, 156173). Significant effort will be needed in the future to conduct comprehensive assessments.

9.3.3.4. Satellite-Based Estimates of Anthropogenic Component of Aerosol Direct Radiative Forcing

Satellite instruments do not measure the aerosol chemical composition needed to discriminate anthropogenic from natural aerosol components. Because anthropogenic aerosols are predominantly sub-micron, the fine-mode fraction derived from POLDER, MODIS, or MISR might be used as a tool for deriving anthropogenic aerosol optical depth. This could provide a feasible way to conduct measurement-based estimates of anthropogenic component of aerosol direct radiative forcing (Kaufman et al., 2002, 190956). Such method derives anthropogenic AOD from satellite measurements by empirically correcting contributions of natural sources (dust and maritime aerosol) to the sub-micron AOD (Kaufman et al., 2005, 155891). The MODIS-based estimate of anthropogenic AOD is about 0.033 over oceans, consistent with model assessments of 0.030~0.036 even though the total AOD from MODIS is 25-40% higher than the models (Kaufman et al., 2005, 155891). This accounts for 21 ± 7% of the MODIS-observed total aerosol optical depth, compared with about 33% of anthropogenic contributions estimated by the models. The anthropogenic fraction of AOD should be much larger over land (i.e., 47 ± 9% from a composite of several models) (Bellouin et al., 2005, 155684), comparable to the 40% estimated by Yu et al. (2006, 156173). Similarly, the non-spherical fraction from MISR or POLDER can be used to separate dust from spherical aerosol (Kahn et al., 2001, 190969; Kalashnikova and Kahn, 2006, 190962), providing another constraint for distinguishing anthropogenic from natural aerosols.

There have been several estimates of anthropogenic component of DRF in recent years. Table 9-10 lists such estimates of anthropogenic component of TOA DRF that are from model simulations (Schulz et al., 2006, 190381) and constrained to some degree by satellite observations (Bellouin et al., 2005, 155684; Bellouin et al., 2008, 189999; Christopher et al., 2006, 155729; Chung et al., 2005, 155733; Kaufman et al., 2005, 155891; Matsui et al., 2006, 190495; Quaas et al., 2008, 190916; Yu et al., 2006, 156173; Zhao et al., 2008, 190936). The satellite-based clear-sky DRF by anthropogenic aerosols is estimated to be -1.1 ± 0.37 W/m^2 over ocean, about a factor of 2 stronger than model simulated -0.6 W/m^2. Similar DRF estimates are rare over land, but a few studies do suggest that the anthropogenic DRF over land is much more negative than that over ocean (Bellouin et al., 2005, 155684; Bellouin et al., 2008, 189999; Yu et al., 2006, 156173). On global average, the measurement-based estimate of anthropogenic DRF ranges from -0.9 to -1.9 W/m^2, again stronger than the model-based estimate of -0.8 W/m^2. Similar to DRF estimates for total aerosols, satellite-based estimates of anthropogenic component of DRF are rare over land.

On global average, anthropogenic aerosols are generally more absorptive than natural aerosols. As such the anthropogenic component of DRF is much more negative at the surface than at TOA. Several observation-constrained studies estimate that the global average, clear-sky, anthropogenic component of DRF at the surface ranges from -4.2 to -5.1 W/m^2 (Bellouin et al., 2005, 155684; Chung et al., 2005, 155733; Matsui et al., 2006, 190495; Yu et al., 2004, 190926), which is about a factor of 2 larger in magnitude than the model estimates (e.g., Reddy et al., 2005, 190208).

Uncertainties in estimates of the anthropogenic component of aerosol DRF are greater than for the total aerosol, particularly over land. An uncertainty analysis (Yu et al., 2006, 156173) partitions the uncertainty for the global average anthropogenic DRF between land and ocean more or less evenly. Five parameters, namely fine-mode fraction (ff) and anthropogenic fraction of fine-mode fraction (faf) over both land and ocean, and τ over ocean, contribute nearly 80% of the overall uncertainty in the anthropogenic DRF estimate, with individual shares ranging from 13-20% (Yu et al., 2006, 156173). These uncertainties presumably represent a lower bound because the sources of error are assumed to be independent. Uncertainties associated with several parameters are also not well defined. Nevertheless, such uncertainty analysis is useful for guiding future research and documenting advances in understanding.

Table 9-10. Estimates of anthropogenic components of aerosol optical depth (T_{ant}) and clear-sky DRF at the TOA from model simulations.

Data Sources	Ocean		Land		Global		Estimated uncertainty or model diversity for DRF
	T_{ant}	DRF (W/m^2)	T_{ant}	DRF (W/m^2)	T_{ant}	DRF (W/m^2)	
Kaufman et al. (2005, 155891)	0.033	-1.4					30%
Bellouin et al. (2005, 155684)	0.028	-0.8	0.13		0.062	-1.9	15%
Chung et al. (2005, 155733)						-1.1	
Yu et al. (2006, 156173)	0.031	-1.1	-.088	-1.8	0.048	-1.3	47% (ocean), 845 (land), and 62% (global)
Christopher et al. (2006, 155729)		-1.4					65%
Matsui and Pielke (2006, 190495)		-1.6					30°S-30°N oceans
Quaas et al. (2008, 190916)		-0.7		-1.8		-0.9	45%
Bellouin et al. (2008, 189999)	0.021	-0.6	0.107	-3.3	0.043	-1.3	Update to Bellouin et al. (2005, 155684) with MODIS Collection 5 data
Zhao et al. (2008, 190936)		-1.25					35%
Schulz et al. (2006, 190381)	0.022	-0.59	0.065	-1.14	0.036	-0.77	30-40%; same emissions prescribed for all models

Sources: Schulz et al., (2006, 190381) approaches constrained by satellite observations, Kaufman et al. (2005, 155891); Bellouin et al. (2005, 155684) 2008; Chung et al. (2005, 155733); Yu et al. (2006, 156173); Christopher et al. (2006, 155729); Matsui and Pielke (2006, 190495); Quaas et al. (2008, 190916); Zhao et al. (2008, 190936).

9.3.3.5. Aerosol-Cloud Interactions and Indirect Forcing

Satellite views of the Earth show a planet whose albedo is dominated by dark oceans and vegetated surfaces, white clouds, and bright deserts. The bright white clouds overlying darker oceans or vegetated surface demonstrate the significant effect that clouds have on the Earth's radiative balance. Low clouds reflect incoming sunlight back to space, acting to cool the planet, whereas high clouds can trap outgoing terrestrial radiation and act to warm the planet. In the Arctic, low clouds have also been shown to warm the surface (Garrett and Zhao, 2006, 190570). Changes in cloud cover, in cloud vertical development, and cloud optical properties will have strong radiative and therefore, climatic impacts. Furthermore, factors that change cloud development will also change precipitation processes. These changes may alter amounts, locations and intensities of local and regional rain and snowfall, creating droughts, floods and severe weather.

Cloud droplets form on a subset of aerosol particles called cloud condensation nuclei (CCN). In general, an increase in aerosol leads to an increase in CCN and an increase in drop concentration. Thus, for the same amount of liquid water in a cloud, more available CCN will result in a greater number but smaller size of droplets (Twomey, 1977, 190533). A cloud with smaller but more numerous droplets will be brighter and reflect more sunlight to space, thus exerting a cooling effect. This is the first aerosol indirect radiative effect, or "albedo effect." The effectiveness of a particle as a CCN depends on its size and composition so that the degree to which clouds become brighter for a given aerosol perturbation, and therefore the extent of cooling, depends on the aerosol size distribution and its size-dependent composition. In addition, aerosol perturbations to cloud microphysics may involve feedbacks; for example, smaller drops are less likely to collide and coalesce; this will inhibit growth, suppressing precipitation, and possibly increasing cloud lifetime (Albrecht, 1989, 045783). In this case clouds may exert an even stronger cooling effect.

A distinctly different aerosol effect on clouds exists in thin Arctic clouds (LWP <25 gm^{-2}) having low emissivity. Aerosol has been shown to increase the longwave emissivity in these clouds, thereby warming the surface (Garrett and Zhao, 2006, 190570; Lubin and Vogelmann, 2006, 190466).

Some aerosol particles, particularly black carbon and dust, also act as ice nuclei (IN) and in so doing, modify the microphysical properties of mixed-phase and ice-clouds. An increase in IN will generate more ice crystals, which grow at the expense of water droplets due to the

difference in vapor pressure over ice and water surfaces. The efficient growth of ice particles may increase the precipitation efficiency. In deep convective, polluted clouds there is a delay in the onset of freezing because droplets are smaller. These clouds may eventually precipitate, but only after higher altitudes are reached that result in taller cloud tops, more lightning and greater chance of severe weather (Andreae et al., 2004, 155658; Rosenfeld and Lansky, 1998, 190230). The present state of knowledge of the nature and abundance of IN, and ice formation in clouds is extremely poor. There is some observational evidence of aerosol influences on ice processes, but a clear link between aerosol, IN concentrations, ice crystal concentrations and growth to precipitation has not been established. This report therefore only peripherally addresses ice processes. More information can be found in a review by the WMO/IUGG International Aerosol-Precipitation Scientific Assessment (Levin and Cotton, 2008, 190375).

In addition to their roles as CCN and IN, aerosols also absorb and scatter light, and therefore they can change atmospheric conditions (temperature, stability, and surface fluxes) that influence cloud development and properties (Ackerman et al., 2000, 002987; Hansen et al., 1997, 043104). Thus, aerosols affect clouds through changing cloud droplet size distributions, cloud particle phase, and by changing the atmospheric environment of the cloud.

9.3.3.6. Remote Sensing of Aerosol-Cloud Interactions and Indirect Forcing

The AVHRR satellite instruments have observed relationships between columnar aerosol loading, retrieved cloud microphysics, and cloud brightness over the Amazon Basin that are consistent with the theories explained above (Feingold et al., 2001, 190544; Kaufman and Fraser, 1997, 190958; Kaufman and Nakajima, 1993, 190959), but do not necessarily prove a causal relationship. Other studies have linked cloud and aerosol microphysical parameters or cloud albedo and droplet size using satellite data applied over the entire global oceans (Han et al., 1998, 190594; Nakajima et al., 2001, 190552; Wetzel and Stowe, 1999, 190636). Using these correlations with estimates of aerosol increase from the pre-industrial era, estimates of anthropogenic aerosol indirect radiative forcing fall into the range of -0.7 to -1.7 W/m^2 (Nakajima et al., 2001, 190552).

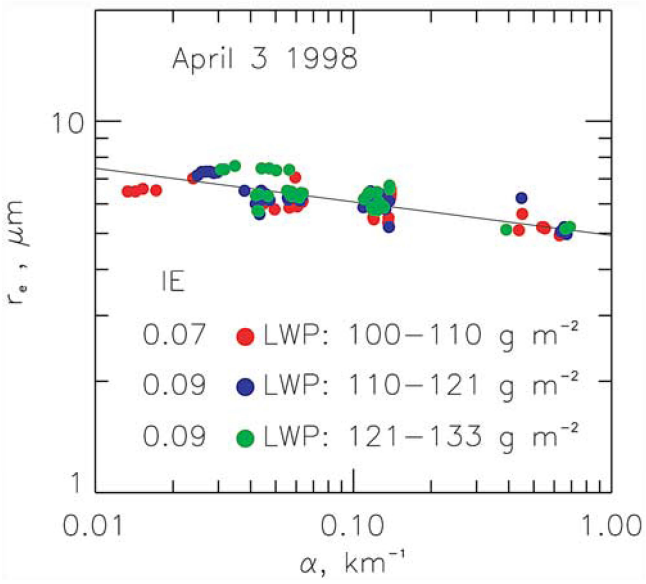
Introduction of the more modern instruments (POLDER and MODIS) has allowed more detailed observations of relationships between aerosol and cloud parameters. Cloud cover can both decrease and increase with increasing aerosol loading (Kaufman et al., 2005, 155891; Koren et al., 2004, 190187; Koren et al., 2005, 190188; Matheson et al., 2005, 190494; Sekiguchi et al., 2003, 190385; Yu et al., 2007, 093173). The same is true of LWP (Han et al., 2002, 049181; Matsui et al., 2006, 190498). Aerosol absorption appears to be an important factor in determining how cloud cover will respond to increased aerosol loading (Jiang and Feingold, 2006, 190976; Kaufman and Koren, 2006, 190951; Koren et al., 2008, 190193). Different responses of cloud cover to increased aerosol could also be correlated with atmospheric thermodynamic and moisture structure (Yu et al., 2007, 093173). Observations in the MODIS data show that aerosol loading correlates with enhanced convection and greater production of ice anvils in the summer Atlantic Ocean (Koren et al., 2005, 190188), which conflicts with previous results that used AVHRR and could not isolate convective systems from shallow clouds (Sekiguchi et al., 2003, 190385).

In recent years, surface-based remote sensing has also been applied to address aerosol effects on cloud microphysics. This method offers some interesting insights, and is complementary to the global satellite view. Surface remote sensing can only be applied at a limited number of locations, and therefore lacks the global satellite view. However, these surface stations yield high temporal resolution data and because they sample aerosol below, rather than adjacent to clouds they do not suffer from "cloud contamination." With the appropriate instrumentation (lidar) they can measure the local aerosol entering the clouds, rather than a column-integrated aerosol optical depth. Under well-mixed conditions, surface in situ aerosol measurements can be used. Surface remote-sensing studies are discussed in more detail below, although the main science issues are common to satellite remote sensing.

Feingold et al. (2001, 190544) used data collected at the ARM Southern Great Plains (SGP) site to allow simultaneous retrieval of aerosol and cloud properties. A combination of a Doppler cloud radar and a microwave radiometer was used to retrieve cloud drop effective radius re profiles in non-precipitating (radar reflectivity Z <-17 dBZ), ice-free clouds. Simultaneously, sub-cloud aerosol extinction profiles were measured with a lidar to quantify the response of drop sizes to changes in aerosol properties. Cloud data were binned according to liquid water path (LWP) as measured with a microwave radiometer, consistent with Twomey's (1977, 190533) conceptual view of the aerosol impact on cloud microphysics. With high temporal/spatial resolution data (on the order of 20s or 100s of meters), realizations of aerosol-cloud interactions at the large eddy scale were obtained, and quantified in terms of the relative decrease in re in response to a relative increase in aerosol extinction (dln re/dln extinction), as shown in Figure 9-70. Examining the dependence in this way reduces reliance on absolute measures of cloud and aerosol parameters and minimizes sensitivity to measurement error, provided errors are unbiased. This formulation permitted these responses to be related to cloud microphysical theory. Restricting the examination to updrafts only (as determined from the radar Doppler signal) permitted examination of the role of updraft in determining the response of re to changes in aerosol (via changes in drop number

concentration Nd). Analysis of data from 7 days showed that turbulence intensifies the aerosol impact on cloud microphysics.

In addition to radar/microwave radiometer retrievals of aerosol and cloud properties, measurements of cloud optical depth by surface based radiometers such as the MFRSR (Michalsky et al., 2001, 190537) have been used in combination with measurements of cloud LWP by microwave radiometer to measure an average value of re during daylight when the solar elevation angle is sufficiently high (Min and Harrison, 1996, 190538). Using this retrieval, Kim et al. (2003, 155899) performed analyses of the re response to changes in aerosol at the same continental site, using a surface measurement of the aerosol light scattering coefficient instead of using extinction near cloud base as a proxy for CCN. Variance in LWP was shown to explain most of the variance in cloud optical depth, exacerbating detection of an aerosol effect. Although a decrease in re was observed with increasing scattering coefficient, the relation was not strong, indicative of other influences on re and/or decoupling between the surface and cloud layer. A similar study was conducted by Garrett et al. (2004, 190568) at a location in the Arctic.



Source: Adapted with Permission of the American Geophysical Union from Feingold et al. (2003, 190551).

Figure 9-70. Scatter plots showing mean cloud drop effective radius (re) versus aerosol extinction coefficient (unit: km-1) for various liquid water path (LWP) bands on April 3, 1998 at ARM SGP site.

They suggested that summertime Arctic clouds are more sensitive to aerosol perturbations than clouds at lower latitudes. The advantage of the MFRSR/microwave radiometer combination is that it derives re from cloud optical depth and LWP and it is not as sensitive to large drops as the radar is. A limitation is that it can be applied only to clouds with extensive horizontal cover during daylight hours.

More recent data analyses by Feingold et al. (2003, 190551), Kim et al. (2008, 130785) and McComiskey et al. (2008, 190525) at a variety of locations, and modeling work (Feingold, 2003, 190547) have investigated (i) the use of different proxies for cloud condensation nuclei, such as the light scattering coefficient and aerosol index; (ii) sensitivity of cloud microphysical/optical properties to controlling factors such as aerosol size distribution, entrainment, LWP, and updraft velocity; (iii) the effect of optical- as opposed to radar-retrievals of drop size; and (iv) spatial heterogeneity. These studies have reinforced the importance of LWP and vertical velocity as controlling parameters. They have also begun to reconcile the reasons for the large discrepancies between various approaches, and platforms (satellite, aircraft in situ, and surface-based remote sensing). These investigations are important because satellite measurements that use a similar approach are being employed in GCMs to represent the albedo indirect effect (Quaas and Boucher, 2005, 190573). In fact, the weakest albedo indirect effect in IPCC (2007, 092765) derives from satellite measurements that have very weak responses of re to changes in aerosol. The relationship between these aerosol-cloud microphysical responses and cloud radiative forcing has been examined by

McComiskey and Feingold (2008, 190517). They showed that for plane-parallel clouds, a typical uncertainty in the logarithmic gradient of a re-aerosol relationship of 0.05 results in a local forcing error of -3 to -10 W/m^2, depending on the aerosol perturbation. This sensitivity reinforces the importance of adequate quantification of aerosol effects on cloud microphysics to assessment of the radiative forcing, i.e., the indirect effect. Quantification of these effects from remote sensors is exacerbated by measurement errors. For example, LWP is measured to an accuracy of 25 g m-2 at best, and since it is the thinnest clouds (i.e., low LWP) that are most susceptible (from a radiative forcing perspective) to changes in aerosol, this measurement uncertainty represents a significant uncertainty in whether the observed response is related to aerosol, or to differences in LWP. The accuracy and spatial resolution of satellite-based LWP measurements is much poorer and this represents a significant challenge. In some cases important measurements are simply absent, e.g., updraft is not measured from satellite-based remote sensors.

Finally, cloud radar data from CloudSat, along with the A-train aerosol data, is providing great opportunity for inferring aerosol effects on precipitation (e.g., Stephens and Haynes, 2007, 190413). The aerosol effect on precipitation is far more complex than the albedo effect because the instantaneous view provided by satellites makes it difficult to establish causal relationships.

9.3.3.7. In Situ Studies of Aerosol-Cloud Interactions

In situ observations of aerosol effects on cloud microphysics date back to the 1950s and 1960s (Brenguier et al., 2000, 189966; Gunn and Phillips, 1957, 190595; Leaitch et al., 1992, 045270; Radke et al., 1989, 156034; Squires, 1958, 045608; Warner, 1968, 157114; Warner and Twomey, 1967, 045616; to name a few). These studies showed that high concentrations of CCN from anthropogenic sources, such as industrial pollution or the burning of sugarcane can increase cloud droplet number concentration Nd, thus increasing cloud microphysical stability and potentially reducing precipitation efficiency. As in the case of remote sensing studies, the causal link between aerosol perturbations and cloud microphysical responses (e.g., re or Nd) is much better established than the relationship between aerosol and changes in cloud fraction, LWC, and precipitation (see also Levin and Cotton, 2008, 190375).

In situ cloud measurements are usually regarded as “ground truth” for satellite retrievals but in fact there is considerable uncertainty in measured parameters such liquid water content (LWC), and size distribution, which forms the basis of other calculations such as drop concentration, re and extinction. It is not uncommon to see discrepancies in LWC on the order of 50% between different instruments, and cloud drop size distributions are difficult to measure, particularly for droplets <10 μm where Mie scattering oscillations generate ambiguities in drop size. Measurement uncertainty in re from in situ probes is assessed, for horizontally homogeneous clouds, to be on the order of 15- 20%, compared to 10% for MODIS and 15-20% for other spectral measurements (Feingold et al., 2003, 190551). As with remote measurements it is prudent to consider relative (as opposed to absolute) changes in cloud microphysics related to relative changes in aerosol. An added consideration is that in situ measurements typically represent a very small sample of the atmosphere akin to a thin pencil line through a large volume. For an aircraft flying at 100 m/s and sampling at 1 Hz, the sample volume is on the order of 10 cm^3. The larger spatial sampling of remote sensing has the advantage of being more representative but it removes small-scale (i.e., sub sampling volume) variability, and therefore, may obscure important cloud processes.

Measurements at a wide variety of locations around the world have shown that increases in aerosol concentration lead to increases in Nd. However the rate of this increase is highly variable and always sub-linear, as exemplified by the compilation of data in Ramanathan et al. (2001, 042681). This is because, as discussed previously, Nd is a function of numerous parameters in addition to aerosol number concentration, including size distribution, updraft velocity (Leaitch et al., 1996, 190354), and composition. In stratocumulus clouds, characterized by relatively low vertical velocity (and low supersaturation) only a small fraction of particles can be activated whereas in vigorous cumulus clouds that have high updraft velocities, a much larger fraction of aerosol particles is activated. Thus the ratio of Nd to aerosol particle number concentration is highly variable.

In recent years there has been a concerted effort to reconcile measured Nd concentrations with those calculated based on observed aerosol size and composition, as well as updraft velocity. These so-called “closure experiments” have demonstrated that on average, agreement in Nd between these approaches is on the order of 20% (Conant et al., 2004, 190010). This provides confidence in theoretical understanding of droplet activation, however, measurement accuracy is not high enough to constrain the aerosol composition effects that have magnitudes <20%.

One exception to the rule that more aerosol particles result in larger Nd is the case of giant CCN (sizes on the order of a few microns), which, in concentrations on the order of 1 cm^3 (i.e., ~ 1% of the total concentration) can lead to significant suppression in cloud supersaturation and reductions in Nd (O'Dowd et al., 1999, 090414). The measurement of these large particles is difficult and hence the importance of this effect is hard to assess. These same giant CCN, at concentrations as low as 1/liter, can significantly affect the initiation of precipitation in

moderately polluted clouds (Johnson, 1982, 190973) and in so doing alter cloud albedo (Feingold et al., 1999, 190540).

The most direct link between the remote sensing of aerosol-cloud interactions discussed in Section 9.3.3.6 and in situ observations is via observations of relationships between drop concentration Nd and CCN concentration. Theory shows that if re-CCN relationships are calculated at constant LWP or LWC, their logarithmic slope is -1/3 that of the Nd-CCN logarithmic slope (i.e., dlnre/dlnCCN = -1/3 dlnNd/ dlnCCN). In general, Nd-CCN slopes measured in situ tend to be stronger than equivalent slopes obtained from remote sensing – particularly in the case of satellite remote sensing (McComiskey and Feingold, 2008, 190517). There are a number of reasons for this: (i) in situ measurements focus on smaller spatial scales and are more likely to observe the droplet activation process as opposed to remote sensing that incorporates larger spatial scales and includes other processes such as drop coalescence that reduce Nd, and therefore the slope of the Nd- CCN relationship (McComiskey et al., 2008, 190525). (ii) Satellite remote sensing studies typically do not sort their data by LWP, and this has been shown to reduce the magnitude of the re-CCN response (Feingold, 2003, 190547).

In conclusion, observational estimates of aerosol indirect radiative forcings are still in their infancy. Effects on cloud microphysics that result in cloud brightening have to be considered along with effects on cloud lifetime, cover, vertical development and ice production. For in situ measurements, aerosol effects on cloud microphysics are reasonably consistent (within ~ 20%) with theory but measurement uncertainties in remote sensing of aerosol effects on clouds, as well as complexity associated with three-dimensional radiative transfer, result in considerable uncertainty in radiative forcing. The higher order indirect effects are poorly understood and even the sign of the microphysical response and forcing may not always be the same. Aerosol type and specifically the absorption properties of the aerosol may cause different cloud responses. Early estimates of observationally based aerosol indirect forcing range from -0.7 to -1.7 W/m^2 (Nakajima et al., 2001, 190552) and -0.6 to -1.2 W/m^2 (Sekiguchi et al., 2003, 190385), depending on the estimate for aerosol increase from pre-industrial times and whether aerosol effects on cloud fraction are also included in the estimate.

9.3.4. Outstanding Issues

Despite substantial progress, as summarized in Sections 9.3.2 and 9.3.3, most measurement-based studies so far have concentrated on influences produced by the sum of natural and anthropogenic aerosols on solar radiation under clear sky conditions. Important issues remain:

- Because accurate measurements of aerosol absorption are lacking and land surface reflection values are uncertain, DRF estimates over land and at the ocean surface are less well constrained than the estimate of TOA DRF over ocean.
- Current estimates of the anthropogenic component of aerosol direct radiative forcing have large uncertainties, especially over land.
- Because there are very few measurements of aerosol absorption vertical distribution, mainly from aircraft during field campaigns, estimates of direct radiative forcing of above-cloud aerosols and profiles of atmospheric radiative heating induced by aerosol absorption are poorly constrained.
- There is a need to quantify aerosol impacts on thermal infrared radiation, especially for dust.
- The diurnal cycle of aerosol direct radiative forcing cannot be adequately characterized with currently available, sun-synchronous, polar orbiting satellite measurements.
- Measuring aerosol, cloud, and ambient meteorology contributions to indirect radiative forcing remains a major challenge.
- Long-term aerosol trends and their relationship to observed surface solar radiation changes are not well understood.

The current status and prospects for these areas are briefly discussed below.

Measuring Aerosol Absorption and Single-Scattering Albedo

Currently, the accuracy of both in situ and remote sensing aerosol SSA measurements is generally ± 0.03 at best, which implies that the inferred accuracy of clear sky aerosol DRF would be larger than 1 W/m^2 (see Chapter 1 of the CSSP SAP2.3). Recently developed photoacoustic (Arnott et al., 1999, 020650) and cavity ring down extinction cell (Strawa et al., 2002, 190421) techniques for measuring aerosol absorption produce SSA with improved accuracy over previous methods. However, these methods are still experimental, and must be deployed on aircraft. Aerosol absorption retrievals from satellites using the UV-technique have large uncertainties associated with its sensitivity to the height of the aerosol layer(s) (Torres et al., 2005, 190507), and it is unclear how the UV results can be extended to visible wavelengths. Views in and out of sunglint can be used to retrieve total aerosol extinction and scattering, respectively, thus constraining aerosol absorption over oceans (Kaufman et al., 2002, 190955). However, this technique requires retrievals of aerosol scattering properties, including the real part of the refractive index, well beyond what has so far been demonstrated

from space. In summary, there is a need to pursue a better understanding of the uncertainty in SSA from both in situ measurements and remote sensing retrievals and, with this knowledge, to synthesize different data sets to yield a characterization of aerosol absorption with well-defined uncertainty (Leahy et al., 2007, 190232). Laboratory studies of aerosol absorption of specific known composition are also needed to interpret in situ measurements and remote sensing retrievals and to provide updated database of particle absorbing properties for models.

Estimating the Aerosol Direct Radiative Forcing over Land

Land surface reflection is large, heterogeneous, and anisotropic, which complicates aerosol retrievals and DRF determination from satellites. Currently, the aerosol retrievals over land have relatively lower accuracy than those over ocean (Section 9.3.2.5) and satellite data are rarely used alone for estimating DRF over land (Section 9.3.3). Several issues need to be addressed, such as developing appropriate angular models for aerosols over land (Patadia et al., 2008, 190558) and improving land surface reflectance characterization. MODIS and MISR measure land surface reflection wavelength dependence and angular distribution at high resolution (Martonchik et al., 1998, 190484; Martonchik et al., 2002, 190490; Moody et al., 2005, 190548). This offers a promising opportunity for inferring the aerosol direct radiative forcing over land from satellite measurements of radiative fluxes (e.g., CERES) and from critical reflectance techniques (Fraser and Kaufman, 1985, 190567; Kaufman, 1987, 190960). The aerosol direct radiative forcing over land depends strongly on aerosol absorption and improved measurements of aerosol absorption are required.

Distinguishing Anthropogenic from Natural Aerosols

Current estimates of anthropogenic components of AOD and direct radiative forcing have larger uncertainties than total aerosol optical depth and direct radiative forcing, particularly over land (see Section 9.3.3.4), because of relatively large uncertainties in the retrieved aerosol microphysical properties (see Section 9.3.2). Future measurements should focus on improved retrievals of such aerosol properties as size distribution, particle shape, and absorption, along with algorithm refinement for better aerosol optical depth retrievals. Coordinated in situ measurements offer a promising avenue for validating and refining satellite identification of anthropogenic aerosols (Anderson et al., 2005, 189993; 2005, 189991). For satellite-based aerosol type characterization, it is sometimes assumed that all biomass-burning aerosol is anthropogenic and all dust aerosol is natural (Kaufman et al., 2005, 155891). The better determination of anthropogenic aerosols requires a quantification of biomass burning ignited by lightning (natural origin) and mineral dust due to human induced changes of land cover/land use and climate (anthropogenic origin). Improved emissions inventories and better integration of satellite observations with models seem likely to reduce the uncertainties in aerosol source attribution.

Profiling the Vertical Distributions of Aerosols

Current aerosol profile data are far from adequate for quantifying the aerosol radiative forcing and atmospheric response to the forcing. The data have limited spatial and temporal coverage, even for current spaceborne lidar measurements. Retrieving aerosol extinction profile from lidar measured attenuated backscatter is subject to large uncertainties resulting from aerosol type characterization. Current space-borne Lidar measurements are also not sensitive to aerosol absorption. Because of lack of aerosol vertical distribution observations, the estimates of DRF in cloudy conditions and dust DRF in the thermal infrared remain highly uncertain (Lubin et al., 2002, 190463; Schulz et al., 2006, 190381; Sokolik et al., 2001, 190404). It also remains challenging to constrain the aerosol-induced atmospheric heating rate increment that is essential for assessing atmospheric responses to the aerosol radiative forcing (e.g., Feingold et al., 2005, 190550; Lau et al., 2006, 190223; Yu et al., 2002, 190923).

Progress in the foreseeable future is likely to come from (1) better use of existing, global, space-based backscatter lidar data to constrain model simulations, and (2) deployment of new instruments, such as high-spectral-resolution lidar (HSRL), capable of retrieving both extinction and backscatter from space. The HSRL lidar system will be deployed on the EarthCARE satellite mission tentatively scheduled for 2013 (http://asimov/esrin.esi.it/esaLP/ASESMYNW9SC_Lpearthcare_1.html).

Characterizing the Diurnal Cycle of Aerosol Direct Radiative Forcing

The diurnal variability of aerosol can be large, depending on location and aerosol type (Smirnov et al., 2002, 190398), especially in wildfire situations, and in places where boundary layer aerosols hydrate or otherwise change significantly during the day. This cannot be captured by currently available, sun-synchronous, polar orbiting satellites. Geostationary satellites provide adequate time resolution (Christopher and Zhang, 2002, 190031; Wang et al., 2003, 157106), but lack the information required to characterize aerosol types. Aerosol type information from low earth orbit satellites can help improve accuracy of geostationary satellite

aerosol retrievals (Costa et al., 2004, 190006; 2004, 192022). For estimating the diurnal cycle of aerosol DRF, additional efforts are needed to adequately characterize the anisotropy of surface reflection (Yu et al., 2004, 190926) and daytime variation of clouds.

Studying Aerosol-Cloud Interactions and Indirect Radiative Forcing

Remote sensing estimates of aerosol indirect forcing are still rare and uncertain. Improvements are needed for both aerosol characterization and measurements of cloud properties, precipitation, water vapor, and temperature profiles. Basic processes still need to be understood on regional and global scales. Remote sensing observations of aerosol-cloud interactions and aerosol indirect forcing are for the most part based on simple correlations among variables, from which cause-and-effects cannot be deduced. One difficulty in inferring aerosol effects on clouds from the observed relationships is separating aerosol from meteorological effects, as aerosol loading itself is often correlated with the meteorology. In addition, there are systematic errors and biases in satellite aerosol retrievals for partly cloud-filled scenes. Stratifying aerosol and cloud data by liquid water content, a key step in quantifying the albedo (or first) indirect effect, is usually missing. Future work will need to combine satellite observations with in situ validation and modeling interpretation. A methodology for integrating observations (in situ and remote) and models at the range of relevant temporal/spatial scales is crucial to improve understanding of aerosol indirect effects and aerosol-cloud interactions.

Quantifying Long-Term Trends of Aerosols at Regional Scales

Because secular changes are subtle and are superposed on seasonal and other natural variability, this requires the construction of consistent, multi-decadal records of climate-quality data. To be meaningful, aerosol trend analysis must be performed on a regional basis. Long-term trends of aerosol optical depth have been studied using measurements from surface remote sensing stations (e.g., Augustine et al., 2008, 189913; Hoyt and Frohlich, 1983, 190621; Luo et al., 2001, 190467) and historic satellite sensors (Massie et al., 2004, 190492; Mishchenko and Geogdzhayev, 2007, 190545; Mishchenko et al., 2007, 190542; Zhao et al., 2008, 190935). An emerging multiyear climatology of high quality AOD data from modern satellite sensors (e.g., Kahn et al., 2005, 190966; Remer et al., 2008, 190224) has been used to examine the interannual variations of aerosol (e.g., Koren et al., 2007, 190189; Mishchenko and Geogdzhayev, 2007, 190545)

and contribute significantly to the study of aerosol trends. Current observational capability needs to be continued to avoid any data gaps. A synergy of aerosol products from historical, modern and future sensors is needed to construct as long a record as possible. Such a data synergy can build upon understanding and reconciliation of AOD differences among different sensors or platforms (Jeong et al., 2005, 190977). This requires overlapping data records for multiple sensors. A close examination of relevant issues associated with individual sensors is urgently needed, including sensor calibration, algorithm assumptions, cloud screening, data sampling and aggregation, among others.

Linking Aerosol Long-Term Trends with Changes of Surface Solar Radiation

Analysis of the long-term surface solar radiation record suggests significant trends during past decades (e.g., Alpert et al., 2005, 190047; Pinker et al., 2005, 190569; Stanhill and Cohen, 2001, 042121; Wild et al., 2005, 156156). Although a significant and widespread decline in surface total solar radiation (the sum of direct and diffuse irradiance) occurred up to 1990 (so-called solar dimming), a sustained increase has been observed during the subsequent decade. Speculation suggests that such trends result from decadal changes of aerosols and the interplay of aerosol direct and indirect radiative forcing (Norris and Wild, 2007, 190555; Ruckstuhl et al., 2008, 190356; Stanhill and Cohen, 2001, 042121; Streets et al., 2006, 190425; Wild et al., 2005, 156156). However, reliable observations of aerosol trends are required to test these ideas. In addition to aerosol optical depth, changes in aerosol composition must also be quantified, to account for changing industrial practices, environmental regulations, and biomass burning emissions (Novakov et al., 2003, 048398; Streets and Aunan, 2005, 156106; Streets et al., 2004, 190423). Such compositional changes will affect the aerosol SSA and size distribution, which in turn will affect the surface solar radiation (e.g., Qian et al., 2007, 190572). However, such data are currently rare and subject to large uncertainties. Finally, a better understanding of aerosol-radiation-cloud interactions and trends in cloudiness, cloud albedo, and surface albedo is badly needed to attribute the observed radiation changes to aerosol changes with less ambiguity.

9.3.5. Concluding Remarks

Since the concept of aerosol-radiation-climate interactions was first proposed around 1970, substantial progress has been made in determining the mechanisms and magnitudes of

these interactions, particularly in the last 10 years. Such progress has greatly benefited from significant improvements in aerosol measurements and increasing sophistication of model simulations. As a result, knowledge of aerosol properties and their interaction with solar radiation on regional and global scales is much improved. Such progress plays a unique role in the definitive assessment of the global anthropogenic radiative forcing, as "virtually certainly positive" in IPCC AR4 (Haywood and Schulz, 2007, 190600).

In Situ Measurements of Aerosols

New in situ instruments such as aerosol mass spectrometers, photoacoustic techniques, and cavity ring down cells provide high accuracy and fast time resolution measurements of aerosol chemical and optical properties. Numerous focused field campaigns and the emerging ground-based aerosol networks are improving regional aerosol chemical, microphysical, and radiative property characterization. Aerosol closure studies of different measurements indicate that measurements of submicrometer, spherical sulfate and carbonaceous particles have a much better accuracy than that for dust-dominated aerosol. The accumulated comprehensive data sets of regional aerosol properties provide a rigorous "test bed" and strong constraint for satellite retrievals and model simulations of aerosols and their direct radiative forcing.

Remote Sensing Measurements of Aerosols

Surface networks, covering various aerosol regimes around the globe, have been measuring aerosol optical depth with an accuracy of 0.01~0.02, which is adequate for achieving the accuracy of 1 W/m^2 for cloud-free TOA DRF. On the other hand, aerosol microphysical properties retrieved from these networks, especially SSA, have relatively large uncertainties and are only available in very limited conditions. Current satellite sensors can measure AOD with an accuracy of about 0.05 or 15-20% in most cases. The implementation of multi-wavelength, multi-angle, and polarization measuring capabilities has also made it possible to measure particle properties (size, shape, and absorption) that are essential for characterizing aerosol type and estimating anthropogenic component of aerosols. However, these microphysical measurements are more uncertain than AOD measurements.

Observational Estimates of Clear-Sky Aerosol Direct Radiative Forcing

Closure studies based on focused field experiments reveal DRF uncertainties of about 25% for sulfate/carbonaceous aerosol and 60% for dust at regional scales. The high-accuracy of MODIS, MISR and POLDER aerosol products and broadband flux measurements from CERES make it feasible to obtain observational constraints for aerosol TOA DRF at a global scale, with relaxed requirements for measuring particle microphysical properties. Major conclusions from the assessment are:

- A number of satellite-based approaches consistently estimate the clear-sky diurnally averaged TOA DRF (on solar radiation) to be about -5.5 ± 0.2 W/m^2 (mean ± standard error from various methods) over global ocean. At the ocean surface, the diurnally averaged DRF is estimated to be -8.7 ± 0.7 W/m^2. These values are calculated for the difference between today's measured total aerosol (natural plus anthropogenic) and the absence of all aerosol.
- Overall, in comparison to that over ocean, the DRF estimates over land are more poorly constrained by observations and have larger uncertainties. A few satellite retrieval and satellite-model integration yield the overland clear-sky diurnally averaged DRF of -4.9 ± 0.7 W/m^2 and -11.8 ± 1.9 W/m2 at the TOA and surface, respectively. These values over land are calculated for the difference between total aerosol and the complete absence of all aerosol.
- Use of satellite measurements of aerosol microphysical properties yields that on a global ocean average, about 20% of AOD is contributed by human activities and the clear-sky TOA DRF by anthropogenic aerosols is -1.1 ± 0.4 W/m^2. Similar DRF estimates are rare over land, but a few measurement-model integrated studies do suggest much more negative DRF over land than over ocean.
- These satellite-based DRF estimates are much greater than the model-based estimates, with differences much larger at regional scales than at a global scale.

Measurements of Aerosol-Cloud Interactions and Indirect Radiative Forcing

In situ measurement of cloud properties and aerosol effects on cloud microphysics suggest that theoretical understanding of the activation process for water cloud is reasonably well-understood. Remote sensing of aerosol effects on droplet size associated with the albedo effect tends to underestimate the magnitude of the response compared to in situ measurements. Recent efforts trace this to a combination of lack of stratification of data by cloud water, the relatively large spatial scale over which measurements are averaged (which includes variability in cloud fields, and processes that obscure the aerosol-cloud processes), as well as measurement uncertainties (particularly in broken cloud fields). It remains a major challenge

to infer aerosol number concentrations from satellite measurements. The present state of knowledge of the nature and abundance of IN, and ice formation in clouds is extremely poor.

Despite the substantial progress in recent decades, several important issues remain, such as measurements of aerosol size distribution, particle shape, absorption, and vertical profiles, and the detection of aerosol long-term trend and establishment of its connection with the observed trends of solar radiation reaching the surface, as discussed in Section 9.3.4. Furthering the understanding of aerosol impacts on climate requires a coordinated research strategy to improve the measurement accuracy and use the measurements to validate and effectively constrain model simulations. Concepts of future research in measurements are discussed in Chapter 4 "Way Forward" (of the CCSP SAP2.3).

9.3.6. Modeling the Effect of Aerosols on Climate

9.3.6.1. Introduction

The IPCC Fourth Assessment Report (AR4) (IPCC, 2007, 092765) concludes that man's influence on the warming climate is in the category of "very likely". This conclusion is based on, among other things, the ability of models to simulate the global and, to some extent, regional variations of temperature over the past 50-100 years. When anthropogenic effects are included, the simulations can reproduce the observed warming (primarily for the past 50 years); when they are not, the models do not get very much warming at all. In fact, all of the models runs for the IPCC AR4 assessment (more than 20) produce this distinctive result, driven by the greenhouse gas increases that have been observed to occur.

These results were produced in models whose average global warming associated with a doubled CO_2 forcing of 4 W/m^2 was about 3°C. This translates into a climate sensitivity (surface temperature change per forcing) of about 0.75°C/(W/m^2). The determination of climate sensitivity is crucial to projecting the future impact of increased greenhouse gases, and the credibility of this projected value relies on the ability of these models to simulate the observed temperature changes over the past century. However, in producing the observed temperature trend in the past, the models made use of very uncertain aerosol forcing. The greenhouse gas change by itself produces warming in models that exceeds that observed by some 40% on average (IPCC, 2007, 092765). Cooling associated with aerosols reduces this warming to the observed level. Different climate models use differing aerosol forcings, both direct (aerosol scattering and absorption of short and longwave radiation) and indirect (aerosol effect on cloud cover reflectivity and lifetime), whose magnitudes vary markedly from one model to the next. Kiehl (2007, 190949) using nine of the IPCC (2007, 092765) AR4 climate models found that they had a factor of three forcing differences in the aerosol contribution for the 20th century. The differing aerosol forcing is the prime reason why models whose climate sensitivity varies by almost a factor of three can produce the observed trend. It was thus concluded that the uncertainty in IPCC (2007, 092765) anthropogenic climate simulations for the past century should really be much greater than stated (Kerr, 2007, 190950; Schwartz et al., 2007, 190384), since, in general, models with low/high sensitivity to greenhouse warming used weaker/stronger aerosol cooling to obtain the same temperature response (Kiehl, 2007, 190949). Had the situation been reversed and the low/high sensitivity models used strong/weak aerosol forcing, there would have been a greater divergence in model simulations of the past century.

Figure 9-71. Sampling the Arctic Haze. Pollution and smoke aerosols can travel long distances, from mid-latitudes to the Arctic, causing "Arctic Haze." Photo taken from the NASA DC-8 aircraft during the ARCTAS field experiment over Alaska in April 2008. Credit: Mian Chin, NASA.

Therefore, the fact that a model has accurately reproduced the global temperature change in the past does not imply that its future forecast is accurate. This state of affairs will remain until a firmer estimate of radiative forcing (RF) by aerosols, in addition to that by greenhouse gases, is available.

Two different approaches are used to assess the aerosol effect on climate. "Forward modeling" studies incorporate different aerosol types and attempt to explicitly calculate the aerosol RF. From this approach, IPCC (2007, 092765) concluded that the best estimate of the global aerosol direct RF (compared with preindustrial times) is -0.5 (-0.9 to -0.1) W/m^2. The RF due to the cloud albedo or brightness effect (also referred to as first indirect or Twomey effect) is estimated to be -0.7 (-1.8 to -0.3) W/m^2. No estimate was specified for the effect associated with cloud lifetime. The total negative RF due to aerosols according to IPCC (2007, 092765) estimates is then -1.3 (-2.2 to -0.5) W/m^2. In comparison, the positive radiative forcing (RF) from greenhouse gases (including tropospheric ozone) is estimated to be +2.9 ± 0.3 W/m^2; hence tropospheric aerosols reduce the influence from greenhouse gases by about 45% (15-85%). This approach however inherits large uncertainties in aerosol amount, composition, and physical and optical properties in modeling of atmospheric aerosols. The consequences of these uncertainties are discussed in the next section.

The other method of calculating aerosol forcing is called the "inverse approach" – it is assumed that the observed climate change is primarily the result of the known climate forcing contributions. If one further assumes a particular climate sensitivity (or a range of sensitivities), one can determine what the total forcing had to be to produce the observed temperature change. The aerosol forcing is then deduced as a residual after subtraction of the greenhouse gas forcing along with other known forcings from the total value. Studies of this nature come up with aerosol forcing ranges of -0.6 to -1.7 W/m^2 (Knutti et al., 2002, 190178;

Knutti et al., 2003, 190180); IPCC AR4 Chap.9); -0.4 to -1.6 W/m^2 (Gregory et al., 2002, 190593); and -0.4 to -1.4 W/m^2 (Stott, 2006, 190419). This approach however provides a bracket of the possible range of aerosol forcing without the assessment of current knowledge of the complexity of atmospheric aerosols.

This chapter of the CCSP SAP2.3 reviews the current state of aerosol RF in the global models and assesses the uncertainties in these calculations. First representation of aerosols in the forward global chemistry and transport models and the diversity of the model simulated aerosol fields are discussed; then calculation of the aerosol direct and indirect effects in the climate models is reviewed; finally the impacts of aerosols on climate model simulations and their implications are assessed.

9.3.6.2. Modeling of Atmospheric Aerosols

The global aerosol modeling capability has developed rapidly in the past decade. In the late 1990s, there were only a few global models that were able to simulate one or two aerosol components, but now there are a few dozen global models that simulate a comprehensive suite of aerosols in the atmosphere. As introduced in Chapter 1 (of the CCSP SAP2.3), aerosols consist of a variety of species including dust, sea salt, sulfate, nitrate, and carbonaceous aerosols (black and organic carbon) produced from natural and man-made sources with a wide range of physical and optical properties. Because of the complexity of the processes and composition, and highly inhomogeneous distribution of aerosols, accurately modeling atmospheric aerosols and their effects remains a challenge. Models have to take into account not only the aerosol and precursor emissions, but also the chemical transformation, transport, and removal processes (e.g., dry and wet depositions) to simulate the aerosol mass concentrations. Furthermore, aerosol particle size can grow in the atmosphere because the ambient water vapor can condense on the aerosol particles. This "swelling" process, called hygroscopic growth, is most commonly parameterized in the models as a function of relative humidity.

Estimates of Emissions

Aerosols have various sources from both natural and anthropogenic processes. Natural emissions include wind-blown mineral dust, aerosol and precursor gases from volcanic eruptions, natural wild fires, vegetation, and oceans. Anthropogenic sources include emissions from fossil fuel and biofuel combustion, industrial processes, agriculture practices, and human-induced biomass burning.

Following earlier attempts to quantify manmade primary emissions of aerosols (Penner et al., 1993, 045457; Turco et al., 1983, 190529) systematic work was undertaken in the late 1990s to calculate emissions of black carbon (BC) and organic carbon (OC), using fuel-use data and measured emission factors (Cooke and Wilson, 1996, 190046; Cooke et al., 1999, 156365; Liousse et al., 1996, 078158). The work was extended in greater detail and with improved attention to source-specific emission factors in Bond et al. (2004, 056389), which provides global inventories of BC and OC for the year 1996, with regional and source-category discrimination that includes contributions from industrial, transportation, residential solid-fuel combustion, vegetation and open biomass burning (forest fires, agricultural waste burning, etc.), and diesel vehicles.

Emissions from natural sources—which include wind-blown mineral dust, wildfires, sea salt, and volcanic eruptions—are less well quantified, mainly because of the difficulties of measuring emission rates in the field and the unpredictable nature of the events. Often, emissions must be inferred from ambient observations at some distance from the actual source. As an example, it was concluded (Lewis and Schwartz, 2004, 192023) that available information on size-dependent sea salt production rates could only provide order-of-magnitude estimates. The natural emissions in general can vary dramatically over space and time.

Aerosols can be produced from trace gases in the atmospheric via chemical reactions, and those aerosols are called secondary aerosols, as distinct from primary aerosols that are directly emitted to the atmosphere as aerosol particles. For example, most sulfate and nitrate aerosols are secondary aerosols that are formed from their precursor gases, sulfur dioxide (SO_2) and nitrogen oxides (NO and NO_2, collectively called NO_X), respectively. Those sources have been studied for many years and are relatively well known. By contrast, the sources of secondary organic aerosols (SOA) are poorly understood, including emissions of their precursor gases (called volatile organic compounds, VOC) from both natural and anthropogenic sources and the atmospheric production processes.

Globally, sea salt and mineral dust dominate the total aerosol mass emissions because of the large source areas and/or large particle sizes. However, sea salt and dust also have shorter atmospheric lifetimes because of their large particle size, and are radiatively less active than aerosols with small particle size, such as sulfate, nitrate, BC, and particulate organic matter (POM, which includes both carbon and non-carbon mass in the organic aerosol), most of which are anthropogenic in origin.

Because the anthropogenic aerosol RF is usually evaluated (e.g., by the IPCC) as the anthropogenic perturbation since the pre-industrial period, it is necessary to estimate the

historical emission trends, especially the emissions in the pre-industrial era. Compared to estimates of present-day emissions, estimates of historical emission have much larger uncertainties. Information for past years on the source types and strengths and even locations are difficult to obtain, so historical inventories from preindustrial times to the present have to be based on limited knowledge and data. Several studies on historical emission inventories of BC and OC (e.g., Bond et al., 2007, 190050; Fernandes et al., 2007, 190554; Ito and Penne, 2005, 190626; Junker and Liousse, 2008, 190971; Novakov et al., 2003, 048398), SO_2 (Stern, 2005, 190416), and various species (Dentener et al., 2006, 088434; Van Aardenne et al., 2001, 055564) are available in the literature; there are some similarities and some differences among them, but the emission estimates for early times do not have the rigor of the studies for present-day emissions. One major conclusion from all these studies is that the growth of primary aerosol emissions in the 20th century was not nearly as rapid as the growth in CO2 emissions. This is because in the late 19th and early 20th centuries, particle emissions such as BC and POM were relatively high due to the heavy use of biofuels and the lack of particulate controls on coal-burning facilities; however, as economic development continued, traditional biofuel use remained fairly constant and particulate emissions from coal burning were reduced by the application of technological controls (Bond et al., 2007, 190050). Thus, particle emissions in the 20th century did not grow as fast as CO2 emissions, as the latter are roughly proportional to total fuel use—oil and gas included. Another challenge is estimating historical biomass burning emissions. A recent study suggested about a 40% increase in carbon emissions from biomass burning from the beginning to the end of last century (Mouillot et al., 2006, 190549), but it is difficult to verify.

Table 9-11. Anthropogenic emissions of aerosols and precursors for 2000 and 1750.

Source	Species*	Emission# 2000 (Tg/yr)	Emission 1750 (Tg/yr)
Biomass burning	BC	3.1	1.03
	POM	34.7	12.8
	S	4.1	1.46
Biofuel	BC	9.1	0.39
	POM	9.6	1.56
	S		0.12
Fossil fuel	BC	3.0	
	POM	3.2	
	S	98.9	

Data source for 2000 emission: biomass burning – Global Fire Emission Dataset (GFED); biofuel BC and POM – Speciated Pollutant Emission Wizard (SPEW); biofuel sulfur – International Institute for Applied System Analysis (IIASA); fossil fuel BC and POM – SPEW; fossil fuel sulfur – Emission Database for Global Atmospheric Research (EDGAR) and IIASA. Fossil fuel emission of sulfur (S) is the sum of emission from industry, power plants, and transportation listed in Dentener et al. (2006, 088434).
* S=sulfur, including SO_2 and particulate SO_4^{2-}. Most emitted as SO_2, and 2.5% emitted as SO_4^{2-}.

Source: Adapted from Dentener et al. (2006, 088434)

As an example, Table 9-11 shows estimated anthropogenic emissions of sulfur, BC and POM in the present day (year 2000) and pre-industrial time (1750) compiled by Dentener et al. (2006, 088434) These estimates have been used in the Aerosol Comparisons between Observations and Models (AeroCom) project (Experiment B, which uses the year 2000 emission; and Experiment PRE, which uses pre-industrial emissions), for simulating atmospheric aerosols and anthropogenic aerosol RF. The AeroCom results are discussed below and in Section 9.3.6.3.

Aerosol Mass Loading and Optical Depth

In the global models, aerosols are usually simulated in the successive steps of sources (emission and chemical formation), transport (from source location to other area), and removal processes (dry deposition, in which particles fall onto the surface, and wet deposition by rain) that control the aerosol lifetime. Collectively, emission, transport, and removal determine the amount (mass) of aerosols in the atmosphere. Aerosol optical depth (AOD), which is a measure of solar or thermal radiation being attenuated by aerosol particles via scattering or absorption, can be related to the atmospheric aerosol mass loading as follows:

$$AOD = MEE \bullet M$$

Equation 9-3

where M is the aerosol mass loading per unit area (g m-2), MEE is the mass extinction efficiency or specific extinction in unit of m^2/g, which is

$$MEE = \frac{3Q_{est}}{4\pi pr_{eff}} \bullet \int$$

Equation 9-4

where Qext is the extinction coefficient (a function of particle size distribution and refractive index), reff is the aerosol particle effective radius, ρ is the aerosol particle density, and f is the ratio of ambient aerosol mass (wet) to dry aerosol mass M. Here, M is the result from model-simulated atmospheric processes and MEE embodies the aerosol physical (including microphysical) and optical properties. Since Qext varies with radiation wavelength, so do MEE and AOD. AOD is the quantity that is most commonly obtained from remote sensing measurements and is frequently used for model evaluation (see Chapter 2 of the CCSP SAP2.3). AOD is also a key parameter determining aerosol radiative effects.

Here the results from the recent multiple global-model studies by the AeroCom project are summarized, as they represent the current assessment of model-simulated atmospheric aerosol loading, optical properties, and RF for the present-day. AeroCom aims to document differences in global aerosol models and compare the model output to observations. Sixteen global models participated in the AeroCom Experiment A (AeroCom-A), for which every model used their own configuration, including their own choice of estimating emissions (Kinne et al., 2006, 155903; Textor et al., 2006, 190456). Five major aerosol types: sulfate, BC, POM, dust, and sea salt, were included in the experiments, although some models had additional aerosol species. Of those major aerosol types, dust and sea-salt are predominantly natural in origin, whereas sulfate, BC, and POM have major anthropogenic sources.

Table 9-12 summarizes the model results from the AeroCom-A for several key parameters: Sources (emission and chemical transformation), mass loading, lifetime, removal rates, and MEE and AOD at a commonly used, mid-visible, wavelength of 550 nanometer (nm). These are the globally averaged values for the year 2000. Major features and conclusions are:

- Globally, aerosol source (in mass) is dominated by sea salt, followed by dust, sulfate, POM, and BC. Over the non-desert land area, human activity is the major source of sulfate, black carbon, and organic aerosols.
- Aerosols are removed from the atmosphere by wet and dry deposition. Although sea salt dominates the emissions, it is quickly removed from the atmosphere because of its large particle size and near-surface distributions, thus having the shortest lifetime. The median lifetime of sea salt from the AeroCom-A models is less than half a day, whereas dust and sulfate have similar lifetimes of 4 days and BC and POM 6-7 days.
- Globally, small-particle-sized sulfate, BC, and POM make up a little over 10% of total aerosol mass in the atmosphere. However, they are mainly from anthropogenic activity, so the highest concentrations are in the most populated regions, where their effects on climate and air quality are major concerns.
- Sulfate and BC have their highest MEE at mid-visible wavelengths, whereas dust is lowest among the aerosol types modeled. That means for the same amount of aerosol mass, sulfate and BC are more effective at attenuating (scattering or absorbing) solar radiation than dust. This is why the sulfate AOD is about the same as dust AOD even though the atmospheric amount of sulfate mass is 10 times less than that of the dust.
- There are large differences, or diversities, among the models for all the parameters listed in Table 9-12. The largest model diversity, shown as the % standard deviation from the all-model-mean and the range (minimum and maximum values) in Table 9-12, is in sea salt emission and removal; this is mainly associated with the differences in particle size range and source parameterizations in each model. The diversity of sea salt atmospheric loading however is much smaller than that of sources or sinks, because the largest particles have the shortest lifetimes even though they comprise the largest fraction of emitted and deposited mass.

Table 9-12. Summary of statistics of AeroCom Experiment A results from 16 global models.

Quantity	Mean	Median	Range	Stddev/mean*
SOURCES (TG/YR)				
SO_4^{2-}	179	186	98-232	22%
BC	11.9	11.3	7.8-19.4	23%
Organic matter	96.6	96.0	53-138	26%
Dust	1840	1640	672-4040	49%
Sea salt	16600	6280	2180-121000	199%
REMOVAL RATE (DAY-)				
SO_4^{2-}	0.25	0.24	0.19-0.39	18%
BC	0.15	0.15	0.066-0.19	21%
Organic matter	0.16	0.16	0.09-0.23	24%
Dust	0.31	0.25	0.14-0.79	62%
Sea salt	5.07	2.50	0.95-35.0	188%
LIFETIME (DAY)				
SO_4^{2-}	4.12	4.13	2.6-5.4	18%
BC	7.12	6.54	5.3-15	33%
Organic matter	6.54	6.16	4.3-11	27%
Dust	4.14	4.04	1.3-7.0	43%
Sea salt	0.48	0.41	0.03-1.1	58%
MASS LOADING (TG)				
SO_4^{2-}	1.99	1.98	0.92-2.70	25%
BC	0.24	0.21	0.046-0.51	42%
Organic matter	1.70	1.76	0.46-2.56	27%
Dust	19.2	20.5	4.5-29.5	40%
Sea salt	7.52	6.37	2.5-13.2	54%
MEE AT 550 NM (M2G-1)				
SO_4^{2-}	11.3	9.5	4.2-28.3	56%
BC	9.4	9.2	5.3-18.9	36%
Organic matter	5.7	5.7	3.7-9.1	26%
Dust	0.99	0.95	0.46-2.05	45%
Sea salt	3.0	3.1	0.97-7.5	55%
AOD AT 550 NM				
SO_4^{2-}	0.035	0.034	0.015-0.051	33%
BC	0.004	0.004	0.002-0.009	46%
Organic matter	0.018	0.019	0.006-0.030	36%
Dust	0.032	0.033	0.012-0.054	44%
Sea salt	0.033	0.030	0.02-0.067	42%
TOTAL AOT AT 550 NM	***0.124***	***0.127***	***0.056-0.151***	***18%***

Stddev/mean was used as the term "diversity" in Textor et al. (2006, 190456).

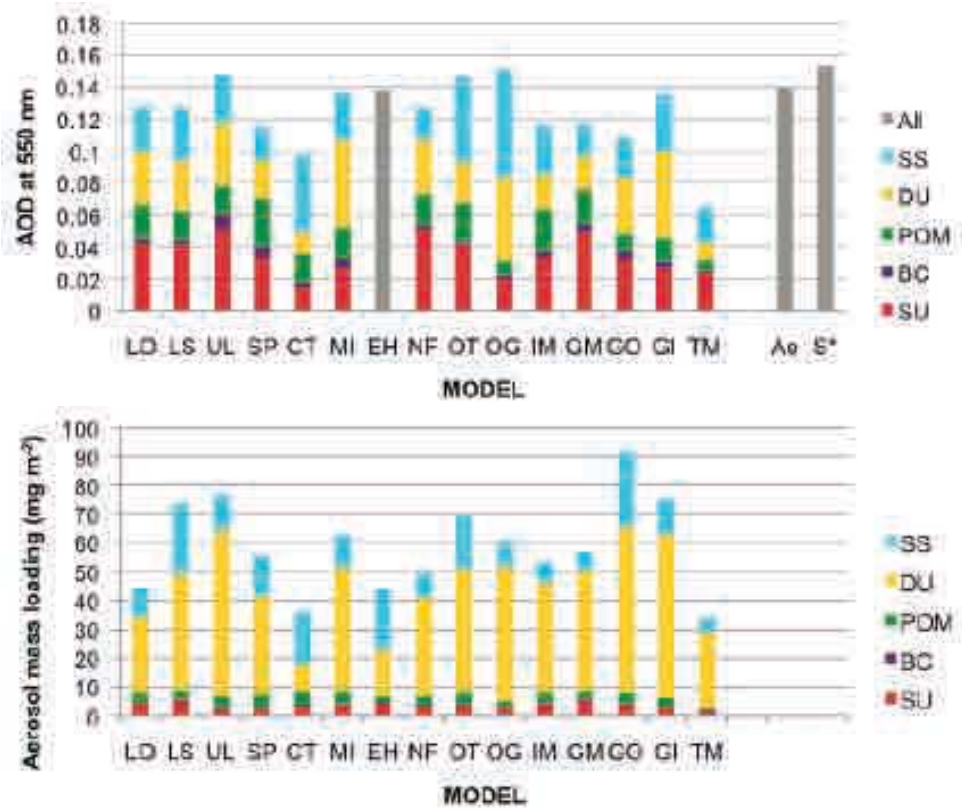
Source: Textor et al. (2006, 190456) and Kinne et al. (2006, 155903), and AeroCom website http://nansen.ipsl.jussieu.fr/AEROCOM/data.html

- Among the key parameters compared in Table 9-12, the models agree best for simulated total AOD – the % of standard deviation from the model mean is 18%, with the extreme values just a factor of 2 apart. The median value of the multi-model simulated global annual mean total AOD, 0.127, is also in agreement with the global mean values from recent satellite measurements. However, despite the general agreement in total AOD, there are significant diversities at the individual component level for aerosol optical thickness, mass loading, and mass extinction efficiency. This indicates that uncertainties in assessing aerosol climate forcing are still large, and they depend not only on total AOD but also on aerosol absorption and scattering direction (called asymmetry factor), both of which are determined by aerosol physical and optical properties. In addition, even with large differences in mass loading and MEE among different models, these terms could compensate for each other (Equation 9-3) to produce similar AOD. This is illustrated in Figure 9-72. For example, model LO and LS have quite different mass loading (44 and 74 mg m^{-2}, respectively), especially for dust and sea salt amount, but they produce nearly identical total AOD (0.127 and 0.128, respectively).
- Because of the large spatial and temporal variations of aerosol distributions, regional and seasonal diversities are even larger than the diversity for global annual means.

To further isolate the impact of the differences in emissions on the diversity of simulated aerosol mass loading, identical emissions for aerosols and their precursor were used in the AeroCom Experiment B exercise in which 12 of the 16 AeroCom-A models participated (Textor et al., 2007, 190458). The comparison of the results and diversity between AeroCom-A and –B for the same models showed that using harmonized emissions does not significantly reduce model diversity for the simulated global mass and AOD fields, indicating that the differences in atmospheric processes, such as transport, removal, chemistry, and aerosol microphysics, play more important roles than emission in creating diversity among the models. This outcome is somewhat different from another recent study, in which the differences in calculated clear-sky aerosol RF between two models (a regional model STEM and a global model MOZART) were attributed mostly to the differences in emissions (Bates et al., 2006, 189912), although the conclusion was based on only two model simulations for a few focused regions. It is highly recommended from the outcome of AeroCom-A and -B that, although more detailed evaluation for each individual process is needed, multi-model ensemble results, e.g., median values of multi-model output variables, should be used to estimate aerosol RF, due to their greater robustness, relative to individual models, when compared to observations (Schulz et al., 2006, 190381; Textor et al., 2006, 190456; Textor et al., 2007, 190458).

9.3.6.3. Calculating Aerosol Direct Radiative Forcing

The three parameters that define the aerosol direct RF are the AOD, the single scattering albedo (SSA), and the asymmetry factor (g), all of which are wavelength dependent. AOD is indicative of how much aerosol exists in the column, SSA is the fraction of radiation being scattered versus the total attenuation (scattered and absorbed), and the g relates to the direction of scattering that is related to the size of the particles (see Chapter 1 of the CCSP SAP2.3). An indication of the particle size is provided by another parameter, the Ångström exponent (Å), which is a measure of differences of AOD at different wavelengths. For typical tropospheric aerosols, Å tends to be inversely dependent on particle size; larger values of Å are generally associated with smaller aerosols particles. These parameters are further related; for example, for a given composition, the ability of a particle to scatter radiation decreases more rapidly with decreasing size than does its ability to absorb, so at a given wavelength varying Å can change SSA. Note that AOD, SSA, g, Å, and all the other parameters in Equation 9-3 and Equation 9-4 vary with space and time due to variations of both aerosol composition and relative humidity, which influence these characteristics.



Source: Adapted from Kinne et al. (2006, 155903)

Figure 9-72. Global annual averaged AOD (upper panel) and aerosol mass loading (lower panel) with their components simulated by 15 models in AeroCom- A (excluding one model which only reported mass). SU=SO_4^{2-}, BC=black carbon, POM=particulate OC, DU=dust, SS=sea salt. Model abbreviations: LO=LOA (Lille, Fra), LS=LSCE (Paris, Fra), UL=ULAQ (L'Aquila, Ita), SP=SPRINTARS (Kyushu, Jap), CT=ARQM (Toronto, Can), MI=MIRAGE (Richland, USA), EH=ECHAM5 (MPI-Hamburg, Ger), NF=CCM-Match (NCAR Boulder, USA), OT=Oslo-CTM (Oslo, Nor), OG=OLSO-GCM (Oslo, Nor) [prescribed background for DU and SS], IM=IMPACT (Michigan, USA), GM=GFDLMozart (Princeton, NJ, USA), GO=GOCART (NASA-GSFC, Washington DC, USA), GI=GISS (NASA-GISS, New York, USA), TM=TM5 (Utrecht, Net). Also shown in the upper panel are the averaged observation data from AERONET (Ae) and the satellite composite (S*).

In the recent AeroCom project, aerosol direct RF for the solar spectral wavelengths (or shortwave) was assessed based on the 9 models that participated in both Experiment B and PRE in which identical, prescribed emissions for present (year 2000) and pre-industrial time (year 1750) listed in Table 9-11 were used across the models (Schulz et al., 2006, 190381). The anthropogenic direct RF was obtained by subtracting Aero- Com-PRE from AeroCom-B simulated results. Because dust and sea salt are predominantly from natural sources, they were not included in the anthropogenic RF assessment although the land use practice can contribute to dust emissions as "anthropogenic". Other aerosols that were not considered in the AeroCom forcing assessment were natural sulfate (e.g., from volcanoes or ocean) and POM (e.g., from biogenic hydrocarbon oxidation), as well as nitrate. The aerosol direct forcing in the AeroCom assessment thus comprises three major anthropogenic aerosol components sulfate, BC, and POM.

Table 9-13. SO_4^{2-} mass loading, MEE and AOD at 550 nm, shortwave radiative forcing at the top of the atmosphere, and normalized forcing with respect to AOD and mass. All values refer to anthropogenic perturbation.

Model	Mass load (mg m^{-2})	MEE ($m^2 g^{-1}$)	AOD att 550 nm	TOA Forcing (W/m^2)	Forcing/AOD (W/m^2)	Forcing/Mass ($W g^{-1}$)
PUBLISHED SINCE IPCC 2001						
A CCM3	2.23			-0.56		-251
B GEOSCHEM	1.53	11.8	0.018	-0.33	-18	-216
C GISS	3.30	6.7	0.022	-0.65	-30	-197
D GISS	3.27			-0.96		-294
E GISS*	2.12			-0.57		-269
F SPRINTARS	1.55	9.7	0.015	-0.21		-135
G LMD	2.76			-0.42		-152
H LOA	3.03	9.9	0.03	-0.41	-14	-135
I GATORG	3.06			-0.32		-105
J PNNL	5.50	7.6	0.042	-0.44	-10	-80
K UIO-CTM	1.79	10.6	0.019	-0.37	-19	-207
L UIO-GCM	2.28			-0.29		-127
AEROCOM: IDENTICAL EMISSIONS USED FOR YEAR 2000 AND 1750						
M UMI	2.64	7.6	0.02	-0.58	-29	-220
N UIO-CTM	1.70	11.2	0.019	-0.36	-19	-212
O LOA	3.64	9.6	0.035	-0.49	-14	-135
P LSCE	3.01	7.6	0.023	-0.42	-18	-140
Q ECHAMS-HAM	2.47	6.5	0.016	-0.46	-29	-186
R GISS**	1.34	4.5	0.006	-0.19	-32	-142
S UIO-GCM	1.72	7.0	0.012	-0.25	-21	-145
T SPRINTARS	1.19	10.9	0.013	-0.16	-12	-134
U ULAQ	1.62	12.3	0.02	-0.22	-11	-136
Average A-L	2.70	9.4	0.024	-00.46	-18	-181
Average M-U	2.15	8.6	0.018	-0.35	-21	-161
Minimum A-U	1.19	4.5	0.006	-0.96	-32	-294
Maximum A-U	5.50	12.3	0.042	-0.16	-10	-80
Std dev A-L	1.09	1.9	0.010	0.202	7	68
Std dev M-U	0.83	2.6	0.008	0.149	8	35
%Stddev/avg A-L	40%	20%	41%	44%	38%	385
%Stddev/avg M-U	39%	30%	45%	43%	37%	22%

Model abbreviations: CCM3=Community Climate Model; GEOSCHEM=Goddard Earth Observing System-Chemistry; GISS=Goddard nstitute for Space Studies; SPRINTARS=Spectral Radiation-Transport Model for Aerosol Species; LMD=Laboratoire de Meteorologie Dynamique; LOA=Laboratoire d'Optique Atmospherique; GATORG=Gas, Aerosol Transport and General circulation model; PNNL=Pacific Northwest National Laboratory; UIO-CTM=Univeristy of Oslo CTM; UIO-GCM=University of Oslo GCM; UMI=University of Michigan; LSCE=Laboratoire des Sciences du Climat et de l'Environment; ECHAMS5-HAM=European Centre Hamburg with Hamburg Aerosol Module; ULAQ=University of IL'Aquila.

Source: Adapted from IPCC AR4 (2007, 092765) and Schulz et al. (2006, 190381)

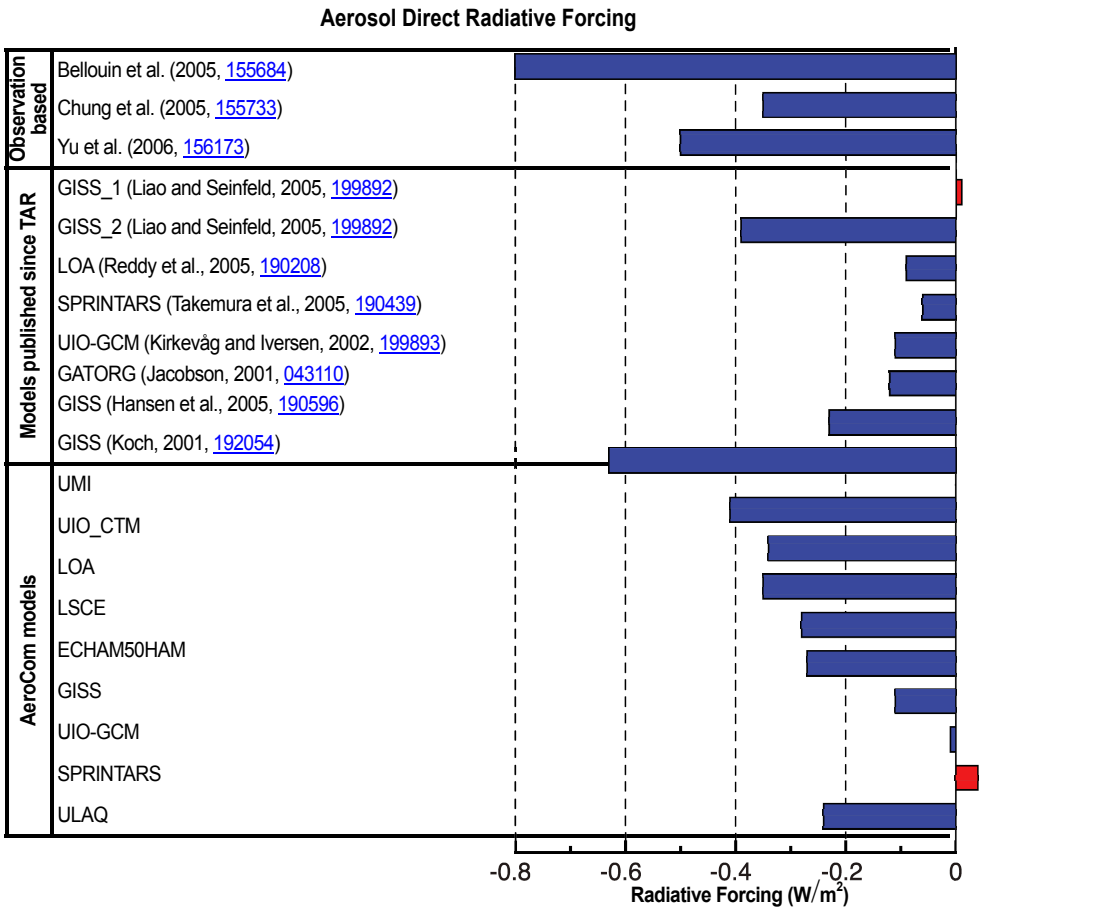
Table 9-14. Particulate organic matter (POM) and BC mass loading, AOD at 550 nm, shortwave radiative forcing at the top of the atmosphere, and normalized forcing with respect to AOD and mass.

Model	Mass load ($mg\ m^{-2}$)	MEE ($m^2 g^{-1}$)	AOD at 550 nm	TOA Forcing (W/m^2)	Forcing/ AOD (W/m^2)	Forcing/ Mass ($W\ g^{-1}$)	Mass load ($mg\ m^{-2}$)	MEE ($m^2 g^{-1}$)	AOD at 550 nm	TOA Forcing (W/m^2)	Forcing/ AOD (W/m^2)	Forcing/ Mass ($W\ g^{-1}$)
PUBLISHED SINCE IPCC 2001												
A SPRINTARS				-0.24		-107				0.36		
B LOA	2.33	6.9	0.016	-0.25	-16	-140	0.37			0.55		
C GISS	1.86	9.1	0.017	-0.26	-15	-161	0.29			0.61		
D GISS	1.86	8.1	0.015	-0.30	-20	-75	0.29			0.35		
E GISS*	2.39			-0.18		-92	0.39			0.50		
F GISS	2.49			-0.23		-101	0.43			0.53		
G SPRINTARS	2.67	10.9	0.029	-0.27	-9	-23	0.53			0.42		
H GATORG	2.56			-0.06		-112	0.39			0.55		
I MOZGN	3.03	5.9	0.018	-0.34	-19							
J CCM							0.33			0.34		
K UIO-CTM							0.30			0.19		
AEROCOM: IDENTICAL EMISSIONS FOR YEAR 2000 & 1750												
L UMI	1.16	5.2	0.0060	-0.23	-38	-198	0.19	6.8	1.29	0.25	194	1316
M UIO-CTM	1.12	5.2	0.0058	-0.16	-28	-143	0.19	7.1	1.34	0.22	164	1158
N LOA	1.41	6.0	0.0085	-0.16	-19	-113	0.25	7.9	1.98	0.32	162	1280
OLSCE	1.50	5.3	0.0079	-0.17	-22	-113	0.25	4.4	1.11	0.30	270	1200
P ECHAMS-HAM	1.00	7.7	0.0077	-0.10	-13	-100	0.16	7.7	1.23	0.20	163	1250
Q GISS**	1.22	4.9	0.0060	-0.14	-23	-115	0.24	7.6	1.83	0.22	120	917
R UIO-GCM	0.88	5.2	0.0046	-0.06	-13	-68	0.19	10.3	1.95	0.36	185	1895
S SPRINTARS	1.84	10.9	0.0200	-0.10	-5	-54	0.37	9.5	3.50	0.32	91	865
T ULAQ	1.71	4.4	0.0075	-0.09	-12	-53	0.38	7.6	2.90	0.08	28	211
Average A-K	2.40	8.2	0.019	-0.24	-16	-102	0.37			0.44		1242
Average L-T	1.32	6.1	0.008	-0.13	-19	-106	0.25	7.7	1.90	0.25	153	1121
Minimum A-T	0.88	4.4	0.005	-0.34	-38	-198	0.16	4.4	1.11	0.08	28	211
Maximum A-T	3.03	10.9	0.029	-0.06	-5	-23	0.53	10.3	3.50	0.61	270	2103
Std dev A-K	0.39	1.7	0.006	0.09	4	41	0.08			0.06		384
Std dev L-T	0.32	2.0	0.005	0.05	10	46	0.08	1.6	0.82	0.09	68	450
%Stddev/avg A-K	16%	21%	30%	36%	26%	41%	22%			23%		31%
%Stddev/avg L-T	25%	33%	56%	39%	52%	43%	32%	21%	43%	34%	45%	40%

Source: Based on IPCC AR4 (2007, 092765) and Schulz et al. (2006, 190381).

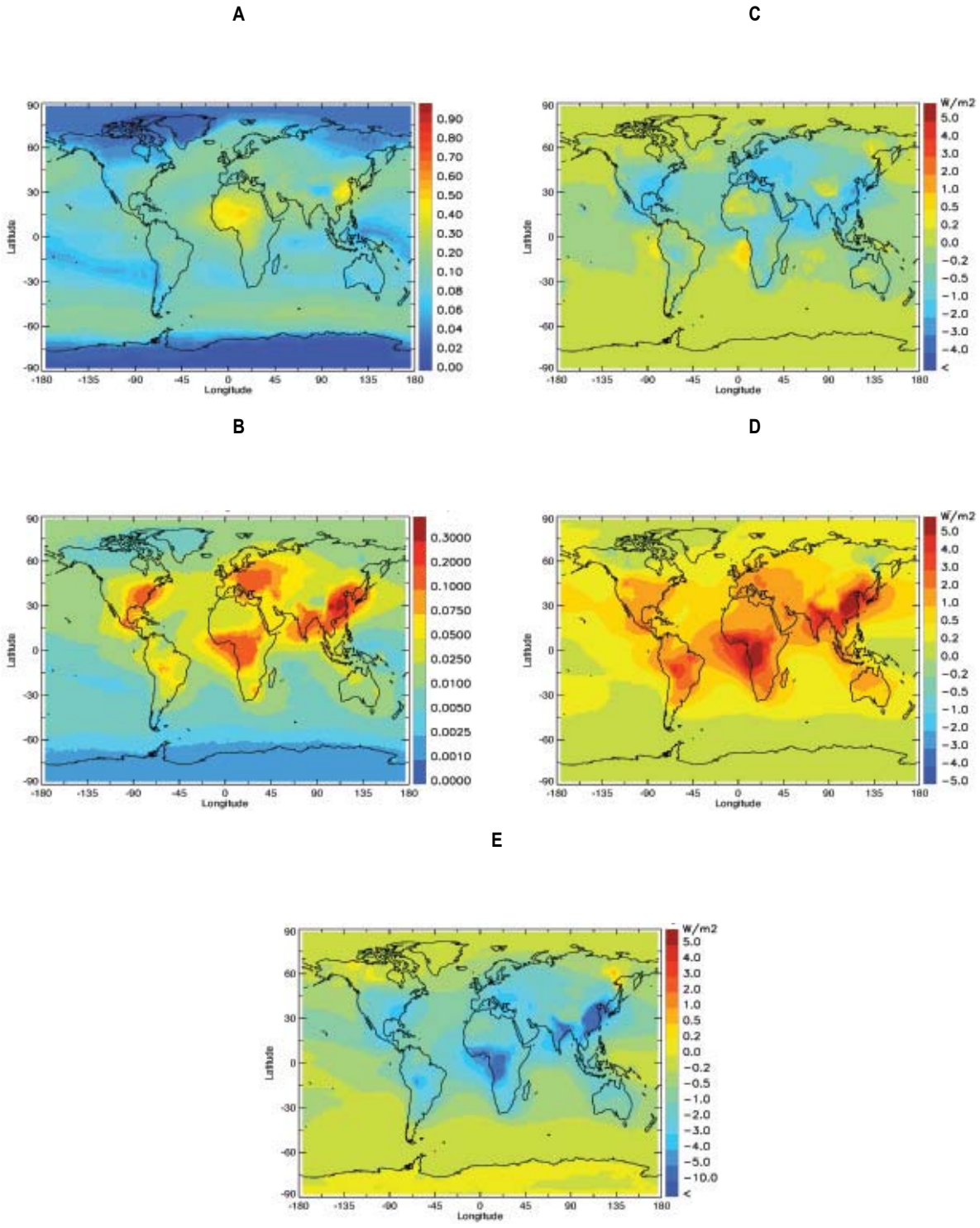
The IPCC AR4 (2007, 092765) assessed anthropogenic aerosol RF based on the model results published after the IPCC TAR in 2001, including those from the AeroCom study discussed above. These results (adopted from IPCC AR4) are shown in Table 9-13 for sulfate and Table 9-14 for carbonaceous aerosols (BC and POM), respectively. All values listed in Table 9-13 and Table 9-14 refer to anthropogenic perturbation, i.e., excluding the natural fraction of these aerosols. In addition to the mass burden, MEE, and AOD, Table 9-13 and Table 9-14 also list the "normalized forcing", also known as "forcing efficiency", one for the forcing per unit AOD, and the other the forcing per gram of aerosol mass (dry). For some models, aerosols are externally mixed, that is, each aerosol particle contains only one aerosol type such as sulfate, whereas other models allow aerosols to mix internally to different degrees, that is, each aerosol particle can have more than one component, such as black carbon coated with sulfate. For models with internal mixing of aerosols, the component values for AOD, MEE, and forcing were extracted (Schulz et al., 2006, 190381).

Considerable variation exists among these models for all quantities in Table 9-13 and Table 9-14. The RF for all the components varies by a factor of 6 or more: Sulfate from 0.16 to 0.96 W/m^2, POM from -0.06 to -0.34 W/m^2, and BC from +0.08 to +0.61 W/m^2, with the standard deviation in the range of 30 to 40% of the ensemble mean. It should be noted that although BC has the lowest mass loading and AOD, it is the only aerosol species that absorbs strongly, causing positive forcing to warm the atmosphere, in contrast to other aerosols that impose negative forcing to cool the atmosphere. As a result, the net anthropogenic aerosol forcing as a whole becomes less negative when BC is included. The global average anthropogenic aerosol direct RF at the top of the atmosphere (TOA) from the models, together with observation-based estimates (see Chapter 2 of the CCSP SAP2.3), is presented in Figure 9-73. Note the wide range for forcing in Figure 9-73. The comparison with observation-based estimates shows that the model estimated forcing is in general lower, partially because the forcing value from the model is the difference between present-day and pre-industrial time, whereas the observation-derived quantity is the difference between an atmosphere with and without anthropogenic aerosols, so the "background" value that is subtracted from the total forcing is higher in the models. The discussion so far has dealt with global average values. The geographic distributions of multi-model aerosol direct RF has been evaluated among the AeroCom models, which are shown in Figure 9-74 for total and anthropogenic AOD at 550 nm and anthropogenic aerosol RF at TOA, within the atmospheric column, and at the surface. Globally, anthropogenic AOD is about 25% of total AOD (Figure 9-74A and B) but is more concentrated over polluted regions in Asia, Europe, and North America and biomass burning regions in tropical southern Africa and South America. At TOA, anthropogenic aerosol causes negative forcing over mid-latitude continents and oceans with the most negative values (-1 to -2 W/m^2) over polluted regions (Figure 9-74C). Although anthropogenic aerosol has a cooling effect at the surface with surface forcing values down to -10 W/m^2 over China, India, and tropical Africa (Figure 9-74E), it warms the atmospheric column with the largest effects again over the polluted and biomass burning regions. This heating effect will change the atmospheric circulation and can affect the weather and precipitation (e.g., Kim et al., 2006, 190917).



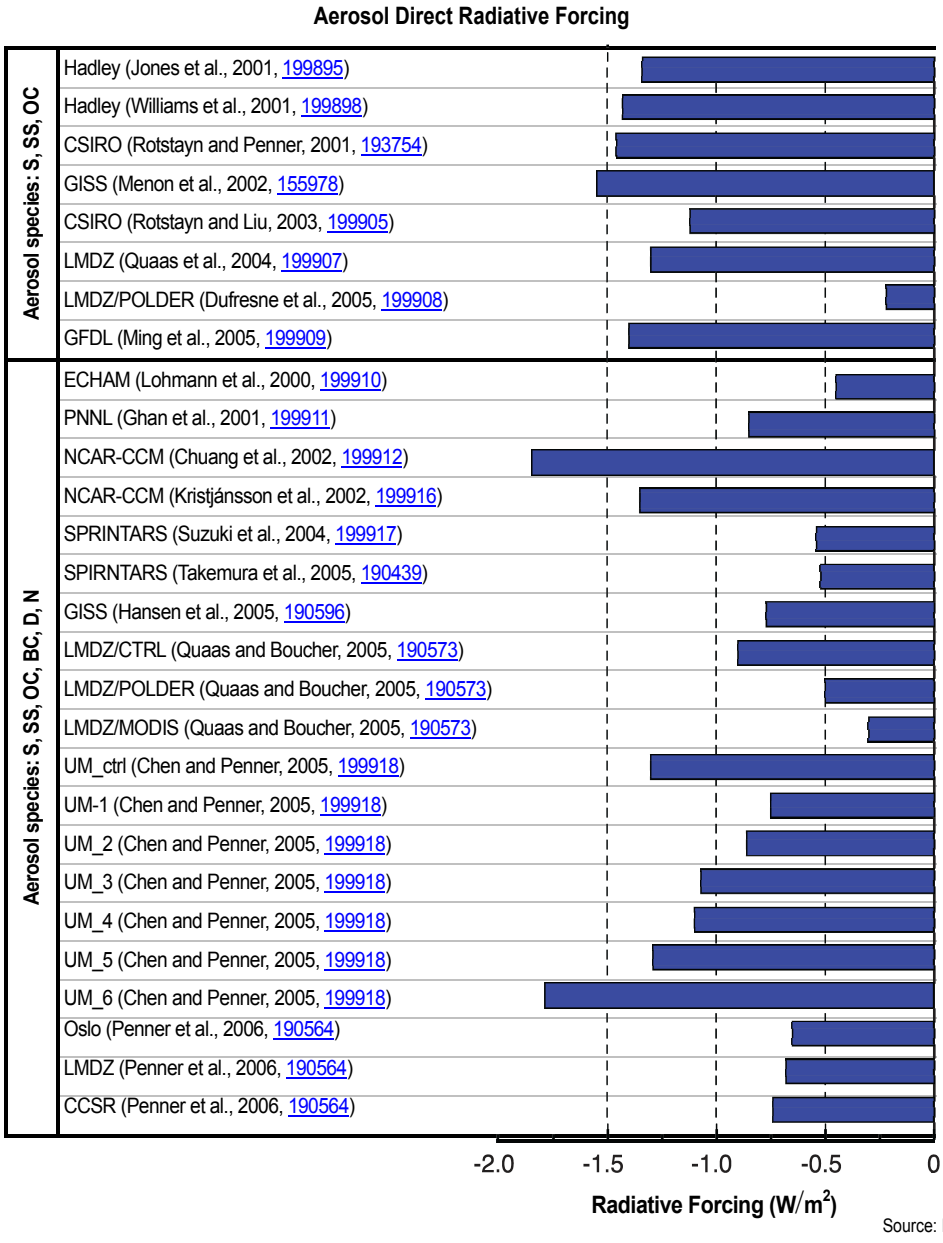
Source: IPCC (2007, 092765).

Figure 9-73. Aerosol direct radiative forcing in various climate and aerosol models. Observed values are shown in the top section.



Source: Schulz et al. (2006, 190381) and AeroCom image catalog (http://nansen.ipsl.jussieu.fr/AEROCOM/aerocomhome.html)

Figure 9-74. Aerosol optical thickness and anthropogenic shortwave all-sky radiative forcing from the AeroCom study. Shown in the figure: total AOD (A) and anthropogenic AOD (B) at 550 nm, and radiative forcing at TOA (C), atmospheric column (D), and surface (E).



Source: IPCC (2007, 092765).

Figure 9-75. Radiative forcing from the cloud albedo effect (1st aerosol indirect effect) in the global climate models used from IPCC (2007, 092765), Chapter 2, Figure 2.14, of the IPCC AR4. Species included in the lower panel are SO_4^{2-}, sea salt, organic and BC, dust and nitrates; in the top panel, only SO_4^{2-}, sea salt and OC are included.

Basic conclusions from forward modeling of aerosol direct RF are:

- The most recent estimate of all-sky shortwave aerosol direct RF at TOA from anthropogenic sulfate, BC, and POM (mostly from fossil fuel/biofuel combustion and biomass burning) is -0.22 ± 0.18 W/m^2 averaged globally, exerting a net cooling effect. This value would represent the low-end of the forcing magnitude, since some potentially significant anthropogenic aerosols, such as nitrate and dust from human activities are not included because of their highly uncertain sources and processes. IPCC AR4 had adjusted the total anthropogenic aerosol direct RF to -0.5 ± 0.4 W/m^2 by adding estimated anthropogenic nitrate and dust forcing values based on limited modeling studies and by considering the observation-based estimates (see Chapter 2 of the CCSP SAP2.3).
- Both sulfate and POM cause negative forcing whereas BC causes positive forcing because of its highly absorbing nature. Although BC comprises only a small fraction of anthropogenic aerosol mass load and AOD, its forcing efficiency (with respect to either AOD or mass) is an order of magnitude stronger than sulfate and POM, so its positive shortwave forcing largely offsets the negative forcing from sulfate and POM. This points out the importance of improving the model ability to simulate each individual aerosol components more accurately, especially black carbon. Separately, it is estimated from recent model studies that anthropogenic sulfate, POM, and BC forcings at TOA are -0.4, -0.18, +0.35 W/m^2, respectively. The anthropogenic nitrate and dust forcings are estimated at -0.1 W/m^2 for each, with uncertainties exceeds 100% (IPCC, 2007, 092765).
- In contrast to long-lived greenhouse gases, anthropogenic aerosol RF exhibits significant regional and seasonal variations. The forcing magnitude is the largest over the industrial and biomass burning source regions, where the magnitude of the negative aerosol forcing can be of the same magnitude or even stronger than that of positive greenhouse gas forcing.
- There is a large spread of model-calculated aerosol RF even in the global annual averaged values. The AeroCom study shows that the model diversity at some locations (mostly East Asia and African biomass burning regions) can reach ± 3 W/m^2, which is an order of magnitude above the global averaged forcing value of -0.22 W/m^2. The large diversity reflects the low level of current understanding of aerosol radiative forcing, which is compounded by uncertainties in emissions, transport, transformation, removal, particle size, and optical and microphysical (including hygroscopic) properties.
- In spite of the relatively small value of forcing at TOA, the magnitudes of anthropogenic forcing at the surface and within the atmospheric column are considerably larger: -1 to -2 W/m^2 at the surface and +0.8 to +2 W/m^2 in the atmosphere. Anthropogenic aerosols thus cool the surface but heat the atmosphere, on average. Regionally, the atmospheric heating can reach annually averaged values exceeding 5 W/m^2. Source: Schulz et al. (2006, 190381) and AeroCom Image Catalog (http://nansen.ipsl.jussieu.fr/AEROCOM/aerocomhome.html)
- Figure 9-74D). These regional effects and the negative surface forcing are expected to exert an important effect on climate through alteration of the hydrological cycle.

9.3.6.4. Calculating Aerosol Indirect Forcing

Aerosol Effects on Clouds

A subset of the aerosol particles can act as cloud condensation nuclei (CCN) and/or ice nuclei (IN). Increases in aerosol particle concentrations, therefore, may increase the ambient concentrations of CCN and IN, affecting cloud properties. For a fixed cloud liquid water content, a CCN increase will lead to more cloud droplets so that the cloud droplet size will decrease. That effect leads to brighter clouds, the enhanced albedo then being referred to as the "cloud albedo effect" (Twomey, 1977, 190533), also known as the first indirect effect. If the droplet size is smaller, it may take longer to rainout, leading to an increase in cloud lifetime, hence the "cloud lifetime" effect (Albrecht, 1989, 045783), also called the second indirect effect. Approximately one-third of the models used for the IPCC 20th century climate change simulations incorporated an aerosol indirect effect, generally (though not exclusively) considered only with sulfates.

Shown in Figure 9-75 are results from published model studies indicating the different RF values from the cloud albedo effect. The cloud albedo effect ranges from -0.22 to -1.85 W/m^2; the lowest estimates are from simulations that constrained representation of aerosol effects on clouds with satellite measurements of drop size vs. aerosol index. In view of the difficulty of quantifying this effect remotely (discussed later), it is not clear whether this constraint provides an improved estimate. The estimate in the IPCC AR4 ranges from +0.4 to -1.1 W/m^2, with a "best-guess" estimate of 0.7 W/m^2.

The representation of cloud effects in GCMs is considered below. However, it is becoming increasingly clear from studies based on high resolution simulations of aerosol-

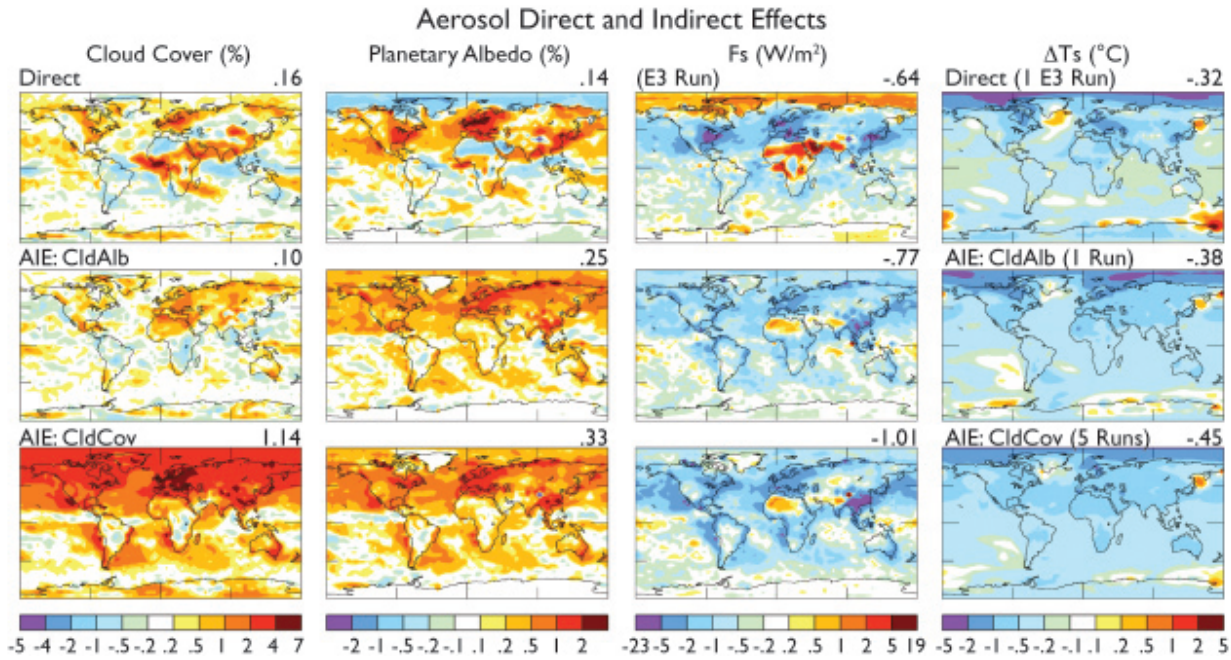
cloud interactions that there is a great deal of complexity that is unresolved in climate models. This point is examined below (High Resolution Modeling).

Most models did not incorporate the "cloud lifetime effect." Hansen et al. (2005, 059087) compared this latter influence (in the form of time-averaged cloud area or cloud cover increase) with the cloud albedo effect. In contrast to the discussion in IPCC (2007, 092765), they argue that the cloud cover effect is more likely to be the dominant one, as suggested both by cloud-resolving model studies (Ackerman et al., 2004, 190056) and satellite observations (Kaufman et al., 2005, 155891). The cloud albedo effect may be partly offset by reduced cloud thickness accompanying aerosol pollutants, producing a meteorological (cloud) rather than aerosol effect (see the discussion in Lohman and Feichter, 2005, 155942). The distinction between meteorological feedback and aerosol forcing can become quite opaque; as noted earlier, the term feedback is restricted here to those processes that are responding to a change in temperature. Nevertheless, both aerosol indirect effects were utilized in Hansen et al. (2005, 059087), with the second indirect effect calculated by relating cloud cover to the aerosol number concentration, which in turn is a function of sulfate, nitrate, black carbon and organic carbon concentration. Only the low altitude cloud influence was modeled, principally because there are greater aerosol concentrations at low levels, and because low clouds currently exert greater cloud RF. The aerosol influence on high altitude clouds, associated with IN changes, is a relatively unexplored area for models and as well for process-level understanding.

Hansen et al. (2005, 059087) used coefficients to normalize the cooling from aerosol indirect effects to between -0.75 and -1 W/m^2, based on comparisons of modeled and observed changes in the diurnal temperature range as well as some satellite observations. The response of the GISS model to the direct and two indirect effects is shown in Figure 9-76. As parameterized, the cloud lifetime effect produced somewhat greater negative RF (cooling), but this was the result of the coefficients chosen. Geographically, it appears that the "cloud cover" effect produced slightly more cooling in the Southern Hemisphere than did the "cloud albedo" response, with the reverse being true in the Northern Hemisphere (differences on the order of a few tenths °C).

Model Experiments

There are many different factors that can explain the large divergence of aerosol indirect effects in models (Figure 9-75). To explore this in more depth, Penner et al. (2006, 190564) used three general circulation models to analyze the differences between models for the first indirect effect, as well as a combined first plus second indirect effect. The models all had different cloud and/or convection parameterizations. In the first experiment, the monthly average aerosol mass and size distribution of, effectively, sulfate aerosol were prescribed, and all models followed the same prescription for parameterizing the cloud droplet number concentration (CDNC) as a function of aerosol concentration. In that sense, the only difference among the models was their separate cloud formation and radiation schemes. The different models all produced similar droplet effective radii, and therefore shortwave cloud forcing, and change in net outgoing whole sky radiation between pre-industrial times and the present. Hence the first indirect effect was not a strong function of the cloud or radiation scheme. The results for this and the following experiments are presented in Figure 9-77, where the experimental results are shown sequentially from left to right for the whole sky effect and in Table 9-15 for the clear-sky and cloud forcing response as well.



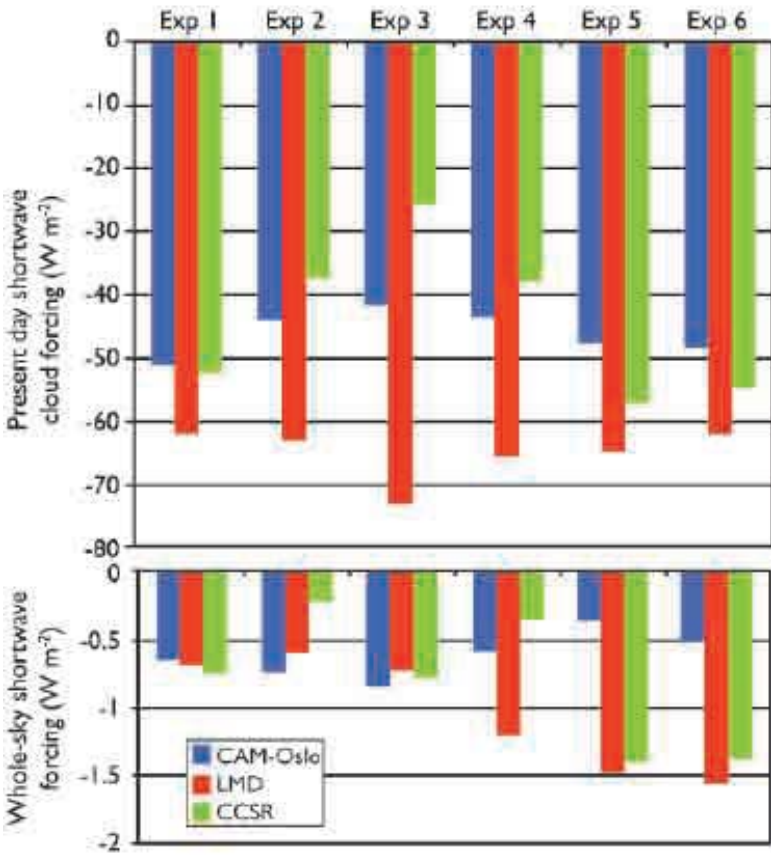
Source: Reprinted with Permission of Bioresource Technology from Hansen et al. (2005, 059087).

Figure 9-76. Anthropogenic impact on cloud cover, planetary albedo, radiative flux at the surface (while holding sea surface temperatures and sea ice fixed) and surface air temperature change from the direct aerosol forcing (top row), the first indirect effect (second row) and the second indirect effect (third row). The temperature change is calculated from year 81-120 of a coupled atmosphere simulation with the GISS model.

The change in cloud forcing is the difference between whole sky and clear sky outgoing radiation in the present day minus pre-industrial simulation. The large differences seen between experiments 5 and 6 are due to the inclusion of the clear sky component of aerosol scattering and absorption (the direct effect) in experiment 6.

In the second experiment, the aerosol mass and size distribution were again prescribed, but now each model used its own formulation for relating aerosols to droplets. In this case one of the models produced larger effective radii and therefore a much smaller first indirect aerosol effect (Figure 9-77, Table 9-15. However, even in the two models where the effective radius change and net global forcing were similar, the spatial patterns of cloud forcing differ, especially over the biomass burning regions of Africa and South America.

The third experiment allowed the models to relate the change in droplet size to change in precipitation efficiency (i.e., they were now also allowing the second indirect effect – smaller droplets being less efficient rain producers – as well as the first). The models utilized the same relationship for autoconversion of cloud droplets to precipitation. Changing the precipitation efficiency results in all models producing an increase in cloud liquid water path, although the effect on cloud fraction was smaller than in the previous experiments. The net result was to increase the negative radiative forcing in all three models, albeit with different magnitudes: for two of the models the net impact on outgoing shortwave radiative increased by about 20%, whereas in the third model (which had the much smaller first indirect effect), it was magnified by a factor of three.



Source: Adapted from Penner et al. (2006, 190564).

Figure 9-77. Global average present-day short wave cloud forcing at TOA (top) and change in whole sky net outgoing shortwave radiation (bottom) between the present-day and pre-industrial simulations for each model in each experiment.

Table 9-15. Differences in present day and pre-industrial outgoing solar radiation (W/m^2) in the different experiments.

Model	EXP 1	EXP 2	EXP 3	EXP 4	EXP 5	EXP 6
WHOLE-SKY						
CAM-Oslo	-0.648	-0.726	-0.833	-0.580	-0.365	-0.518
LMD-Z	-0.682	-0.597	-0.722	-1.194	-1.479	-1.553
CCSR	-0.739	-0.218	-0.733	-0.350	-1.386	-1.386
CLEAR-SKY						
CAM-Oslo	-0.063	-0.066	-0.026	0.014	-0.054	-0.575
LMD-Z	-0.054	0.019	0.030	-0.066	-0.126	-1.034
CCSR	0.018	-0.007	-0.045	-0.008	0.018	-1.160
CLOUD-FORCING						
CAM-Oslo	-0.548	-0.660	-0.807	-0.595	-0.311	0.056
LMD-Z	-0.628	-0.616	-0.752	-1.128	-1.353	-0.518
CCSR	-0.757	-0.212	-0.728	-0.345	-1.404	-0.200

EXP1: tests cloud formation and radiation schemes
EXP2: tests formulation for relating aerosols to droplets
EXP3: tests inclusion of droplet size influence on precipitation efficiency
EXP4: tests formulation of droplet size influence on precipitation efficiency
EXP5: tests model aerosol formulation from common sources
EXP6: added the direct aerosol effect

Source: Adapted from Penner et al. (2006, 190564).

In the fourth experiment, the models were now each allowed to use their own formulation to relate aerosols to precipitation efficiency. This introduced some additional changes in the whole sky shortwave forcing (Figure 9-77).

In the fifth experiment, models were allowed to produce their own aerosol concentrations, but were given common sources. This produced the largest changes in the RF in several of the models. Within any one model, therefore, the change in aerosol concentration has the largest effect on droplet concentrations and effective radii. This experiment too resulted in large changes in RF.

In the last experiment, the aerosol direct effect was included, based on the full range of aerosols used in each model. While the impact on the whole-sky forcing was not large, the addition of aerosol scattering and absorption primarily affected the change in clear sky radiation (Table 9-15).

The results of this study emphasize that in addition to questions concerning cloud physics, the differences in aerosol concentrations among the models play a strong role in inducing differences in the indirect effect(s), as well as the direct one.

Observational constraints on climate model simulations of the indirect effect with satellite data (e.g., MODIS) have been performed previously in a number of studies (e.g., Lohmann et al., 2006, 190451; Menon et al., 2008, 190534; Quaas et al., 2006, 190915; Storlevmo et al., 2006, 190418).

These have been somewhat limited since the satellite retrieved data used do not have the vertical profiles needed to resolve aerosol and cloud fields (e.g., cloud droplet number and liquid water content); the temporal resolution of simultaneous aerosol and cloud product retrievals are usually not available at a frequency of more than one a day; and higher level clouds often obscure low clouds and aerosols. Thus, the indirect effect, especially the second indirect effect, remains, to a large extent, unconstrained by satellite observations. However, improved measurements of aerosol vertical distribution from the newer generation of sensors on the A-train platform may provide a better understanding of changes to cloud properties from aerosols. Simulating the top-of-atmosphere reflectance for comparison to satellite measured values could be another way to compare model with observations, which would eliminate the inconsistent assumptions of aerosol optical properties and surface reflectance encountered when compared the model calculated and satellite retrieved AOD values.

Additional Aerosol Influences

Various observations have empirically related aerosols injected from biomass burning or industrial processes to reductions in rainfall (e.g., Andreae et al., 2004, 155658; Eagan et al., 1974, 190231; Rosenfeld, 2000, 002234; Warner, 1968, 157114). There are several potential mechanisms associated with this response.

In addition to the two indirect aerosol effects noted above, a process denoted as the "semidirect" effect involves the absorption of solar radiation by aerosols such as black carbon and dust. The absorption increases the temperature, thus lowering the relative humidity and producing evaporation, hence a reduction in cloud liquid water. The impact of this process depends strongly on what the effective aerosol absorption actually is; the more absorbing the aerosol, the larger the potential positive forcing on climate (by reducing low level clouds and allowing more solar radiation to reach the surface). This effect is responsible for shifting the critical value of SSA (separating aerosol cooling from aerosol warming) from 0.86 with fixed clouds to 0.91 with varying clouds (Hansen et al., 1997, 043104). Reduction in cloud cover and liquid water is one way aerosols could reduce rainfall.

More generally, aerosols can alter the location of solar radiation absorption within the system, and this aspect alone can alter climate and precipitation even without producing any change in net radiation at the top of the atmosphere (the usual metric for climate impact). By decreasing solar absorption at the surface, aerosols (from both the direct and indirect effects) reduce the energy available for evapotranspiration, potentially resulting in a decrease in precipitation. This effect has been suggested as the reason for the decrease in pan evaporation over the last 50 years (Roderick and Farquhar, 2002, 042788). The decline in solar radiation at the surface appears to have ended in the 1990s (Wild et al., 2005, 156156), perhaps because of reduced aerosol emissions in industrial areas (Kruger and Grasl, 2002, 190200), although this issue is still not settled.

Energy absorption by aerosols above the boundary layer can also inhibit precipitation by warming the air at altitude relative to the surface, i.e., increasing atmospheric stability. The increased stability can then inhibit convection, affecting both rainfall and atmospheric circulation (Chung and Zhang, 2004, 190054; Ramanathan et al., 2001, 042681). To the extent that aerosols decrease droplet size and reduce precipitation efficiency, this effect by itself could result in lowered rainfall values locally.

In their latest simulations, Hansen et al. (2007, 190597) did find that the indirect aerosol effect reduced tropical precipitation; however, the effect is similar regardless of which of the two indirect effects is used, and also similar to the direct effect. So it is likely that the reduction of tropical precipitation is because of aerosol induced cooling at the surface and the consequent reduced evapotranspiration. Similar conclusions were reached by Yu et al. (2002, 190923) and Feingold et al. (2005, 190550). In this case, the effect is a feedback and not a forcing.

The local precipitation change, through its impacts on dynamics and soil moisture, can have large positive feedbacks. Harvey (2004, 190598) concluded from assessing the response to aerosols in eight coupled models that the aerosol impact on precipitation was larger than on temperature. He also found that the precipitation impact differed substantially among the models, with little correlation among them.

Recent GCM simulations have further examined the aerosol effects on hydrological cycle. Ramanathan et al. (2005, 190199) showed from fully coupled ocean-atmosphere GCM experiments that the "solar dimming" effect at the surface, i.e., the reduction of solar radiation reaching the surface, due to the inclusion of absorbing aerosol forcing causes a reduction in surface evaporation, a decrease in meridional sea surface temperature (SST) gradient and an increase in atmospheric stability, and a reduction in rainfall over South Asia. Lau and Kim (2006, 190226) examined the direct effects of aerosol on the monsoon water cycle variability from GCM simulations with prescribed realistic global aerosol forcing and proposed the "elevated heat pump" effect, suggesting that atmospheric heating by absorbing aerosols (dust and black carbon), through water cycle feedback, may lead to a strengthening of the South Asia monsoon. These model results are not necessarily at odds with each other, but rather illustrate the complexity of the aerosol-monsoon interactions that are associated with different mechanisms, whose relative importance in affecting the monsoon may be strongly dependent on spatial and temporal scales and the timing of the monsoon. These results may be model dependent and should be further examined.

High Resolution Modeling

Largely by its nature, the representation of the interaction between aerosol and clouds in GCMs is poorly resolved. This stems in large part from the fact that GCMs do not resolve convection on their large grids (order of several hundred km), that their treatment of cloud microphysics is rather crude, and that as discussed previously, their representation of aerosol needs improvement. Superparametrization efforts (where standard cloud parameterizations in the GCM are replaced by resolving clouds in each grid column of the GCM via a cloud resolving model) (e.g.,Grabowski, 2004, 190590) could lead the way for the development of more realistic cloud fields and thus improved treatments of aerosol cloud interactions in large-scale models. However, these are just being incorporated in models that resolve both cloud and

aerosols. Detailed cloud parcel models have been developed to focus on the droplet activation problem (that asks under what conditions droplets actually start forming) and questions associated with the first indirect effect. The coupling of aerosol and cloud modules to dynamical models that resolve the large turbulent eddies associated with vertical motion and clouds [large eddy simulations (LES) models, with grid sizes of ~100 m and domains ~10 km] has proven to be a powerful tool for representing the details of aerosol-cloud interactions together with feedbacks (e.g., Ackerman et al., 2004, 190056; Feingold et al., 1994, 190535; 1999, 190540; Kogan et al., 1994, 190186; Stevens et al., 1996, 190417).

This section explores some of the complexity in the aerosol indirect effects revealed by such studies to illustrate how difficult parameterizing these effects properly in GCMs could really be.

The First Indirect Effect

The relationship between aerosol and drop concentrations (or drop sizes) is a key piece of the first indirect effect puzzle. (It should not, however, be equated to the first indirect effect which concerns itself with the resultant RF). A huge body of measurement and modeling work points to the fact that drop concentrations increase with increasing aerosol. The main unresolved questions relate to the degree of this effect, and the relative importance of aerosol size distribution, composition and updraft velocity in determining drop concentrations (for a review, see Mcfiggans et al., 2006, 190532). Studies indicate that the aerosol number concentration and size distribution are the most important aerosol factors. Updraft velocity (unresolved by GCMs) is particularly important under conditions of high aerosol particle number concentration.

Although it is likely that composition has some effect on drop number concentrations, composition is generally regarded as relatively unimportant compared to the other parameters (Dusek et al., 2006, 155756; Ervens et al., 2005, 190527; Feingold et al., 2003, 190551; Fitzgerald, 1975, 095417). Therefore, it has been stated that the significant complexity in aerosol composition can be modeled, for the most part, using fairly simple parameterizations that reflect the soluble and insoluble fractions (e.g., Rissler et al., 2004, 190225). However, composition cannot be simply dismissed. Furthermore, chemical interactions also cannot be overlooked. A large uncertainty remains concerning the impact of organic species on cloud droplet growth kinetics, thus cloud droplet formation. Cloud drop size is affected by wet scavenging, which depends on aerosol composition especially for freshly emitted aerosol. And future changes in composition will presumably arise due to biofuels/biomass burning and a reduction in sulfate emissions, which emphasizes the need to include composition changes in models when assessing the first indirect effect. The simple soluble/insoluble fraction model may become less applicable than is currently the case.

The updraft velocity, and its change as climate warms, may be the most difficult aspect to simulate in GCMs because of the small scales involved. In GCMs it is calculated in the dynamics as a grid box average, and parameterized on the small scale indirectly because it is a key part of convection and the spatial distribution of condensate, as well as droplet activation. Numerous solutions to this problem have been sought, including estimation of vertical velocity based on predicted turbulent kinetic energy from boundary layer models (Larson et al., 2001, 190212; Lohmann et al., 1999, 190443) and PDF representations of subgrid quantities, such as vertical velocity and the vertically-integrated cloud liquid water ('liquid water path,' or LWP) (Golaz et al., 2002, 190587; 2002, 190589; Larson et al., 2005, 190220; Pincus and Klein, 2000, 190565). Embedding cloud-resolving models within GCMs is also being actively pursued (Grabowski et al., 1999, 190592; Randall et al., 2003, 190201). Numerous other details come into play; for example, the treatment of cloud droplet activation in GCM frameworks is often based on the assumption of adiabatic conditions, which may overestimate the sensitivity of cloud to changes in CCN (Sotiropoulou et al., 2006, 190406; Sotiropoulou et al., 2007, 190405). This points to the need for improved theoretical understanding followed by new parameterizations.

Other Indirect Effects

The second indirect effect is often referred to as the "cloud lifetime effect", based on the premise that non-precipitating clouds will live longer. In GCMs the "lifetime effect" is equivalent to changing the representation of precipitation production and can be parameterized as an increase in cloud area or cloud cover (e.g., Hansen et al., 2005, 059087). The second indirect effect hypothesis states that the more numerous and smaller drops associated with aerosol perturbations, suppress collision-induced rain, and result in a longer cloud lifetime. Observational evidence for the suppression of rain in warm clouds exists in the form of isolated studies (e.g., Warner, 1968, 157114) but to date there is no statistically robust proof of surface rain suppression (Levin and Cotton, 2008, 190375). Results from ship-track studies show that cloud water may increase or decrease in the tracks (Coakley and Walsh, 2002, 192025) and satellite studies suggest similar results for warm boundary layer clouds (Han et al., 2002, 049181). Ackerman et al. (2004, 190056) used LES to show that in stratocumulus, cloud water may increase or decrease in response to increasing aerosol depending on the relative humidity of the air overlaying the cloud. Wang et al. (2003, 157106) showed that all

else being equal, polluted stratocumulus clouds tend to have lower water contents than clean clouds because the small droplets associated with polluted clouds evaporate more readily and induce an evaporation-entrainment feedback that dilutes the cloud. This result was confirmed by Xue and Feingold (2006, 190920) and Jiang and Feingold (2006, 190976) for shallow cumulus, where pollution particles were shown to decrease cloud fraction. Furthermore, Xue et al. (2008, 190921) suggested that there may exist two regimes: the first, a precipitating regime at low aerosol concentrations where an increase in aerosol will suppress precipitation and increase cloud cover (Albrecht, 1989, 045783); and a second, non-precipitating regime where the enhanced evaporation associated with smaller drops will decrease cloud water and cloud fraction.

The possibility of bistable aerosol states was proposed earlier by Baker and Charlson (1990, 190016) based on consideration of aerosol sources and sinks. They used a simple numerical model to suggest that the marine boundary layer prefers two aerosol states: a clean, oceanic regime characterized by a weak aerosol source and less reflective clouds; and a polluted, continental regime characterized by more reflective clouds. On the other hand, study by Ackerman et al. (1994, 189975) did not support such a bistable system using a somewhat more sophisticated model. Further observations are needed to clarify the nature of cloud/aerosol interactions under a variety of conditions.

Finally, the question of possible effects of aerosol on cloud lifetime was examined by Jiang et al. (2006, 133165), who tracked hundreds of cumulus clouds generated by LES from their formative stages until they dissipated. They showed that in the model there was no effect of aerosol on cloud lifetime, and that cloud lifetime was dominated by dynamical variability.

It could be argued that the representation of these complex feedbacks in GCMs is not warranted until a better understanding of the processes is at hand. Moreover, until GCMs are able to represent cloud scales, it is questionable what can be obtained by adding microphysical complexity to poorly resolved clouds. A better representation of aerosol-cloud interactions in GCMs therefore depends on the ability to improve representation of aerosols and clouds, as well as their interaction, in the hydrologic cycle. This issue is discussed further in the next chapter.

9.3.6.5. Aerosol in the Climate Models

Aerosol in the IPCC AR4 Climate Model Simulations

To assess the atmospheric and climate response to aerosol forcing, e.g., changes in surface temperate, precipitation, or atmospheric circulation, aerosols, together with greenhouse gases should be an integrated part of climate model simulation under the past, present, and future conditions. Table 9-16 lists the forcing species that were included in 25 climate modeling groups used in the IPCC AR4 (2007, 092765) assessment. All the models included long-lived greenhouse gases, most models included sulfate direct forcing, but only a fraction of those climate models considered other aerosol types. In other words, aerosol RF was not adequately accounted for in the climate simulations for the IPCC AR4. Put still differently, the current aerosol modeling capability has not been fully incorporated into the climate model simulations. As pointed out in Section 9.3.6.4, fewer than one-third of the models incorporated an aerosol indirect effect, and most considered only sulfates.

The following discussion compares two of the IPCC AR4 climate models that include all major forcing agencies in their climate simulation: the model from the NASA Goddard Institute for Space Studies (GISS) and from the NOAA Geophysical Fluid Dynamics Laboratory (GFDL). The purpose in presenting these comparisons is to help elucidate how modelers go about assessing their aerosol components, and the difficulties that entail. A particular concern is how aerosol forcings were obtained in the climate model experiments for IPCC AR4. Comparisons with observations have already led to some improvements that can be implemented in climate models for subsequent climate change experiments (e.g., Koch et al., 2006, 190184, for GISS model). This aspect is discussed further in Chapter 4 of the CCSP SAP2.3.

Table 9-16. Forcings used in IPCC AR4 simulations of 20th century climate change. This table is adapted from SAP 1.1 Table 5.2 (compiled using information provided by the participating modeling centers, see http://www.pcmdi.llnl.gov/ipcc/model-documentation/ipcc_model_documentation.php) plus additional information from that website. Eleven different forcings are listed: well-mixed greenhouse gases (G), tropospheric and stratospheric ozone (O), SO_4^{2-} aerosol direct (SD) and indirect effects (S), black carbon (BC) and organic carbon aerosols (OC), mineral dust (MD), sea salt (SS), land use/land cover (LU), solar irradiance (SO), and volcanic aerosols (V). Check mark denotes inclusion of a specific forcing. As used here, "inclusion" means specification of a time-varying forcing, with changes on interannual and longer timescales.

	Model	Country	G	O	SD	SI	BC	OC	MD	SS	LU	SO	V
1	BCC-CMI	China	√	√	√								
2	BCCR-BCM2.0	Norway	√		√				√	√			
3	CCSM3	USA	√	√	√		√	√				√	√
4	CGCM3.1(T47)	Canada	√		√								
5	CGCM3.1(T63)	Canada	√		√								
6	CNRM-CM3	France	√	√	√		√						
7	CSIRO-Mk3.0	Australia	√		√								
8	CSIRO-Mk3.5	Australia	√		√								
9	ECHAMS/MPI-OM	Germany	√	√	√	√							
10	ECHO-G	Germany/ Korea	√	√	√	√						√	√
11	FGOALS-g1.0	China	√		√								
12	GFDL-CM2.0	USA	√	√	√		√				√	√	√
13	GFDL-CM2.1	USA	√	√	√		√				√	√	√
14	GISS-AOM	USA	√		√					√			
15	GISS-EH	USA	√	√	√	√	√	√	√	√	√	√	√
16	GISS-ER	USA	√	√	√	√	√	√	√	√	√	√	√
17	INGV-SXG	Italy	√	√	√								
18	INM-CM3.0	Russia	√		√							√	
19	IPSL-CM4	France	√		√	√							
20	MICROC3.2(hires)	Japan	√	√	√		√	√	√	√	√	√	√
21	MICROC3.2(medres)	Japan	√	√	√		√	√	√	√	√	√	√
22	MRI-CGCM2.3.2	Japan	√		√							√	√
23	PCM	USA	√	√	√							√	√
24	UKMO-HasCM3	U.K.	√	√	√	√							
25	UKMO-HadGEM1	U.K.	√	√	√	√	√	√				√	√

The GISS Model

There have been many different configurations of aerosol simulations in the GISS model over the years, with different emissions, physics packages, etc., as is apparent from the multiple GISS entries in the preceding figures and tables. There were also three different GISS GCM submissions to IPCC AR4, which varied in their model physics and ocean formulation.

(Note that the aerosols in these three GISS versions are different from those in the AeroCom simulations described in Sections 9.3.6.2 and 9.3.6.3.) The GCM results discussed

below all relate to the simulations known as GISS model ER (Schmidt et al., 2006, 190373) (see Table 9-16). Although the detailed description and model evaluation have been presented in Liu et al. (2006, 190422), below are the general characteristics of aerosols in the GISS ER:

Aerosol fields: The aerosol fields used in the GISS ER is a prescribed "climatology" which is obtained from chemistry transport model simulations with monthly averaged mass concentrations representing conditions up to 1990. Aerosol species included are sulfate, nitrate, BC, POM, dust, and sea salt. Dry size effective radii are specified for each of the aerosol types, and laboratory-measured phase functions are employed for all solar and thermal wavelengths. For hygroscopic aerosols (sulfate, nitrate, POM, and sea salt), formulas are used for the particle growth of each aerosol as a function of relative humidity, including the change in density and optical parameters. With these specifications, the AOD, single scattering albedo, and phase function of the various aerosols are calculated. While the aerosol distribution is prescribed as monthly mean values, the relative humidity component of the extinction is updated each hour. The global averaged AOD at 550 nm is about 0.15.

Global distribution: When comparing with AOD from observations by multiple satellite sensors of MODIS, MISR, POLDER, and AVHRR and surface based sunphotometer network AERONET (see Chapter 2 of the CCSP SAP2.3 for detailed information about data), qualitative agreement is apparent, with generally higher burdens in Northern Hemisphere summer, and seasonal variations of smoke over southern Africa and South America, as well as wind blown dust over northern African and the Persian Gulf. Aerosol optical depth in both model and observations is smaller away from land. There are, however, considerable discrepancies between the model and observations. Overall, the GISS GCM has reduced aerosol optical depths compared with the satellite data (a global, clear-sky average of about 80% compared with MODIS and MISR data), although it is in better agreement with AERONET ground-based measurements in some locations (note that the input aerosol values were calibrated with AERONET data). The model values over the Sahel in Northern Hemisphere winter and the Amazon in Southern Hemisphere winter are excessive, indicative of errors in the biomass burning distributions, at least partially associated with an older biomass burning source used (the source used here was from (Liousse et al., 1996, 078158)).

Seasonal variation: A comparison of the seasonal distribution of the global AOD between the GISS model and satellite data indicates that the model seasonal variation is in qualitative agreement with observations for many of the locations that represent major aerosol regimes, although there are noticeable differences. For example, in some locations the seasonal variations are different from or even opposite to the observations.

Particle size parameter: The Ångström exponent (Å), which is determined by the contrast between the AOD at two or more different wavelengths and is related to aerosol particle size (discussed in Section 9.3.6.3). This parameter is important because the particle size distribution affects the efficiency of scattering of both short and long wave radiation, as discussed earlier. Å from the GISS model is biased low compared with AERONET, MODIS, and POLDER data, although there are technical differences in determining the Å. This low bias suggests that the aerosol particle size in the GISS model is probably too large. The average effective radius in the GISS model appears to be 0.3-0.4 μm, whereas the observational data indicates a value more in the range of 0.2-0.3 μm (Liu et al., 2006, 190422).

Single scattering albedo: The model-calculated SSA (at 550 nm) appears to be generally higher than the AERONET data at worldwide locations (not enough absorption), but lower than AERONET data in Northern Africa, the Persian Gulf, and the Amazon (too much absorption). This discrepancy reflects the difficulties in modeling BC, which is the dominant absorbing aerosol, and aerosol sizes. Global averaged SSA at 550 nm from the GISS model is at about 0.95.

Aerosol direct RF: The GISS model calculated anthropogenic aerosol direct shortwave RF is -0.56 W/m^2 at TOA and -2.87 W/m^2 at the surface. The TOA forcing (upper left, Figure 9-78) indicates that, as expected, the model has larger negative values in polluted regions and positive forcing at the highest latitudes. At the surface (lower left, Figure 9-78) GISS model values exceed -4 W/m^2 over large regions. Note there is also a longwave RF of aerosols (right column), although they are much weaker than the shortwave RF.

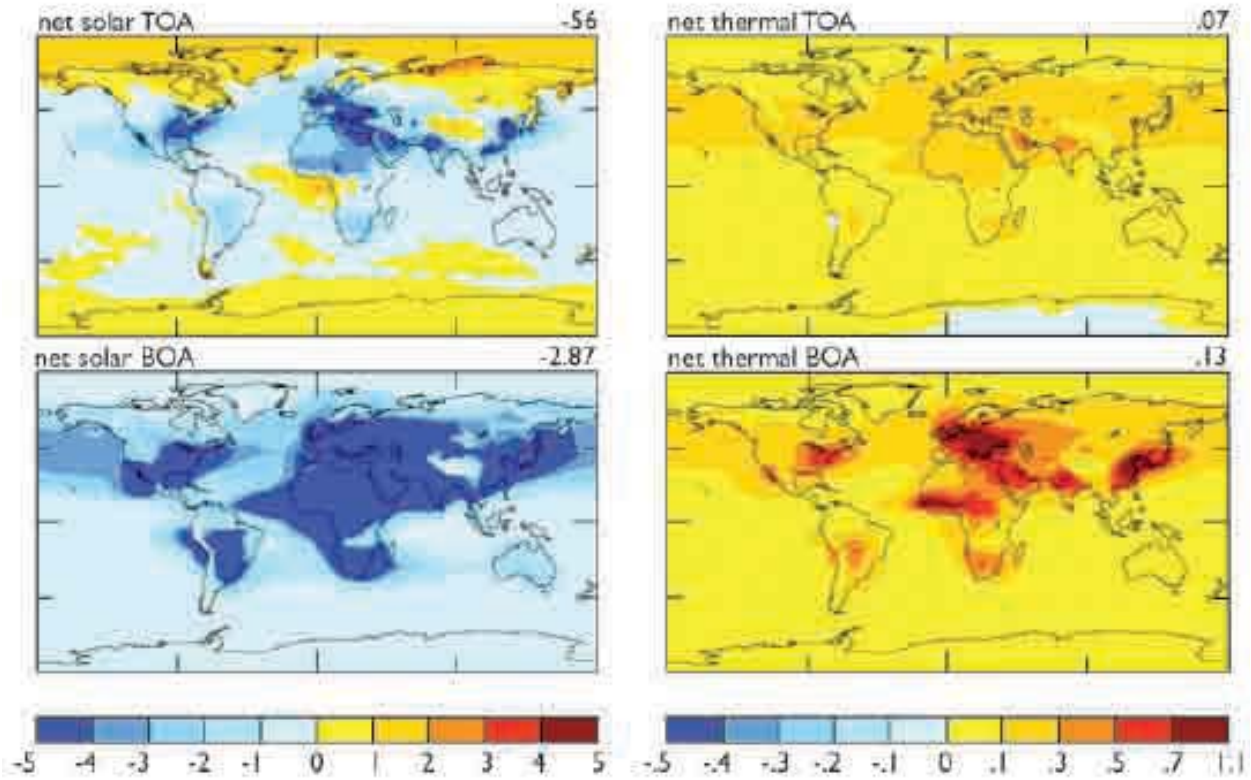
There are several concerns for climate change simulations related to the aerosol trend in the GISS model. One is that the aerosol fields in the GISS AR4 climate simulation (version ER) are kept fixed after 1990. In fact, the observed trend shows a reduction in tropospheric aerosol optical thickness from 1990 through the present, at least over the oceans (Mishchenko and Geogdzhayev, 2007, 190545). Hansen et al. (2007, 190597) suggested that the deficient warming in the GISS model over Eurasia post-1990 was due to the lack of this trend. Indeed, a possible conclusion from the Penner et al. (2002, 190562) study was that the GISS model overestimated the AOD (presumably associated with anthropogenic aerosols) poleward of 30°N. However, when an alternate experiment reduced the aerosol optical depths, the polar warming became excessive (Hansen et al., 2007, 190597). The other concern is that the GISS model may underestimate the organic and sea salt AOD, and overestimate the influence of black carbon aerosols in the biomass burning regions (Liu et al., 2006, 190422; deduced from Penner et al., 2002, 190562). To the extent that is true, it would indicate the GISS model underestimates the aerosol direct cooling effect in a substantial portion of the tropics, outside of biomass burning areas. Clarifying those issues requires numerous modeling experiments and various types of observations.

The GFDL Model

A comprehensive description and evaluation of the GFDL aerosol simulation are given in Ginoux et al. (2006, 190582). Below are the general characteristics:

Aerosol fields: The aerosols used in the GFDL climate experiments are obtained from simulations performed with the MOZART 2 model (Model for Ozone and Related chemical Tracers) (Horowitz, 2006, 190620; Horowitz et al., 2003, 057770). The exceptions were dust, which was generated with a separate simulation of MOZART 2, using sources from Ginoux et al. (2001, 190579) and wind fields from NCEP/NCAR reanalysis data; and sea salt, whose monthly mean concentrations were obtained from a previous study by Haywood et al. (1999, 040453). It includes most of the same aerosol species as in the GISS model (although it does not include nitrates), and, as in the GISS model, relates the dry aerosol to wet aerosol optical depth via the model's relative humidity for sulfate (but not for organic carbon); for sea salt, a constant relative humidity of 80% was used. Although the parameterizations come from different sources, both models maintain a very large growth in sulfate particle size when the relative humidity exceeds 90%.

Global distributions: Overall, the GFDL global mean aerosol mass loading is within 30% of that of other studies (Chin et al., 2002, 189996; Reddy et al., 2005, 190207; Tie et al., 2005, 190459), except for sea salt, which is 2 to 5 times smaller. However, the sulfate AOD (0.1) is 2.5 times that of other studies, whereas the organic carbon value is considerably smaller (on the order of 1/2). Both of these differences are influenced by the relationship with relative humidity. In the GFDL model, sulfate is allowed to grow up to 100% relative humidity, but organic carbon does not increase in size as relative humidity increases. Comparison of AOD with AVHRR and MODIS data for the time period 1996-2000 shows that the global mean value over the ocean (0.15) agrees with AVHRR data (0.14) but there are significant differences regionally, with the model overestimating the value in the northern mid latitude oceans and underestimating it in the southern ocean. Comparison with MODIS also shows good agreement globally (0.15), but in this case indicates large disagreements over land, with the model producing excessive AOD over industrialized countries and underestimating the effect over biomass burning regions. Overall, the global averaged AOD at 550 nm is 0.17, which is higher than the maximum values in the AeroCom-A experiments (Table 9-12) and exceeds the observed value too (Ae and S* in Figure 9-72).



Source: Figure provided by A. Lacis, GISS.

Figure 9-78. Direct radiative forcing by anthropogenic aerosols in the GISS model (including sulfates, BC, OC and nitrates). Short wave forcing at TOA and surface are shown in the top left and bottom left panels. The corresponding thermal forcing is indicated in the right hand panels.

Composition: Comparison of GFDL modeled species with in situ data over North America, Europe, and over oceans has revealed that the sulfate is overestimated in spring and summer and underestimated in winter in many regions, including Europe and North America. Organic and black carbon aerosols are also overestimated in polluted regions by a factor of two, whereas organic carbon aerosols are elsewhere underestimated by factors of 2 to 3. Dust concentrations at the surface agree with observations to within a factor of 2 in most places where significant dust exists, although over the southwest U.S. it is a factor of 10 too large. Surface concentrations of sea salt are underestimated by more than a factor of 2. Over the oceans, the excessive sulfate AOD compensates for the low sea salt values except in the southern oceans.

Size and single-scattering albedo: No specific comparison was given for particle size or single-scattering albedo, but the excessive sulfate would likely produce too high a value of reflectivity relative to absorption except in some polluted regions where black carbon (an absorbing aerosol) is also overestimated.

As in the case of the GISS model, there are several concerns with the GFDL model. The good global-average agreement masks an excessive aerosol loading over the Northern Hemisphere (in particular, over the northeast U.S. and Europe) and an underestimate over biomass burning regions and the southern oceans. Several model improvements are needed, including better parameterization of hygroscopic growth at high relative humidity for sulfate and organic carbon; better sea salt simulations; correcting an error in extinction coefficients; and improved biomass burning emissions inventory (Ginoux et al., 2006, 190582).

Comparisons between GISS and GFDL Model

Both GISS and GFDL models were used in the IPCC AR4 climate simulations for climate sensitivity that included aerosol forcing. It would be constructive, therefore, to compare the similarities and differences of aerosols in these two models and to understand what their

impacts are in climate change simulations. Figure 9-79 shows the percentage AOD from different aerosol components in the two models.

Sulfate: The sulfate AOD from the GISS model is within the range of that from all other models (Table 9-13), but that from the GFDL model exceeds the maximum value by a factor of 2.5. An assessment in SAP 3.2 (CCSP, 2008, 192028; Shindell et al., 2008, 190393) also concludes that GFDL had excessive sulfate AOD compared with other models. The sulfate AOD from GFDL is nearly a factor of 4 large than that from GISS, although the sulfate burden differs only by about 50% between the two models. Clearly, this implies a large difference in sulfate MEE between the two models.

BC and POM: Compared to observations, the GISS model appears to overestimate the influence of BC and POM in the biomass burning regions and underestimate it elsewhere, whereas the GFDL model is somewhat the reverse: it overestimates it in polluted regions, and underestimates it in biomass burning areas. The global comparison shown in Table 9-14 indicates the GISS model has values similar to those from other models, which might be the result of such compensating errors. The GISS and GFDL models have relatively similar global-average black carbon contributions, and the same appears true for POM.

Sea salt: The GISS model has a much larger sea salt contribution than does GFDL (or indeed other models).

Global and regional distributions: Overall, the global averaged AOD is 0.15 from the GISS model and 0.17 from GFDL. However, as shown in Figure 9-79, the contribution to this AOD from different aerosol components shows greater disparity. For example, over the Southern Ocean where the primary influence is due to sea salt in the GISS model, but in the GFDL it is sulfate. The lack of satellite observations of the component contributions and the limited available in situ measurements make the model improvements at aerosol composition level difficult.

Climate simulations: With such large differences in aerosol composition and distribution between the GISS and GFDL models, one might expect that the model simulated surface temperature might be quite different. Indeed, the GFDL model was able to reproduce the observed temperature change during the 20th century without the use of an indirect aerosol effect, whereas the GISS model required a substantial indirect aerosol contribution (more than half of the total aerosol forcing) (Hansen et al., 2007, 190597). It is likely that the reason for this difference was the excessive direct effect in the GFDL model caused by its overestimation of the sulfate optical depth. The GISS model direct aerosol effect (see Section 9.3.6.6) is close to that derived from observations (Chapter 2 of the CCSP SAP2.3); this suggests that for models with climate sensitivity close to 0.75°C/(W/m^2) (as in the GISS and GFDL models), an indirect effect is needed.

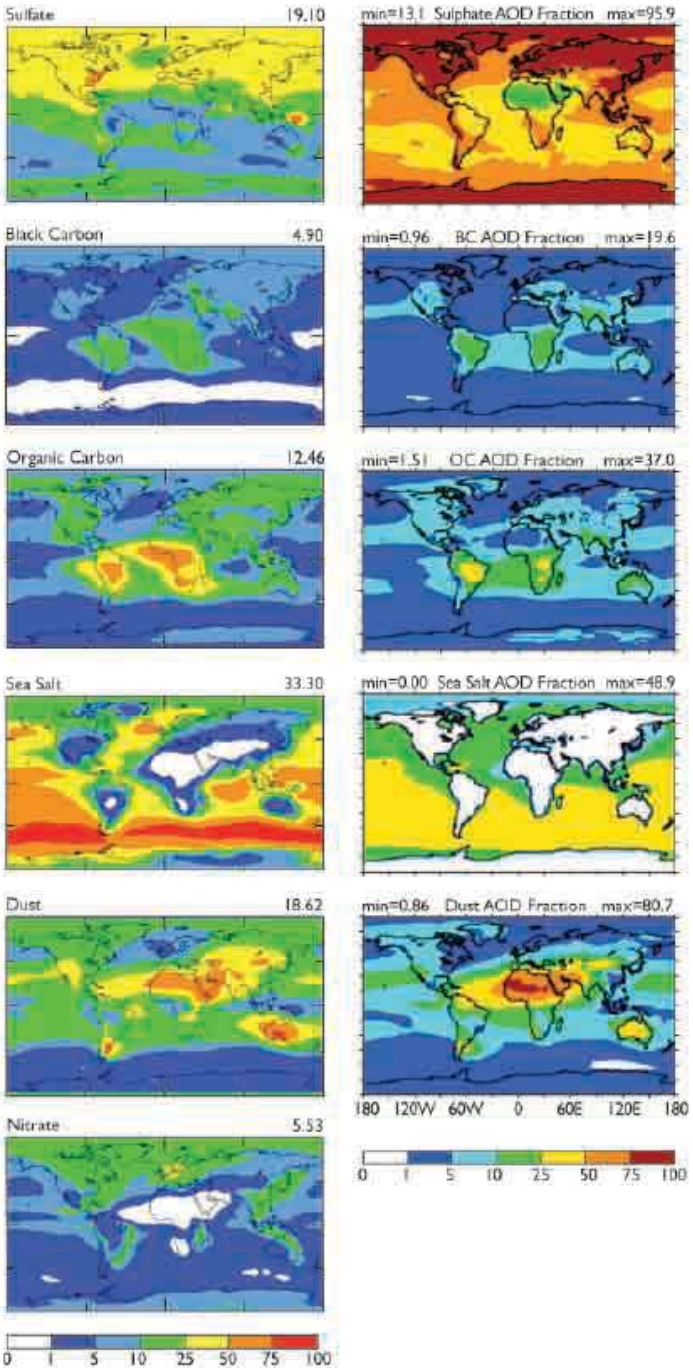


Figure 9-79. Percentage of aerosol optical depth in the GISS, left, based on Liu et al. (2006, 190422), provided by A. Lacis, GISS, and GFDL, right, from Ginoux et al. (2006, 190582). Models associated with the different components: SO_4^{2-} (1st row), BC (2nd row), OC (3rd row), sea-salt (4th row), dust (5th row), and nitrate (last row). Nitrate not available in GFDL model). Numbers on the GISS panels are global average, but on the GFDL panels are maximum and minimum.

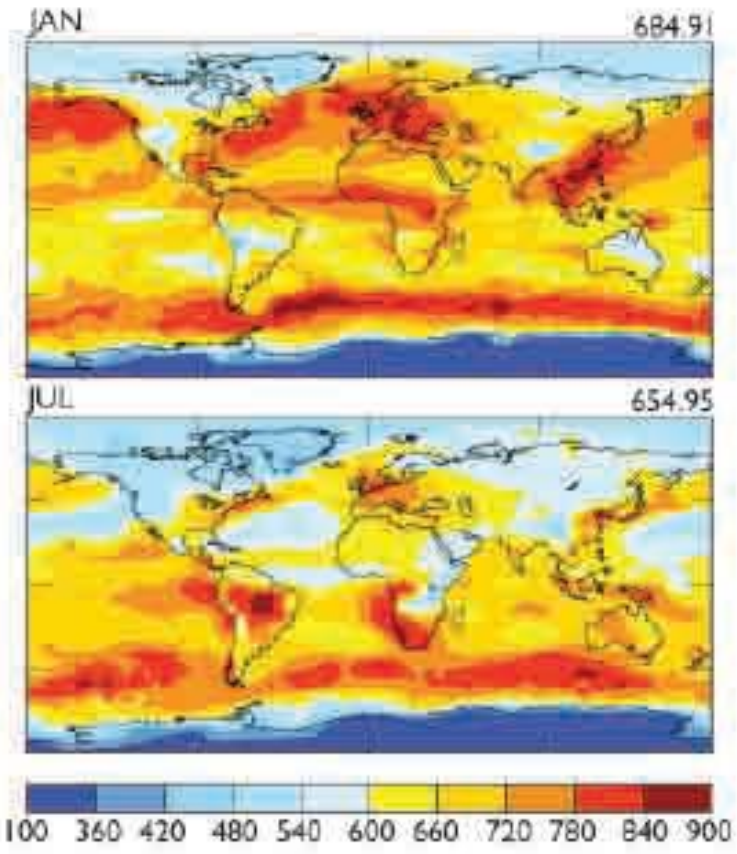
Additional Considerations

Long wave aerosol forcing: So far only the aerosol RF in the shortwave (solar) spectrum has been discussed. Figure 9-78 (right column) shows that compared to the shortwave forcing, the values of anthropogenic aerosol long wave (thermal) forcing in the GISS model are on the order of 10%. Like the shortwave forcing, these values will also be affected by the particular aerosol characteristics used in the simulation.

Aerosol vertical distribution: Vertical distribution is particularly important for absorbing aerosols, such as BC and dust in calculating the RF, particularly when longwave forcing is considered (e.g., Figure 9-78) because the energy they reradiate depends on the temperature (and hence altitude), which affects the calculated forcing values. Several model inter-comparison studies have shown that the largest difference among model simulated aerosol distributions is the vertical profile (e.g., Lohmann et al., 2001, 190448; Penner et al., 2002, 190562; Textor et al., 2006, 190456), due to the significant diversities in atmospheric processes in the models (e.g., Table 9-12). In addition, the vertical distribution also varies with space and time, as illustrated in Figure 9-80 from the GISS ER simulations for January and July showing the most probable altitude of aerosol vertical locations. In general, aerosols in the northern hemisphere are located at lower altitudes in January than in July, and vice versa for the southern hemisphere.

Mixing state: Most climate model simulations incorporating different aerosol types have been made using external mixtures, i.e., the evaluation of the aerosols and their radiative properties are calculated separately for each aerosol type (assuming no mixing between different components within individual particles). Observations indicate that aerosols commonly consist of internally mixed particles, and these "internal mixtures" can have very different radiative impacts. For example, the GISS-1 (internal mixture) and GISS-2 (external mixture) model results shows very different magnitude and sign of aerosol forcing from slightly positive (implying slight warming) to strong negative (implying significant cooling) TOA forcing (Figure 9-73), due to changes in both radiative properties of the mixtures, and in aerosol amount. The more sophisticated aerosol mixtures from detailed microphysics calculations now being used/developed by different modeling groups may well end up producing very different direct (and indirect) forcing values.

Cloudy sky vs. clear sky: The satellite or AERONET observations are all for clear sky only because aerosol cannot be measured in the remote sensing technique when clouds are present. However, almost all the model results are for all-sky because of difficulty in extracting cloud-free scenes from the GCMs. So the AOD comparisons discussed earlier are not completely consistent. Because AOD can be significantly amplified when relative humidity is high, such as near or inside clouds, all-sky AOD values are expected to be higher than clear sky AOD values. On the other hand, the aerosol RF at TOA is significantly lower for all-sky than for clear sky conditions; the IPCC AR4 and AeroCom RF study (Schulz et al., 2006, 190381) have shown that on average the aerosol RF value for all-sky is about 1/3 of that for clear sky although with large diversity (63%). These aspects illustrate the complexity of the system and the difficulty of representing aerosol radiative influences in climate models whose cloud and aerosol distributions are somewhat problematic. And of course aerosols in cloudy regions can affect the clouds themselves, as discussed in Section 9.3.6.5.



Source: A. Lacis, GISS.

Figure 9-80. Most probable aerosol altitude (in pressure, hPa) from the GISS model in January (top) and July (bottom).

9.3.6.6. Impacts of Aerosols on Climate Model Simulations

Surface Temperature Change

It was noted in the introduction that aerosol cooling is essential in order for models to produce the observed global temperature rise over the last century, at least models with climate sensitivities in the range of 3°C for doubled CO2 (or ~0.75°C/(W/m^2)). The implications of this are discussed here in somewhat more detail. Hansen et al. (2007, 190597) show that in the GISS model, well-mixed greenhouse gases produce a warming of close to 1°C between 1880 and the present (Table 9-17). The direct effect of tropospheric aerosols as calculated in that model produces cooling of close to -0.3°C between those same years, while the indirect effect (represented in that study as cloud cover change) produces an additional cooling of similar magnitude (note that the general model result quoted in IPCC AR4 is that the indirect RF is twice that of the direct effect).

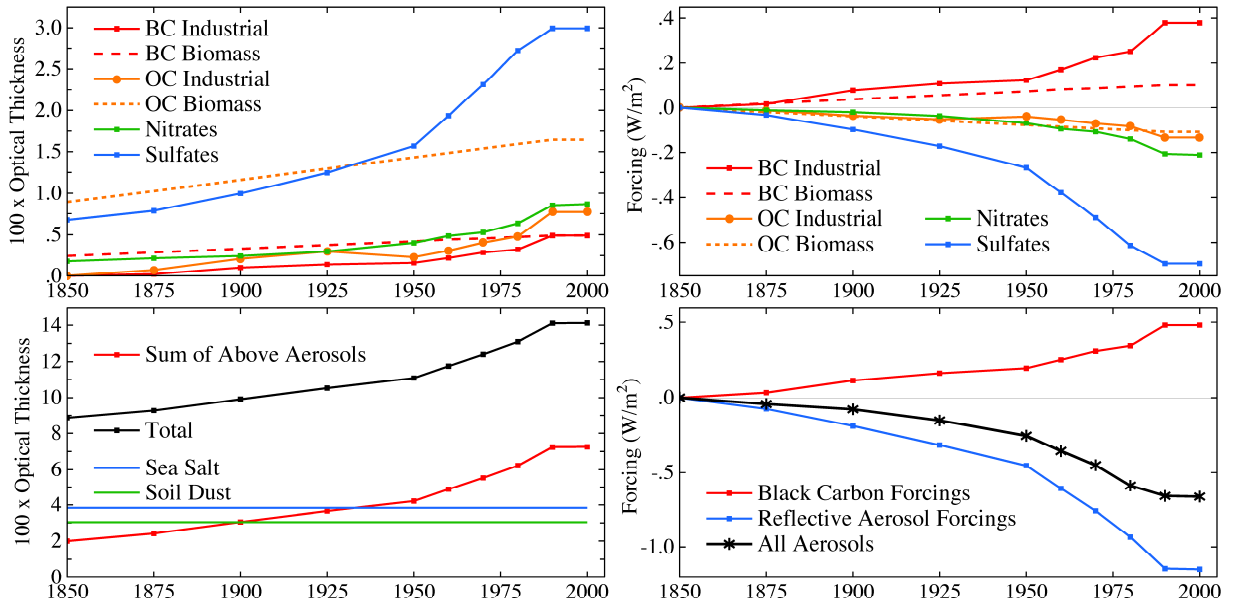
Table 9-17. Climate forcings (1880-2003) used to drive GISS climate simulations, along with the surface air temperature changes obtained for several periods.

Forcing Agent	Forcing Wm^{-2} (1880-2003)				ΔT Surface °C (year to 2003)			
	Fi	Fa	Fs	Fe	1880	1900	1950	1979
Well-mixed GHGs	2.62	2.50	2.65	2.72	0.96	0.93	0.74	0.43
Stratospheric H_2O			0.06	0.05	0.03	0.01	0.05	0.00
O_3	0.44	0.28	0.26	0.23	0.p08	0.05	0.00	-0.01
Land use			-0.09	-0.09	-0.05	-0.p07	-0.04	-0.02
Snow albedo	0.05	0.05	0.14	0.14	0.03	0.00	0.02	-0.01
Solar irradiance	0.23	0.24	0.23	0.22	0.07	0.07	0.01	0.02
Stratospheric aerosols	0.00	0.00	0.00	0.00	-0.08	-0.03	-0.06	0.04
Trop. aerosol direct forcing	-0.41	-0.38	-0.52	-0.60	-0.28	-0.23	-0.18	-0.10
Trop. aerosol indirect forcing			-0.87	-0.77	-0.27	-0.29	-0.14	-0.05
Sum of above			1.86	1.90	0.49	0.44	0.40	0.30
All forcings at once			1.77	1.75	0.53	0.61	0.44	0.29

Source: Reprinted with Permission of Springer Publishing from Hansen et al. (2007, 190597).
Instantaneous (Fi), adjusted (Fa), fixed SST (Fs) and effective (Fe) forcings are defined in Hansen et al. (2005, 059087)

The time dependence of the total aerosol forcing used as well as the individual species components is shown in Figure 9-81. The resultant warming, 0.53 (± 0.04) °C including these and other forcings (Table 9-17), is less than the observed value of 0.6-0.7°C from 1880-2003. Hansen et al. (2007, 190597) further show that a reduction in sulfate optical thickness and the direct aerosol effect by 50%, which also reduced the aerosol indirect effect by 18%, produces a negative aerosol forcing from 1880-2003 of -0.91 W/m^2 (down from -1.37 W/m^2 with this revised forcing). The model now warms 0.75°C over that time. Hansen et al. (2007, 190597) defend this change by noting that sulfate aerosol removal over North America and western Europe during the 1990s led to a cleaner atmosphere. Note that the comparisons shown in the previous section suggest that the GISS model already underestimates aerosol optical depths; it is thus trends that are the issue here.

The magnitude of the indirect effect used by Hansen et al. (2005, 190596) is roughly calibrated to reproduce the observed change in diurnal temperature cycle and is consistent with some satellite observations. However, as Anderson et al. (2003, 054820) note, the forward calculation of aerosol negative forcing covers a much larger range than is normally used in GCMs; the values chosen, as in this case, are consistent with the inverse reasoning estimates of what is needed to produce the observed warming, and hence generally consistent with current model climate sensitivities. The authors justify this approach by claiming that paleoclimate data indicate a climate sensitivity of close to 0.75 (± 0.25)°C/(W/m^2), and therefore something close to this magnitude of negative forcing is reasonable. Even this stated range leaves significant uncertainty in climate sensitivity and the magnitude of the aerosol negative forcing. Furthermore, IPCC (2007, 092765) concluded that paleoclimate data are not capable of narrowing the range of climate sensitivity, nominally 0.375-1.13 °C/(W/m^2), because of uncertainties in paleoclimate forcing and response; so from this perspective the total aerosol forcing is even less constrained than the GISS estimate. Hansen et al. (2007, 190597) acknowledge that "an equally good match to observations probably could be obtained from a model with larger sensitivity and smaller net forcing, or a model with smaller sensitivity and larger forcing".



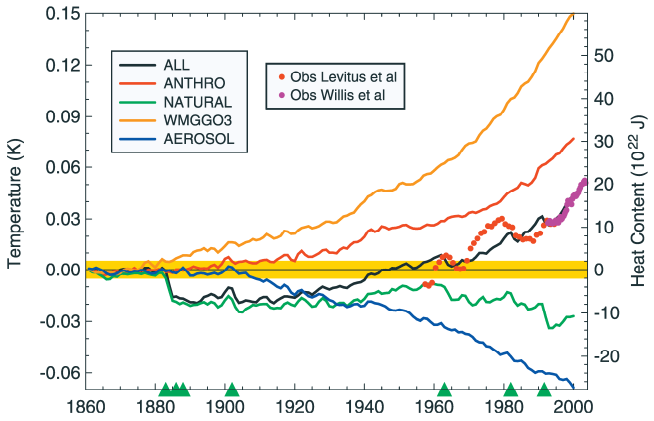
Source: Reprinted with Permission of Springer from Hansen et al. (2007, 190597).

Figure 9-81. Time dependence of aerosol optical thickness (left) and climate forcing (right). Note that as specified, the aerosol trends are all "flat" from 1990-2000.

The GFDL model results for global mean ocean temperature change (down to 3 km depth) for the time period 1860-2000 is shown in Figure 9-82, along with the different contributing factors (Delworth et al., 2005, 190055). This is the same GFDL model whose aerosol distribution was discussed previously. The aerosol forcing produces a cooling on the order of 50% that of greenhouse warming (generally similar to that calculated by the GISS model, Table 9-17). Note that this was achieved without any aerosol indirect effect.

The general model response noted by IPCC, as discussed in the introduction, was that the total aerosol forcing of -1.3 W/m^2 reduced the greenhouse forcing of near 3 W/m^2 by about 45%, in the neighborhood of the GFDL and GISS forcings. Since the average model sensitivity was close to 0.75 °C/(W/m^2), similar to the sensitivities of these models, the necessary negative forcing is therefore similar. The agreement cannot therefore be used to validate the actual aerosol effect until climate sensitivity itself is better known.

Is there some way to distinguish between greenhouse gas and aerosol forcing that would allow the observational record to indicate how much of each was really occurring? This question of attribution has been the subject of numerous papers, and the full scope of the discussion is beyond the range of this (CCSP SAP2.3) report. It might be briefly noted that Zhang et al. (2006, 157722) using results from several climate models and including both spatial and temporal patterns, found that the climate responses to greenhouse gases and sulfate aerosols are correlated, and separation is possible only occasionally, especially at global scales. This conclusion appears to be both model and method-dependent: using time-space distinctions as opposed to trend detection may work differently in different models (Gillett et al., 2002, 190576). Using multiple models helps primarily by providing larger-ensemble sizes for statistics (Gillett et al., 2002, 190578). However, even separating between the effects of different aerosol types is difficult. Jones et al. (2005, 155885) concluded that currently the pattern of temperature change due to black carbon is indistinguishable from the sulfate aerosol pattern. In contrast, Hansen et al. (2005, 059087) found that absorbing aerosols produce a different global response than other forcings, and so may be distinguishable. Overall, the similarity in response to all these very different forcings is undoubtedly due to the importance of climate feedbacks in amplifying the forcing, whatever its nature.



Source: Courtesy of the American Geogphysical Union from Delworth et al. (2005, 190055).

Figure 9-82. Change in global mean ocean temperature (left axis) and ocean heat content (right axis) for the top 3000 m due to different forcings in the GFDL model. WMGG includes all greenhouse gases and ozone; NATURAL includes solar and volcanic aerosols (events shown as green triangles on the bottom axis). Observed ocean heat content changes are shown as well.

Distinctions in the climate response do appear to arise in the vertical, where absorbing aerosols produce warming that is exhibited throughout the troposphere and into the stratosphere, whereas reflective aerosols cool the troposphere but warm the stratosphere (Hansen et al., 2005, 059087; IPCC, 2007, 092765). Delworth et al. (2005, 190055) noted that in the ocean, the cooling effect of aerosols extended to greater depths, due to the thermal instability associated with cooling the ocean surface. Hence the temperature response at levels both above and below the surface may provide an additional constraint on the magnitudes of each of these forcings, as may the difference between Northern and Southern Hemisphere changes (IPCC, 2007, 092765, Chapter 9). The profile of atmospheric temperature response will be useful to the extent that the vertical profile of aerosol absorption, an important parameter to measure, is known.

Implications for Climate Model Simulations

The comparisons in Sections 9.3.6.2 and 9.3.6.3 suggest that there are large differences in model calculated aerosol distributions, mainly because of the large uncertainties in modeling the aerosol atmospheric processes in addition to the uncertainties in emissions. The fact that the total optical depth is in better agreement between models than the individual components means that even with similar optical depths, the aerosol direct forcing effect can be quite different, as shown in the AeroCom studies. Because the diversity among models and discrepancy between models and observations are much larger at the regional level than in global average, the assessment of climate response (e.g., surface temperature change) to aerosol forcing would be more accurate for global average than for regional or hemispheric differentiation. However, since aerosol forcing is much more pronounced on regional than on global scales because of the highly variable aerosol distributions, it is insufficient or even misleading to just get the global average right.

The indirect effect is strongly influenced by the aerosol concentrations, size, type, mixing state, microphysical processes, and vertical profile. As shown in previous sections, very large differences exist in those quantities even among the models having similar AOD. Moreover, modeling aerosol indirect forcing presents more challenges than direct forcing because there is so far no rigorous observational data, especially on a global scale, that one can use to test the model simulations. As seen in the comparisons of the GISS and GFDL model climate simulations for IPCC AR4, aerosol indirect forcing was so poorly constrained that it was completely ignored by one model (GFDL) but used by another (GISS) at a magnitude that is more than half of the direct forcing, in order to reproduce the observed surface temperature trends. A majority of the climate models used in IPCC AR4 do not consider indirect effects; the ones that did were mostly limited to highly simplified sulfate indirect effects (Table 9-16). Improvements must be made to at least the degree that the aerosol indirect forcing can no longer be used to mask the deficiencies in estimating the climate response to greenhouse gas and aerosol direct RF.

9.3.6.7. Outstanding Issues

Clearly there are still large gaps in assessing the aerosol impacts on climate through modeling. Major outstanding issues and prospects of improving model simulations are discussed below.

Aerosol composition

Many global models are now able to simulate major aerosol types such as sulfate, black carbon, and POM, dust, and sea salt, but only a small fraction of these models simulate nitrate aerosols or consider anthropogenic secondary organic aerosols. And it is difficult to quantify the dust emission from human activities. As a result, the IPCC AR4 estimation of the nitrate and anthropogenic dust TOA forcing was left with very large uncertainty. The next generation of global models should therefore have a more comprehensive suite of aerosol compositions with better-constrained anthropogenic sources.

Aerosol absorption

One of the most critical parameters in aerosol direct RF and aerosol impact on hydrological cycles is the aerosol absorption. Most of the absorption is from BC despite its small contribution to total aerosol short and long-wave spectral ranges, whereas POM absorbs in the near UV. The aerosol absorption or SSA, will have to be much better represented in the models through improving the estimates of carbonaceous and dust aerosol sources, their atmospheric distributions, and optical properties.

Aerosol indirect effects

The activation of aerosol particles into CCN depends not only on particle size but chemical composition, with the relative importance of size and composition unclear. In current aerosol-climate modeling, aerosol size distribution is generally prescribed and simulations of aerosol composition have large uncertainties. Therefore the model estimated “albedo effect” has large uncertainties. How aerosol would influence cloud lifetime/ cover is still in debate. The influence of aerosols on other aspects of the climate system, such as precipitation, is even more uncertain, as are the physical processes involved. Processes that determine aerosol size distributions, hygroscopic growth, mixing state, as well as CCN concentrations, however, are inadequately represented in most of the global models. It will also be difficult to improve the estimate of indirect effects until the models can produce more realistic cloud characteristics.

Aerosol impacts on surface radiation and atmospheric heating

Although these effects are well acknowledged to play roles in modulating atmospheric circulation and water cycle, few coherent or comprehensive modeling studies have focused on them, as compared to the efforts that have gone to assessing aerosol RF at TOA. They have not yet been addressed in the previous IPCC reports. Here, of particular importance is to improve the accuracy of aerosol absorption.

Long-term trends of aerosol

To assess the aerosol effects on climate change the long-term variations of aerosol amount and composition and how they are related to the emission trends in different regions have to be specified. Simulations of historical aerosol trends can be problematic since historical emissions of aerosols have shown large uncertainties – as information is difficult to obtain on past source types, strengths, and even locations. The IPCC AR4 simulations used several alternative aerosol emission histories, especially for BC and POM aerosols.

Climate modeling

Current aerosol simulation capabilities from CTMs have not been fully implemented in most models used in IPCC AR4 climate simulations. Instead, a majority employed simplified approaches to account for aerosol effects, to the extent that aerosol representations in the GCMs, and the resulting forcing estimates, are inadequate. The oversimplification occurs in part because the modeling complexity and computing resource would be significantly increased if the full suite of aerosols were fully coupled in the climate models.

Observational constraints

Model improvement has been hindered by a lack of comprehensive datasets that could provide multiple constraints for the key parameters simulated in the model. The extensive AOD coverage from satellite observations and AERONET measurements has helped a great

deal in validating model-simulated AOD over the past decade, but further progress has been slow. Large model diversities in aerosol composition, size, vertical distribution, and mixing state are difficult to constrain, because of lack of reliable measurements with adequate spatial and temporal coverage (see Chapter 2 of the CCSP SAP2.3).

Aerosol radiative forcing

Because of the large spatial and temporal differences in aerosol sources, types, emission trends, compositions, and atmospheric concentrations, anthropogenic aerosol RF has profound regional and seasonal variations. So it is an insufficient measure of aerosol RF scientific understanding, however useful, for models (or observation-derived products) to converge only on globally and annually averaged TOA RF values and accuracy. More emphasis should be placed on regional and seasonal comparisons, and on climate effects in addition to direct RF at TOA.

9.3.6.8. Conclusions

From forward modeling studies, as discussed in the IPCC (2007, 092765) , the direct effect of aerosols since pre-industrial times has resulted in a negative RF of about -0.5 ± 0.4 W/m^2. The RF due to cloud albedo or brightness effect is estimated to be -0.7 (-1.8 to -0.3) W/m^2. Forcing of similar magnitude has been used in some modeling studies for the effect associated with cloud lifetime, in lieu of the cloud brightness influence. The total negative RF due to aerosols according to IPCC (2007, 092765) estimates is therefore -1.3 (-2.2 to -0.5) W/m^2. With the inverse approach, in which aerosols provide forcing necessary to produce the observed temperature change, values range from -1.7 to -0.4 W/m^2 (IPCC, 2007, 092765) . These results represent a substantial advance over previous assessments (e.g., IPCC TAR), as the forward model estimated and inverse approach required aerosol TOA forcing values are converging. However, large uncertainty ranges preclude using the forcing and temperature records to more accurately determine climate sensitivity.

There are now a few dozen models that simulate a comprehensive suite of aerosols. This is done primarily in the CTMs. Model inter-comparison studies have shown that models have merged at matching the global annual averaged AOD observed by satellite instruments, but they differ greatly in the relative amount of individual components, in vertical distributions, and in optical properties. Because of the great spatial and temporal variations of aerosol distributions, regional and seasonal diversities are much larger than that of the global annual mean. Different emissions and differences in atmospheric processes, such as transport, removal, chemistry, and aerosol microphysics, are chiefly responsible for the spread among the models. The varying component contributions then lead to differences in aerosol direct RF, as aerosol scattering and absorption properties depend on aerosol size and type. They also impact the calculated indirect RF, whose variations are further amplified by the wide range of cloud and convective parameterizations in models. Currently, the largest aerosol RF uncertainties are associated with the aerosol indirect effect. Most climate models used for the IPCC AR4 simulations employed simplified approaches, with aerosols specified from stand-alone CTM simulations. Despite the uncertainties in aerosol RF and widely varying model climate sensitivity, the IPCC AR4 models were generally able to reproduce the observed temperature record for the past century. This is because models with lower/higher climate sensitivity generally used less/more negative aerosol forcing to offset the greenhouse gas warming. An equally good match to observed surface temperature change in the past could be obtained from a model with larger climate sensitivity and smaller net forcing, or a model with smaller sensitivity and larger forcing (Hansen et al., 2007, 190597). Obviously, both greenhouse gases and aerosol effects have to be much better quantified in future assessments.

Progress in better quantifying aerosol impacts on climate will only be made when the capabilities of both aerosol observations and representation of aerosol processes in models are improved. The primary concerns and issues discussed in this chapter of the CCSP SAP2.3 include:

- Better representation of aerosol composition and absorption in the global models
- Improved theoretical understanding of subgrid-scale processes crucial to aerosol-cloud interactions and lifetime
- Improved aerosol microphysics and cloud parameterizations
- Better understanding of aerosol effects on surface radiation and hydrological cycles
- More focused analysis on regional and seasonal variations of aerosols
- More reliable simulations of aerosol historic long-term trends
- More sophisticated climate model simulations with coupled aerosol and cloud processes
- Enhanced satellite observations of aerosol type, SSA, vertical distributions, and aerosol radiative effect at TOA; more coordinated field experiments to provide constraints on aerosol chemical, physical, and optical properties.

9.3.7. Fire as a Special Source of PM Welfare Effects

Much interest has developed in defining more precisely the role of pyrogenic C in the boreal C cycle. This is due to: (1) the resistance of pyrogenic C to decomposition; (2) its influence on soil processes; and (3) the absorption of solar radiation by soot aerosols (Preston and Schmidt, 2006, 156030).

Preston and Schmidt (2006, 156030) reviewed the current state of knowledge regarding atmospheric emissions of pyrogenic C in the boreal zone. They considered chemical structures, analytical methods, formation, characteristics in soil, loss mechanisms, and longevity. Biomass is largely converted to gaseous forms during burning, but up to several percent is converted to pyrogenic C, and this includes charcoal and BC. Charcoal is defined visually; BC is defined chemically by its resistance to oxidation in the laboratory. Andreae and Gelencsér (2006, 156215) reviewed a different category of light-absorbing carbon, referred to as brown carbon.

Within the boreal zone, fire is a critical driver of ecosystem process and nutrient cycling (Hicke et al., 2003, 156545). For example, Bachelet et al. (2005, 156241) estimated that 61% of the C gained in Alaska by primary production of boreal forests between 1922 and 1996 was lost to fire.

An updated modeling effort to evaluate the radiative effects of aerosols was presented by Stier et al. (2007, 157012). Inclusion of refractive indices recommended byBond and Bergstrom (2005, 155696) significantly increased aerosol RF and resulted in better agreement with sun-photometer estimates. Although this stage of climate modeling improved the representation of aerosols, large uncertainties remain regarding the effects of aerosol mixing and aerosol-cloud interactions. Furthermore, Stier et al. (2007, 157012) emphasized that these types of modeling efforts are dependent upon emission estimates that are likely to vary by a factor of 2 or more.

One important reason for the acknowledged uncertainty in estimating global emissions of carbonaceous aerosols is the influence of intermittent fires that can occur at scales large enough to affect hemispheric aerosol concentrations. To better quantify the effects of large-scale fire, Generoso et al. (2007, 155786) used satellite observations of boreal fires in Russia in 2003 to evaluate the performance of a global chemistry and transport model in simulating aerosol optical thickness, transport, and deposition. Emissions estimates of BC and OC were adjusted in the model to better match satellite observations of pollutant transport over the North Pacific. This resulted in an increase in optical thickness and BC deposition by a factor of 2. The adjusted model estimated that the fires contributed 16-33% of the optical thickness and 40-56% of BC deposition north of 75^{o} N in the spring and summer of 2003.

Large fires also occurred over the Iberian Peninsula and Mediterranean coast during 2003. A meso-scale atmospheric transport model was used with ground-based measurements and satellite optical measurements to characterize the dispersion of emitted smoke particles and quantify radiative effects across Europe (Hodzic et al., 2007, 156553). The modeled wildfire emissions resulted in increases in $PM_{2.5}$ concentrations from 20 to 200%. The increased aerosol concentration was estimated to increase radiative forcing by 10-35 W/m^2 during the period of strong fire influence. Absorption of radiation by BC was also estimated to decrease rates of photolysis by 30%. In this simulation, all particles were assumed to be internally mixed, and secondary aerosol formation was not considered. Meteorological conditions in Europe during the exceptionally hot summer of 2003 were linked to enhanced photochemically derived pollutants, increased wild fires, and elevated aerosol concentrations in an analysis by Vautard et al. (2007, 106012).

In addition to incidental fires, routine biomass burning, usually associated with agriculture in eastern Europe, also has been shown to contribute to hemispheric concentrations of carbonaceous aerosols. In the spring of 2006, the most severe air pollution levels in the Arctic to date were recorded (Stohl et al., 2006, 156100). Atmospheric transport modeling coupled with satellite fire detection data identified biomass burning for agriculture as the primary cause of the high pollution levels. Concentrations of $PM_{2.5}$ peaked during the pollution episode at values of an order of magnitude greater than those recorded prior to the episode. The increased transport of pollution into the Arctic during 2006 was attributed to weather conditions that delayed preparations for crop planting into May. Weather patterns favorable for pollutant transport into the Arctic were related to unusually warm weather in late April and May, when the majority of agricultural biomass burning took place that year.

In the summer of 2004, 2.7 million ha were burned by wildfire in Alaska and 3.1 million ha were burned in Canada. Effects on atmospheric air quality were measured throughout the Arctic, although the concentrations of particulates varied considerably. Aerosol optical depths were also

increased at all measurement stations, which indicated that the fires were likely to have had a significant effect on the atmospheric radiation budget for the Arctic (Stohl et al., 2006, 156100). At one site, a pronounced drop in albedo was observed due presumably to high deposition of light absorbing particulates on the snow surface by the North American fires in 2004.

Investigations of the effects of large fires on climate forcing have typically focused on the absorptive effects of BC. However, these fires also release large amounts of CO_2 and CH_4, as well as light scattering compounds such as OC, and can enhance cloud formation. These fires also increase radiative surface absorption through BC deposition on snow and ice, and alter surface albedo and ecosystem energy budgets within the burn perimeter. Randerson et al. (2006, 156038) estimated the net climate forcing of greenhouse gases, aerosols, BC deposition on snow and ice and changes in albedo for the year subsequent to a fire and for 80 years in the future in interior Alaska. The net effect of the fire in the first year was an increase in radiative forcing, but over the 80-year recovery period, average net annual radiative forcing was decreased by the fire.

9.3.8. Radiative Effects of Volcanic Aerosols

Section 9.3.8.1. comes directly from IPCC AR4 Chapter 2, Section 2.7.2, with section, table, and figure numbers changed to be internally consistent with this ISA.

9.3.8.1. Explosive Volcanic Activity

Radiative Effects of Volcanic Aerosols

Volcanic sulfate aerosols are formed as a result of oxidation of the sulfur gases emitted by explosive volcanic eruptions into the stratosphere. The process of gas-to-particle conversion has an e-folding time of roughly 35 days (Bluth et al., 1992, 192029; Read et al., 1993, 192031). The e-folding time (by mass) for sedimentation of sulfate aerosols is typically about 12 to 14 months (Baran and Foot, 1994, 192032; Barnes and Hofmann, 1997, 192044; Bluth et al., 1997, 192045; Lambert et al., 1993, 192231). Also emitted directly during an eruption are volcanic ash particulates (siliceous material). These are particles usually larger than 2 μm that sediment out of the stratosphere fairly rapidly due to gravity (within three months or so), but could also play a role in the radiative perturbations in the immediate aftermath of an eruption. Stratospheric aerosol data incorporated for climate change simulations tends to be mostly that of the sulfates (Ammann et al., 2003, 192057; Hansen et al., 2002, 049177; Ramachandran et al., 2000, 192050; Sato et al., 1993, 192046; Stenchikov et al., 1998, 192049; Tett et al., 2002, 192053). As noted in the Second Assessment Report (SAR) and the TAR, explosive volcanic events are episodic, but the stratospheric aerosols resulting from them yield substantial transitory perturbations to the radiative energy balance of the planet, with both shortwave and longwave effects sensitive to the microphysical characteristics of the aerosols (e.g., size distribution).

Long-term ground-based and balloon-borne instrumental observations have resulted in an understanding of the optical effects and microphysical evolution of volcanic aerosols (Deshler et al., 2003, 192058; Hofmann et al., 2003, 192062). Important ground-based observations of aerosol characteristics from pre-satellite era spectral extinction measurements have been analysed by Stothers (2001, 192233; 2001, 192232), but they do not provide global coverage. Global observations of stratospheric aerosol over the last 25 years have been possible owing to a number of satellite platforms, for example, TOMS and TOVS have been used to estimate SO_2 loadings from volcanic eruptions (Krueger et al., 2000, 192234; Prata et al., 2003, 192235). The Stratospheric Aerosol and Gas Experiment (SAGE) and Stratospheric Aerosol Measurement (SAM) projects (e.g., McCormick and Trepte, 1987, 192328) have provided vertically resolved stratospheric aerosol spectral extinction data for over 20 years, the longest such record. This data set has significant gaps in coverage at the time of the El Chichón eruption in 1982 (the second most important in the 20th century after Mt. Pinatubo in 1991) and when the aerosol cloud is dense; these gaps have been partially filled by lidar measurements and field campaigns (e.g., Antuña et al., 2003, 192251; Thomason and Peter, 2006, 192248).

Volcanic aerosols transported in the atmosphere to polar regions are preserved in the ice sheets, thus recording the history of the Earth's volcanism for thousands of years (Kruysse, 1971, 192236; Mosley-Thompson et al., 2003, 192255; Palmer et al., 2002, 192319). However, the atmospheric loadings obtained from ice records suffer from uncertainties due to imprecise knowledge of the latitudinal distribution of the aerosols, depositional noise that can affect the signal for an individual eruption in a single ice core, and poor constraints on aerosol microphysical properties. The best-documented explosive volcanic event to date, by way of reliable and accurate observations, is the 1991 eruption of Mt. Pinatubo. The growth and decay

of aerosols resulting from this eruption have provided a basis for modeling the RF due to explosive volcanoes. There have been no explosive and climatically significant volcanic events since Mt. Pinatubo. As pointed out in Ramaswamy et al. (2001, 156899), stratospheric aerosol concentrations are now at the lowest concentrations since the satellite era and global coverage began in about 1980. Altitude dependent stratospheric optical observations at a few wavelengths, together with columnar optical and physical measurements, have been used to construct the time-dependent global field of stratospheric aerosol size distribution formed in the aftermath of volcanic events. The wavelength-dependent stratospheric aerosol single-scattering characteristics calculated for the solar and longwave spectrum are deployed in climate models to account for the resulting radiative (shortwave plus longwave) perturbations.

Using available satellite- and ground-based observations, Hansen et al. (2002, 049177) constructed a volcanic aerosols data set for the 1850-1999 period (Sato et al., 1993, 192046). This has yielded zonal mean vertically resolved aerosol optical depths for visible wavelengths and column average effective radii. Stenchikov et al. (2006, 192260) introduced a slight variation to this data set, employing UARS observations to modify the effective radii relative to Hansen et al. (2002, 049177), thus accounting for variations with altitude. Ammann et al. (2003, 192057) developed a data set of total aerosol optical depth for the period since 1890 that does not include the Krakatau eruption. The data set is based on empirical estimates of atmospheric loadings, which are then globally distributed using a simplified parameterization of atmospheric transport, and employs a fixed aerosol effective radius (0.42 μm) for calculating optical properties. The above data sets have essentially provided the bases for the volcanic aerosols implemented in virtually all of the models that have performed the 20th-century climate integrations (Stenchikov et al., 2006, 192260). Relative to Sato et al. (1993, 192046), the Ammann et al. (2003, 192057) estimate yields a larger value of the optical depth, by 20 to 30% in the second part of the 20th century, and by 50% for eruptions at the end of 19th and beginning of 20th century, for example, the 1902 Santa Maria eruption (Figure 9-83).

The global mean RF calculated using the Sato et al. (1993, 192046) data yields a peak in radiative perturbation of about -3 W/m^2 for the strong (rated in terms of emitted SO_2) 1860 and 1991 eruptions of Krakatau and Mt. Pinatubo, respectively. The value is reduced to about -2 W/m^2 for the relatively less intense El Chichón and Agung eruptions (Hansen et al., 2002, 049177). As expected from the arguments above, Ammann's RF is roughly 20 to 30% larger than Sato's RF.

Not all features of the aerosols are well quantified, and extending and improving the data sets remains an important area of research. This includes improved estimates of the aerosol size parameters (Bingen et al., 2004, 192262), a new approach for calculating aerosol optical characteristics using SAGE and UARS data (Bauman et al., 2003, 192265), and intercomparison of data from different satellites and combining them to fill gaps (Randall et al., 2001, 192268). While the aerosol characteristics are better constrained for the Mt. Pinatubo eruption, and to some extent for the El Chichón and Agung eruptions, the reliability degrades for aerosols from explosive volcanic events further back in time as there are few, if any, observational constraints on their optical depth and size evolution.

The radiative effects due to volcanic aerosols from major eruptions are manifest in the global mean anomaly of reflected solar radiation; this variable affords a good estimate of radiative effects that can actually be tested against observations. However, unlike RF, this variable contains effects due to feedbacks (e.g., changes in cloud distributions) so that it is actually more a signature of the climate response. In the case of the Mt. Pinatubo eruption, with a peak global visible optical depth of about 0.15, simulations yield a large negative perturbation as noted above of about -3 W/m^2 (Hansen et al., 2002, 049177; Ramachandran et al., 2000, 192050) (see also Section 9.2 of the IPCC AR4). This modeled estimate of reflected solar radiation compares reasonably with ERBS observations (Minnis et al., 1993, 190539). However, the ERBS observations were for a relatively short duration, and the model-observation comparisons are likely affected by differing cloud effects in simulations and measurements. It is interesting to note (Stenchikov et al., 2006, 192260) that, in the Mt. Pinatubo case, the Goddard Institute for Space Studies (GISS) models that use the Sato et al. (1993, 192046) data yield an even greater solar reflection than the National Center for Atmospheric Research (NCAR) model that uses the larger (Ammann et al., 2003, 192057) optical depth estimate.

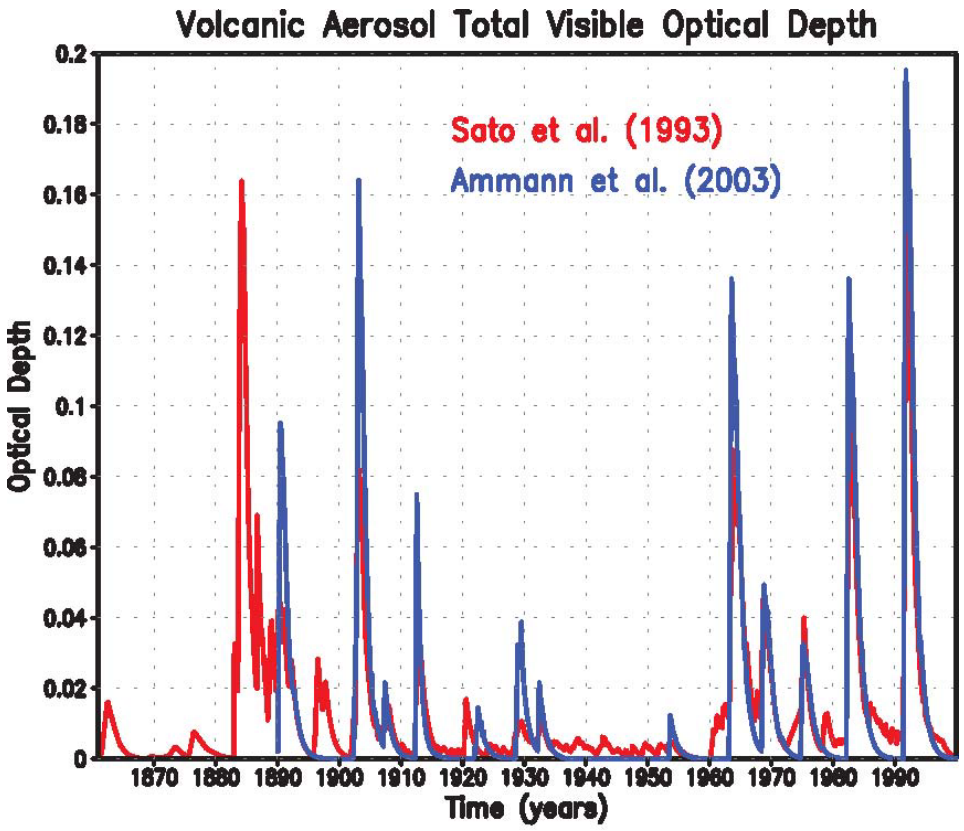


Figure 9-83. Visible (wavelength 0.55 µm) optical depth estimates of stratospheric SO_4^{2-} aerosols formed in the aftermath of explosive volcanic eruptions that occurred between 1860 and 2000. Results are shown from two different data sets that have been used in recent climate model integrations. Note that the Ammann et al. (2003, 192057) data begins in 1890.

Thermal, Dynamical and Chemistry Perturbations Forced by Volcanic Aerosols

Four distinct mechanisms have been invoked with regards to the climate response to volcanic aerosol RF. First, these forcings can directly affect the Earth's radiative balance and thus alter surface temperature. Second, they introduce horizontal and vertical heating gradients; these can alter the stratospheric circulation, in turn affecting the troposphere. Third, the forcings can interact with internal climate system variability (e.g., El Niño-Southern Oscillation, North Atlantic Oscillation, Quasi- Biennial Oscillation) and dynamical noise, thereby triggering, amplifying or shifting these modes (see Section 9.2 of the IPCC AR4) (Stenchikov et al., 2004, 192274; Yang and Schlesinger, 2001, 192270). Fourth, volcanic aerosols provide surfaces for heterogeneous chemistry affecting global stratospheric ozone distributions (Chipperfield et al., 2003, 192275) and perturbing other trace gases for a considerable period following an eruption. Each of the above mechanisms has its own spatial and temporal response pattern. In addition, the mechanisms could depend on the background state of the climate system, and thus on other forcings (e.g., due to well-mixed gases) (Meehl et al., 2004, 192279), or interact with each other.

The complexity of radiative-dynamical response forced by volcanic impacts suggests that it is important to calculate aerosol radiative effects interactively within the model rather than prescribe them (Andronova et al., 1999, 192286; Broccoli et al., 2003, 192283). Despite differences in volcanic aerosol parameters employed, models computing the aerosol radiative effects interactively yield tropical and global mean lower-stratospheric warmings that are fairly consistent with each other and with observations (Hansen et al., 2002, 049177; Ramachandran et al., 2000, 192050; Ramaswamy et al., 2006, 192284; Stenchikov et al., 2004, 192274; Yang and Schlesinger, 2001, 192270); however, there is a considerable range in the responses in the

polar stratosphere and troposphere. The global mean warming of the lower stratosphere is due mainly to aerosol effects in the longwave spectrum, in contrast to the flux changes at the TOA that are essentially due to aerosol effects in the solar spectrum. The net radiative effects of volcanic aerosols on the thermal and hydrologic balance (e.g., surface temperature and moisture) have been highlighted by recent studies (Free and Angell, 2002, 192281; Jones et al., 2003, 192278) (see Chapter 6 of the IPCC AR4). See Chapter 9 (of the IPCC AR4) for significance of the simulated responses and model-observation comparisons for 20th-century eruptions. A mechanism closely linked to the optical depth perturbation and ensuing warming of the tropical lower stratosphere is the potential change in the cross-tropopause water vapour flux (Joshi and Shine, 2003, 192327) (see Section 2.3.7 of the IPCC AR4).

Anomalies in the volcanic-aerosol induced global radiative heating distribution can force significant changes in atmospheric circulation, for example, perturbing the equator-to-pole heating gradient (Ramaswamy et al., 2006, 192273; Stenchikov et al., 2002, 192277) (see Section 9.2 of the IPCC AR4) and forcing a positive phase of the Arctic Oscillation that in turn causes a counterintuitive boreal winter warming at middle and high latitudes over Eurasia and North America (Miller et al., 2005, 192258; Perlwitz and Graf, 2001, 192271; Perlwitz and Harnik, 2003, 192264; Rind et al., 2005, 192261; Shindell et al., 2003, 192069; Shindell et al., 2004, 192267; Stenchikov et al., 2002, 192277; Stenchikov et al., 2004, 192274; Stenchikov et al., 2006, 192260).

Stratospheric aerosols affect the chemistry and transport processes in the stratosphere, resulting in the depletion of ozone (Brasseur and Granier, 1992, 192256; Chipperfield et al., 2003, 192275; Solomon et al., 1996, 192252; Tie et al., 1994, 192253). Stenchikov et al. (2002, 192277) demonstrated a link between ozone depletion and Arctic Oscillation response; this is essentially a secondary radiative mechanism induced by volcanic aerosols through stratospheric chemistry. Stratospheric cooling in the polar region associated with a stronger polar vortex initiated by volcanic effects can increase the probability of formation of polar stratospheric clouds and therefore enhance the rate of heterogeneous chemical destruction of stratospheric ozone, especially in the NH (Tabazadeh et al., 2002, 192250). The above studies indicate effects on the stratospheric ozone layer in the wake of a volcanic eruption and under conditions of enhanced anthropogenic halogen loading. Interactive microphysics-chemistry-climate models (Dameris et al., 2005, 192055; Rozanov et al., 2002, 192070; Rozanov et al., 2004, 192072; Shindell et al., 2003, 192069; Timmreck et al., 2003, 192068) indicate that aerosol-induced stratospheric heating affects the dispersion of the volcanic aerosol cloud, thus affecting the spatial RF. However the models' simplified treatment of aerosol microphysics introduces biases; further, they usually overestimate the mixing at the tropopause level and intensity of meridional transport in the stratosphere (Douglass et al., 2003, 057260; Schoeberl et al., 2003, 057262). For present climate studies, it is practical to utilize simpler approaches that are reliably constrained by aerosol observations.

Because of its episodic and transitory nature, it is difficult to give a best estimate for the volcanic RF, unlike the other agents. Neither a best estimate nor a level of scientific understanding was given in the TAR. For the well-documented case of the explosive 1991 Mt. Pinatubo eruption, there is a good scientific understanding. However, the limited knowledge of the RF associated with prior episodic, explosive events indicates a low level of scientific understanding.

9.3.9. Other Special Sources and Effects

International shipping has been identified as an additional source of carbonaceous aerosols. Simulations with a climate model that included aerosol effects and 3 different emissions inventories showed that shipping contributed 2.3-3.6% of the total SO_4^{2-} atmospheric aerosol content and 0.4-1.4% of the total BC atmospheric aerosol content, based on global means in 2000. This modeling also showed that aerosol optical thickness over the Indian Ocean, the Gulf of Mexico, and the northeastern Pacific Ocean varied by 8 to 10%. The corresponding all-sky (that includes both cloudy and clear skies) direct radiative forcings ranged from -0.011 to -0.013 W/m^2. The greatest effect of aerosols emitted from global shipping is likely to be an increase in cloud formation and the resulting change in reflectivity of shortwave radiation. Aerosols from shipping were estimated to contribute 17-39% of the total anthropogenic aerosol radiation forcing effect.

When BC is deposited to the surface of ice or snow, solar absorption and heating occur at the surface. This can melt additional snow or ice at the surface and the reflectivity of the surface can change. Both factors affect aspects of climate. Jacobson (2003, 155866; 2004, 155870) and Jacobson et al. (2004, 180362) estimated the warming due to fossil fuel BC and organic matter using the Gas, Aerosol, Transport, Radiation, General Circulation, Mesoscale and Ocean Model (GATOR-GCMOM). The modeling effort included consideration of the BC cycle, accounting for emissions, transport, aerosol coagulation, aerosol growth, cloud activation, aerosol-cloud coagulation, cloud-cloud coagulation, rainout, washout, dry deposition, and processes of precipitated and dry-deposited BC in snow and sea ice. Results suggested that BC absorption in snow and sea ice

increased near-surface temperatures over a 10-year simulation by about 0.06°K (Jacobson, 2003, 155868).

BC soot is a potentially important agent of climate warming in the Arctic, and northern boreal wildfires may contribute substantially to this effect. Soot is approximately twice as effective as CO_2 in altering surface air temperature, and can reduce sea ice formation and snow albedo (Hansen and Nazarenko, 2004, 156521).

Kim et al. (2005, 155900) investigated the relationships between northern boreal wildfires and reductions in Arctic sea ice and glacial coverage. They modeled the FROSTFIRE boreal forest control burn (Hinzman et al., 2003, 155845) with respect to BC aerosol transport, dispersion, and deposition. Model results suggested that boreal wildfires could be a major source of BC soot to sea ice and glaciers in Alaska. This may exacerbate summer melting of sea ice and reduce recruitment of first-year ice into multiyear ice, thereby leading to an overall reduction in sea ice. Similarly, increased BC soot on glaciers would be expected to increase summer melting and lead to an overall reduction in glacial coverage (Kim et al., 2005, 155900).

Jacobson (2002, 155865) proposed, based on model simulations with 12 identifiable effects of aerosol particles on climate, emission reductions of fossil fuel particulate BC and associated organic matter could potentially slow warming for a specific period more than reduction of CO_2 or CH_4 for a specific period. Jacobson's (2006, 156599) calculations suggested that fossil fuel BC plus organic matter emissions reductions could eliminate 8-18% of total anthropogenic warming, and 20-45% of net warming after accounting for aerosol cooling, within a period of 3-5 years (Chock et al., 2003, 155727). See also conflicting discussions (Feichter et al., 2003, 155772; Penner, 2003, 156851); and further responses (Jacobson, 2003, 155867; Jacobson, 2003, 155868; Jacobson, 2003, 155869; Penner, 2003, 156851).

Bond and Sun (2005, 156282) reviewed published data regarding the warming potential of BC, compared with CO_2 and other GHG. Climatic effects of GHG are generally compared on the basis of top-of-the-atmosphere, globally averaged changes in radiative balance. On that basis, BC is one of the largest individual warming agents, after CO_2 and perhaps CH_4 (Bond and Sun, 2005, 156282; Jacobson, 2000, 056378; Sato et al., 2003, 156947).

Reddy and Boucher (2007, 156042) conducted an analysis that provided regional estimates of BC emissions from fossil fuels and biofuels. These estimates indicated that East and Southeast Asia contributed over 50% of the global BC burden and its associated direct radiative forcing. Europe was found to be the largest BC contributor in the northern latitudes. The indirect effect of BC deposition on snow was also estimated to be highest for Europe.

To improve understanding of the role of aerosols in climate forcing, Chung and Seinfeld (2002, 155732) estimated the global distribution of BC, primary organic particles (those directly emitted from combustion), secondary organic particles (primary organic compounds partially oxidized in the atmosphere), and SO_4^{2-} aerosols to model the overall radiative forcing of these groups of compounds. The model was run with the assumption that the BC particles do not combine with OC or SO_4^{2-} particles (termed an external mixture), and with the assumption that the particles are represented by a core of BC surrounded by a shell of light scattering aerosols. Modeling results suggested an overall radiative cooling effect from aerosols ranging from -0.39 to -0.78 W/m^2.

Roberts and Jones (2004, 156052) used a climate modeling approach to compare possible effects of BC on climate warming to those attributable to emissions from greenhouse gases. Results suggested that the warming effect from atmospheric BC aerosols may not be large relative to that from greenhouse gases. A different modeling approach by Roeckner et al. (2006, 156920) evaluated the effects of BC and primary OC on climate under two scenarios of carbonaceous aerosol emissions. In the first scenario, BC and primary OC emissions decreased over Europe and China, but increased at lower latitudes. In the second scenario, emissions were frozen at 2000 levels. The effects of both scenarios on mean global temperature were found to be small, but higher aerosol emissions at low latitudes did result in atmospheric heating and corresponding land surface cooling that led to increased precipitation and runoff in this simulation.

Study of BC effects in tropical climates was undertaken by Wang (2007, 156147). Substantial effects of direct radiative forcing by BC on the tropical Pacific were shown in model results that were similar to the El Niño Southern Oscillation activities both in the nature and scale of effects with enhancement of the Indian monsoon circulation. The model suggested that atmospheric heating by radiation absorption by BC can form temperature and pressure anomalies that favor propagation of convection from western to central and eastern Pacific. More work will be needed to distinguish between the aerosol signal and natural factors in controlling tropical precipitation in this region.

Table 9-18. Overview of the different aerosol indirect effects and their sign of the net radiative flux change at the top of the atmosphere (TOA).

Effect	Cloud Types Affected	Process	Sign of Change in TOA Radiation	Potential Magnitude	Scientific Understanding
Cloud albedo effect	All clouds	For the same cloud water or ice content more but smaller cloud particles reflect more solar radiation	Negative	Medium	Low
Cloud lifetime effect	All clouds	Smaller cloud particles decrease the precipitation efficiency thereby presumably prolonging cloud lifetime	Negative	Medium	Very low
Semi-direct effect	All clouds	Absorption of solar radiation by absorbing aerosols affects static stability and the surface energy budget, and may lead to an evaporation of cloud particles	Positive or Negative	Small	Very low
Glaciation indirect effect	Mixed-phase clouds	An increase in IN increases the precipitation efficiency	Positive	Medium	Very low
Thermodynamic effect	Mixed-phase clouds	Smaller cloud droplets delay freezing causing super-cooled clouds to extend to colder temperatures	Positive or Negative	Medium	Very low

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Table 9-19. Overview of the different aerosol indirect effects and their implications for the global mean net shortwave radiation of the surface Fsfc (columns 2-4) and for precipitation (columns 5-7).

Effect	Sign of Change in Fsfc	Potential Magnitude	Scientific Understanding	Sign of Change in Precipitation	Potential Magnitude	Scientific Understanding
Cloud albedo effect	Negative	Medium	Low	n.a.	n.a.	n.a.
Cloud lifetime effect	Negative	Medium	Very low	Negative	Small	Very low
Semi-direct effect	Negative	Large	Very low	Negative	Large	Very low
Glaciation indirect effect	Positive	Medium	Very low	Positive	Medium	Very low
Thermodynamic effect	Positive or Negative	Medium	Very low	Positive or Negative	Medium	Very low

Source: Reprinted with Permission of Cambridge University Press from Denman (2007, 156394)

There are several other kinds of climate effects from aerosol PM. None is well understood or well quantified. The semi-direct effect, which involves absorption of solar radiation by soot particles followed by re-emission as thermal radiation, is expected to heat the air mass and increase its static stability relative to the surface. The semi-direct effect can also cause evaporation of cloud droplets, thereby partially offsetting the cloud albedo indirect effect. The glaciation effect involves an increase in IN, which is expected to cause rapid glaciation of a super-cooled liquid water cloud due to the differences in vapor pressure over ice and water. Unlike cloud droplets, these ice crystals can quickly reach precipitation size, with the potential to turn a non-precipitating cloud into a precipitating cloud. The thermodynamic effect involves a delay in freezing by the smaller cloud droplets, which can cause super cooled clouds to occur under colder temperatures. The possible consequences to radiative flux of all of the processes are outlined in Table 9-18 (top of the atmosphere effects) and Table 9-19 (surface radiative and precipitation effects) (Denman et al., 2007, 156394), though significant uncertainties remain. Nevertheless, the individual processes cannot be considered in isolation because of the numerous feedbacks, and because atmospheric aerosol concentrations and climate are intimately coupled (Denman et al., 2007, 156394; Dentener et al., 2006, 088434).

9.3.9.1. Glaciers and Snowpack

Organic compounds are incorporated into snow by wet and dry deposition processes (Lei and Wania, 2004, 127880; Roth et al., 2004, 056431). Atmospherically deposited organics appear to be ubiquitous in snowpacks at appreciable concentrations (Grannas et al., 2007, 156492). Examples include PAHs, phthalates, alkanes, phenols, low molecular weight carbonyls, POPs, and low molecular weight organic acids (Halsall, 2004, 155822; Nakamura et al., 2000, 156792; Villa et al., 2003, 156139). Humic-like substances found in the snowpack may release VOCs into the atmosphere via photo-oxidation (Grannas et al., 2004, 155803; Grannas et al., 2007, 156492). Several thousand organic species were identified by Grannas et al. (2006, 155804), based on molecular weight, from a single ice core collected in Russia. Little information is available, however, regarding the chemical properties of these chemical constituents. In addition to the diversity of chemicals that are deposited into the snowpack, there are also biological organisms, including bacteria and algae. Their role in influencing snow chemistry and volatilization processes is not understood (Grannas et al., 2007, 156492).

Recent research has explored connections between the atmosphere and the cryosphere (land or sea covered by snow or ice). A seasonal maximum of 40% of the Earth's land surface is covered by snow or ice, as well as several percent of the oceans. Particulate deposition to snow and ice surfaces can affect melting rates. Deposition of PM to glacial ice surfaces can affect the subsequent rate of melting. A thin cover of debris contributes to accelerated melting. A thicker cover of debris, such as that which may result from a volcanic eruption, retards melting. The difference is due to the changing balance between enhanced absorption of shortwave radiation by PM and conductive heat flow (insulation) through a buildup of material having low heat conduction (Kirkbride and Dugmore, 2003, 156645).This issue is particularly important for deposition of large quantities of volcanic material. To a lesser extent, however, the same principles apply to PM deposition derived from air pollution. Under a thin layer of debris, ablation rates are higher than for clean ice. However, as the thickness of the debris layer increases, ablation rates systematically decline (Nicholson and Benn, 2006, 156806). The threshold debris thickness that separates ablation increase from decrease is site specific and depends on local climate and the nature of the debris particles. Nicholson and Benn (2006, 156806) presented a surface energy balance model to calculate ice melt beneath a surface debris layer, based on meteorological data and basic debris characteristics. Modeled melting rates matched observed rates, suggesting that the model produced useful results.

Long-range atmospheric transport of PM delivers a large fraction of the total input of POPs to the Arctic region (Halsall, 2004, 155822). These contaminants can accumulate in Arctic food webs and have become the focus of international research and concern. Nevertheless, fate and transport of POPs within terrestrial and marine Arctic ecosystems are not well understood and are strongly affected by the presence of snow and ice. Sea ice provides a barrier to air-water exchange, and this hinders volatilization and re-emission of previously deposited contaminants (Halsall, 2004, 155822). Thus, the effects of greenhouse gasses and PM on climate in the Arctic region have feedbacks to POP fate, transport, and toxicity. The transfer of POPs among the major abiotic environmental compartments in the Arctic are summarized in Figure 9-84 from Halsall (2004, 155822). Recent studies detailing rate and transport of POPs are summarized in Table 9-20.

Table 9-20. Recent studies highlighting POP occurrence and fate in the major arctic compartments.

ATMOSPHERE		
1	Annual time-series of OC and PCB concentrations in the Norwegian Arctic	Oehme et al. (1996, 156001)
2	Long-term analysis of the chlordane-group and their input to the Arctic with changing sources	Bidleman et al. (2002, 155691)
3	PAH occurrence at monitoring sites across the Arctic, seasonality and gas/particle partitioning	Halsall et al. (1997, 155821)
4	PCB occurrence at monitoring sites across the Arctic, spatial differences and seasonality	Stern et al. (1997, 156096)
5	Long-term analysis of PCB and OC trends in the Canadian Arctic and seasonal patterns	Hung et al. (2001, 155856; 2002, 155857)
6	Trans-Pacific LRAT and impact of Asian sources on the western Canadian Arctic	Bailey et al. (2000, 155670)
FRESHWATER		
7	Annual avg water concentrations in major Russian rivers for selected OC pesticides	Alexeeva et al. (2001, 155651)
8	Long-term (decades) PCB deposition profile in Arctic lake sediments	Muir et al. (1996, 155991)
9	Mass balance of selected OCs in Canadian Arctic lake conducted with data collected over 3 yrs	Helm et al. (2002, 155835)
10	Examining the biodegradation of HCHs in Canadian Arctic watersheds	Helm et al. (2000, 155834)
MARINE		
11	Transport and entry of β-HCH into western Arctic Ocean via Pacific surface waters	Li et al. (2002, 156691)
12	Occurrence of current use pesticides in air, fog and surface seawater in the western Arctic Ocean	Chermyak et al. (1996, 155726)
13	Resolving petrogenic and anthropogenic PAH input to marine sediments in coastal Arctic seas	Yunker et al. (1996, 156175)
14	Quantifying abiotic and biotic degradation of HCHs in the Arctic Ocean water column	Harner et al. (2000, 155829)
15	PCBs and OCs in surface ocean water—Bering and Chukchi seas	Strachan et al. (2001, 156103)
16	Spatial patterns of HCHs and toxaphene in Arctic Ocean surface water	Jantunen and Bidleman (1998, 155877)
SNOW/AIR-FRESHWATER		
17	PAHs (and inorganics) in surface snow layers (snowpit) at Summit, Greenland	Masclet et al. (2000, 155966)
18	PAHs measured in snow and ice layers on Agassiz ice-cap, Ellesmere Island, Canada	Peters et al. (1995, 156856)
19	Modeling OC behaviour and fate in the surface seasonal snow pack at Amituk Lake, Canada	Wania et al. (1998, 156148)
20	OCs, PCBs and PAHs in snow and ice of the Ob-Yenisey watershed of the Russian Arctic	Melnikov et al. (2003, 156753)
OCEAN/AIR		
21	Transfer of α-HCH across the air/water interface in the western Arctic ocean	Jantunen and Bidleman (1996, 155876)
22	Calculated seasonality of OC air/water fluxes in the Canadian high Arctic	Hargrave et al. (1997, 155827)
OCEAN/ICE		
23	Transport potential of contaminants across the Arctic ocean via sea-ice drift	Pfirman et al. (1997, 156864)
24	The importance of eastern Arctic sea-ice drift as a source of contaminants to the Norwegian sea	Korsnes et al. (2002, 156657)

Source: Reprinted with Permission of Elsevier Ltd. from Halsall (2004, 155822)

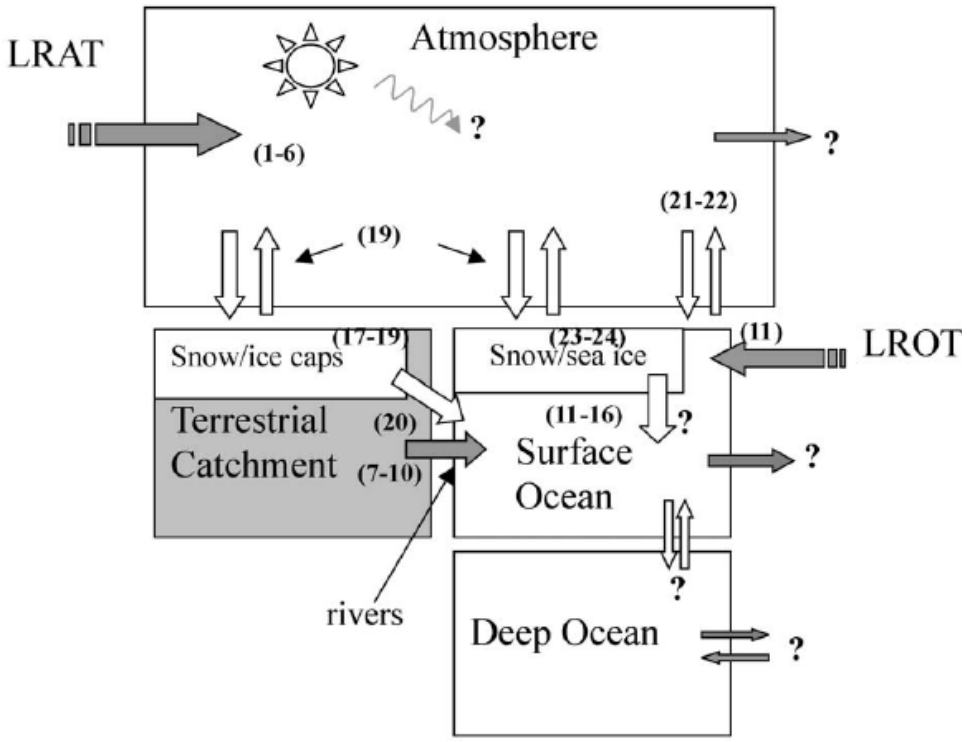


Figure 9-84. The transfer of POPs between the major abiotic compartments of the Arctic. Shaded arrows represent inputs/outputs of POPs to the Arctic. The numbers refer to selected studies detailing the occurrence and behavior of POPs, and are listed in Table 9-20. Question marks represent those areas that are least well understood. LRAT-long range atmospheric transport; LROT – long range oceanic transport.

9.3.9.2. Radiative Forcing by Anthropogenic Surface Albedo Change: BC in Snow and Ice

Section 9.3.9.2 comes directly from IPCC AR4 Chapter 2, Section 2.5.4, with section, table, and figure numbers changed to be internally consistent with this ISA.

The presence of soot particles in snow could cause a decrease in the albedo of snow and affect snowmelt. Initial estimates by Hansen et al. (2000, 042683) suggested that BC could thereby exert a positive RF of +0.2 W/m^2. This estimate was refined by Hansen and Nazarenko (2004, 156521), who used measured BC concentrations within snow and ice at a wide range of geographic locations to deduce the perturbation to the surface and planetary albedo, deriving an RF of +0.15 W/m^2. The uncertainty in this estimate is substantial due to uncertainties in whether BC and snow particles are internally or externally mixed, in BC and snow particle shapes and sizes, in voids within BC particles, and in the BC imaginary refractive index. Jacobson (2004, 155870) developed a global model that allows the BC aerosol to enter snow via precipitation and dry deposition, thereby modifying the snow albedo and emissivity. They found modeled concentrations of BC within snow that were in reasonable agreement with those from many observations. The model study found that BC on snow and sea ice caused a decrease in the surface albedo of 0.4% globally and 1% in the NH, although RFs were not reported. Hansen et al. (2005, 059087) allowed the albedo change to be proportional to local BC deposition according to Koch (2001, 192054) and presented a further revised estimate of 0.08 W/m^2. They also suggested that this RF mechanism produces a greater temperature response by a factor of 1.7 than an equivalent CO2 RF, that is, the 'efficacy' may be higher for this RF mechanism (see Section 2.8.5.7 of the IPCC AR4). This report adopts a best estimate

for the BC on snow RF of +0.10 ± 0.10 W/m^2, with a low level of scientific understanding (Section 2.9, Table 2.11, of the IPCC AR4).

9.3.9.3. Effects on Local and Regional Climate

Most effects of PM on climate, as assessed by IPCC (Stohl et al., 2007, 157015) and summarized in this assessment, focus on global-scale processes and responses. In addition, it is also possible that PM emissions contribute to local and regional climate changes. These might include short-term cycles in rainfall or temperature and rainfall suppression, especially near cities and for orographic precipitation. Rainfall suppression, in particular, is believed to exacerbate water supply problems which are substantial in many regions, especially in the western U.S.

Aerosol particles, directly and through cloud enhancement, may reduce near-surface wind speeds locally. Slower winds, in turn, reduce evaporation. The overall impact can be a reduction in local precipitation. Jacobson and Kaufman (2006, 090942) investigated the effects of PM on spatially-distributed wind speeds and resulting feedbacks to precipitation using the GATOR-GCMOM (Jacobson, 2001, 155864) and supporting evidence from satellite data. The study focused on the South Coast Air Basin (SCAB) in California during February and August, 2002-2004. The modeled precipitation decrease over land in California was 2% of the baseline 1.5 mm/day due to emissions of anthropogenic aerosol particle and precursor gasses in the SCAB domain. However, the reduction over much of the Sierra Nevada, where most precipitation falls, was up to 0.5 mm/day, or 4-5% of the baseline 10-13 mm/day in that mountainous region (Jacobson, 2006, 156599). The probable mechanism was described as follows. Aerosol particles and aerosol-enhanced clouds reduce wind speeds below them by stabilizing the air, reducing the vertical transport of horizontal momentum. In turn, the reduced wind speeds, and associated reduced evaporation and increased cloud lifetime, contributes to reduced local and regional precipitation (Jacobson, 2006, 156599).

Effects of air pollution on regional precipitation were quantified by Givati and Rosenfeld (2004, 156475). They found a 15-25% reduction in the orographic component of precipitation downwind of major coastal urban areas during the 20th century. Their study focused on orographically-forced clouds because these short-lived, shallow clouds are expected to exhibit the largest effect of air pollution on precipitation. Substantially larger precipitation suppression due to aerosol particulate pollution was found between Fresno and Sacramento in California by Givati and Rosenfeld (2004, 156475). Precipitation losses over topographical barriers in the Sierra Nevada amounted to 15-25% of the annual precipitation at elevations less than 2,000 m. This precipitation suppression occurred mainly in the relatively shallow orographic clouds within the cold air mass of cyclones. The suppression that occurred on the upslope side of the mountains was coupled with similar percentage (but lower absolute volume) enhancement on the drier downslope eastern side (Givati and Rosenfeld, 2004, 156475). Similar results were found in studies by Griffith et al. (2005, 156497), Jirak and Cotton (2006, 156612), Rosenfeld and Givati (2006, 156924), and Rosenfeld et al. (2007, 156057). At all of these study locations (California, Israel, Utah, Colorado, China), orographic precipitation decreased by 15-30% downwind of pollution sources, likely due to creation of more and smaller cloud droplets and resulting suppression of precipitation.

The study of Givati and Rosenfeld (2004, 156475) was the first to quantify the microphysical effect of mesoscale precipitation. Following the findings of Givati and Rosenfeld (2004, 156475), the effects of aerosol air pollution on precipitation at high elevation sites in the Front Range of Colorado adjacent to urban areas were investigated by Jirak and Cotton (2006, 156612). Examination of precipitation trends showed that the ratio of upslope precipitation during easterly flows at high elevation west of Denver and Colorado Springs to the upwind urban sites decreased by about 30% over the past half century. These results provide further support for the hypothesis that aerosol pollution suppresses orographic precipitation downwind of pollution source areas.

Griffith et al. (2005, 156497) found similar reductions in mountainous precipitation in Utah, downwind of Salt Lake City and Provo. The ratio of precipitation at mountain stations located in rural settings in Utah and Nevada remained stable, supporting the hypothesis that air pollution decreases Ro (the ratio of precipitation at the downwind site to precipitation at the upwind pollution source) over the mountains to the east of Salt Lake City.

Rosenfeld and Givati (2006, 156924) extended the investigation of the suppression of precipitation by aerosol pollutants to a larger scale by examining the ratio between precipitation amounts over the hills to precipitation over upwind lowland areas throughout the western U.S. from the Pacific Coast to the Rocky Mountains. They found in these paired analyses a pattern of

decreasing precipitation by as much as 24% from the Mexican border to central California, with no decrease in northern California and Oregon and smaller decrease of 14% in Washington east of Seattle and Puget Sound. Similar decreases were found over Arizona and New Mexico (Rosenfeld, 2006, 190233), Utah (Griffith et al., 2005, 156497), and the east slope of the Colorado Rockies (Jirak and Cotton, 2006, 156612).

Suppression of winter orographic precipitation appears to occur up to hundreds of kilometers inland of coastal urban areas (Rosenfeld, 2006, 190233). Decreases in this precipitation ratio occurred during winter orographic precipitation, but not during convective summer precipitation over the same mountain ranges. This finding agrees with the expectation that aerosol-induced changes in the rate of precipitation formation would cause a decrease in precipitation from shallow and short-lived orographic clouds, but not necessarily from deeper and longer-lived thermally-driven convective clouds.

Results of these studies of aerosol effects on orographic precipitation suggest that human-caused air pollution, and fine particles in particular, have had a large effect on precipitation well beyond the local scales of the pollution sources (Rosenfeld, 2006, 190233).

9.3.10. Summary of Effects on Climate

Aerosols affect climate through direct and indirect effects. The direct effect is primarily realized as planet brightening when seen from space because most aerosols scatter most of the visible spectrum light that reaches them. The IPCC AR4 reported that the radiative forcing from this direct effect was -0.5 (±0.4) W/m^2 and identified the level of scientific understanding of this effect as 'Medium-low'. The global mean direct radiative forcing effect from individual components of aerosols was estimated for the first time in the IPCC AR4 where they were reported to be (all in W/m^2 units): -0.4 (±0.2) for sulfate, -0.05 (±0.05) for fossil fuel-derived organic carbon, +0.2 (±0.15) for fossil fuel-derived black carbon, +0.03 (±0.12) for biomass burning, -0.1 (±0.1) for nitrates, and -0.1 (±0.2) for mineral dust. Global loadings of anthropogenic dust and nitrates remain very troublesome to estimate, making the radiative forcing estimates for these constituents particularly uncertain.

Numerical modeling of aerosol effects on climate has sustained remarkable progress since the time of the last PM AQCD, though model solutions still display large heterogeneity in their estimates of the direct radiative forcing effect from anthropogenic aerosols. The clear-sky direct radiative forcing over ocean due to anthropogenic aerosols is estimated from satellite instruments to be on the order of -1.1 (±0.37) W/m^2 while model estimates are -0.6 W/m^2. The models' low bias over ocean is carried through for the global average: global average direct radiative forcing from anthropogenic aerosols is estimated from measurements to range from -0.9 to -1.9 W/m^2, larger than the estimate of -0.8 W/m^2 from the models.

Aerosol indirect effects on climate are primarily realized as an increase in cloud brightness (termed the 'first indirect' or Twomey effect), changes in precipitation, and possible changes in cloud lifetime. The IPCC AR4 reported that the radiative forcing from the Twomey effect was -0.7 (range: -1.1 to +4) and identified the level of scientific understanding of this effect as 'Low' in part owing to the very large unknowns concerning aerosol size distributions and important interactions with clouds. Other indirect effects from aerosols are not considered to be radiative forcing.

Taken together, direct and indirect effects from aerosols increase Earth's shortwave albedo or reflectance thereby reducing the radiative flux reaching the surface from the Sun. This produces net climate cooling from aerosols. The current scientific consensus reported by IPCC AR4 is that the direct and indirect radiative forcing from anthropogenic aerosols computed at the top of the atmosphere, on a global average, is about -1.3 (range: -2.2 to -0.5) W/m^2. While the overall global average effect of aerosols at the top of the atmosphere and at the surface is negative, absorption and scattering by aerosols within the atmospheric column warms the atmosphere between the Earth's surface and top of the atmosphere. In part, this is owing to differences in the distribution of aerosol type and size within the vertical atmospheric column since aerosol type and size distributions strongly affect the aerosol scattering and reradiation efficiencies at different altitudes and atmospheric temperatures. And, although the magnitude of the overall negative radiative forcing at the top of the atmosphere appears large in comparison to the analogous IPCC AR4 estimate of positive radiative forcing from anthropogenic GHG of about +2.9 (± 0.3) W/m^2, the horizontal, vertical, and temporal distributions and the physical lifetimes of these two very different radiative forcing agents are not similar; therefore, the effects do not simply off-set one another.

Overall, the evidence is sufficient to conclude **that a causal relationship exists between PM and effects on climate, including both direct effects on radiative forcing and indirect effects that involve cloud feedbacks that influence precipitation formation and cloud lifetimes.**

9.4. Ecological Effects of PM

9.4.1. Introduction

PM is heterogeneous with respect to chemical composition and size; therefore, it can cause a variety of ecological effects, which have been previously described by the U.S. EPA (2004, 056905) and by Grantz et al. (2003, 155805). Atmospheric PM has been defined, for regulatory purposes, mainly by size fractions and less clearly so in terms of chemical nature, structure, or source. Both fine and coarse-mode particles may affect plants and other organisms; however, PM size classes do not necessarily relate to ecological effects (U.S. EPA, 1996, 079380). More often the chemical constituents drive the ecosystem response to PM (Grantz et al., 2003, 155805).

The previous PM assessment (U.S. EPA, 2004, 056905) included the acidifying effects of particulate N and S. The 2008 NO_XSO_X ISA (U.S. EPA, 2008, 157074) assessed the effects of particle- and gas-phase N and S pollution on acidification, N enrichment, and Hg methylation. Acidification of ecosystems is driven primarily by deposition resulting from SO_X, NO_X, and NH_X pollution. Acidification from the deposition resulting from current emission levels causes a cascade of effects that harm susceptible aquatic and terrestrial ecosystems, including slower growth and injury to forests and localized extinction of fishes and other aquatic species. In addition to acidification, atmospheric deposition of reactive N resulting from current NO_X and NH_X emissions along with other non-atmospheric sources (e.g., fertilizers and wastewater), causes a suite of ecological changes within sensitive ecosystems. These include increased primary productivity in most N-limited ecosystems, biodiversity losses, changes in C cycling, and eutrophication and harmful algal blooms in freshwater, estuarine, and ocean ecosystems. In some watersheds, additional SO_4^{2-} from atmospheric deposition increases Hg methylation rates by increasing both the number and activity of S-reducing bacteria. Methylmercury is a powerful toxin that can bioaccumulate to toxic amounts in food webs at higher trophic levels.

This assessment of PM effects on ecosystems considers both direct and indirect exposure pathways. Atmospheric PM may affect ecological receptors directly following deposition on surfaces or indirectly by changing the soil chemistry or by changing the amount of radiation reaching the Earth's surface. Indirect effects acting through the soil are often thought to be most significant because they can alter nutrient cycling and inhibit nutrient uptake (U.S. EPA, 2004, 056905; U.S. EPA, 2008, 157074). The U.S. EPA (2004, 056905) reported that the effects of PM can be both chemical and physical. Physical effects of particle deposition on vegetation may include abrasion and radiative heating. However, chemical effects may be more significant (U.S. EPA, 2008, 157074).

In general, anthropogenic stressors can result in damaged ecosystems that do not recover readily (Odum, 1993, 076742; Rapport and Whitford, 1999, 004595). Ecosystems sometimes lack the capacity to adapt to an anthropogenic stress and are unable to maintain their normal structure and functions unless the stressor is removed (Rapport and Whitford, 1999, 004595). These stresses result in a process of ecosystem degradation marked by a decrease in biodiversity, reduced primary and secondary production, and a lower capacity to recover and return to the original ecosystem state. In addition, there can be an increased prevalence of disease, reduced nutrient cycling, increased dominance of exotic species, and increased dominance by smaller, short-lived opportunistic species (Odum, 1985, 039482; Rapport and Whitford, 1999, 004595).

Ecosystems are often subjected to multiple stressors, of which atmospheric PM deposition is only one. Additional stressors are also important, including O_3 exposure, climatic variation, natural and human disturbance, the occurrence of invasive non-native plants, native and non-native insect pests, disease, acidification, and eutrophication among others. PM deposition interacts with these other stressors to affect ecosystem patterns and processes.

The possible effects of particulate (and other) air pollutants on ecosystems have been categorized by Guderian (1977, 004150) as follows:

- accumulation of pollutants in plants and other ecosystem components (such as soil and surface- and groundwater),
- damage to consumers as a result of pollutant accumulation,
- changes in species diversity because of shifts in competition,
- disruption of biogeochemical cycles,
- disruption of stability and reduction in the ability to self-regulate,
- breakdown of stands and associations, and
- expansion of denuded zones.

The general conclusion of the last PM assessment (U.S. EPA, 2004, 056905) was that ecosystem response to PM can be difficult to determine because the changes are often subtle. For example, changes in the soil may not be observed until pollutant deposition has occurred for many decades, except in the most severely polluted areas around heavily industrialized point sources. The presence of co-occurring pollutants generally makes it difficult to attribute ecological effects to PM alone or to one constituent in the deposited PM. In other words, the potential for alteration of ecosystem function and structure exists but can be difficult to quantify except in cases of extreme amounts of deposition, especially when there are other pollutants present in the ambient air that may produce additive or synergistic responses.

New information on the ecological effects of coarse and fine particle PM is presented in the following discussion in the context of effects that were known from the last PM AQCD (U.S. EPA, 2004, 056905). The general effects of the chemical constituents of PM are discussed; however, a rigorous assessment of each chemical constituent (e.g., Hg, Cd, Pb, etc.) is not given. Both direct and indirect effects will be discussed and the strength of the scientific evidence will be evaluated using the causality framework.

9.4.1.1. Ecosystem Scale, Function, and Structure

Information presented in this section was collected at multiple scales, ranging from the physiology of a given species to population, community, and ecosystem-level investigations. For this assessment, “ecosystem” is defined as a functional entity consisting of interacting groups of living organisms and their abiotic (chemical and physical) environment. Ecosystems cover a hierarchy of spatial scales and can comprise the entire globe, biomes at the continental scale, or small, well-circumscribed systems such as a small pond.

Ecosystems have both structure and function. Structure may refer to a variety of measurements including the species richness, abundance, community composition and biodiversity as well as

landscape attributes. Competition among and within species and their tolerance to environmental stresses are key elements of survivorship. When environmental conditions are shifted, for example, by the presence of anthropogenic air pollution, these competitive relationships may change and tolerance to stress may be exceeded. "Function" refers to the suite of processes and interactions among the ecosystem components and their environment that involve nutrient and energy flow as well as other attributes including water dynamics and the flux of trace gases. Plant processes including photosynthesis, nutrient uptake, respiration, and C allocation, are directly related to functions of energy flow and nutrient cycling. The energy accumulated and stored by vegetation (via photosynthetic C capture) is available to other organisms. Energy moves from one organism to another through food webs, until it is ultimately released as heat. Nutrients and water can be recycled. Air pollution alters the function of ecosystems when elemental cycles or the energy flow are altered. This alteration can also be manifested in changes in the biotic composition of ecosystems.

There are at least three levels of ecosystem response to pollutant deposition: (1) the individual organism and its environment; (2) the population and its environment; and (3) the biological community composed of many species and their environment (Billings, 1978, 034165). Individual organisms within a population vary in their ability to withstand the stress of environmental change. The response of individual organisms within a population is based on their genetic constitution, stage of growth at time of exposure to stress, and the microhabitat in which they are growing (Levine and Pinto, 1998, 029599). The range within which organisms can exist and function determines the ability of the population to survive. Those able to cope with the stresses survive and reproduce. Competition among different species results in succession (community change over time) and, ultimately, produces ecosystems composed of populations of species that have the capability to tolerate the stresses (Guderian, 1985, 019325; Rapport and Whitford, 1999, 004595). Available information on individual, population and community response to PM will be discussed.

9.4.1.2. Ecosystem Services

Ecosystem structure and function may be translated into ecosystem services. Ecosystem services identify the varied and numerous ways that ecosystems are important to human welfare. Ecosystems provide many goods and services that are of vital importance for the functioning of the biosphere and provide the basis for the delivery of tangible benefits to human society. Hassan et al. (2005, 092759) define these to include supporting, provisioning, regulating, and cultural services:

- Supporting services are necessary for the production of all other ecosystem services. Some examples include biomass production, production of atmospheric O_2, soil formation and retention, nutrient cycling, water cycling, and provisioning of habitat. Biodiversity is a supporting service that is increasingly recognized to sustain many of the goods and services that humans enjoy from ecosystems. These provide a basis for three higher-level categories of services.

- Provisioning services, such as products (Gitay et al., 2001, 092761), i.e., food (including game, roots, seeds, nuts and other fruit, spices, fodder), fiber (including wood, textiles), and medicinal and cosmetic products (including aromatic plants, pigments).

- Regulating services that are of paramount importance for human society such as (a) C sequestration, (b) climate and water regulation, (c) protection from natural hazards such as floods, avalanches, or rock-fall, (d) water and air purification, and (e) disease and pest regulation.

- Cultural services that satisfy human spiritual and aesthetic appreciation of ecosystems and their components.

9.4.2. Deposition of PM

Deposition of PM is discussed in Chapter 3.3.4. Additional material specifically related to ecosystems is discussed in this section.

9.4.2.1. Forms of Deposition

Research summarized by the previous NAAQS PM assessment illustrated the complexity of deposition processes. Airborne particles, their gas-phase precursors, and their transformation products are removed from the atmosphere by wet and dry deposition processes. These deposition processes transfer PM pollutants to other environmental media where they can alter the structure, function, diversity, and sustainability of complex ecosystems. Dry deposition of PM is most effective for coarse particles. These include primary geologic materials and elements such as iron and manganese. By contrast, wet deposition is more effective for fine particles of secondary atmospheric origin and elements such as cadmium, chromium, lead, nickel, and vanadium (Reisinger, 1990, 046737; Smith, 1990, 084015; U.S. EPA, 2004, 056905). The relative magnitudes of the different deposition modes vary with ecosystem type, location, elevation, and chemical burden of the atmosphere (U.S. EPA, 2004, 056905). There are differences in the deposition behavior of fine and coarse particles. Coarse particles generally settle nearer their site of formation than do fine particles. In addition, the chemical constitution of individual particles is correlated with size. For example, much of the base cation and heavy metal burden is present on coarse particles.

Fine PM is often a secondary pollutant that forms within the atmosphere, rather than being directly emitted from a pollution source. It derives from atmospheric gas-to-particle conversion reactions involving nucleation, condensation, and coagulation, and from evaporation of water from contaminated fog and cloud droplets. Fine PM may also contain condensates of VOCs, volatilized metals, and products of incomplete combustion, including polycyclic aromatic hydrocarbons (PAH) and BC (soot) (U.S. EPA, 2004, 056905).

Fine PM may act as a carrier for materials such as herbicides that are phytotoxic. Fine PM provides much of the surface area of particles suspended in the atmosphere, whereas coarse PM provides much of the mass of airborne particles. Surface area can influence ecological effects associated with the oxidizing capacity of fine particles, their interactions with other pollutants, and their adsorption of organic compounds. Fine and coarse particles also respond to changes in atmospheric humidity, precipitation, and wind, and these can alter their deposition characteristics.

Coarse PM is mainly a primary pollutant, having been emitted from pollution sources as fully formed particles derived from abrasion and crushing processes, soil disturbances, desiccation of marine aerosol emitted from bursting bubbles, hygroscopic fine PM expanding with humidity to coarse mode, and/or gas condensation directly onto preexisting coarse particles. Suspended primary coarse PM may contain iron, silica, aluminum, and base cations from soil, plant and insect fragments, pollen, fungal spores, bacteria, and viruses, as well as fly ash, brake lining particles, and automobile tire fragments. Coarse mode particles can be altered by chemical reactions and/or physical interactions with gaseous or liquid contaminants.

Exposure to a given mass concentration of PM may lead to widely differing phytotoxic and other environmental outcomes depending upon the particular mix of PM constituents involved. Especially important in this regard are S and N components of PM, which are addressed in the 2008 NO_XSO_X ISA, and effects of particulate heavy metals and organic contaminants. This variability has not been characterized adequately. Though effects of specific chemical fractions of PM have been described to some extent, there has been relatively little research aimed at defining the effects of unspeciated PM on plants or ecosystems.

9.4.2.2. Components of PM Deposition

Trace Metals

Atmospheric deposition can be the primary source of some metals to some watersheds. Metal inputs can include the primary crustal elements (Al, Ca, K, Fe, Mg, Si, Ti) and the primary anthropogenic elements (Cu, Zn, Cd, Cr, Mn, Pb, V, Hg). The crustal elements are derived largely from weathering and erosion, whereas the anthropogenic elements are derived from combustion, industrial sources, and other man-made sources (Goforth and Christoforou, 2006, 088353).

Heavy metal deposition to ecosystems depends on their location as well as upwind emissions source strength. The deposition velocity tends to be dependent on particle size and chemical species. Larger particles deposit more efficiently than smaller particles. Heavy metals preferentially associate

with fine particles. Fine particles also have the longest atmospheric residence times. Depending on climate and topography, fine particles may remain airborne for days to months and may be transported thousands of kilometers from their source.

Ecosystems immediately downwind of major heavy metal emissions sources may receive locally heavy dry deposition. Trace element investigations conducted in roadside, industrial, and urban environments have also shown that substantial amounts of particulate heavy metals can accumulate on surfaces.

A significant trace metal component of PM is mercury (Hg). Hg is toxic and can move readily through environmental compartments. Atmospheric and depositional inputs of Hg include both natural and anthropogenic sources. Natural geologic contributions to Hg in the environment include geothermal and volcanic activity, geologic metal deposits, and organic-rich sedimentary rocks. These natural emissions combine with anthropogenic emissions from such sources as power plants, landfills, sewage sludge, mine waste, and incineration (Gustin, 2003, 155816; Schroeder and Munthe, 1998, 014559). Emissions from natural sources are controlled by geologic features, including substrate Hg content, rock type, the degree of hydrothermal activity, and the presence of heat sources (Gustin, 2003, 155816). The significance of natural Hg sources relative to anthropogenic sources varies geographically. For example, Nevada occurs within a global mercuriferous belt, with area emissions about three times higher than the value assumed for global modeling (Gustin, 2003, 155816). In Nevada, natural and anthropogenic Hg emissions are approximately equal (Gustin, 2003, 155816).

The U.S. EPA (1997, 157066) compiled an assessment of the sources and environmental effects of Hg in the U.S. A variety of factors were found to influence Hg deposition, fate and transport (Table 9-21). Such factors relate in particular to speciation of the Hg that is emitted, the forms in which it is deposited from the atmosphere, and transformations that occur within the atmosphere and within the aquatic, transitional, and terrestrial compartments of the receiving watershed. There have been studies that have reconstructed, from lake sediment records, the atmospheric depositional history of trace metals and PAHs in lakes adjacent to coal-fired power plants. For example, Donahue et al. (2006, 155751) analyzed sediment from Wababun Lake, which is located in Alberta, Canada in proximity (within 35 km) to 4 power plants built since 1950. Trace metal concentrations of Hg, Cu, Pb, As, and Se in lake sediment increased by 1.2- to 4-fold. The total PAH flux to surface sediments was 730-1,100 $\mu g/m^2/yr$, which was two to five times higher than in 2 lakes situated 20 km to the north and 70 km to the south. Further discussion of Hg effects on ecosystems can be found in Section 9.4.5.

Table 9-21. Factors potentially important in estimating Hg exposure.

Factor	Importance and Possible Effect on Mercury Exposure
Type of anthropogenic source of mercury	Different combustion and industrial process sources are anticipated to have different local scale impacts due to physical source characteristics (e.g., stack height), the method of waste generation (e.g., incineration or mass burn) or mercury control devices and their effectiveness.
Mercury emission rates from stack	Increased emissions will result in a greater chance of adverse impacts on environment.
Mercury species emitted from stack	More soluble species will tend to deposit closer to the source.
Form of mercury emitted from stack	Transport properties can be highly dependent on form.
Deposition differences between vapor and particulate-bound mercury	Vapor-phase forms may deposit significantly faster than particulate-bound forms.
Transformations of mercury after emission from source	Relatively nontoxic forms emitted from source may be transformed into more toxic compounds.
Transformation of mercury in watershed soil	Reduction and revolatilization of mercury in soil limits the buildup of concentration.
Transport of mercury from watershed soils to water body	Mercury in watershed soils can be a significant source to water bodies and subsequently to fish.
Transformation of mercury in water body	Reduction, methylation, and demethylation of mercury in water bodies affect the overall concentration and the MHg fraction, which is bioaccumulated in fish.
Facility locations	Effects of meteorology and terrain may be significant.
Location relative to local mercury source	Receptors located downwind are more likely to have higher exposures. Influence of distance depends on source type.
Contribution from non-local sources of mercury	Important to keep predicted impacts of local sources in perspective.
Uncertainty	Reduces confidence in ability to estimate exposure accurately.

Source: Modified from U.S. EPA (1997, 157066)

Organics

Organic compounds that may be associated with deposited PM include persistent organic pollutants (POPs), pesticides, SOCs, polyaromatic hydrocarbons (PAHs) and flame retardants among others. Organic compounds partition between gas and particle phases, and organic particulate deposition depends largely on the particle sizes available for adsorption (U.S. EPA, 2004, 056905). Dry deposition of organic materials is often dominated by the coarse fraction. Gas-particle phase interconversions are important in determining the amount of dry deposition.

Most persistent organic pollutants (POPs) enter the biosphere via human activities, including synthetic pesticide application, output of polychlorinated dibenzo dioxins (PCDD) from incinerators, and accidental release of PCBs from transformers (Lee, 2006, 088968). Once they are introduced into the environment, their accumulation and magnification in biological systems are determined by physiochemical properties and environmental conditions (Section 9.4.6). Uptake by plants can occur at the soil/plant interface and at the air/plant interface (Krupa et al., 2008, 198696). For lipophilic POPs, such as PCDDs and PCBs, the air/plant response route generally dominates (Lee, 2006, 088968; Thomas et al., 1998, 156118), but uptake through above-ground plant tissue also occurs. In a study of zucchini (*Cucurbita pepo*), Lee et al. (2006, 088968) found chlordane pesticide components in all vegetation tissues examined: root, stem, leaves, fruits.

Many pesticides and SOCs are carcinogenic or estrogenic and pose potential threats to aquatic and terrestrial biota. Although deposition of SOCs was previously reported for the Sierra Nevada Mountains in California and the Rocky Mountains in Colorado, little was previously known about the occurrence, distribution, or sources of SOCs in alpine, sub-Arctic, and Arctic ecosystems in the western U.S. The snowpack is efficient at scavenging of both particulate and gas phase pesticides from the atmosphere (Halsall, 2004, 155822; Lei and Wania, 2004, 127880). Analysis of pesticides in snowpack samples from seven NPs in the western U.S. by Hageman et al. (2006, 156509) illustrated the deposition and fate of 47 pesticides and their degradation products. Correlation analysis with latitude, temperature, elevation, PM, and two indicators of regional pesticide use suggested that regional patterns in historic and current agricultural practices are largely responsible

for the distribution of pesticides in the NPs. Pesticide deposition to parks in Alaska was attributed to long-range atmospheric transport.

PAHs include hundreds of different compounds that are characterized by possessing two or more fused benzene rings. They are widespread contaminants in the environment, and are formed by incomplete combustion of fossil fuels and other organic materials. Eight PAHs are considered carcinogenic and 16 are classified by EPA as priority pollutants. They are common air pollutants in metropolitan areas, derived from vehicular traffic and other urban sources. Especially high concentrations have been found near Söderberg aluminum production industries and areas where heating during winter via wood burning is common. Other sources, in addition to gasoline and diesel engines, include forest fires and various forms of fossil fuel combustion (Sanderson and Farant, 2004, 156942).

The behavior of PAHs is strongly determined by their chemical characteristics, especially their nonpolarity and hydrophobicity. They readily adsorb to particulates in the air and to sediments in water. Srogi (2007, 180049) provided a thorough review of PAH concentrations in various environmental compartments and their use for assessing environmental risks and possible effects on ecosystems and human health.

Deposition and fate of PAH has been an important area of research. Because they are carcinogenic, PAHs are important environmental contaminants. Root-soil behavior of PAHs is an area of active study. Soil-bound PAHs are associated with soil organic matter and are therefore generally not easily available for root uptake. PAHs are readily adsorbed to root surfaces but there seems to be little movement to the interior of the root or movement up to the shoots (Gao and Zhu, 2004, 155782). Paddy rice is the main food crop planted in China. As an aquatic plant having aerial roots, the movement of PAHs into rice roots may be different than their movement into more widely studied land-grown food crops. PAH concentrations in the rice roots were more correlated with the water and air compartments than with the soil (Jiao et al., 2007, 155879).

The total PAH concentration in grasses adjacent to a highway have been measured to be about eight times higher than in grasses from reference sites not close to a highway (Crépineau et al., 2003, 155741). Howe et al. (2004, 155854) found that concentrations of PAHs and hexachlorobenzene (HCB) in spruce (*Picea* spp.) needles at 36 sites in eastern Alaska varied by an order of magnitude. Samples collected near the city of Fairbanks generally had higher concentrations than samples collected from rural areas. The relative importance of combustion sources versus petrogenic sources was highest in the near-coastal areas, as reflected in variation in the concentration of ratios of isomeric PAHs.

Use of flame retardants has increased in recent years in response to fire product safety regulations. However, some flame retardant chemicals are toxic and are readily transported atmospherically. Use of some has been banned in Europe and some of the United States because of their persistence and tendency to bioaccumulate (Hoh et al., 2006, 190378).

Base Cations

With respect to ecosystem effects from PM deposition, the inclusion of base cations (especially Ca, Mg, and K) in atmospheric deposition is generally considered to be a positive effect. Base cations are important plant nutrients that are in some locations present in short supply and that are further depleted by the acidic components of deposition. Increased base cation deposition can help to ameliorate adverse effects of acidification of soils and surface waters and reduce the toxicity of inorganic Al to plant roots and aquatic biota. These topics are covered in detail in the recent 2008 NO_XSO_X ISA (U.S. EPA, 2008, 157074).

Although the effects of base cation deposition inputs to terrestrial ecosystems are most commonly considered to be positive, under very high base cation deposition, plant health can be adversely affected. Dust that is high in base cations can settle on leaves and other plant structures and remain for extended periods of time. This is especially likely in arid environments because rainfall can serve to wash dry deposited materials off the foliage. Extended dust coverage can result in a variety of adverse impacts on plant physiology (Grantz et al., 2003, 155805). For example, van Heerden et al. (2007, 156131) documented decreased chlorophyll content, inhibition of CO_2 assimilation, and uncoupling of the oxygen-evolving complex in desert shrubs exposed to high limestone dust deposition near a limestone quarry in Namibia.

Based on the Integrated Forest Study (IFS) data, the U.S. EPA (2004, 056905) concluded that particulate deposition has a greater effect on base cation inputs to soils than on base cation losses associated with the inputs of sulfur, nitrogen, and H^+. These atmospheric inputs of base cations have considerable significance, not only to the base cation status of these ecosystems, but also to the potential of incoming precipitation to acidify or alkalize the soils in these ecosystems. This topic is discussed in detail in the recent NO_XSO_X ISA (U.S. EPA, 2008, 157074).

9.4.2.3. Magnitude of Dry Deposition

Using Vegetation for Estimating Atmospheric Deposition

Whereas direct real-time measurement of deposition or air concentrations of atmospheric contaminants is desirable, it is not always practical (Howe et al., 2004, 155854). Instead, passive time-integrative methods are frequently used. These can involve analysis of vegetative tissues as a record of pollutant exposure, or analysis of lake sediment cores or ice cores to determine changes in pollutant input over time. There is a general assumption that the concentration of an analyte in vegetation reflects the time-integrated concentration of that analyte in the air. The development of deposition layers in sediment or ice cores allows the possibility of determining the effects of changes in the atmospheric concentration over periods of years, decades, or longer.

Biomonitoring methods are important in air pollution assessment and provide a complement for more typical instrumental analyses. It is well known that mosses can accumulate large amounts of heavy metals in response to atmospheric deposition. Mosses accumulate dissolved materials and PM deposited from the atmosphere and have been used extensively in Europe as surrogate collectors for estimating bulk (wet plus dry) deposition of metals. The ease and low cost of this method has enabled regional assessments to be conducted throughout Europe.

Despite its wide use, however, several papers have pointed out complications in the use of mosses to quantify metal deposition rates. Zechmeister (1998, 156178) found that the uptake efficiency for 12 heavy metals in three species of moss was similar, but that uptake efficiency in a fourth species was uncorrelated with the other species for about half the metals considered. Zechmeister (1998, 156178) also showed that productivity of an individual species can vary greatly among sites. To calculate atmospheric deposition of metals from accumulation in mosses, both the metal concentration and the rate of biomass production is needed. Further complication was shown in the study of Shakya et al. (2008, 156081), which revealed that accumulation of Cu, Zn and Pb decreased chlorophyll content. Sites with greater deposition amounts may therefore have lower rates of productivity than cleaner sites.

Differences in uptake efficiencies among species and productivity among sites has led to the use of a single moss species placed in mesh bags that can be distributed to areas where that species of moss does not grow naturally. Studies to standardize this passive deposition monitoring approach have been limited. Adamo et al. (2007, 155644) evaluated the effects of washing with water, oven drying, and acid washing as preteatments and found little difference in uptake efficiencies, although the ratio of the collecting surface area to mass was found to be a key factor in uptake efficiency.

Couto et al. (2004, 155739) investigated dry versus bulk deposition of metals using transplanted moss bags. This study showed that at some sites dry deposition exceeded bulk deposition, a likely outcome of wash-off of dry deposited particles. This study also documented intercationic displacement and leaching as a result of acidic precipitation. The authors concluded that the accumulated metal concentration represented an unstable equilibrium between inputs and outputs of elements that were a function of the local environment and weather during the exposure period. They also concluded that it was not possible to extrapolate calibrations between metal accumulation in moss and atmospheric deposition of metals to areas with different weather conditions, precipitation pH, and air contaminant concentrations. Zechmeister et al. (2003, 157175) also presented results demonstrating the problems with dry deposited particles that can be washed off by rain. These studies indicate that moss is not a completely effective collector of total particle deposition. Deposition estimates from moss accumulation probably represent values that fall between wet deposition and total deposition.

A European moss biomonitoring network has been in place since 1990 (Harmens et al., 2007, 155828). Sampling surveys are repeated every five years. The survey conducted in 2005/2006

occurred in 32 countries at over 7,000 sites. The network reports metal concentrations associated with live moss tissue. Trends analysis of these data showed statistically significant decreases over time in moss concentrations for As, Cu, V, and Zn. Trends were not observed for Cr, Fe, or Ni. Results for individual countries participating in the survey have also been published. In Hungary, major pollution sources were readily detected by moss sampling (Otvos et al., 2003, 156831). Somewhat higher metal concentrations in mosses in 1997 than in other European countries were attributed to the use of a different moss species in the Hungarian survey (Otvos et al., 2003, 156831). Similar sampling in Romania showed regions with contamination that were among the highest in Europe. These results were consistent with known air quality problems in Romania (Lucaciu et al., 2004, 155947). Because particulate deposition is not well characterized using this method, spatial patterns and temporal trends for particulate metal deposition in Europe only provide crude estimates of relative deposition patterns.

The use of moss to assess heavy metal deposition has received much less attention in the U.S. than in Europe. A study conducted in the Blue Ridge Mountains, VA, found that metal concentrations in moss were related to elevation and canopy species at some sites (Schilling and Lehman, 2002, 113075). However, metal concentrations in moss were not related to concentrations in the O horizon of the soil. Other measurement methods for trace metal deposition were not available to compare with moss concentrations.

Epiphytic lichens have also been used to evaluate heavy metal accumulation. Helena et al. (2004, 155833) found substantially increased concentrations of metals in lichens transplanted from a relatively clean region to an area in proximity to a metal smelter. The presence of specific species of bryophyte or lichen can serve as an effective bioindicator of metal contamination (Cuny et al., 2004, 155742). In some studies, tree bark has been used as a biomonitor for atmospheric deposition of heavy metals (Baptista et al., 2008, 155673; Pacheco and Freitas, 2004, 156011; Rusu et al., 2006, 156062).

Biomonitoring using mosses, lichens, or other types of vegetation has been established as a means of identifying spatial patterns in atmospheric deposition of heavy metals in relation to power plants, industry, and other point and regional emissions sources. More recently, a number of studies (López et al., 2002, 155943; 2003, 155944; 2003, 155945) have used cattle that have been reared predominantly on local forage as a means of monitoring atmospheric inputs of Cu, Ar, Zn, and Hg. For example, Hg emissions from coal fired power plants in Spain had a substantial effect on Hg accumulation by calves (López et al., 2003, 155944). Accumulation of Hg by cattle extended to ~140-200 km downwind from the source.

Yang and Zhu (2007, 156168) investigated the effectiveness of pine needles as passive air samplers for SOCs, such as PAHs, that are partially or completely particle-associated in the atmosphere. PAH distribution patterns are complicated by their properties, which span a broad range of octanol-air partition coefficients. This allows them to be present in both vapor and particle phases. In addition, the air-plant partitioning of PAHs is affected by air temperature and atmospheric stability (Krupa et al., 2008, 198696; Yang and Chen, 2007, 092847). DeNicola et al. (2005, 155747) documented the suitability of a Mediterranean evergreen oak (*Quercus ilex*) to serve as a passive biomonitor for atmospheric contamination with PAH in Italy.

Deposition to Canopies

Tree canopies have been shown to increase dry deposition from the atmosphere, including deposition of PM. Dry deposition rates in the canopy are commonly estimated by the difference between throughfall deposition and deposition measured by an open collector, although the use of this approach to specifically quantify particulate deposition is complicated by gaseous deposition to leaf surfaces and, for some elements, leaching and uptake. Avila and Rodrigo (2004, 155664) found that trace metal deposition in throughfall in a Spanish oak forest were higher than bulk deposition for Cu, Pb, Mn, V, and Ni, but not for Cd and Zn. This study also found that dry deposition of Cu, Pb, Zn, Cd and V occurred, but that canopy uptake of Zn and Cd also occurred. Leaching of Mn and Ni from the foliage was observed as well. Leaching of Ni, Cu, Mn, Rb, and Sr from a red spruce-balsam fir canopy by acidic cloud water was also measured in a study by Lawson et al. (2003, 089371). These studies suggest that leaching of trace metals from forest canopies varies with tree species and the acidity of precipitation. Throughfall therefore cannot be assumed to represent total deposition of heavy metals without evaluating uptake and leaching at the specific study site. Physical models have

provided an alternative to estimating dry deposition to canopies with throughfall measurements. Recently, Pryor and Binkowski (2004, 116805) identified an additional complication in that models typically hold particle size constant. Nevertheless, there may be significant modification of particle size distributions during the deposition process.

The use of pine and oak canopies as bioindicators of atmospheric trace metal pollution was investigated by Aboal et al. (2004, 155642). As an ecosystem pool, metals in leaves were likely to be much more important than those in mosses. The authors concluded, however, that these tree species were not effective bioindicators of atmospheric deposition of heavy metals. Metal concentrations in leaves were found to be one to three orders of magnitude lower than in mosses collected in this study.

The effectiveness of tree canopies in capturing particulates was investigated as a method for improving air quality by Freer-Smith et al. (2004, 156451). This study showed that with consideration of planting design, location of pollution source, and tree species, planting of trees can be effective at reducing particulate air pollution. However, this approach does not address the possible effects of the captured pollution on trees, soils and surface waters.

High-elevation forests generally receive larger particulate deposition loadings than equivalent low elevation sites. Higher wind speeds at high elevation enhance the rate of aerosol impaction. Orographic effects enhance rainfall intensity and composition and increase the duration of occult deposition. High-elevation forests are often dominated by coniferous species with needle-shaped leaves that enhance impaction and retention of PM delivered by all three deposition modes.

Deposition to Soil

As with mosses, accumulation of heavy metals in surface soils provides a general reflection of the spatial distribution of industrial pollution. The distribution of toxic elements in urban soils has been an important area of study (Madrid et al., 2002, 155956; Markiewicz et al., 2005, 155963). Generally, Cu, Pb, Zn, and Ni have accumulated in urban soils compared with their rural counterparts (Yuangen et al., 2006, 156174). In the study of Romic and Romic (2003, 156055), relationships were found between urban activities and concentrations of metals in soils in developed areas surrounding Zagreb, Croatia. Goodarzi et al. (2002, 155801) compared deposition estimated by moss bags to concentrations of metals in A-horizon soils in the vicinity of a large smelter. Statistically significant correlations were observed between the moss bag deposition estimates and the soil metal concentrations for Cd, Pb, Zn, and in some cases also Cu. These correlations suggested that atmospheric deposition of metals caused elevated metal concentrations in the upper mineral horizon of these soils. No correlations were found for Hg or As in this study.

Studies have also been conducted to assess metal accumulation in peat because of the tendency of most metals to be immobilized through binding with organic matter. Steinnes et al. (2005, 156095) presented geographical patterns of metal concentrations in surface peat throughout Norway that corresponded to pollution sources, although the peat samples were collected in 1979. Zaccone et al. (2007, 179930) found that variations of metal concentrations with depth in a single Swiss peat core corresponded with the depositional history that would be expected from the industrial revolution, although Cs^{137} activity exhibited a distribution in the profile that was not fully consistent with the Chernobyl nuclear reactor accident. A detailed study of Finnish peat showed that relationships between depth profiles of metal concentrations and deposition history can match well for some metals at some sites, but not well for the same metals at other sites (Roberts et al., 2003, 156051). They also found that Zn and Cd accumulation rates were independent of deposition history at each of three study sites.

Metal deposition to soil is also a significant concern adjacent to roadways. Urban stormwater can be rich in heavy metals and other contaminants derived from atmospheric deposition, and can be a major source of pollutant inputs to water bodies in urban settings. Urban stormwater runoff can also be toxic to aquatic biota, partly due to trace metal concentrations (Greenstein et al., 2004, 155808; Sabin et al., 2005, 088300; Schiff et al., 2002, 156959). These processes are largely a function of the impervious nature of much of the ground surface in urban areas (i.e., buildings, roads, sidewalks, parking lots, construction sites). Dry-deposited pollutants can build up, especially in arid and semi-arid environments, and then be washed into surface waters with the first precipitation event. The concentrations of Cd, Ca, Cu, Pb, and Zn in road runoff were found to be significantly higher during winter in Sweden. This seasonal pattern was attributed to the intense wearing of the

pavement that occurred during winter due to the use of studded tires in combination with chemical effects of deicing salts (Bäckström et al., 2003, 156242).

9.4.3. Direct Effects of PM on Vegetation

Exposure to airborne PM can lead to a range of phytotoxic responses, depending on the particular mix of deposited particles. This was well known at the time of the previous PM criteria assessment, as summarized below. Most direct phytotoxic effects occur in severely polluted areas surrounding industrial point sources, such as limestone quarries and other mining activities, cement kilns, and metal smelting facilities (U.S. EPA, 2004, 056905). Experimental application of PM constituents to foliage typically elicits little response at the more common ambient concentrations. The diverse chemistry and size characteristics of ambient PM and the lack of clear distinction between effects attributed to phytotoxic particles and to other air pollutants further confound the understanding of the direct effects on foliar surfaces.

Deposition of PM can cause the accumulation of heavy metals on vegetative surfaces. Low solubility limits foliar uptake and direct heavy metal toxicity because trace metals must be brought into solution before they can enter into the leaves or bark of vascular plants. In those instances when trace metals are absorbed, they are frequently bound in leaf tissue and are lost when the leaf drops off (Hughes, 1981, 053595).

Depending on the size of the particles, the PM deposited on the leaf surface can affect the plant's metabolism and photosynthesis by blocking light, obstructing stomatal apertures, increasing leaf temperature and altering pigment and mineral content (Naidoo and Chirkoot, 2004, 190449) (Section 9.4.3.1.). Fine PM has been shown to enter the leaf through the stomata and penetrate into the mesophyll layers where it alters leaf chemistry (Da et al., 2006, 190190). Kuki et al. (2008, 155346) also showed increased leaf permeability and increased activity of enzymes in response to fine PM lead (Section 9.4.5.).

Studies of the direct toxic effects of particles on vegetation have not yet advanced to the stage of reproducible exposure experiments. In general, phytotoxic gases are deposited more readily, assimilated more rapidly, and lead to greater direct injury of vegetation as compared with most common particulate materials. The dose-response functions obtained in early experiments following the exposure of plants to phytotoxic gases generally have not been observed following the application of particles (U.S. EPA, 2004, 056905).

9.4.3.1. Effects of Coarse-mode Particles

The current state of scientific knowledge regarding the direct effects of coarse PM on plants has not changed since publication of the previous PM criteria assessment (U.S. EPA, 2004, 056905). The summary provided here is taken from that report. In many rural areas and some urban areas, the majority of the mass in the coarse particle mode derives from the elements Si, Al, Ca, and Fe, suggesting a crustal origin as fugitive dust from disturbed land, roadways, agriculture tillage, or construction activities. Large particles tend to deposit near their source (Grantz et al., 2003, 155805) and rapid sedimentation of coarse particles tends to restrict their direct effects on vegetation largely to roadsides and forest edges, which often receive the greatest deposition (U.S. EPA, 2004, 056905)

Dust

Dust can cause both physical and chemical effects. Consequences are often mediated via impacts on leaf cuticles and waxes. Deposition of inert PM on above-ground plant organs sufficient to coat them with a layer of dust may result in changes in radiation received, a rise in leaf temperature, and the blockage of stomata. Crust formation can reduce photosynthesis and the formation of carbohydrates needed for normal growth, induce premature leaf-fall, damage leaf tissues, inhibit growth of new tissue, and reduce starch storage. Dust may decrease photosynthesis, respiration, and transpiration; and it may result in the condensation and reactivity of gaseous pollutants with PM, thereby causing visible injury symptoms and decreased productivity (U.S. EPA, 2004, 056905). Leaves with trichomes may be more prone to the accumulation of dust on leaf surfaces (Kuki et al., 2008, 155346).

The chemical composition of PM is usually the key phytotoxic factor leading to plant injury. For example, cement-kiln dust liberates calcium hydroxide on hydration. It can then penetrate the epidermis and enter the mesophyll, causing an increase in leaf surface pH. In turn, surface pH can be important for surface microbial colonization and wax formation and degradation.

Salt

Sea-salt particles can serve as nuclei for the absorption and subsequent reaction of other gaseous and particulate air pollutants. Direct effects on vegetation reflect these inputs and salt injury caused by the sodium and chloride that constitute the bulk of these particles. The source of most salt spray near the coast is aerosolized ocean water. Sea salt can cause damage to plants; however, it is not covered in this assessment because it is not of anthropogenic origin. However particulate salt may be input to an ecosystem from deicing salt.

Injury to vegetation from the application of deicing salt is caused by salt spray blown or drifting from the highways (Viskari and Karenlampi, 2000, 019101). The most severe injury is often observed nearest the highway. Conifers planted near roadway margins in the eastern U.S. often exhibit foliar injury due to toxic amounts of saline aerosols deposited from deicing solutions (U.S. EPA, 2004, 056905).

9.4.4. PM and Altered Radiative Flux

The effects of PM on radiative flux and the subsequent effects on vegetation have been described in Section 4.2.3.2 of the previous PM assessment (U.S. EPA, 2004, 056905); a brief overview is presented below. Atmospheric PM can affect ambient radiation, which can be considered in both its direct and diffuse components. Foliar interception by canopy elements occurs for both up- and down-welling radiation. Therefore, the effect of atmospheric PM on atmospheric turbidity influences canopy processes both by radiation attenuation and by changing the efficiency of radiation interception in the canopy through conversion of direct to diffuse radiation (Hoyt, 1978, 046638). Diffuse radiation is more uniformly distributed throughout the canopy and increases canopy photosynthetic productivity by distributing radiation to lower leaves. The enrichment in photosynthetically active radiation (PAR) present in diffuse radiation may offset a portion of the effect of an increased atmospheric albedo due to atmospheric particles. Mercado et al. (2009, 190444) estimated the effects of variations in diffuse light on the terrestrial carbon sink during the last century using a global model. The results indicated that the terrestrial carbon sink increased by approximately 25% during the "global dimming"' period (1950-1980), likely driven by increased diffuse light despite decreased PAR. However, under a future scenario in which SO_4^{2-} and BC aerosols decline, the diffuse-radiation and the associated terrestrial C sink also decline (Mercado et al., 2009, 190444).

The effects of regional haze on the yield of crops because of reduction in solar radiation were examined by Chameides et al. (1999, 011184) in China, where regional haze is especially severe. Based on model results, it was estimated that approximately 70% of crops were being depressed by at least 5-30% by regional scale air pollution and its associated haze (Chameides et al., 1999, 011184; U.S. EPA, 2004, 056905).

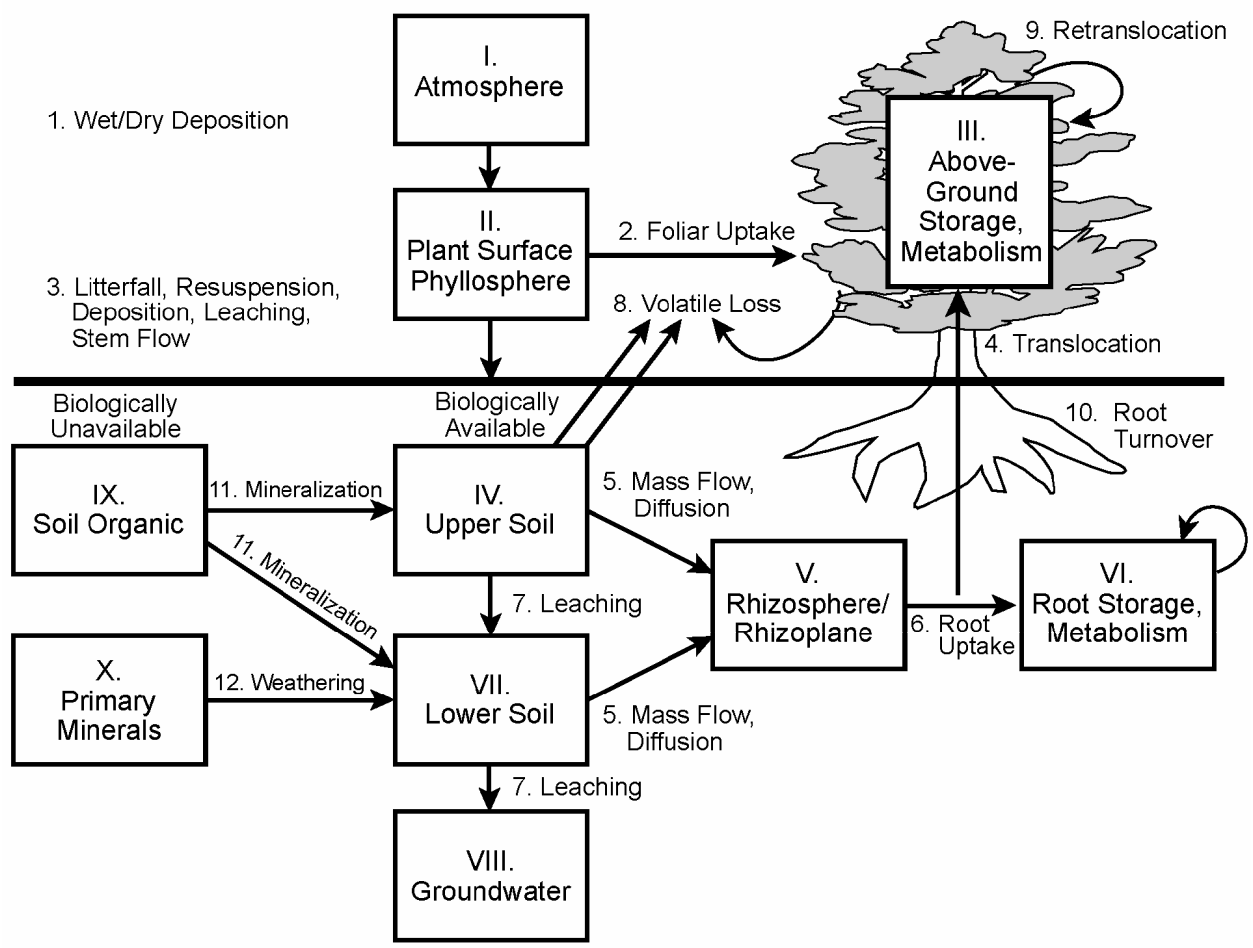
9.4.5. Effects of Trace Metals on Ecosystems

Trace metals may enter the ecosystems as both fine and coarse particles. All but 10 of the 90 elements that comprise the inorganic fraction of the soil occur at concentrations of <0.1% (1,000 µg/g) and are termed "trace" elements or trace metals. Trace metals with a density greater than 6 g/cm^3, referred to as "heavy metals" (e.g., Cd, Cu, Pb, Cr, Hg, Ni, Zn), are of particular interest because of their potential toxicity to plants and animals. Although some trace metals are essential for vegetative growth or animal health, they are all toxic in large quantities. Most trace elements exist in the atmosphere in particulate form as metal oxides (Ormrod, 1984, 046892). Aerosols containing trace elements derive predominantly from industrial activities. Generally, only the heavy metals Cd, Cr, Ni, and Hg are released from stacks in the vapor phase (McGowan et al., 1993, 046731). Atmospherically deposited PM can interact with a variety of biogeochemical

processes. The potential pathways of accumulation of trace metals in terrestrial ecosystems, as well as the possible consequences of trace metal deposition on ecosystem functions, are summarized in Figure 9-85 (U.S. EPA, 2004, 056905). A number of mass balance approaches (Macleod et al., 2005, 155954; Toose and Mackay, 2004, 156123), and metal speciation and transport models (Bhavsar et al., 2004, 155689; Bhavsar et al., 2004, 155690; Gandhi et al., 2007, 155781) have been developed in recent years.

Atmospheric Pb is a component of PM in some regions. The effects of Pb on ecosystems were discussed in the 2006 Pb AQCD (U.S. EPA, 2006, 090110), which concluded that, due to the deposition of Pb from past human practices (e.g., leaded gasoline, ore smelting) and the long residence time of Pb in many aquatic and terrestrial ecosystems, a legacy of environmental Pb burden exists, over which is superimposed much lower contemporary atmospheric Pb loadings. The potential for ecological effects of the combined legacy and contemporary Pb burden to occur is a function of the bioavailability or bioaccessibility of the Pb. This, in turn, is highly dependent upon numerous site factors (e.g., soil OC content, pH, water hardness). Although the more localized ecosystem impacts observed around smelters are often striking, effects generally cannot be attributed solely to Pb, because of the presence of many other stressors (e.g., other heavy metals, oxides of sulfur and nitrogen) that can also act singly or in concert with Pb to cause readily observable environmental effects (U.S. EPA, 2004, 056905; U.S. EPA, 2008, 157074).

Effects of fine particle trace elements were described by the U.S. EPA (2004, 056905), and some additional more recent research has also been conducted, especially on the topic of vegetative uptake of trace elements from the soil. The state of scientific understanding as presented by the U.S. EPA (2004, 056905) as well as a discussion of more recent research findings are presented below.



Source: U.S. EPA (2004, 056905)

Figure 9-85. Relationship of plant nutrients and trace metals with vegetation. Compartments (roman numerals) represent potential storage sites; whereas arrows (Arabic numerals) represent potential transfer routes.

9.4.5.1. Effects on Soil Chemistry

Trace metals are naturally found in small amounts in soils, ground water, and vegetation. Many are essential micronutrients required for growth by plants and animals. Naturally occurring mineralization can produce metal concentrations in soils and vegetation that are high compared to atmospheric sources. Many metals are bound by chemical processes in the soil, reducing their availability to biota. However, epiphytic or parasitic root colonizing microorganisms can solubilize and transport metals for root uptake (Lingua et al., 2008, 155935). It can be difficult to assess the extent to which observed heavy metal concentrations in soil are of anthropogenic origin. This is because soil parent material, pedogenesis, and anthropogenic inputs all influence the amounts and distribution of trace elements in soil. Trace element concentrations in some natural soils that are remote from air pollution can be higher than soils derived from other parent materials that receive anthropogenic inputs (Burt et al., 2003, 155709). The general effects of metals from atmospheric deposition are presented in the following discussion.

There is not a standard method available for quantifying the bioavailability of heavy metals in soil. A variety of models, isotopic studies, and sequential extraction methods have been used (Collins et al., 2003, 155737; Feng et al., 2005, 155774; Shan et al., 2003, 156972). Total metal concentration in soil does not give a good indication of potential biological effects because soils vary in their

ability to bind metals in forms that are not bioavailable. There are various methods available for assessing bioavailability of metals, but soils are heterogeneous and there is no ideal method for evaluating what conditions the soil biota experience. Almås et al. (2004, 155654) argued that the actual measurement of biological effects is the best criterion for determining bioavailability. In particular, the replacement of metal-sensitive microorganisms by metal-tolerant organisms within each functional group may be one of the most sensitive indicators of metal exposure. An increase in microbial trace metal tolerance *per se* would not be problematic if it was not for the fact that this increase in tolerance is generally accompanied by a decrease in microbial diversity (Almas et al., 2004, 155654; Lakzian et al., 2002, 156671).

Heavy metals deposited from the atmosphere to forests accumulate either in the organic forest floor or in the upper mineral soil layers and metal concentration tends to decrease with soil depth. The accumulation of heavy metals in soil is influenced by a variety of soil characteristics, including pH, Fe and Al oxide content, amount of clay and organic material, and cation exchange capacity (CEC) (Hernandez et al., 2003, 155841). Thus, the pattern of distribution of heavy metals in soils depends on both the soil characteristics and the metal characteristics.

Burt et al. (2003, 155709) investigated the concentrations and chemical forms of trace metals in smelter-contaminated soils collected in the Anaconda and Deer Lodge Valley area of Montana, one of the major mining districts of the world for over a century (1864-1983). The relative distributions of trace metals within the more soluble soil extraction forms were similar to their respective total concentrations. This suggested a relationship between the concentrations of total trace elements and concentrations of soluble mobile fractions. Sequential extractions do not provide direct characterization of trace metal speciation, but rather an indication of chemical reactivity (Burt et al., 2003, 155709; Ramos et al., 1994, 046736). Soluble and exchangeable forms are considered readily mobile and bioavailable. Those bound to clay minerals or organic matter are considered generally unavailable.

There is concern that Pb contamination of forest soil could move into groundwater. This would be important in view of the large quantity of Pb deposited from the atmosphere in the 1960s and 1970s in response to combustion of leaded gasoline. This issue was investigated by Watmough et al. (2004, 077809) who applied a stable isotope (^{207}Pb) to the forest floors of white pine (*Pinus strobus*) and sugar maple (*Acer saccharum*) stands. Added Pb was rapidly lost from the forest floor, likely due to high litter turnover in these forest types. However, Pb concentrations in the upper 30 cm of mineral soil were strongly correlated with soil OM, suggesting that Pb does not readily move down the soil profile to the ground water, but rather is associated with the organic content of the upper soil layers (Watmough et al., 2004, 077809).

The upper soil layers are typically an active site of litter decomposition and plant root uptake, both processes may be affected by metal components of PM. Surface litter decomposition is reduced in soils having high metal concentrations. This is likely due to the sensitivity to metals of microbial decomposers and reduced palatability of plant litter having high metal concentration (Johnson and Hale, 2008, 155881). Root decomposition is a key component of nutrient cycling. Johnson and Hale (2008, 155881) measured in situ fine root decomposition at Sudbury, Ontario and Rouyn-Noranda, Quebec. Elevated soil metal concentrations (Cu, Ni, Pb, Zn) did not necessarily reduce fine root decomposition. Only at sites having high concentrations of metals did decomposing roots show increased metal concentrations over time.

9.4.5.2. Effects on Soil Microbes and Plant Uptake via Soil

Upon entering the soil environment, PM pollutants can alter ecological processes of energy flow and nutrient cycling, inhibit nutrient uptake, change ecosystem structure, and affect ecosystem biodiversity. Many of the most important effects occur in the soil. The soil environment is one of the most dynamic sites of biological interaction in nature. It is inhabited by microbial communities of bacteria, fungi, and actinomycetes. These organisms are essential participants in the nutrient cycles that make elements available for plant uptake. Changes in the soil environment that influence the role of the bacteria and fungi in nutrient cycling determine plant and ultimately ecosystem response.

Many of the major indirect plant responses to PM deposition are chiefly soil-mediated and depend on the chemical composition of the individual components of deposited PM. Effects may result in changes in biota and in soil conditions that affect ecological processes, such as nutrient cycling and uptake by plants.

The soil environment is rich in biota. Bacteria and fungi are usually most abundant in the rhizosphere, the soil around plant roots that all mineral nutrients must pass through. Bacteria and fungi benefit from the nutrients that are present in root exudates and make mineral nutrients available for plant uptake. The soil-mediated ecosystem impacts of PM are largely determined by effects on the growth of bacteria and mycorrhizal fungi that are involved in nutrient cycling and plant nutrient uptake.

Soil Nutrient Cycling

Accumulation of heavy metals in litter can interfere with nutrient cycling. Microorganisms are responsible for decomposition of organic matter, which contributes to soil fertility. Toxic effects on the microflora can be caused by Zn, Cd, and Cu. The U.S. EPA (2004, 056905) judged that addition of only a few mg of Zn per kg of soil can inhibit sensitive microbial processes. Enzymes involved in the cycling of N, P, and S (especially arylsulfatase and phosphatase) seem to be most affected (Kandeler et al., 1996, 094392).

Soil organic matter cycling is known to be sensitive to disturbance due to heavy metal pollution. This can cause increased litter accumulation at sites close to metal emissions point sources. The relative importance of the various processes that might be responsible for this observation is poorly known. Boucher et al. (2005, 155699) conducted CO_2 evolution studies in microcosms having metal-rich and metal-poor plant materials. Their results suggested that there was a pool of less readily decomposable C that appeared to be preferentially preserved in the presence of high metal (Zn, Pb, Cd) concentrations in the leaves of the metallophyte *Arabidopsis halleri*. An additional possibility is that increased lignification of the cell walls increased the amount of insoluble C (Mayo et al., 1992, 155974).

Yuangen et al. (2006, 156174) found that urban soil basal respiration rates were positively correlated with soil acetic acid-extractable Cd, Cu, Ni, and Zn. The soil microbial biomass was negatively correlated with the concentrations of Pb fractions, but not with other metals. Overall microbial biomass was lower for urban soils as compared with rural soils (Yuangen et al., 2006, 156174).

Metal Toxicity to Microbial Communities

It is believed that increased accumulation of litter in metal-contaminated areas is due to the effects of metal toxicity on microorganisms. Smith (1991, 042566) reported the effects of Cd, Cu, Ni, and Zn on the symbiotic activity of fungi, bacteria, and actinomycetes. In particular, the formation of mycorrhizae has been shown to be reduced when Zn, Cu, Ni, and Cd were added to the soil.

Most studies of the effects of heavy metals on soils have been conducted under laboratory conditions. However, Oliveira and Pampulha (2006, 156827) performed a field study to evaluate long-term changes in soil microbiological characteristics in response to heavy metal contamination. Dehydrogenase activity, soil ATP content, and enumeration of major soil microbial groups illustrated the effects of contamination. There was a marked decrease in total numbers of the different microbial groups. In particular, asymbiotic nitrogen-fixers and heterotrophic bacteria were found to be sensitive. Dehydrogenase activity was confirmed to be a good assay for determining the effect of heavy metals on physiologically active soil microbial biomass.

The toxic effects of heavy metals on soil microorganisms are well known. However, less is known about the relative sensitivity of different types of soil microorganisms (Rajapaksha et al., 2004, 156035). Vaisvalavicius et al. (2006, 157080) assessed the toxicity of high concentrations of Pb (839 mg/kg), Zn (844 mg/kg), and Cu (773 mg/kg) in the upper 0-0.1 m soil layer. Microbial abundance of all groups was reduced and enzymatic activity was lower than for uncontaminated soil. In particular, actinomycetes, oligonitrophobic and mineral N assimilating bacteria were most affected.

Effects of heavy metals in soil on microbes depends on soil pH, organic content, and the type of heavy metal exposure (Kucharski and Wyszkowska, 2004, 156662). Some studies have shown that heavy metals inhibit microbial activity in soil (Smejkalova et al., 2003, 156987; Vasundhara et al., 2004, 156133). However, Wyszkowska et al. (2007, 179948) showed that heavy metals can either

inhibit or stimulate the growth of soil microbes. Populations of *Azotobacter* spp. decreased, but populations of oligotrophic and copiotrophic bacteria, actinomyces, and fungi increased in response to heavy metal exposure. Acute metal stress causes a decrease in microbial biomass as metal-sensitive microbes are inhibited (Joynt et al., 2006, 155887).

Studies of the impacts of metal stress on the microbial community composition in soil have generally been based on microbial culturing techniques that can select only a subset of the natural soil population of microbes. More recent culture-independent studies have been conducted using phospholipids or nucleic acid biomarkers to reveal information regarding changes in microbial community structure (Joynt et al., 2006, 155887). Using this approach, Joynt et al.(2006, 155887) demonstrated that soils contaminated with both metals (Pb, Cr) and organic solvent compounds over a period of several decades had undergone changes in community composition, but still contained a phytogenetically diverse group of bacteria. This may reflect adaptation to the potentially toxic conditions through such processes as natural selection, gene exchange, and immigration. Comparison between a severely contaminated soil with a similar soil that had much lower amounts of contamination showed considerably lower microbial diversity in the contaminated soil, particularly for asymbiotic nitrogen fixers and heterotrophic bacteria (Oliveira and Pampulha, 2006, 156827).

As pollution increases, it is expected that the more sensitive species will be lost and the more tolerant species remain. This gives rise to the concept of pollution-induced community tolerance (PICT), which has been demonstrated for populations of bacteria and fungi (Davis et al., 2004, 155744). These researchers assessed the effects of long-term Zn exposure on the metabolic diversity and tolerance to Zn of a soil microbial community across a gradient of Zn pollution. PICT was found to correlate better with total soil Zn than with the concentration of Zn in soil pore water.

Soil Microbe Interactions with Plant Uptake of Metals

Atmospherically-deposited metals accumulate in upper soil horizons where fine roots are most developed. The availability for plant uptake of metals in soil depends on metal speciation and soil pH. In addition, metal binding to dissolved organic matter (DOM) reduces bioavailability (Sauvé, 2001, 156948). Because organic matter typically decreases with soil depth, the affinity of metals for organic matter can influence metal bioavailability at different soil depths. Fine roots (<2 mm diameter) provide the major site of uptake and transport to the above-ground plant and generally contain a large proportion of the total metals found in plants (Gordon and Jackson, 2000, 155802).

Fine roots are often colonized by mycorrhiza and interact with other soil microbes. Recent published evidence supports that mycorrizha and bacteria influence plant uptake and tolerance of metals. Mycorrhiza are fungi that colonize plant roots to form a symbiosis. Mycorrhiza take up nutrients from the soil and transfer them to the plant in exchange for carbon from the plant. Like plants, some species and strains of mycorrhiza are more tolerant of metals in the soil (Ray et al., 2005, 190473), so that unpolluted and polluted sites may host different species and strains of mycorrhiza (Vogel-Mikus et al., 2005, 190501).

Mycorrhiza have been observed to cause a range of effects on plants. In some cases, plants colonized with mycorrhiza showed improved nutrient uptake and decreased metal uptake (Berthelsen et al., 1995, 078058; Nogueira et al., 2004, 190460; Vogel-Mikus et al., 2006, 190502). Mycorrhiza have been shown to accumulate metals and act as a sink (Berthelsen et al., 1995, 078058; Carvalho et al., 2006, 155715) often preventing the metals in the roots from allocation to shoots (Kaldorf et al., 1999, 190399; Soares and Siqueira, 2008, 190482; Zhang et al., 2005, 192083). For example, estuarine salt marshes are often located close to urban and industrial areas and receive elevated amounts of trace metal contaminants from point and non-point (including atmospheric deposition) sources. Vegetation is important in the retention and accumulation of heavy metals in salt marshes. Carvalho et al. (2006, 155715) conducted experiments on the effects of arbuscular mycorrhizal fungi (AMF) on the uptake of Cd and Cu by *Aster tripolium*, a common plant species in polluted salt marshes and a host of AMF. Carvalho et al. (2006, 155715) found that AMF colonization increased metal accumulation in the root system of *Aster tripolium* without enhancing translocation to the shoot. By trapping toxic metals in the roots, this plant species may reduce the extent of vegetative stress caused by metal exposure and act as an effective sink for these metals. In a review paper Christie et al. (2004, 190174) concluded that mycorrhiza may directly improve plant tolerance to

metals by binding and immobilizing metals and indirectly improve plant tolerance by improving uptake of nutrients that increase plant growth.

There is recent evidence that bacteria and mycorrhiza act together to improve plant tolerance to metals. Like mycorrhiza some bacteria are more tolerant to metals than others (Vivas et al., 2003, 190499). Combined inoculation of *Trifolium sp.* by the arbuscular mycorrhiza, *Glomus mosseae,* and the bacterium, *Brevivacillus sp.,* conferred tolerance to Cd by increasing nutrient status and rooting development and by decreasing Cd uptake by the plant (Vivas et al., 2003, 190499). A similar result was observed for Zn uptake (Vivas et al., 2006, 190500).

In some cases, mycorrhizae will not prevent metal uptake (Weissenhorn et al., 1995, 073826). In fact, mycorrhiza may facilitate the accumulation of metals in plants and enhance the translocation of metals from the root to the shoot (Citterio et al., 2005, 190176; Vogel-Mikus et al., 2005, 190501; Zimmer et al., 2009, 192085). There is evidence of variable responses depending on the combination of mycorrhiza and bacteria species. Zimmer et al. (2009, 192085) recently showed that the willow tree (*Salix sp.*) colonized with the ectomycorrhizal fungus, *Hebeloma crustuliniforme*, and the bacteria, *Micrococcus luters*, increased total Cd and Zn accumulation due to enhanced mycorrhizal formation. In these cases where soil microbes cause increased metal accumulation, there is a potential to use the system for phytoremediation.

Plants also vary in the extent to which they take up heavy metals from the soil. Variability has been shown to occur in response to different plant species and different metals. For example, Szabó and Fodor (2006, 156109) exposed winter wheat (*Triticum aestivum*), maize (*Zea mays*) and sunflower (*Helianthus annuus*) to a variety of micro-pollutants. Cadmium accumulation was significant in both vegetative and reproductive plant parts. Vegetative winter wheat accumulated substantial amounts of Hg, but the other species did not. Lead, Cu, and Zn showed only moderate enrichment in crops (Szabó and Fodor, 2006, 156109).

There is some evidence to support that shallow-rooted plant species are most likely to take up metals from the soil (Martin and Coughtrey, 1981, 047727). However, there is little evidence confirming this observation. It may be more likely that shallow roots of species are likely to take up metals because the metal often accumulates in shallow soil layers. Even though atmospheric PM will usually deposit on soils before being taken up by plants, it could also be deposited to aquatic systems with subsequent transfer to terrestrial plants. Contamination of stream sediments by heavy metals can impact adjacent terrestrial ecosystems when high flows cause resuspension and subsequent streamside deposition of sediment particles. For example, Ozdilek et al. (2007, 156010) showed that metal concentrations in vegetation along the Blackstone River in Massachusetts and Rhode Island were generally inversely related to the distance from the riverbank, with higher metal concentrations in plant tissues located near the river. The ability of plants to take up metals from soil is an important part of metal cycling in the environment. This uptake process allows the metals to enter the food web, where they might exert mutagenic, carcinogenic, and teratogenic effects (Hunaiti et al., 2007, 156579).

9.4.5.3. Plant Response to Metals

Some metals, including Cu, Co, Ni, and Zn, are essential micronutrients needed for plant growth. Others, including Hg, Cd, and Pb are not essential for plants. Though all heavy metals can be directly toxic at sufficiently high concentrations, only Cu, Ni, and Zn have been documented as being frequently toxic to plants (U.S. EPA, 2004, 056905), while toxicity due to Cd, Co, and Pb has been observed less frequently (Smith, 1990, 046896). Toxic doses depend on the type of ion, ion concentration, plant species and the stage of plant growth (Memon and Schroder, 2009, 190442). Toxicity response is also dependent on the nutritional status of the plant and the development of mycorrhizae (Strandberg et al., 2006, 156105). Plants respond to high concentrations of metals in soil through a variety of mechanisms and there are substantial differences among plant species in their response to heavy metal exposure. Mechanisms of metal tolerance included exclusion or excretion rates, genetics (Patra et al., 2004, 081976; Yang et al., 2005, 192104), mycorrhizal interactions (Gohre and Paszkowski, 2006, 190355), storage capability and accumulation (Clemens, 2006, 190179), and various cellular detoxification mechanisms (Gratao et al., 2005, 190364; Hall, 2002, 190365).

One of the most important mechanisms that increases plant tolerance to metals is chelation with phytochelatins, such as metallothioneins and peptide ligands that are synthesized within the plant from glutathione (Memon and Schroder, 2009, 190442). Phytochelatins are intracellular

metal-binding peptides that act as specific indicators of metal stress. Because they are produced by plants as a response to sublethal concentrations of heavy metals, they can indicate that heavy metals play a role in forest decline (Gawel et al., 1996, 012278). Phytochelatin concentrations have previously been measured in coniferous trees in the northeastern U.S. The U.S. EPA (2004, 056905) and Grantz et al. (2003, 155805) summarized studies indicating that both the number of dead red spruce trees and phytochelatin concentrations increased sharply with elevation in the northeastern U.S. Red spruce stands showing varying degrees of decline indicated a systematic and significant increase in phytochelatin concentrations associated with the extent of tree injury. These data suggest that metal stress might contribute to tree injury and forest decline in the northeastern U.S. The extent to which low to moderate amounts of heavy metal deposition, which might occur at locations that are not in close proximity to a large point source, contribute to adverse impacts on forest vegetation is not known. Although the phytochelatin data suggest a linkage, more direct experimental data would be needed to confirm such a finding.

In general, plant growth is negatively correlated with trace metal and heavy metal concentration in soils and plant tissue (Audet and Charest, 2007, 190169). Trace metals, particularly heavy metals, can influence forest growth. Growth suppression of foliar microflora has been shown to result from Fe, Al, and Zn. These three metals can also inhibit fungal spore formation, as can Cd, Cr, Mg, and Ni (see Smith, 1990, 046896). Metals cause stress and decreased photosynthesis (Kucera et al., 2008, 190408) and disrupt numerous enzymes and metabolic pathways (Strydom et al., 2006, 190486). Excessive concentrations of metals result in phytotoxicity through: (i) changes in the permeability of the cell membrane; (ii) reactions of sulfydryl (-SH) groups with cations; (iii) affinity for reacting with phosphate groups and active groups of ADP or ATP; and (iv) replacement of essential ions (Patra et al., 2004, 081976).

In addition to disrupting photosynthesis and other metabolic pathways, metals have been shown to alter frost hardiness and impair nutrition. A recent review by Taulavuori (2005, 190489) suggests that metal- induced stress reduces frost hardiness of plants, a particular concern at high elevation sites. Kim et al. (2003, 155899) found decreased concentration of K in needles and Ca in stems of *Pinus sylvestris* seedlings exposed to Cd addition. This response suggests a disturbance of nutrition in response to Cd. Pollutant-caused needle loss can reduce the interception of pollutants from the atmosphere, and therefore reduce their concentrations in stemflow. This may be responsible for the observation that species diversity of lichens is sometimes higher on trees affected by die-back (Hauck, 2003, 155830).

Da Silva et al. (2006, 190190) have shown that PM had anatomical and physiological effects on plants growing near an iron pelletization factory in Brazil. The effects of PM occurred due to foliar uptake. Structural characteristics such as peltate trichomes may have formed a barrier lessening the penetration of metallic iron into the mesophyll in some species. Iron was shown to penetrate the trichomes, epidermic cells (adaxial and abaxial surfaces), stomata, xylem cells, collenchyma, endodermis and mesophyll tissues. Once entering the stomata, the PM penetrates within the mesophyll, it may modify the chemical balance of the mesophyll (Da et al., 2006, 190190).

A greenhouse study evaluated the combined effects of iron dust on restinga vegetation (coastal vegetation of Brazil) that commonly grows near iron ore industries. Kuki et al. (2008, 155346) found that iron dust had differing effects on gas exchange, chlorophyll content, iron content and antioxidant enzyme activity on two plant species common to the restinga. *Schinus terebinthifolius* (an invasive exotic in the U.S.) was not affected by the iron dust. However, *Sophora tomentosa* showed increased iron content and membrane permeability to the leaves, increasing activity of antioxidant enzymes. These results showed that the plants used different strategies to cope with PM pollution. *S. terebinthifolius* avoided stress, while *S. tomentosa* used antioxidant enzyme systems to partially neutralize oxidative stress.

Plant foliage can accumulate elemental Hg over time in response to air exposure and concentrations in soil (Ericksen et al., 2003, 155769; Frescholtz et al., 2003, 190352). A mesocosm experiment was conducted by Ericksen et al. (2003, 155769) where aspen trees were grown in gas-exchange chambers in Hg-enriched soil (12.3 ± 1.3 µg/g) and the Hg content in the foliage was analyzed. Foliar Hg increased with leaf age for 2-3 mo and then stabilized at leaf concentrations near 150 ng/g. About 80% of the Hg found in above-ground biomass was present in the leaves. The concentration of Hg in trees grown in the same mesocosms in containers of low Hg soil (0.03 ± 0.01 µg/g) exhibited foliar Hg concentrations that were similar to those of trees grown in Hg-enriched soil. Almost all of the foliar Hg originated from the atmosphere. Clearly, plant foliage

can be a major sink for airborne Hg, which can subsequently enter the soil after litterfall (Ericksen et al., 2003, 155769). However, this study did not determine the extent to which atmospheric Hg was dry-deposited on the foliage, as opposed to gaseous uptake through the stomata. Foliar/air Hg exchange has been shown to be dynamic and bi-directional (Millhollen et al., 2006, 190447). These investigators compared foliar Hg accumulation over time in three tree species with fluxes measured using a plant gas-exchange system subsequent to soil amendment with $HgCl_2$. Root tissue Hg concentrations were strongly correlated with soil Hg concentrations, suggesting that below-ground accumulation of Hg by roots may be an important process in the biogeochemical cycling of Hg in soil systems. Nevertheless, measured foliar Hg fluxes indicated that deposition of atmospheric Hg constituted the dominant flux of Hg to the leaf surface (Millhollen et al., 2006, 190447). Grigal (2003, 155811) also found that Hg in vegetation is derived almost exclusively from the atmosphere. Mercury uptake from soil is limited, partly because roots adsorb Hg but transport it to foliage very poorly (Grigal, 2002, 156498). Grigal (2003, 155811) provided a thorough review of the sequestration of Hg in forest and peatland ecosystems. A fundamental aspect of Hg cycling is its strong relationship to organic matter. For that reason, peatlands sequester much larger quantities of Hg than would be expected on the basis of their land area. Thus, if global climate change affects C storage, it may indirectly affect Hg storage because of the strong relationship between Hg and organic matter (Grigal, 2003, 155811).

Arbuscular mycorrhizal (AM) fungi can play important roles in mitigating toxicity of heavy metals in plants. For example, AM symbiosis is known to be involved in plant adaptation to As-contaminated soils. Higher plants that are adapted to As contaminated soils are generally associated with mycorrhizal fungi (Gonzalez-Chavez et al., 2002, 155800). It has also been shown that AM symbioses can influence plant coexistence and community diversity (O'Connor, 2002). Some plants associated with AM fungi can successfully colonize sites that are heavily contaminated by heavy metals (Pennisi, 2004, 156018).

Dong et al. (2008, 192106) cultivated white clover (*Trifolium repens*) and ryegrass (*Lolium perenne*) in As-contaminated soil (water extractable As 82.7 mg/kg). The growth and P nutrition of both species largely depended on AM symbiosis. The AM-inoculated plants showed selective uptake and transfer of P over As.

PM pollution has the potential to alter species composition over long time scales. Kuki et al. (2009, 190411) showed that early establishment stages of *Sophora tomentosa* species were negatively affected by the combination of iron ore and acidifying particles. The deleterious effects of the PM included deficient germination and toxic concentrations in roots. In contrast, *S. terebinthifolius* was not affected by the PM revealing species resistance to the pollution. The difference among species response suggests that over a long time period the imbalance will likely change the species composition (Kuki et al., 2009, 190411).

The process of removing toxins from soil or water using photoautotrophs is referred to as phytoremediation. Some plant species have good ability to extract heavy metals from soil, thereby offering potential for phytoremediation (Clemens, 2006, 190179; Hooda, 2007, 190382; Padmavathiamma and Li, 2007, 190465) . For example, several species of willow (*Salix* spp.) accumulate high concentrations of Zn and Cd in aboveground biomass (Lunácková et al., 2003, 155948; Meers et al., 2007, 155977; Rosselli et al., 2003, 156058). A first estimation of the order of magnitude of potential metal removal by willow was 2 to 27 kg/ha/yr of Zn and 0.25 to 0.65 kg/ha/yr for Cd (Meers et al., 2007, 155977). Build-up of high concentrations of trace metals in soil is difficult to remediate because of the long residence times of metals in the environment. Plants that survive on heavy metal-contaminated soils have been studied to elucidate the mechanisms that allow them to tolerate such conditions and interactions between soil contamination and vegetation composition (Becker and Brändel, 2007, 156260; Hall, 2002, 190365). There are numerous other plants that have been investigated for application to phytoremediation. Plants that hyperaccumulate metals have special potential for remediation of metal-contaminated sites. About 400 species have been reported. Brassicaceae has the largest numbers of taxa, with 11 genera and 87 species known to hyperaccumulate one or more metal contaminants (Prasad and DeOliveira, 2003, 156885).

Plant uptake is often the first step for a metal to enter higher levels of the food web. Consumers of vegetation may often receive heavy loading of metals from their diets. Metals may also bioaccumulate in some species and tissue concentrations are magnified at the higher trophic levels, so-called biomagnifications (see Section 9.4.5.7. on Biomagnification).

9.4.5.4. Effects on Aquatic Ecosystems

The atmospheric deposition of PM into the ocean has important implications for primary productivity and carbon sequestration. In part, metals in PM deposition may limit phytoplankton growth in parts of the ocean (Crawford et al., 2003, 156370). In particular, Fe and Zn can influence the productivity of algae that are involved in $CaCO_3$ production. The production of both particulate organic C and $CaCO_3$ drive the ocean's biological carbon pump (Shulz et al., 2004, 156087). Thus, in oceanic areas of trace metal limitation, changes in trace metal atmospheric deposition can affect biogenic calcification, with potential consequences for CO_2 partitioning between the ocean and atmosphere.

A study by Sheesley et al. (2004, 156084) illustrated the value of bioassay procedures to provide an initial screening of ambient PM toxicity. They used two species of green algae and two extraction methods to compare the toxicities of atmospheric PM collected at two urban/industrial sites and one rural site near the southern shore of Lake Michigan. Toxicities varied by site, by extraction solvent, and by bioassay. Results suggested that toxicity was not related to the total mass of PM in the extract, but to the chemical components of the PM. It is noteworthy that the concentrations of contaminants in PM in this type of short-term and acute toxicity testing are much higher than would be found in the natural environment. Thus, the purpose of this type of testing is to provide an initial screening-level comparison of relative toxicities of atmospheric PM from different source areas. It does not provide the data that would be needed to assess risk (Sheesley et al., 2004, 156084).

9.4.5.5. Effects on Animals

There has been little work focusing on animal indicators of PM effects in the field. However, there have been several recent studies on snails, amphibians, earthworms, and bivalves that are discussed below.

Bioindicator organisms can be especially useful for monitoring PM effects over geographical and temporal scales. Terrestrial invertebrates have been used to monitor contaminants in both air and soil. Snails (*Helix* sp.) accumulate trace metals and agrochemicals, and can be used as effective biomonitors for urban air pollution (Beeby and Richmond, 2002, 155680; Regoli et al., 2006, 156046; Viard et al., 2004, 055675). Demonstrated biological effects include growth inhibition, impairment of reproduction, and induction of metallothioneins that are involved in metal detoxification (Gomot-de and Kerhoas, 2000, 155798; Regoli et al., 2006, 156046). The use of sentinel species to detect the effects of complex mixtures of air pollutants is of particular value because the chemical constituents are difficult to characterize, exhibit varying bioavailability, and are subject to various synergistic effects.

Regoli et al. (2006, 156046) caged land snails (*Helix aspersa*) at five locations in the urban areas of Ancona, Italy. After four weeks of exposure to ambient air pollution, the snails were analyzed for trace metals and PAHs. Biomarkers were measured that correlated with contaminant accumulation, including concentrations of metallothioneins, activity of biotransformation enzymes, and peroxisomal proliferation. In addition, indicators of oxidative stress were measured, such as oxyradical scavenging capacity, onset of cellular damage, and loss of DNA integrity. Results documented substantial accumulation of metals and PAHs in snail digestive tissues in urban areas having high traffic congestion. Cellular reactivity was also found, suggesting that this species is an effective bioindicator for multipollutant air quality and PM monitoring.

Some amphibian ecotoxicological research has focused on heavy metal exposure. Contaminant uptake can occur by oral, pulmonary, and dermal exposure (James et al., 2004, 155874; Johnson et al., 1999, 155880; Lambert, 1997, 155916). This is potentially important because of documented declines in amphibian populations in the U.S. and elsewhere in recent decades (Houlahan et al., 2000, 155853). Toads were shown to be fairly tolerant of Cd exposure (James et al., 2004, 155874). It is not clear whether current amounts of terrestrial metal contamination pose an increased risk to amphibians in general.

Estuarine and marine bivalves provide potential bioindicators for Hg bioaccumulation. For example, Coelho et al. (2006, 190181) investigated Hg concentrations in *Scrobicularia plana*, a long-lived, deposit-feeding bivalve in southern Europe. Annual bioaccumulation rates were shown to be strongly correlated with Hg concentrations in suspended particulate matter (SPM), a response to

their deposit-feeding tactics (Verdelhos et al., 2005, 190497). The ability to predict annual accumulation rates for indicator species, such as this bivalve, may facilitate management actions to avoid deleterious effects on humans through consumption of bivalves above a certain age/size class.

Earthworms often constitute a large percentage of soil animal biomass and they are considered to be relatively sensitive indicators of soil metal contamination. They are continuously exposed to the soil via dermal contact in the soil solution or ingestion of large quantities of soil pore water, polluted food and/or soil particles (Lanno et al., 2004, 190415). Hobbelen et al. (2006, 190371) determined the important metal pools for bioaccumulation by earthworms *Lumbricus rubellus*, which live in the upper 5cm of soil and *Aporrectodea caliginosa*, which live in the upper 25 cm of soil. Soil concentration explained much of earthworm concentrations, however Cd concentration in *A. calinginosa* was best explained by pore water concentrations and no variable tested explained Zn tissue concentrations. Massicotte et al. (2003, 155968) compared the cell viability and phagocytic potential of three earthworm species (*Lumbricus terrestris*, *Eisenia andrei*, and *Aporrectodea tuberculata*) in response to atmospheric emissions of metals from a cement factory in Quebec, Canada. Cell viability actually increased in proximity (0.5 km) to the cement factory for *A. tuberculata*, and this might have been due to beneficial effects of increased Ca deposition. There were no significant differences observed for the other two species (Massicotte et al., 2003, 155968).

Biogeochemical cycling of Hg in the Arctic has been investigated, in part because observed Hg concentrations in marine animals may pose health risks for local human populations. The lifetime of gaseous elemental Hg (GEM) in the atmosphere, which constitutes about 95% of atmospheric Hg, is generally about one year (Lin and Pehkonen, 1999, 190426). However, during spring (typically March through June), the lifetime of GEM in the Arctic is much shorter, and atmospheric GEM can be depleted in less than one day during atmospheric Hg depletion episodes (AMDE) (Lindberg et al., 2002, 190429; Skov et al., 2004, 190481). During the AMDE, GEM is rapidly oxidized to reactive gaseous Hg that can be deposited to the ground surface (Skov et al., 2004, 190481). Because of the increased solar flux to the Arctic during spring and seasonal melting of sea ice, there may be an increased efficiency of Hg bioaccumulation in Arctic food webs than would be expected based on data collected at mid-latitudes. Skov et al. (2004, 190481) developed a simple parameterization for AMDE and included it in the Danish Eulerian Hemispheric Model (DEHM). The model was shown to reproduce the general structure of AMDE, suggesting that the limiting factor for AMDE may be the surface temperature of sea ice.

9.4.5.6. Biomagnification across Trophic Levels

Biomagnification is the progressive accumulation of chemicals with increasing trophic level (LeBlanc, 1995, 155921). Organic Hg is the most likely metal to biomagnify, in part because organisms can efficiently assimilate methylmercury and it is slowly eliminated (Croteau et al., 2005, 156373; Reinfelder et al., 1998, 156047). Of the trace metals, there is also evidence that Cd, Pb, Zn, Cu and Se biomagnify.

The study of trophic transfer and biomagnification is limited by the difficulty in discriminating food webs and the uncertainty associated with assignment of trophic position to individual species (Croteau et al., 2005, 156373). Use of stable isotopes can help to establish linkages. However, it is difficult to determine the extent to which biomagnification occurs in a given ecosystem without thoroughly investigating physiological biodynamics, habitat, food web structure, and trophic position of relevant species. Thus, development of an understanding of ecosystem complexity is necessary to determine what species might be at greatest risk from toxic metal exposure (Croteau et al., 2005, 156373).

Terrestrial

Bioaccumulation of heavy metals can occur through the plant-herbivore and litter-detrivore food webs. The U.S. EPA (2004, 056905) concluded that Cd and Zn can bioaccumulate in earthworms. Other invertebrates inhabiting soil litter may also accumulate metals. Although food web accumulation of a metal may not result in mortality, it might reduce breeding potential or result in other non-lethal effects that adversely affect organism responses to environmental cues.

Metal accumulation in litter can be found mainly around brass works, cement factories, and Pb and Zn smelters. Organisms that feed on earthworms living in soils with elevated metal

concentrations may also accumulate Pb and Zn. Increased concentrations of heavy metals have been found in a variety of mammals living in areas with elevated heavy metal concentrations in the soils.

The transfer of metals from plants to terrestrial snails is an interesting system for biomagnifications because snails accumulate metals in their soft tissue and can contribute significantly to the transfer of pollutants to primary consumers and terrestrial predators (Dallinger et al., 2001, 192109). Notten et al. (2005, 190461) studied the transfer of Cu, Zn, Cd and Pb in terrestrial soil-plant-snail food chains in metal-polluted soils of the Netherlands. The food chain included perennial plant species *Urtica dioica* and the herbivorous snail *Cepaea nemoralis*. The transfer of metal from the soil to the plant compartment was low (coefficient of determination $R^2 = 0.20$). Total concentration of metals in soils was a poor predictor of leaf concentration. Low metal concentration in the leaves was thought to be due to low pore water metal concentrations and was also thought to be partly caused by low translocation from roots within the plant. The Cu, Zn and Cd concentrations in the snails were always higher than concentrations in the leaves indicating bioaccumulation. The metal transfer from the leaf to snail was highest among all routes tested, suggesting that transfer from diet is important. Similar results were found by Beeby and Richmond (2002, 155680) with the snail, *Helix aspersa*, and the plant, *Taraxacum sp.*, for Zn, Pb, Cd, but not for Cu.

Many types of predators including shrews, thrushes and beetle larvae include snails as part of their diet (Gomot-De and Pihan, 2002, 190357; Seifert et al., 1999, 190480). Seifert et al. (1999, 190480) found the shrews eating snails with elevated Cd had critical levels of Cd in their kidneys. Scheifler et al. (2007, 190379) found that Cd in snails lead to toxic levels in beetle larvae that caused increased amounts of mortality.

Aquatic

In general, it has been assumed that metal biomagnification in aquatic ecosystems is an exception rather than the rule (Gray, 2002, 155806). More recent research has demonstrated aquatic biomagnification of certain metals. For example, Stewart et al. (2004, 156097) used stable isotopes of C and N to show biomagnification of Se in San Francisco Bay food webs. Croteau et al. (2005, 156373) identified trophic position of estuarine organisms and food web structure in the delta of San Francisco Bay to document Cd biomagnification in invertebrates that live on macrophytes and also in fish. Concentrations of Cd were biomagnified 15 times within two trophic links in each food web. In contrast, no tendency towards biomagnification was observed for Cu.

In aquatic ecosystems, biomagnification of trace metals does not necessarily occur. Nguyen et al. (2005, 155997) found biodiminution for most metals in Lake Balaton, Hungary, with the exception of slight enrichment of Zn from PM to zooplankton and of Cd from sediment to mussels.

Once transported to aquatic ecosystems, trace metals often preferentially bind to sediment particles. Some of these sediment-bound metals may be unavailable to biota; in contrast, metals bound to sediment organic matter may exhibit varying degrees of bioavailability (Di Toro et al., 2005, 155750). Piol et al. (2006, 156028) studied the bioavailability of sediment-bound Cd to the freshwater oligochaete *Lumbriculus variegatus*. They found that Cd uptake depended on the amount of free dissolved Cd(II), and the Cd contribution from sedimentary particles to biological uptake was negligible.

Marine bivalve mollusks bioaccumulate trace metals and other contaminants (LaBrecque et al., 2004, 155913) and therefore may be used as bioindicators of contamination. In addition, they constitute an important link to human health by virtue of their importance as a food source (Cheggour et al., 2005, 155723; Li et al., 2002, 156691).

9.4.5.7. Effects near Smelters and Roadsides

The high PM concentrations in proximity to mining, smelting, roadsides and other industrial sources result in heavy metal loadings that may be particularly damaging to nearby ecosystems.

Smelters

The Harjavalta region is one of the most intensively studied heavy metal polluted areas in the world. Kiikkilä et al. (2003, 156637) reviewed available data on heavy metal deposition and environmental effects in this area. Emissions from the smelter were as high as 1,100 t/yr of dust, 140 t/yr Cu, 96 t/yr Ni, 162 t/yr Zn, and 94 t/yr Pb in 1987. Deposition amounts decreased substantially after 1990, to only a few percent of the amounts that occurred during the 1980s.

Kiikkilä (2003, 156637) investigated the effects of heavy metal pollution in proximity to a Cu-Ni smelter at Harjavalta, Finland. The deposition of heavy metals increased within 30 km of the smelter. Only slight changes in the understory vegetation were observed at distances greater than 8 km from the smelter. At 4 km distance, species composition of vegetation, insects, birds, and soil microbiota changed and tree growth was reduced. Within about 1 km, only the most resistant organisms were surviving.

The number of soil organisms clearly decreased and their community structure was altered close to the Harjavalta smelter (Kiikkilä, 2003, 156637). However, this effect was only pronounced within about 2 km of the smelter. This suggests that the soil microfauna are relatively resistant to metal pollution effects.

Soil microbial activity decreased close to the Harjavalta smelter (Kiikkilä, 2003, 156637), as reflected by microbial respiration, distribution of species within physiological groups, and microbial and fungal biomass. The fungi appeared to be more sensitive to metal contamination than the bacteria (Pennanen et al., 1996, 156016). The rate of litter decomposition decreased, causing an accumulation of needle litter on top of the forest floor near the smelter (Fritze et al., 1989, 079635).

Inhibition of nutrient cycling and displacement by Cu and Ni of base cations from cation exchange sites on the soil resulted in a decrease in base cation concentrations in the organic soil layer (Derome and Lindroos, 1998, 155749; Kiikkilä, 2003, 156637) close to the Harjavalta smelter. In addition, Mg, Ca, and Mn concentrations in Scots pine (*Pinus sylvestris*) needles were low, and this was attributed by Kiikkilä (2003, 156637) to the toxic effects of Cu and Ni to plant fine roots and also to ectomycorrhizal root tips (Helmisaari et al., 1999, 155836). Nutrient translocation during fall was also affected close to the smelter; as a consequence needle concentrations of K were relatively high (Nieminen et al., 1999, 155998).

Tree growth (Scots pine) has been poor (Malkönen et al., 1999, 155961) and most vegetation was absent within 0.5 km of the smelter. Effects on plant species occurrence close to the smelter were almost entirely negative. In contrast, some animal species responded positively, including a leaf miner, three species of aphid, and some ants, beetles, and spiders.

Salemaa et al. (2004, 156069) investigated heavy metal concentrations in understory plant species growing at varying distances from the Harjavalta Cu-Ni smelter. Heavy metal concentrations (except Mn) were highest in bryophytes, followed by lichens, and were lowest in vascular plants. Vascular plants are generally able to restrict the uptake of toxic elements, and therefore were able to grow closer to the smelter than lichens. A pioneer moss (*Pohlia nutans*) was unusual in that it survived close to the smelter despite its accumulation of high amounts of Cu and Ni.

Changes in breeding success of cavity-nesting passerine birds close to the Harjavalta smelter were attributed to habitat changes in response to metal toxicity (Eeva et al., 2000, 155761; Kiikkilä, 2003, 156637). Calcium supply is also well known to be important for breeding success in passerine bird species. Eggshell thickness, egg size, clutch size, and hatchability of pied flycatcher (*Ficedula hypoleuca*) were found to be depressed near the Cu smelter at Harjavalta, SW Finland (Eeva and Lehikoinen, 2004, 155762). Availability of Ca-rich food to the birds was estimated by counting snail shells in the nests postfledging. The number of snail shells correlated positively with the Ca concentration of nestling feces and adult breeding success. In addition, the negative impact of Cu on the number of fledglings was stronger at locations where Ca concentration was low (Eeva and Lehikoinen, 2004, 155762).

Documentation of effects on individual species, such as was reported above, does not reveal what the impacts might be on ecosystem function. Nevertheless, the mere fact that multiple species, operating at different trophic levels, have been shown to be affected by the ambient deposition in proximity to the smelter suggests that effects on ecosystem function may indeed have occurred. More research is needed, however, to fully evaluate effects on function as opposed to abundance of individual species.

Roadsides

Heavy metal particles are important constituents of road dust. These particles accumulate on the road surface from brake linings, road paint, tire debris, diesel exhaust, road construction materials, and catalyst materials. Road dust can be suspended in the atmosphere and contribute metals to soil, air, and urban runoff (Adachi and Tainosho, 2004, 081380; Davis et al., 2001, 024933; Smolders and Degryse, 2002, 156091). In particular, Zn oxide comprises 0.4-4.3% of tire tread (Smolders and Degryse, 2002, 156091) and tire wear is a substantial source of environmental Zn pollution. Adachi and Tainosho (2004, 081380) used a field emission screening electron microscope equipped with an energy dispersive x-ray spectrometer to characterize heavy metal particles embedded in tire dust. Samples were classified into four likely source categories, based on cluster analysis. Based on morphology and chemical composition, the samples were identified as having derived from yellow paint ($CrPbO_4$ particles), brake dust (particulate Ti, Fe, Cu, Sb, Zr, Ba and heavy minerals [Y, Zr, La, Ce]), and tire tread (Zn oxide).

Since publication of EPA's 2004 PM criteria assessment, some additional research has been conducted on the effects of windblown PM. Effects on physical, chemical, and biological attributes of both plants and animals have been documented (Englert, 2004, 087939; Gleason et al., 2007, 155794; Kappos et al., 2004, 087922). Experiments by Gleason et al. (2007, 155794) suggest that most direct effects on plants of windblown PM originating from on-road surfaces occur within 40 m of the source. Windblown PM from roads or agriculture can cover plant photosynthetic structures (Sharifi et al., 1999, 156082), cause impact damage (Armbrust and Retta, 2002, 156225), or interfere with physiological mechanisms (Burkhardt et al., 2002, 155708). As previously discussed in Section 9.4.5.5, land snails in urban areas have been shown to be a good indicator of traffic pollution.

9.4.5.8. Toxicity to Mosses and Lichens

At the time of the most recent air quality criteria report for PM (U.S. EPA, 2004, 056905), trace metal toxicity to lichens had been demonstrated in relatively few cases. Nash (1975, 016763) documented Zn toxicity in the vicinity of a Zn smelter near Palmerton, PA. Experimental data had suggested that lichen tolerance to Zn and Cd generally ranges between 200 and 600 ppm (Nash, 1975, 016763).

The effects of deposited metals on the mosses have not been well studied. Tremper et al. (2004, 156126) exposed mosses of two species to roadside conditions and sampled them over a period of 3 mo. Under field conditions, chlorophyll concentrations in moss tissue were not affected by metal contamination and accumulation

Mosses and lichens readily take up metals from atmospheric deposition. Otnyukova (2007, 156009) demonstrated vertical gradients within a coniferous forest canopy in the fruticose lichen genus *Usnea* with respect to lichen thallus morphology and heavy metal concentration. Abnormal thalli at the tree-top level contained higher concentrations of Al, Fe, Zn, F, Sr, and Pb. This vertical pattern within the tree canopy is in general accordance with known deposition of PM to plants (Otnyukova, 2007, 156009).

There is an extensive literature on the use of mosses and lichens for estimating deposition (biomonitors) and indicating metal exposure in ecosystems (bioindicators) (see Section 9.4.2.3.).

9.4.6. Organic Compounds

VOCs in the atmosphere are partitioned between the gas and particle phases. As described by the U.S. EPA (2004, 056905), the partitioning depends on vapor pressure, temperature, surface area of the particles, and the nature of the particles and of the chemical being adsorbed. A wide variety of organic contaminants are deposited from the atmosphere. These include chemicals such as DDT, PCBs, and PAHs.

Important organic atmospheric contaminants are generally those that are transported long distances in the atmosphere, subsequently deposited into remote locations, and bioaccumulated to sufficient concentrations that they can affect humans, wildlife, or other biota (Swackhamer et al., 2004, 190488). Certain physical and chemical properties facilitate the movement of these contaminants from land and water surfaces into the atmosphere, provide stability, and enhance accumulation in lipids. Some, including the relatively small (up to 4 rings) PAHs degrade relatively

rapidly in the atmosphere or at the surface subsequent to atmospheric deposition. Below is a summary of the findings of the U.S. EPA (2004, 056905), followed by discussion of more recent research findings.

Plants may be used as passive monitors to compare the deposition of organic compounds between sites. Vegetation can be used semi-quantitatively to indicate organic pollutant amounts if the mechanism of accumulation is considered. Organic compounds can enter the plant via the roots or be deposited as particles on the leaves and be taken up through the cuticle or stomata. The pathways depend on the chemical and its physical properties. These include, for example, lipophilicity, water solubility, vapor pressure, and Henry's law constant. Environmental conditions can also be important, including temperature and organic content of soil, plant species, and the foliar surface area and lipid content.

Organic particulates in the atmosphere are diverse in their makeup and sources. Vegetation itself is an important source of hydrocarbon aerosols. Terpenes, particularly α-pinene, β-pinene, and limonene, released from tree foliage may react in the atmosphere to form submicron particles. These naturally generated organic particles contribute significantly to the blue-haze aerosols formed naturally over forested areas (Geron et al., 2000, 019095; U.S. EPA, 2004, 056905).

The low water solubility and high lipo-affinity of many organic xenobiotics control their interaction with the vegetative components of natural ecosystems. Foliar surfaces are covered with a waxy cuticle layer that helps reduce moisture loss and short-wave radiation stress. This epicuticular wax consists largely of long-chain esters, polyesters, and paraffins, which accumulate lipophilic compounds. Organic air contaminants in the particulate or vapor phase can be adsorbed to, and accumulate in, the epicuticular wax of leaf surfaces. Direct uptake of organic contaminants through the cuticle and vapor-phase uptake through the stomata are not well characterized for most trace organics.

Soil acts as an important storage compartment for POPs, including PCBs and PAHs. There is a continuous process of partitioning between the soil pool and the atmosphere, and this controls the regional and global transport of these compounds (Backe et al., 2004, 155668; Wania and Mackay, 1993, 157110). Over time, POPs move towards equilibrium between the environmental compartments, and this process can be described using the fugacity concept (Backe et al., 2004, 155668; Mackay, 1991, 042941). Fugacity reflects the tendency of a chemical constituent to escape one environmental compartment and move to another. When an equilibrium distribution is achieved, the fugacity quotient values in each compartment will be equal. Soil/air partitioning is controlled by a variety of factors. These include soil properties, such as organic matter content, moisture, porosity, texture, and structure, as well as the physiochemical properties of the pollutant, including vapor pressure and water solubility.

The accumulation of PAHs in vegetation, due to their lipophilic nature, could contribute to human and other animal exposure via food consumption. As a result, plant uptake of PAHs has been an important area of research (Gao and Zhu, 2004, 155782). Most bioaccumulation of PAHs by plants occurs by leaf uptake (Tao et al., 2006, 156112). Root uptake also occurs. It appears that roots preferentially accumulate the lower molecular weight PAHs due to their greater water solubility (Wild and Jones, 1992, 156155).

Various models have been developed to simulate plant uptake of organic contaminants. The simple partition-limited model of Chiou et al. (2001, 156342) has been further expanded to increase complexity and to include root uptake pathways (e.g., Fryer and Collins, 2003, 156454; Yang et al., 2005, 192104; Zhu et al., 2004, 156184).

In evaluating receptor choice for studies of contaminant exposure to plants, and also remediation potential, it is important to consider differences among species. For example, Parrish et al. (2006, 156014) assessed the bioavailability of PAHs in soil. During the first growing season, zucchini (*Cucurbita pepo* ssp. *pepo*) accumulated significantly more PAHs than did other related plant species, including up to three orders of magnitude greater concentrations of the six-ring PAHs. Parrish et al. (2006, 156014) also noted differences in PAH uptake by two different species of earthworm.

The leaves of *Quercus ilex* have been shown to readily accumulate PAHs *in situ*. Young leaves accumulated PAHs within three weeks of bud break. Mature leaves showed seasonality, with higher PAH concentrations during winter (Alfani et al., 2005, 154319).

It is difficult to discriminate between PAHs that are adsorbed to plant root surfaces as opposed to those that are actually taken up by the roots. In general, soil bound PAHs are associated with soil organic matter and are therefore not readily available for root uptake (Fismes et al., 2002, 141156;

Jiao et al., 2007, 155879). Wild et al. (2005, 156156) used two-photon excitation microscopy to visualize the uptake and transport of two PAHs (anthracene and phenanthrene) from a contaminated soil into living wheat and maize roots. Jiao et al. (2007, 155879) developed a sequential extraction method to discriminate between PAH adsorption in rice roots.

Maize roots and tops of plants have been shown to directly accumulate PAHs from aqueous solution and from air in proportion to exposure amounts. Root concentration factors are log-linear functions of log-based octanol-water partition coefficients (log K_{ow}); similarly, leaf concentration factors are log-linear functions of log-based octanol-air partition coefficients (log K_{oa}) (Lin et al., 2007, 155933). Although the bulk concentrations of PAHs in various plant tissues can differ greatly, the observed differences disappear after they are normalized to lipid content (Lin et al., 2007, 155933). This suggests that the lipid content of different plant tissues may influence PAH distribution within the plant.

Previously, there was relatively little information available regarding incorporation of atmospherically deposited PAHs into aquatic food webs. It is known that PAHs can be transferred to higher trophic levels, including fish, and that this transfer can be mediated by aquatic invertebrates, which generally comprise an important part of fish diets. High mountain lakes offer an effective receptor for quantification of biomagnification in aquatic ecosystems from atmospheric PM deposition. There are typically no sources of organic contaminants in their watersheds, and atmospheric inputs dominate as sources of contamination. In addition, such lakes tend to have relatively simple food webs. Vives et al. (2005, 157099) investigated PAH content of brown trout (*Salmo trutta*) and their food items. Total PAH concentrations tended to be highest in organisms that occupy littoral habitats, and lowest in pelagic organisms. This may reflect more efficient transfer of PAHs to underlying sediments in shallower water and associated degradation within the water column.

Some atmospheric organic contaminants have been shown to accumulate in biota at remote locations. For example, polybrominated diphenyl ethers (PBDEs), which are man-made chemicals used as flame retardants in materials manufacturing, have been found to accumulate in lichens and mosses collected at King George Island, maritime Antarctica (Yogui and Sericano, 2008, 189971). Because contaminant concentrations were not statistically different at sites close to and distant from human facilities in Antarctica, the authors concluded that long-range atmospheric transport was the likely primary source of PBDEs to King George Island. Law et al. (2003, 190420) reviewed available data for accumulation of PBDEs and other brominated flame retardants in wildlife. These compounds have become widely distributed in the environment, including in the deep-water, oceanic food webs.

Ohyama et al. (2004, 190462) chose salmonid fish, mainly rainbow trout (Oncorhyncus mykiss), as an indicator species to evaluate the transport and bioaccumulation of organochloride compounds in the northern and central Sierra Nevada. They found that elevation was an important factor affecting residual concentrations of polychlorinated biphenyls (PCBs) in fish muscle tissue. On this basis, Ohyama et al. (2004, 190462) concluded that PCB residue in rainbow trout, a widely distributed salmonid species, provided a good monitoring tool for studying the effects of mountainous topography on the long-range transport and distribution of persistent organic pollutants.

Semivolatile compounds can undergo repeated volatilization on surfaces, such as plant foliage, in response to diel changes in temperature. As a consequence, such compounds can be deposited, re-emitted, and re-deposited multiple times. This behavior can cause these compounds to move large distances in a leap-frog fashion (Krupa et al., 2008, 198696). It is believed that POPs can be atmospherically transported throughout the world because of their volatility and response to changes in temperature. This "global distillation theory" (Holmqvist et al., 2006, 190380; Wania and Mackay, 1993, 157110) predicts that POPs in the northern hemisphere are generally transported towards the Arctic, and in the southern hemisphere they are transported toward the Antarctic. In general, POP concentrations measured in the Arctic are higher than in the Antarctic. They have been detected in all levels of the Arctic food web (Oehme et al., 1995, 011267). Bioconcentration of organochlorines has been shown in the Arctic food web, including fish, seals, and polar bears (Oehme et al., 1995, 011267). Concentrations measured in Arctic polar bears are especially high (AMAP, 2004, 190168).

Holmqvist et al. (2006, 190380) measured levels of PCBs in longfin eels (*Anguilla dieffenbachii*) in 17 streams on the west coast of South Island, New Zealand. The PCBs were at low levels, and were believed to originate from atmospheric transport from industrial areas in Asia. Characteristics of the longfin eel that make it susceptible to bioaccumulation of lipophilic persistent

pollutants include high lipid content (up to 40%), long lifespan (up to 90 yrs), and position near the top of the food chain (Holmqvist et al., 2006, 190380).

Long-range transport of atmospherically deposited contaminants can be augmented by biotransport. A good example of this phenomenon was documented by Ewald et al. (1998, 190348), who showed that biotransport by migrating sockeye salmon (*Oncorhynchus nerka*) in the Copper River watershed, Alaska, had a greater influence than atmospheric transport on bioaccumulation of PCBs and DDT in lake food webs. Organic pollutants accumulated by salmon during their ocean residence were effectively transferred 410 km inland to their spawning lake. Arctic grayling (*Thymallus arcticus*) in the salmon spawning lake were found to contain organic pollutants more than twice as high as arctic grayling in a near-by salmon-free lake. The pollutant composition of the grayling in the salmon spawning lake was similar to that of the migrating salmon (Ewald et al., 1998, 190348), suggesting that salmon migration contributed to bioaccumulation of organic contaminants in the lake used for spawning by the salmon.

An assessment of the ecological effects of airborne metals and SOCs was conducted for eight NPs by the Western Airborne Contaminants Assessment Project (WACAP) (Landers et al., 2008, 191181). From 2002-2007, WACAP researchers conducted analysis of the biological effects of airborne contaminants in seven ecosystem compartments: air, snow, water, sediments, lichens, conifer needles and fish. The goals were to identify where the pollutants were accumulating, identify ecological indicators for those pollutants causing ecological harm, and to determine the source of the air masses most likely to have transported the contaminants to the parks.

The results from WACAP were summarized by Landers et al. (2008, 191181), which concluded that bioaccumulation of SOCs were observed throughout park ecosystems. Vegetation tended to accumulate PAHs, CUPs, and HCHs. Conifer needles were a good indicator of pesticides, however the ecological consequences of this accumulation are unexamined. SOCs in vegetation and air showed different patterns, possibly because each medium absorbs different types of SOCs with varying efficiencies. Mean ammonium nitrate concentration in ambient fine particulates <2.5 μm diameter was a good predictor of dacthal, endosulfan, chloradane, trifluralin, DDT and PAH concentrations in vegetation.

Concentrations of SOCs were five to seven orders of magnitude higher in fish tissue than in sediments. Fish accumulated more PCBs, chlordanes, DDT and dieldrin than vegetation. Fish lipid and age were the most reliable predictors of SOC concentrations. Most fish appeared normal during field necropsies; however, individuals with both male and female reproductive organs were collected at two sites. The incidence of this condition has increased since the pre-organic pollutant era. Additionally, elevated concentrations of vitellogenin, a female protein involved in egg production, were found in male fish from three sites, and directly related to the concentration of several organochlorines at one site.

The lake sediment records showed steadily increasing mercury deposition over time at lakes in two parks, Mt. Ranier NP and Rocky Mountain NP. Apportionment of the mercury to its atmospheric sources is not quantified at this time; however, the pattern in the sediment suggests a local source rather than a global source. Mercury concentrations in fish exceeded contaminant health thresholds for some piscivorous fish, mammals and birds in most parks. The average mercury concentration in fish from one site and individual fish from three additional sites exceeded the U.S. EPA contaminant health thresholds for humans.

Although this assessment focuses on chemical species that are components of PM, it does not specifically assess the effects of particulate versus gas-phase forms; therefore, in most cases it is difficult to apply the results to this assessment based on particulate concentration and size fraction.

9.4.7. Summary of Ecological Effects of PM

Ecological effects of PM include direct effects to metabolic processes of plant foliage; contribution to total metal loading resulting in alteration of soil biogeochemistry and microbiology, plant and animal growth and reproduction; and contribution to total organics loading resulting in bioaccumulation and biomagnification across trophic levels. These effects were well-characterized in the 2004 PM AQCD (U.S. EPA, 2004, 056905). Thus, the summary below builds upon the conclusions provided in that review.

PM deposition comprises a heterogeneous mixture of particles differing in origin, size, and chemical composition. Exposure to a given concentration of PM may, depending on the mix of deposited particles, lead to a variety of phytotoxic responses and ecosystem effects. Moreover, many

of the ecological effects of PM are due to the chemical constituents (e.g., metals, organics, and ions) and their contribution to total loading within an ecosystem.

Investigations of the direct effects of PM deposition on foliage have suggested little or no effects on foliar processes, unless deposition levels were higher than is typically found in the ambient environment. However, consistent and coherent evidence of direct effects of PM has been found in heavily polluted areas adjacent to industrial point sources such as limestone quarries, cement kilns, and metal smelters (Sections 9.4.3 and 9.4.5.7). Where toxic responses have been documented, they generally have been associated with the acidity, trace metal content, surfactant properties, or salinity of the deposited materials.

An important characteristic of fine particles is their ability to affect the flux of solar radiation passing through the atmosphere, which can be considered in both its direct and diffuse components. Foliar interception by canopy elements occurs for both up- and down-welling radiation. Therefore, the effect of atmospheric PM on atmospheric turbidity influences canopy processes both by radiation attenuation and by changing the efficiency of radiation interception in the canopy through conversion of direct to diffuse radiation. Crop yields can be sensitive to the amount of radiation received, and crop losses have been attributed to increased regional haze in some areas of the world such as China. On the other hand, diffuse radiation is more uniformly distributed throughout the canopy and may increase canopy photosynthetic productivity by distributing radiation to lower leaves. The enrichment in photosynthetically active radiation (PAR) present in diffuse radiation may offset a portion of the effect of an increased atmospheric albedo due to atmospheric particles. Further research is needed to determine the effects of PM alteration of radiative flux on the growth of vegetation in the U.S.

The deposition of PM onto vegetation and soil, depending on its chemical composition, can produce responses within an ecosystem. The ecosystem response to pollutant deposition is a direct function of the level of sensitivity of the ecosystem and its ability to ameliorate resulting change. Many of the most important ecosystem effects of PM deposition occur in the soil. Upon entering the soil environment, PM pollutants can alter ecological processes of energy flow and nutrient cycling, inhibit nutrient uptake, change ecosystem structure, and affect ecosystem biodiversity. The soil environment is one of the most dynamic sites of biological interaction in nature. It is inhabited by microbial communities of bacteria, fungi, and actinomycetes, in addition to plant roots and soil macro-fauna. These organisms are essential participants in the nutrient cycles that make elements available for plant uptake. Changes in the soil environment can be important in determining plant and ultimately ecosystem response to PM inputs.

There is strong and consistent evidence from field and laboratory experiments that metal components of PM alter numerous aspects of ecosystem structure and function. Changes in the soil chemistry, microbial communities and nutrient cycling, can result from the deposition of trace metals. Exposures to trace metals are highly variable, depending on whether deposition is by wet or dry processes. Although metals can cause phytotoxicity at high concentrations, few heavy metals (e.g., Cu, Ni, Zn) have been documented to cause direct phytotoxicity under field conditions. Exposure to coarse particles and elements such as Fe and Mg are more likely to occur via dry deposition, while fine particles, which are more often deposited by wet deposition, are more likely to contain elements such as Ca, Cr, Pb, Ni, and V. Ecosystems immediately downwind of major emissions sources can receive locally heavy deposition inputs. Phytochelatins produced by plants as a response to sublethal concentrations of heavy metals are indicators of metal stress to plants. Increased concentrations of phytochelatins across regions and at greater elevation have been associated with increased amounts of forest injury in the northeastern U.S.

Overall, the ecological evidence is sufficient to conclude **that a causal relationship is likely to exist between deposition of PM and a variety of effects on individual organisms and ecosystems, based on information from the previous review and limited new findings in this review.** However, in many cases, it is difficult to characterize the nature and magnitude of effects and to quantify relationships between ambient concentrations of PM and ecosystem response due to significant data gaps and uncertainties as well as considerable variability that exists in the components of PM and their various ecological effects.

9.5. Effects on Materials

Effects of air pollution on materials are related to both aesthetic appeal and physical damage. Deposited particles, primarily carbonaceous compounds, cause soiling of building materials and culturally important items, such as statues and works of art. Physical damage from dry deposition of PM also can accelerate natural weathering processes. The major deterioration phenomenon affecting building materials in response to atmospheric deposition is most likely sulfation, leading to secondary salt crystallization which forms gypsum (Marinoni et al., 2003, 092520).

This section (a) summarizes information on exposure-related effects on materials associated with particulate pollutants as addressed in the 2004 PM AQCD (U.S. EPA, 2004, 056905); and (b) presents relevant information derived from very limited research conducted and published since completion of that document. Most recent work on this topic has been conducted outside the U.S.

There is a variety of factors that contribute to the deterioration of monuments and buildings of cultural significance. They include: (1) biodeterioration processes; (2) weathering of materials exposed to the air; and (3) air pollution from both anthropogenic and natural sources (Herrera and Videla, 2004, 155843). Because of the diversity in climate, proximity to marine aerosol sources, and pollution of various types, the magnitude and relative importance of these causal agents vary by location.

Much existing literature on damage to structural materials of cultural heritage has not seriously considered the importance of biodeterioration processes and the relationship that often exists between environmental characteristics and the microbial communities that colonize monuments and buildings. In general, high humidity, high temperature, and air pollution often enhance the biodeterioration hazard. Herrera and Videla (2004, 155843) concluded that heterotrophic bacteria, fungi, and cyanobacteria were the main microbial colonizers of buildings that they investigated in Latin America. Their analyses suggested that the major deterioration mechanism of limestone at the Mayan site of Uxmal in a non-polluted rural environment was biosolubilization induced by metabolic acids produced by bacteria and fungi. The rock decay at Tulum, near the seashore, was mainly attributed to the marine influence. At Medellin, it appeared that biodeterioration effects from microbes synergistically enhanced the effects of atmospheric factors on material decay. Deterioration of structural material in the Cathedral of La Plata, located in a mixed urban/industrial environment, was attributed mainly to atmospheric pollutants (Herrera and Videla, 2004, 155843).

Ambient particles can cause soiling of man-made surfaces. Soiling generally is considered an optical effect. Soiling changes the reflectance from opaque materials and reduces the transmission of light through transparent materials. Soiling can represent a significant detrimental effect, requiring increased frequency of cleaning of glass windows and concrete structures, washing and repainting of structures, and, in some cases, reduces the useful life of the object. Particles, especially carbon, may also help catalyze chemical reactions that result in the deterioration of materials (U.S. EPA, 2004, 056905).

Soiling is dependent on atmospheric particle concentration, particle size distribution, deposition rate, and the horizontal or vertical orientation and texture of the exposed surface (Haynie, 1986, 157198). The chemical composition and morphology of the particles and the optical properties of the surface being soiled will determine the time at which soiling is perceived by human observers (Nazaroff and Cass, 1991, 044577).

Ferm et al. (2006, 155135) reported development of a simple passive particle collector for estimating dry deposition to objects of cultural heritage. The observed mass of deposited particles mainly belonged to the coarse particulate mode. The sampler collects particles from all directions. It replicates at least some of the complexity of particle deposition to actual objects, and is easier to analyze than a precious object (Ferm et al., 2006, 155135).

Soiling of urban buildings constitutes a visual nuisance that leads to the loss of architectural value. Soiling can include reversible darkening of the building surfaces and also irreversible damage. Water runoff patterns on the building surfaces are influenced by the type of surface material, architectural elements, and climate. Therefore, soiling does not occur uniformly across the building. Public perception of soiling entails complex interactions between the extent of soiling, architecture, and aesthetics (Grossi and Brimblecombe, 2004, 155813).

One of the most significant air pollution damage features affecting urban buildings and monuments is the formation of black crusts. Quantification of different forms of carbon in black crusts is difficult. There is often a carbonate component which is derived from the building material, plus OC and EC, derived from air pollution. EC is considered to be a tracer for combustion sources,

whereas OC may derive from multiple sources, including atmospheric deposition of primary and secondary pollutants, and the decay of protective organic treatments (Bonazza et al., 2005, 155695). Bonazza et al. (2005, 155695) quantified OC and EC in damage layers on European cultural heritage structures. OC predominated over EC at almost all locations investigated. Traffic appeared to be the major source of fine carbonaceous particles, with organic matter as the main component (Putaud et al., 2004, 055545). Viles and Gorbushina (2003, 156138) found that soiling in Oxford, U.K. showed a relationship with traffic and NO_2 concentrations.

In addition to the soiling effects of EC, much soiling appears to be largely of microbiological origin (Viles and Gorbushina, 2003, 156138). Microbial biofilms, composed mainly of fungi, can stain exposed rock surfaces with yellow, orange, brown, gray, or black colors. Microorganisms may be able to trap PM more efficiently than the stone surface itself. In addition, microbial growth may be stimulated by organic or nutrient constituents in PM deposition.

Viles et al. (2002, 156137) investigated the nature of soiling on limestone tablets in relation to ambient air pollution and climate at three contrasting sites in Great Britain over periods of one to eight years. Spectrophotometer and microscope observations suggested that there were not consistent trends in soiling over time at the study sites. Each site behaved differently in terms of the temporal development of soiling and the differences between sheltered and exposed limestone tablets. In addition, organisms played important roles in the soiling response, even at the highly polluted site.

Some work has been conducted on public perception regarding the lightness of historic buildings and the aesthetic need for cleaning subsequent to soiling by air pollution. Brimblecombe and Grossi (2005, 155703) found a strong relationship between the perceived lightness of a building and the opinion that it was dirty. This relationship was used to establish levels of blackening that might be publicly acceptable.

Recently, the importance of organic contaminant deposition to the overall air pollution damage to building materials has been recognized. Low molecular weight organic anions such as formate, acetate, and oxalate are ubiquitous in black crusts in damage layers on stones and mortars sampled from monuments and buildings throughout Europe (Sabbioni et al., 2003, 049282). This has been observed at urban, suburban, and rural sites.

9.5.1. Effects on Paint

Studies have evaluated the soiling effects of particles on painted surfaces (U.S. EPA, 2004, 056905). Particles composed of EC, acids, and various other constituents are responsible for the soiling of structural painted surfaces. Coarse-mode particles (>2.5 μm) initially contribute more soiling of horizontal and vertical painted surfaces than do fine-mode particles (<2.5 μm), but are more easily removed by rain (Haynie and Lemmons, 1990, 044579). Rain interacts with coarse particles, dissolving the particle and leaving stains on the painted surface (Creighton et al., 1990, 044578; Haynie and Lemmons, 1990, 044579). Particle deposition contributes to increased frequency of cleaning of painted surfaces and physical damage to the painted surface. Air pollution affects the durability of paint finishes by promoting discoloration, chalking, loss of gloss, erosion, blistering, and peeling (U.S. EPA, 2004, 056905). There have been no new developments in this field subsequent to the review of the U.S. EPA (2004, 056905).

9.5.2. Effects on Metal Surfaces

Metals undergo natural weathering processes. The effects of air pollutants on natural weathering processes depend on the nature of the pollutant(s), the deposition rate, and the presence of moisture (U.S. EPA, 2004, 056905). Pollutant effects on metal surfaces are governed by such factors as the presence of protective corrosion films and surface electrolytes, the orientation of the metal surface, and surface moisture. Surface moisture facilitates particulate deposition and promotes corrosive reactions. Formation of hygroscopic salts increases the duration of surface wetness and enhances corrosion.

A corrosion film, such as for example the rust layer on the surface of some metals, may provide some protection against further corrosion. Its effectiveness in retarding the corrosion process is affected by the solubility of the corrosion layer and the pollutant exposure. Other than the effects of acidifying compounds, there has not been additional research conducted in recent years on the effects of PM deposition on metal corrosion.

9.5.3. Effects on Stone

Air pollutants can enhance the natural weathering processes on building stone. The development of crusts on stone monuments has been attributed to the interaction of the stone's surface with pollutants, wet or dry deposition of atmospheric particles, and dry deposition of gypsum particles. Because of a greater porosity and specific surface, mortars have a high potential for reacting with environmental pollutants (Zappia et al., 1998, 012037).

Most research evaluating the effects of air pollutants on stone structures has concentrated on gaseous pollutants (U.S. EPA, 2004, 056905). The dark color of gypsum is attributed to soiling by carbonaceous particles. A lighter gray colored crust is attributed to soil dust and metal deposits (Ausset et al., 1998, 040480; Camuffo, 1995, 076278; Lorusso et al., 1997, 084534; Moropoulou et al., 1998, 040485). Lorusso et al. (1997, 084534) attributed the need for frequent cleaning and restoration of historic monuments in Rome to exposure to total suspended particulates.

Grossi et al. (2003, 155812) investigated the black soiling rates of building granite, marble, and limestone in two urban environments with different climates. Horizontal specimens were exposed, both sheltered and unsheltered from rainfall. Limestone showed soiling proportional to the square root of the time of exposure, but granite and marble did not.

Black soiling is caused mainly by particulate EC (PEC). For that reason, it is most prevalent in urban environments due to the formation of carbonaceous fine particles from the incomplete combustion of fossil fuels. Traffic emissions, especially from diesel engines, and wood burning are important sources of PEC (Grossi et al., 2003, 155812).

Kamh (2005, 155888) studied the effects of weathering on Conway Castle, an historical structure in Great Britain built about 1289 AC. The weathering was identified as honeycomb, blackcrust, exfoliation, and discoloration, with white salt efflorescence at some parts. These features are diagnostic for salt weathering (Goudie et al., 2002, 156486), and this was confirmed by laboratory analyses, including scanning electron microscopy and x-ray diffraction. The authors concluded that the salt was derived from three sources: sea spray, chemical alteration of the carbonate in mortar into SO_4^{2-} salts by acidic deposition, and wet deposition of air pollutants on the stone surface. The salt content on the rock surface fills the rock pores and then exerts high pressure on the rock texture due to hydration of the salt in the cold humid environment. In particular, $CaSO_4$ and Na_2SO_4 exert enough pressure on hydration as to deteriorate construction rock at both the micro- and macroscale (Moses and Smith, 1994, 156785).

9.5.4. Summary of Effects on Materials

Building materials (metals, stones, cements, and paints) undergo natural weathering processes from exposure to environmental elements (wind, moisture, temperature fluctuations, sunlight, etc.). Metals form a protective film of oxidized metal (e.g., rust) that slows environmentally induced corrosion. However, the natural process of metal corrosion is enhanced by exposure to anthropogenic pollutants. For example, formation of hygroscopic salts increases the duration of surface wetness and enhances corrosion.

A significant detrimental effect of particle pollution is the soiling of painted surfaces and other building materials. Soiling changes the reflectance of opaque materials and reduces the transmission of light through transparent materials. Soiling is a degradation process that requires remediation by cleaning or washing, and, depending on the soiled surface, repainting. Particulate deposition can result in increased cleaning frequency of the exposed surface and may reduce the usefulness of the soiled material. Attempts have been made to quantify the pollutant exposure at which materials damage and soiling have been perceived. However, to date, insufficient data are available to advance the knowledge regarding perception thresholds with respect to pollutant concentration, particle size, and chemical composition. Nevertheless, the evidence is sufficient to conclude that **a causal relationship exists between PM and effects on materials.**

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Annex A. Atmospheric Science

A.1. Ambient Air Particle Monitoring

A.1.1. Measurements and Analytical Specifications

Table A-1. Summary of integrated and continuous samplers included in the field comparison.

Abbreviation	Instrument	Manufacturer / Research Institute
INTEGRATED PARTICLE OR GAS/PARTICLE INSTRUMENTS		
Dichot	Dichotomous Sampler with Virtual Impactor	Andersen Instruments (Smyrna, GA)
AND-241 Dichot	Thermo Andersen Series 241 Dichotomous Sampler	Andersen Instruments
AND-246 Dichot	Thermo Andersen SA-246B Dichotomous Sampler	Andersen Instruments
AND-hIVOL10 FRM	Thermo Andersen GMW-1200 HiVol PM_{10} FRM Sampler	Andersen Instruments
ARA-PCM	ARA Particle Composition Monitor	Atmospheric Research and Analysis Inc. (Plano, TX)
CMU	CMU Speciation Sampler	Carnegie Mellon University (CMU), (Pittsburgh, PA)
DRI-SFS	DRI Sequential Filter Sampler	Desert Research Institute (Reno, NV)
HEADS (or HI)	Harvard EPA Annular Denuder System (or Harvard Impactor)	Harvard School of Public Health (Boston, MA)
IMPROVE_SS[b]	IMPROVE Speciation Sampler	URG Corp. (Chapel Hill, NC)
URG-3000N[b]	Modified IMPROVE Module C Sampler for Carbon	URG Corp.
MASS-400[b]	URG Mass Aerosol Speciation Sampler Model 400	URG Corp.
MASS-450[b]	URG Mass Aerosol Speciation Sampler Model 450	URG Corp.
MiniVol	Battery-Powered Portable Low-Volume Sampler	Air Metrics Inc. (Eugene, OR)
PC-BOSS	Particle Concentrator-Brigham Young University Organic Sampling System	Brigham Young University (Provo, UT)
SAMPLING SYSTEM		
PQ-200 FRM	BGI PQ-200 FRM Sampler	BGI Inc. (Waltham, MA)
PQ-200 FRMA	BGI PQ-200A FRM Audit Sampler	BGI Inc.
R&P-ACCU	R&P-Automated Cartridge Collector Unit Sampler	Rupprecht & Patashnick, Co. (Albany, NY)
R&P-2000 FRM	R&P Partisol-2000 FRM Sampler	Rupprecht & Patashnick, Co.
R&P-2000 FRMA	R&P Partisol-2000 FRM Audit Sampler	Rupprecht & Patashnick, Co.
R&P-2025 Dichot[b]	R&P Partisol 2025 Dichotomous Sequential Air Sampler	Rupprecht & Patashnick, Co.
R&P-2025 FRM	R&P Partisol-Plus Model 2025 $PM_{2.5}$ Sequential Samplers	Rupprecht & Patashnick, Co.
R&P-2300[b]	R&P Partisol 2300 Chemical Speciation Sampler	Rupprecht & Patashnick, Co.

Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISA) and the Integrated Risk Information System (IRIS).

Abbreviation	Instrument	Manufacturer / Research Institute
RAAS-100 FRM	Thermo Andersen Reference Ambient Air Sampler Model 100	Andersen Instruments
FRM SAMPLER		
RAAS-200 FRM	Thermo Andersen RAAS Model 200 FRM Audit Sampler	Andersen Instruments
RAAS-300 FRM	Thermo Andersen RAAS Model 300 FRM Sampler	Andersen Instruments
RAAS-400[b]	Thermo Andersen RAAS Model 400 Speciation Sampler	Andersen Instruments
SASSb	MetOne Spiral Ambient Speciation Sampler	Met One Instruments (Grants Pass, OR)
SCS	$PM_{2.5}$ Sequential Cyclone Sampler	New York University (New York, NY)
URG-PCM[b]	URG Particle Composition Monitor	URG Corp. (Chapel Hill, NC)
VAPS	URG Versatile Air Pollution Sampler	URG Corp.
CONTINUOUS MASS INSTRUMENTS		
BAM	B-Attenuation Monitor Model 1020	Met One Instruments
nano-BAM	Met One BAM Model 1020 with 150 nm impactor	Met One Instruments
CAMM	Continuous Ambient Mass Monitor	Developed by Harvard School of Public Health, commercialized by Thermo Andersen Instruments; now withdrawn from market
RAMS	Real-Time Ambient Mass Sampler (modified Tapered Element Oscillation Microbalance with diffusion denuder and Nafion dryer)	Brigham Young University
TEOM	Tapered Element Oscillating Microbalance	Rupprecht & Patashnick, Co.
30 °C-TEOM	TEOM operated at 30 °C	Rupprecht & Patashnick, Co.
50 °C-TEOM	TEOM operated at 50 °C	Rupprecht & Patashnick, Co.
SES-TEOM	TEOM 1400a Series with Sample Equilibration System	Rupprecht & Patashnick, Co.
D-TEOM	Differential TEOM	Rupprecht & Patashnick, Co.
FDMS-TEOM	Filter Dynamics Measurement System TEOM	Rupprecht & Patashnick, Co.
ACCU-TEOM	TEOM 1400 Series with an automated cartridge collection unit	Rupprecht & Patashnick, Co.
CONTINUOUS PARTICLE LIGHT SCATTERING INSTRUMENTS		
Dust Trak	Dust Trak nephelometer	TSI Inc. (Shoreview, MN)
EcoTech	EcoTech Model M9003 nephelometer	EcoTech Pty Ltd., Australia (American EcoTech, Warren, RI)
NGN	NGN-2 nephelometer	Optec Inc. (Lowell, MI)
RR-M903	Radiance Research Nephelometer Model M903	Radiance Research Inc. (Seattle, WA)
CONTINUOUS ELEMENT INSTRUMENTS		
GFAAS	Graphite Furnace Atomic Absorption Spectrometry—aerosol collection as preconcentrate slurry	University of Maryland (College Park, MD)
SEAS	Semicontinuous Elements in Aerosol Sampler	University of Maryland
CONTINUOUS NITRATE INSTRUMENTS		
ADI-N	Aerosol Dynamics Inc. Flash Volatilization Analyzer	Aerosol Dynamics Inc. (Berkeley, CA)
ARA-N	Atmospheric Research and Analysis NO_3-Analyzer	Atmospheric Research and Analysis Inc.
R&P-8400N	R&P-8400N Flash Volatilization Continuous NO_3- Analyzer	Rupprecht & Patashnick, Co.
CONTINUOUS SULFATE INSTRUMENTS		
ADI-S	Aerosol Dynamics Inc. Flash Volatilization Analyzer	Aerosol Dynamics Inc.
CASM	Continuous Ambient Sulfate Monitor (prototype of the TE-5020 by Thermo Electron [Franklin, MA])	Harvard School of Public Health
R&P-8400S	R&P-8400S Flash Volatilization Continuous SO_4^{2-} Analyzer	Rupprecht & Patashnick, Co.
TE-5020	Thermo Electron Model 5020 SO_4^{2-} Particulate Analyzer	Thermo Electron Corp. (Franklin, MA)

Abbreviation	Instrument	Manufacturer / Research Institute
CONTINUOUS MULTI-ION INSTRUMENTS		
AIM	Ambient Ion Monitor Model 9000 (Cl^-,NO_2^- ,NO_3^-,PO_4^{3-}, SO_4^{2-}, NH_4^+,Na^+,$Mg^{2+}$$K^+$,$Ca^{2+}$)	URG Corp.
Dionex-IC	Dionex Ion Chromatograph (F^-, Cl^-, NO_2^-, Br^- NO_3^-, PO_4^{3-}, SO_4^{2-}, Li^+, NH_4^+ ,Na^+,Mg^{2+},K^+,Ca^{2+})	Dionex Corp.
ECN	Energy Research Center of the Netherlands IC-based sampler (Cl^-, NO_3^-, SO_4^{2-}, NH_4^+ ,Na^+, Mg^{2+},K^+, Ca^{2+})	Energy Research Center of the Netherlands (Petten, the Netherlands
PILS-IC	Particle into Liquid Sampler, coupled with IC (Cl^-, NO_2^-, NO_3^-, PO_4^{3-}, SO_4^{2-}, NH_4^+ ,Na+,Mg^{2+},K^+, Ca^{2+})	Georgia Institute of Technology (Atlanta, GA)
TT	Texas Tech IC-based sampler (NO_3^-, SO_4^{2-})	Texas Tech University (Lubbock, TX)
CONTINUOUS CARBON INSTRUMENTS		
OC and EC		
ADI-C	ADI Flash Volatilization Carbon Analyzer	Aerosol Dynamics Inc.
RU-OGI	Rutgers University/Oregon Graduate Institute in-situ carbon analyzer (OC, EC)	Rutgers University (Camden, NJ)/Oregon Graduate Institute (Beaverton, OR)
R&P-5400	R&P-5400 continuous ambient carbon analyzer	Rupprecht & Patashnick, Co.
Sunset OCEC	Sunset Semi-Continuous Real-Time Carbon Aerosol Analysis Instrument	Sunset Laboratory, Inc. (Tigard, OR)
BC		
Aethalometer		Magee Scientific Co. (Berkeley, CA)
AE-16	Magee AE-16 aethalometer (BC)	Magee Scientific Co.
AE-20	Magee AE-20 dual wavelength aethalometer (BC)	Magee Scientific Co.
AE-21	Magee AE-21 dual-wavelength aethalometer (BC)	Magee Scientific Co.
AE-31	Magee AE-31 seven color aethalometer (BC)	Magee Scientific Co.
DRI-PA	DRI Photoacoustic Analyzer (BC)	Droplet Measurement Technologies, Inc. (Boulder, CO)
MAAP	Multi-Angle Absorption Photometer, Model 5012 (BC)	Thermo Scientific Corp. (Franklin, MA)
PSAP	Particle Soot Absorption Photometer (BC)	Radiance Research Inc. (Seattle, WA)
Other Carbon		
PAS-PAH	Photo-Ionization Monitor for PAHs (Model PAS 2000)	EcoChem Analytics (League City, TX)
PILS-WSOC	PILS-WSOC Analyzer, combination of PILS and total organic analyzer (TOA)	Georgia Institute of Technology
PARTICLE SIZING INSTRUMENTS FOR MASS AND CHEMICAL SPECIATION		
DRUM-3	Davis Rotating-Drum Uniform Size-Cut Monitor (0.1-2.5 µm in 3 stages)	University of California–Davis (Davis, CA)
DRUM-8	Davis Rotating-Drum Uniform Size-Cut Monitor (0.09- > 5.0 µm in 8 stages)	University of California–Davis
ELPI	Electrical Low Pressure Impactor (0.007-10 µm in 12 stages)	Dekati (Tampere, Finland)
LPI	Low Pressure Impactor (0.03-10 µm in 13 stages)	Aerosol Dynamics, Inc.
MOUDI	Micro Orifice Uniform Deposit Impactor	MSP Corp. (Minneapolis, MN)
MOUDI-100	MOUDI Model 100 (0.18-18 µm in 8 stages)	MSP Corp.
MOUDI-110	MOUDI Model 110 (0.056-18 µm in 10 stages)	MSP Corp.
Nano-MOUDI	Nano MOUDI (0.010-0.056 µm in 3 stages coupled to MOUDI Model 110)	MSP Corp.
PARTICLE NUMBER / VOLUME INSTRUMENTS		
APS	Aerodynamic Particle Sizer	TSI Inc.
APS-3320	TSI Model 3320 (0.5-20 µm)	TSI Inc.

Abbreviation	Instrument	Manufacturer / Research Institute
APS-3321	TSI Model 3321 (0.5-20 µm; replaced TSI Model 3320)	TSI Inc.
DMA	Differential Mobility Analyzer	TSI Inc.
DMA-3081	TSI Model 3081 (0.01-1.0 µm)	TSI Inc.
DMA-3085	TSI Model 3085 (0.002-0.15 µm)	TSI Inc.
EEPS	Engine Exhaust Particle Sizer (EEPS 0.056-0.56 µm)	TSI Inc.
FMPS	Fast Mobility Particle Sizer (FMPS 0.056-0.56 µm)	TSI Inc.
GRIMM-1108	Optical Particle Counter (OPC; 0.3-20 µm)	GRIMM Technologies, Inc. (Douglasville, GA)
SMPS	Scanning Mobility Particle Sizer	TSI Inc.
SMPS-3936	TSI Model 3936L (0.01-1.0 µm)	TSI Inc.
Nano-SMPS-3936	TSI Model 3936N (0.002-0.15 µm)	TSI Inc.
SMPS + C	SMPS and Condensation Nucleus Counter (0.005-0.35 or 0.01-0.875 µm)	GRIMM Technologies, Inc.
SMPS-custom	DMA Model 3071 and CPC Model 3010	TSI Inc.
WPS	Wide-Range Particle Spectrometer (0.01-10.0 µm)	MSP Corp.
SINGLE PARTICLE INSTRUMENTS		
AMS	Aerosol Mass Spectrometer (0.04-2 µm)	Aerodyne Research Inc. (Billerica, MA)
ATOFMS	Aerosol Time of Flight Mass Spectrometer (0.3-2.5 µm)	TSI Inc.
CNC, CPC	Condensation Nucleus Counters, Condensation Particle Counter	Various vendors
DAASS	Dry-Ambient Aerosol Size Spectrometer consisting of two SMPS and One APS (0.003-10 µm)	Carnegie Mellon University
LIBS	Laser-Induced Breakdown Spectroscopy	National Research Council, Industrial Materials Institute (Boucherville, Quebec, Canada)
PALMS	Particle Analysis by Laser Mass Spectrometer (0.22-2.5 µm)	NOAA (Boulder, CO)
RSMS-II	Rapid Single Particle Mass Spectrometer -II (0.035-1.1 µm)	University of Delaware (Newark, DE)
RSMS-III	Rapid Single Particle Mass Spectrometer III (0.01-2.0 µm)	University of Delaware
LABORATORY INSTRUMENTS		
DRI Model 2001	DRI Model 2001 Thermal/Optical Carbon Analyzer (OC, EC, Eight Carbon Fractions with reflectance and transmittance laser correction)	Atmoslytic, Inc. (Calabasas, CA)
SEM	Scanning Electron Microscopy	Various vendors

[a]Now with Thermo Scientific, Franklin, MA.
[b]EPA-approved speciation sampler used in the Speciation Trends Network (STN).
[c]Now commercialized by Applikon Analytical, the Netherlands, and marketed under the name "MARGA" (Monitor for Aerosols and Gases in Ambient Air).
[d]Not available.

Source: Chow et al. (2008, 156355)

Table A-2. Summary of $PM_{2.5}$ and PM_{10} FRM and FEM samplers.

Manufacturer[a]	Sampler Name	Size Cut[b]	Description	FRM or FEM[c]	Designation #	FRN
BGI Inc.	PQ-100	PM_{10}	Louvered PM_{10} inlet; operates at flow rate of 16.7 L/min; 24-h integrated sampler; uses a mass flow meter to adjust to equivalent volumetric flow at ambient temperature and pressure.	FRM	RFPS-1298-124	Vol. 63, p. 69625, 12/17/98
BGI Inc.	PQ-200	PM_{10}		FRM	RFPS-1298-125	Vol. 63, p. 69625, 12/17/98
BGI Inc.	PQ-200	$PM_{2.5}$	Identical to PM_{10} sampler but uses a WINS[d] impactor downstream of the PM_{10} inlet for $PM_{2.5}$ fractionation at 16.7 L/min; 24-h integrated sampler.	FRM	RFPS-0498-116	Vol. 63, p. 18911, 04/16/98 Vol. 63, p. 31993, 06/11/98
BGI Inc.	PQ-200-VSCC or PQ-200A-VSCC	$PM_{2.5}$	Same as BGI PQ200 $PM_{2.5}$ sampler but with BGI VSCC instead of WINS impactor; PQ200A is a portable audit sampler, similar in design to PQ-200, but more compact in nature.	FEM (II)	EQPM-0202-142	Vol. 67, p. 15567, 04/02/02
R&P	R&P-2000	PM_{10}	R&P Partisol FRM Model 2000 PM_{10} sampler with louvered PM_{10} inlet; operates at flow rate of 16.7 L/min; 24-h integrated sampler; uses a mass flow meter to adjust to equivalent volumetric flow at ambient temperature and pressure; single-channel sampler.	FRM	RFPS-1298-126	Vol. 63, p. 69625, 12/17/98
R&P	R&P-2000	$PM_{2.5}$	R&P Partisol FRM Model 2000 $PM_{2.5}$ sampler, identical to PM_{10} sampler but uses a WINS impactor downstream of the PM_{10} inlet for $PM_{2.5}$ fractionation at 16.7 L/min; 24-h integrated sampler; R&P2000A is a portable audit sampler.	FRM	RFPS-0498-117	Vol. 63, p. 18911, 04/16/98
R&P	R&P2000A	$PM_{2.5}$		FRM	RFPS-0499-129	Vol. 64, p. 19153, 04/19/99
R&P	R&P-2025	PM_{10}	R&P Partisol-Plus Model 2025 PM_{10} sequential sampler with louvered PM_{10} inlet; operates at 16.7 L/min; 24-h integrated sampler; uses a mass flow meter to adjust to equivalent volumetric flow at ambient temperature and pressure; sequential sampler with a capacity of 16 filter cassettes, allowing for two weeks of unattended daily sampling; filter exchange is performed pneumatically.	FRM	RFPS-1298-127	Vol. 63, p. 69625, 12/17/98
R&P	R&P-2025	$PM_{2.5}$	R&P Partisol-Plus Model 2025 $PM_{2.5}$ sequential sampler, identical to R&P-2025 PM_{10} sampler but uses a WINS impactor downstream of the PM_{10} inlet for $PM_{2.5}$ fractionation at 16.7 L/min.	FRM	RFPS-0498-118	Vol. 63, p. 18911, 04/16/98
R&P	R&P2000-VSCC	$PM_{2.5}$	Same as R&P-2000 $PM_{2.5}$ sampler but with BGI VSCC, instead of WINS impactor for $PM_{2.5}$ separation.	FEM (II)	EQPM-0202-143	Vol. 67, p. 15567, 04/02/02
R&P	R&P2000A-VSCC	$PM_{2.5}$	Same as R&P-2000A $PM_{2.5}$ sampler but with BGI VSCC instead of WINS impactor for $PM_{2.5}$ separation.	FEM (II)	EQPM-0202-144	Vol. 67, p. 15567, 04/02/02
R&P	R&P-2025-VSCC	$PM_{2.5}$	Same as R&P-2025 $PM_{2.5}$ sampler but with BGI VSCC instead of WINS impactor, for $PM_{2.5}$ separation.	FEM (II)	EQPM-0202-145	Vol. 67, p. 15567, 04/02/02
Andersen	RAAS-100	PM_{10}	Andersen Instruments, Inc. Model RAAS10-100 PM_{10} sampler with louvered PM_{10} inlet; operates at flow rate of 16.7 L/min; 24-h integrated sampler; volumetric flow measured by dry test meter at pump outlet modulates pump speed to maintain flow rate; single-channel.	FRM	RFPS-0699-130	Vol. 64, p. 33481, 06/23/99
Andersen	RAAS-100	$PM_{2.5}$	Graseby Andersen Model RAAS2.5-100 $PM_{2.5}$ sampler, similar to RAAS-100 PM_{10} with a WINS impactor for $PM_{2.5}$ separation.	FRM	RFPS-0598-119	Vol 63, p. 31991, 06/11/98
Andersen	RAAS200A	PM_{10}	Andersen Instruments, Inc. Model RAAS10-200 and RAAS2.5-100 Audit Samplers, portable compact version; similar to RAAS-100.	FRM	RFPS-0699-131	Vol. 64, p. 33481, 06/23/99
Andersen	RAAS-200A	$PM_{2.5}$		FRM	RFPS-0299-128	Vol. 64, p. 12167, 03/11/99
Andersen	RAAS-300	PM_{10}	Andersen Instruments, Inc. Model RAAS10-300, sequential sampler with louvered PM_{10} inlet, operates at 16.7 L/min; capacity to hold eight filter-holders for multiple day operation.	FRM	RFPS-0699-132	Vol. 64, p. 33481, 06/23/99
Andersen	RAAS-300	$PM_{2.5}$	Graseby Andersen Model RAAS2.5-300 $PM_{2.5}$ sampler, similar to RAAS-300 PM_{10} sampler with a WINS impactor for $PM_{2.5}$ separation.	FRM	RFPS-0598-120	Vol. 63, p. 31991, 06/11/98

Manufacturer[a]	Sampler Name	Size Cut[b]	Description	FRM or FEM[c]	Designation #	FRN
Thermo Scientific, Inc.	CAPS	$PM_{2.5}$	Model 605 Computer Assisted Particle Sampler (CAPS), 24-h integrated. Not available commercially.	FRM	RFPS-1098-123	Vol. 63, p. 8036, 10/29/98
Thermo Scientific, Inc.	RAAS 100-VSCC	$PM_{2.5}$	Same as RAAS-100 $PM_{2.5}$ sampler but with BGI VSCC, instead of WINS impactor.	FEM (II)	EQPM-0804-153	Vol. 69, p. 47924, 08/06/04
Thermo Scientific, Inc.	RAAS 200-VSCC	$PM_{2.5}$	Same as RAAS-200 $PM_{2.5}$ sampler but with BGI VSCC instead of WINS impactor.	FEM (II)	EQPM-0804-154	Vol. 69, p. 47924, 08/06/04
Thermo Scientific, Inc.	RAAS 300-VSCC	$PM_{2.5}$	Same as RAAS-300 $PM_{2.5}$ sampler but with BGI VSCC instead of WINS impactor.	FEM (II)	EQPM-0804-155	Vol. 69, p. 47925, 08/06/04
URG Corp.	MASS-100	$PM_{2.5}$	Model MASS100 $PM_{2.5}$ sampler with louvered PM_{10} inlet followed by WINS impactor, operates at 16.7 L/min; 24-h integrated, volumetric flow measured by dry test meter at pump outlet modulates pump speed to maintain flow rate; single channel.	FRM	RFPS-0400-135	Vol. 65, p. 26603, 05/08/00
URG Corp.	MASS-300	$PM_{2.5}$	Model MASS300 $PM_{2.5}$ sampler with louvered PM_{10} inlet followed by WINS impactor, operates at 16.7 L/min; 24-h integrated, sequential sampler with circular tray holding six filters.	FRM	RFPS-0400-136	Vol. 65, p. 26603, 05/08/00
Tisch Environmental, Inc.	TE-6070 HiVol	PM_{10}	Model TE-6070 PM_{10} High-Volume Sampler, with TE-6001 PM_{10} size selective inlet; 8" x 10" filter holder.	FRM	RFPS-0202-141	Vol. 67, p. 15566, 04/02/02
Met One	BAM	PM_{10}	Models BAM 1020, GBAM 1020, BAM 1020-1, and GBAM 1020-1, with BX-802 inlet; glass-fiber filter tape with 1-h filter change frequency.	FEM	EQPM-0798-122	Vol. 63, p. 41253, 08/03/98

[a] BGI Inc.: BGI Incorporated, Waltham, MA. R&P: Rupprecht & Patashnick Company, Inc., Albany, NY, now Thermo Scientific, Inc., Franklin, MA. Andersen: Graseby Andersen, later Andersen Instruments, Inc., Smyrna, GA, now Thermo Scientific, Inc., Franklin, MA. Thermo Environmental Instruments, Inc., now Thermo Scientific, Inc., Franklin, MA. URG Corp.: URG Corporation, Chapel Hill, NC. Tisch Environmental, Inc., Cleves, OH. Met One Instruments, Inc., Grants Pass, OR

[b] The efficiency of an inlet (Watson et al., 1983, 045084) is determined by its 50% cut-point (d50, the diameter at which half of the particles penetrate through the inlet, while the other half is retained by the inlet, while the other half is retained by the inlet) and the geometric standard deviation (GSD, which is an indicator of the sharpness of the separation, and is derived by the square root of the ratio of particle diameters at penetrations of 16% andc 84%, $[d_{16}/d_{84}]^{0.5}$).

[c] FRM: Federal Reference Method; FEM: Federal Equivalent Method. Roman numeral within parenthesis indicates FEM class.

[d] Particle separation in WINS is achieved by means of a single-jet round nozzle with flow directed into an impaction reservoir. The impaction surface consists of a Gelman Type A/E glass-fiber filter immersed in 1 mL of Dow Corning (Midland, MI) 704 diffusion pump oil housed in a reservoir.

Note: The geometric standard deviation (GSD, which is an indicator of the sharpness of the separation, and is derived by the square root of the ratio of particle diameters at penetrations of 16% and 84%, [d16/d84]0.5).

Source: Chow et al. (2008, 156355)

Table A-3. Measurement and analytical specifications for filter analysis of mass, elements, ions, and carbon.

Observable	Analytical Accuracy[a]	Precisionb	Minimum Detectable Limit (MDL)	Interferences	Comparability	Data Completeness
$PM_{2.5}$ mass	± 5% [4]	± 10% [4]	0.04 µg/m^3 [c] to ~1 µg/m^3 [d 5,6]	Electrostatic charges need to be neutralized before measurement; positive (e.g., OC adsorption) and negative artifacts (e.g., nitrate volatilization)	Within 20% [4]	90 to 100% [h 6,7]
Elements	± 2-5% [4]	± 10% [4]	XRF: 0.4-30 ng/m^3 [g 8] PIXE: 6-360 ng/m^3 [d 9] ICP/MS: 0.004-25 ng/m^3 [10] 0.05-11.7 ng/m^3 [9,11] AAS: 0.02-7.15 ng/m^3 [12]	Volatile compounds may evaporate from filters due to vacuum in XRF and PIXE. Potential contamination during extraction and incomplete extraction efficiency for ICP-MS and AAS. Matrix interference and peak overlap may occur on heavily loaded samples.	10 to 30% depending on species [4]	90 to 100% [h 6,7]
Nitrate	± 6% with spiked concentrations on Teflon4 and ± 1−14% on nylon filters13	± 5 to 10% on replicate analysis [4,13,14] co-located precision ± 5-7% [14-16]	0.06 µg/m^3 [e] to 0.2 µg/m^3 [d 1,6,17]	Subject to volatilization from Teflon or quartz-fiber filters	Within 35% and probably greater [4]	85 to 100% [6,7]
Sulfate	± 5% [4]	± 6 to 10% [4,14,15]	0.06 µg/m^3 [e] to 0.2 µg/m^3 [d 1,6,13]	N/A	Typically within 10%; MOUDIs [13] to 20% lower than speciation samplers [4,17-19]	85 to 100% [6,7,20,21]
Ammonium	± 5% [4]	± 10% [4]	0.06 µg/m^3 [e] to 0.07 µg/m^3 [d 1,6]	Subject to volatilization from Teflon or quartz-fiber filters	Within 30% [4]	86 to 100% [6,7]
OC, EC, TC	± 5% for TC and OC. No standard exists to determine EC accuracy	OC: ± 20% EC: ± 20% TC: ± 10% [4]	OC: 0.1 µg/m^3 [f] to 0.8 µg/m^3 [d] EC: 0.03 µg/m^3 [d] to 0.1 µg/m^3 [f] TC: 0.8 µg/m^3 [d 1,6]	Subject to adsorption (positive artifact) and volatilization (negative artifact) of organic gases to and from quartz-fiber filters	OC: Within 20 to 50% EC: Within 20 to 200% TC: Within 20% [4,17,22]	86 to 100% [6,7]
Total mass of WSOC	DRI Model 2001 Carbon Analyzer: ± 5% [23] TOA: ± 3-7% [24,25]	DRI Model 2001 Carbon Analyzer: ± 10% [23] Sunset Carbon Analyzer: ± 3% [26] TOA: ± 5-10% [27]	DRI Model 2001 Carbon Analyzer: 0.1-0.23 µg C/m^3 [23] Sunset Carbon Analyzer: 0.05-0.22 µg C/m^3 [26,28] Elemental High TOC II: 0.05 µg C/m^3 [29] TOA: 0.12 µg C/m^3 [26]	Extraction efficiency and volume reduction steps	Within 17% [26]	N/A
Elements in water soluble matter: C, H, N, and S	C: 1.5%; H: 3%; N: 3%; S: 5% [30]	± 2% [30]	C: 0.3 µg/m^3 H:0.09 µg/m^3 N: 0.03 µg/m^3 S: 0.10 µg/m^3 [30]	Contamination during sample drying step	N/A	N/A
Dissolved organic nitrogen	N/A	± 5-30% [31]	0.001µg N/m^3 while inorganic nitrogen is low; ≥ 0.071µg N/m^3 while inorganic nitrogen is high [31]	Concentration of inorganic nitrogen	Good correlation between UV and persulfate oxidation methods (R^2 = 0.87) [31]	N/A

Observable	Analytical Accuracy[a]	Precisionb	Minimum Detectable Limit (MDL)	Interferences	Comparability	Data Completeness
Neutral polyols and polyether	GC/MS: ± 4-8% [32]	GC/MS: ± 23% [33,34] Typically ± 20%, ranged from ± 10 to ± 30% [l 32,35,36,37,38] HPLC/MS: ± 5-26% [39]	GC/MS: Levoglucosan: 10 ng/m^3 [g 40] 2.08 ng/m^3 [j 31] 0.01-0.03 ng/m^3 [33,41] HPLC/MS: 9-648 pg/m^3 [39]	GCMS: Extraction recovery interfered by sample matrix Derivatization efficiency IC/PAD: Overlapping peaks in chromatogram	IC/PAD: Good correlation (R^2 = 0.97) with HPLC/MS; and (R^2 = 0.89) with GC/MS Method [42]	N/A
Mono- and Di-carboxylic acids	N/A	GC/MS: ±5-11% on 3 replicates, ± 8 % in avg [43,44] IC: ± 10-15% [45]	GC/MS: 0.04-1.12 ng/m^3 [46] IC: 0.01-0.12 ng/m^3 [47]	GC/MS: Extraction recovery interfered by sample matrix Derivatization efficiency IC: Overlapping peaks in chromatogram	GC/MS: Within 50% for less volatile compounds 46	N/A
Amino acids	N/A	± 9% [48]	1.65-23.6 pg/m^3 [k 48]	Derivatization efficiency Stability of derivatives Overlapping peaks in chromatogram	N/A	N/A
Mass of humic-like substances (HULIS)	N/A	N/A	0.083 ng/m^3 [l 49]	Separation efficiency	N/A	N/A

[a] Accuracy is the ability of analytical methods to quantify the observable of a standard reference material correctly; it does not refer to measurement accuracy if no standards available.50
[b] Refers to precision of co-located measurements, unless specified otherwise.
[c] Based on 1 µg/filter limit of detection for 24-h samples, assuming a flow rate of 16.7 L/min
[d] Based on field blanks collected with FRM samplers; µg/filter converted to µg/m^3 basis assuming a flow rate of 16.7 L/min for 24-h
[e] Based on ½ of a 47-mm filter extracted in 15 mL deionized-distilled water (DDW) for 24-h samples, assuming a flow rate of 16.7 L/min
[f] Based on 0.2 µg/cm^2 detection limit and 13.8 cm^2 deposit area for a 47-mm filter, assuming a flow rate of 16.7 L/min for 24-h
[g] Based on 24-h samples at a flow rate of 16.7 L/min and analyzed by XRF
[h] Except for samples from one FRM sampler at Atlanta Supersite, for which data recovery was 50%[7]; reason not reported.
[i] Reported as uncertainty in literature
[j] Based on 24-h samples at a flow rate of 16.7 L/min
[k] Based on 13.8 cm^2 deposit area for a 47-mm filter and extracted into a final volume of 200 µL, assuming a flow rate of 16.7 L/min for 24-h and molecular weight of amino acid = 150
[l] Based on 13.8 cm^2 deposit area for a 47-mm filter and extracted into a final volume of 200 µL, assuming a flow rate of 16.7 L/min for 24-h
N/A: Not available

[1]Chow (1995, 077012); [2]Watson and Chow (2001, 157123); [3] Watson et al. (1983, 045084); [4]Fehsenfeld et al. (2004, 157360); [5]Solomon et al. (2001, 157193); [6]Watson et al. (2005, 157124); [7]Mikel (2001, 156762); [8]Watson et al. (1999, 020949); [9]Solomon and Sioutas (2006, 156995); [10]Graney et al. (2004, 053756); [11]Tanaka et al. (1998, 157041); [12]Pancras et al. (2005, 098120); [13]John et al. (1988, 045903); [14]Hering and Cass (1999, 084958); [15]Fitz et al. (1989, 077387); [16]Hering et al. (1988, 036012); [17]Solomon et al. (2003, 156994); [18]Cabada et al. (2004, 148859); [19]Fine et al. (2003, 155775); [20]Hogrefe et al. (2004, 099003); [21]Drewnick et al. (2003, 099160); [22]Watson et al. (2005, 157125); [23]Ho et al. (2006, 156552); [24]Decesari et al. (2005, 144536); [25] Mayol-Bracero et al. (2002, 045010); [26]Yang et al. (2003, 156167); [27] Turšic et al. (2006, 157063); [28]Mader et al.(2004, 156724); [29]Xiao and Liu (2004, 056801); [30]Kiss et al. (2002, 156646); [31]Cornell and Jickells (1999, 156367); [32] Zheng et al. (2002, 026100); [33]Fraser et al. (2002, 140741); [34] Fraser et al. (2003, 042231) [35]Schauer er al. (2000, 012225); [36]Fine et al. (2004, 141283); [37]Yue et al. (2004, 157169); [38]Rinehart et al. (2006, 115184); [39]Wan and Yu (2006, 157104); [40]Poore (2000, 012839); [41]Fraser et al. (2003, 040266); [42]Engling et al. (2006, 156422); [43]Yu et al. (2005, 157167); [44]Tran et al. (2000, 013025); [45]Yao et al. (2004, 102213); [46]Li and Yu (2005, 156692); [47]Henning et al. (2003, 156539); [48]Zhang and Anastasio (2003, 157182); [49]Emmenegger et al. (2007, 156418); [50] Watson et al. (1989, 046318); [51]Greaves et al. (1985, 156494); [52]Waterman et al. (2000, 157116); [53]Waterman et al. (2001, 157117); [54]Falkovich and Rudich (2001, 156427); [55]Chow et al. (2007, 157209); [56]Miguel et al. (2004, 123260); [57]Crimmins and Baker (2006, 097008); [58]Ho and Yu (2004, 156551); [59]Jeon et al. (2001, 016636); [60]Mazzoleni et al. (2007, 098038); [61]Poore (2002, 051444); [62]Butler et al. (2003, 156313); [63]Chow et al. (2006, 146622); [64]Russell et al. (2004, 082453); [65]Grover et al. (2006, 138080); [66]Grover et al. (2005, 090044); [67]Schwab et al. (2006, 098449); [68]Hauck et al. (2004, 156525); [69]Jaques et al. (2004, 155878); [70]Rupprecht and Patashnick (2003, 157207); [71]Pang et al (2002, 030353); [72]Eatough et al. (2001, 010303); [73]Lee et al. (2005, 128139); [74]Lee et al. (2005, 156680); [75]Babich et al. (2000, 156239); [76]Lee et al. (2005, 155925); [77]Lee et al. (2005, 128139); [78]Anderson and Ogren (1998, 156213); [79]Chung et al. (2001, 156357); [80]Kidwell and Ondov (2004, 155898); [81]Lithgow et al. (2004, 126616); [82]Weber et al. (2003, 157129); [83]Harrison et al. (2004, 136787); [84]Rattigan et al. (2006, 115897); [85]Wittig et al. (2004, 103413); [86]Vaughn et al. (2005, 157089); [87]Chow et al. (2005, 099030); [88]Weber et al (2001, 024640) ; [89]Schwab et al. (2006, 098785); [90]Lim et al. (2003, 037037); [91]Watson and Chow (2002, 037873); [92]Venkatachari et al. (2006, 105918); [93]Bae et al. (2004, 156243); [94]Arhami et al. (2006, 156224); [95]Park et al. (2005, 156843); [96]Bae et al. (2004, 098680); [97]Chow et al. (2006, 156350); [98]Arnott et al. (2005, 156227); [99]Bond et al. (1999, 156281); [100]Virkkula et al. (2005, 157097); [101]Petzold et al. (2002, 156863); [102]Park et al. (2006, 098104); [103]Arnott et al. (1999, 020650); [104]Peters et al. (2001, 016925); [105]Pitchford et al. (1997, 156872); [106]Rees et al. (2004, 097164); [107]Watson et al. (2000, 010354); [108]Lee et al. (2005, 156680); [109]Hering et al. (2004, 155837); [110]Watson et al. (1998, 198805); [111]Chakrabarti et al. (2004, 157426); [112]Mathai et al. (1990, 156741); [113]Kidwell and Ondov (2001, 017092); [114]Stanier et al. (2004, 095955); [115]Khlystov et al. (2005, 156635); [116]Takahama et al. (2004, 157038); [117]Chow et al. (2005, 156348); [118]Zhang et al. (2002, 157181); [119]Subramanian et al. (2004, 081203); [120]Chow et al. (2006, 155207); [121]Birch and Cary (1996, 026004); [122]Birch (1998, 024953); [123]Birch and Cary (1996, 002352); [124]NIOSH (1996, 156810); [125]NIOSH (1999, 156811); [126]Chow et al. (1993, 077459); [127]Chow et al. (2007, 156354); [128]Ellis and Novakov (1982, 156416); [129]Peterson and Richards (2002, 156861); [130]Schauer et al. (2003, 037014); [13]1Middlebrook et al. (2003, 042932); [132]Wenzel et al. (2003, 157139); [133]Jimenez et al. (2003, 156611); [134]Phares et al. (2003, 156866); [135]Qin and Prather (2006, 156895); [136]Zhang et al. (2005, 157185); [137]Bein et al. (2005, 156265); [138]Drewnick et al. (2004, 155754); [139]Drewnick et al. (2004, 155755); [140]Lake et al. (2003, 156669); [141]Lake et al. (2004, 088411)

Source: Chow et al. (2008, 156355))

Table A-4. Measurement and analytical specifications for filter analysis of organic species.

Organic Species	Analytical Accuracy		Precision		MDL		Interferences		Comparability
	TD	Solvent Extraction	TD	Solvent Extraction	TD	Solvent Extraction	TD	Solvent Extraction	
PAHs	± 2.8-24.1%[51] ± 4.4-29.4%[52] 13.8-26.5%[53] ± 0.5-12.9%[54] 0.05-4.83%[55]	Z-score values 0 to -1.9 [56] ± 4-8%[32] ± 6.5-22%[57]	Avg ± 3.2%, ranged from ± 0.05 to ± 11.5%[55]	Avg ± 8%, ranged from ± 3.8 to ± 15%[56] ± 23%[56] Avg ± 2.6%, ranged from ± 0.6 to ± 9.5%[57] typically ± 20%, ranged from ± 10 to ± 30%[c 32,35-37]	0.016-0.48 ng/m[3 a 58] 0.030-0.45 ng/m[3 a 55]	0.83-1.66 ng/m[3 b 38] 0.033-3.85 ng/m[3 b 56] 0.01-0.03 ng/m[3 33,34,37] 0.76-276 pg/m[3 b 57]	Fragmentation of labile compounds	Possible contaminants from solvents and complicated extraction procedures. Loss of volatile compounds during the extraction and pretreatment steps. Possible carryover from injection port.	R^2s for solvent extraction were 0.95 [58], 0.97[55], and 0.98 [59]
n-Alkanes	N/A	± 4-8%[32]	Avg ± 3.2%, ranged from ± 0.05 to ± 11.5%[55]	± 23%[56] Typically ± 20 %, from ± 10 to ± 30%c [32,35-37]	0.081-0.86 ng/m[3 a 58] 0.061-0.97 ng/m[3 a 55]	0.01-0.03 ng/m[3 33,34,37]	Same as PAHs	Same as PAHs	R^2s for solvent extraction are 0.94 [58] and 0.98 [55,59]
Hopanes	N/A	N/A	Avg ± 3.2%, ranged from ± 0.05 to ± 11.5%[55]	± 23%[56] Typically ± 20 %, from ± 10 to ± 30%[c 32,35-37]	0.030-0.14 ng/m[3 a 55]	0.83-1.66 ng/m[3 b 38] 0.01-0.03 ng/m[3 33,41] 0.01 ng/m[3 37]	Same as PAHs	Same as PAHs	R^2s for solvent extraction are 0.99 [55] and 0.998 [59]
Steranes	N/A	N/A	Avg ± 3.2%, ranged from ± 0.05 to ± 11.5%[55]	N/A	0.018-0.063 ng/m[3 a 55]	0.83-1.66 ng/m[3 b 60]	Same as PAHs	Same as PAHs	R^2s for solvent extraction are 0.97 [55] and 0.998 [59]
Organic acids (including n-alkanoic acids, n-alkenoic acids, alkane dicarboxylic acids, aromatic carboxylic acids, resin acids)	N/A	± 4-8%[32]	± 10 to ± 29%[55]	± 24%[41] ± 23%[56] Typically ± 20 %, from ± 10 to ± 30%[c 32,35-37]	Mono-carboxylic acids (C8, C12, and C16): 0.79, 2.0, and 3.2 ng/m[3 a 54]	0.01-0.03 ng/m[3 33,41]	Fragmentation of labile compounds. Loss of polar species due to absorption onto the surface of the injector. Improper stationary phase column used during TD analysis. Incomplete thermal desorption of analytes because of strong affinity with filter matrix.	Possible contaminants from solvents and complicated extraction procedures. Loss of volatile compounds during the extraction and pretreatment steps. Possible carryover from injection port . Low derivatization efficiency .	Correlation with solvent extraction method R^2 = 0.731 [59]

	Analytical Accuracy		Precision		MDL		Interferences		
Polyols and sugars, including guaiacol and substituted guaiacols, syringol and substituted syringols, anhydrosugars	N/A	± 4-8%[32]	N/A	± 23%[56] Typically ± 20 %, from ± 10 to ± 30%[c 32,35-37]	N/A	Levoglucosa: [10] ng/m[3 61] 2.08 ng/m[3 b 38] 0.01-0.03 ng/m[3 33,41]	Same as organic acids	Same as organic acids	N/A

[a] Assumes 2.9 cm^2 filter used in analysis from a deposit area of 13.8 cm^2, and sample collection at a flow rate of 16.7 L/min for 24-h

[b] Assumes sample collection at a flow rate of 16.7 L/min for 24-h.

[c] Reported as uncertainty in literature.

[d] Assumes a final extract volume of 1 mL and sample collection at a flow rate of 16.7 L/min for 24-h.

N/A: Not available

[1]Chow (1995, 077012); [2]Watson and Chow (2001, 157123); [3] Watson et al. (1983, 045084); [4]Fehsenfeld et al. (2004, 157360); [5]Solomon et al. (2001, 157193); [6]Watson et al. (2005, 157124); [7]Mikel (2001, 156762); [8]Watson et al. (1999, 020949); [9]Solomon and Sioutas (2006, 156995); [10]Graney et al. (2004, 053756); [11]Tanaka et al. (1998, 157041); [12]Pancras et al. (2005, 098120); [13]John et al. (1988, 045903); [14]Hering and Cass (1999, 084958); [15]Fitz et al. (1989, 077387); [16]Hering et al. (1988, 036012); [17]Solomon et al. (2003, 156994); [18]Cabada et al. (2004, 148859); [19]Fine et al. (2003, 155775); [20]Hogrefe et al. (2004, 099003); [21]Drewnick et al. (2003, 099160); [22]Watson et al. (2005, 157125); [23]Ho et al. (2006, 156552); [24]Decesari et al. (2005, 144536); [25] Mayol-Bracero et al. (2002, 045010); [26]Yang et al. (2003, 156167); [27]Turšic et al. (2006, 157063); [28]Mader et al.(2004, 156724); [29]Xiao and Liu (2004, 056801); [30]Kiss et al. (2002, 156646); [31]Cornell and Jickells (1999, 156367); [32] Zheng et al. (2002, 026100); [33]Fraser et al. (2002, 140741); [34] Fraser et al. (2003, 042231) [35]Schauer er al. (2000, 012225); [36]Fine et al. (2004, 141283); [37]Yue et al. (2004, 157169); [38]Rinehart et al. (2006, 115184); [39]Wan and Yu (2006, 157104); [40]Poore (2000, 012839); [41]Fraser et al. (2003, 040266); [42]Engling et al. (2006, 156422); [43]Yu et al. (2005, 157167); [44]Tran et al. (2000, 013025); [45]Yao et al. (2004, 102213); [46]Li and Yu (2005, 156692); [47]Henning et al. (2003, 156539); [48]Zhang and Anastasio (2003, 157182); [49]Emmenegger et al. (2007, 156418); [50] Watson et al. (1989, 046318); [51]Greaves et al. (1985, 156494); [52]Waterman et al. (2000, 157116); [53]Waterman et al. (2001, 157117); [54]Falkovich and Rudich (2001, 156427); [55]Chow et al. (2007, 157209); [56]Miguel et al. (2004, 123260); [57]Crimmins and Baker (2006, 097008); [58]Ho and Yu (2004, 156551); [59]Jeon et al. (2001, 016636); [60]Mazzoleni et al. (2007, 098038); [61]Poore (2002, 051444); [62]Butler et al. (2003, 156313); [63]Chow et al. (2006, 146622); [64]Russell et al. (2004, 082453); [65]Grover et al. (2006, 138080); [66]Grover et al. (2005, 090044); [67]Schwab et al. (2006, 098449); [68]Hauck et al. (2004, 156525); [69]Jaques et al. (2004, 155878); [70]Rupprecht and Patashnick (2003, 157207); [71]Pang et al (2002, 030353); [72]Eatough et al. (2001, 010303); [73]Lee et al. (2005, 128139); [74]Lee et al. (2005, 156680); [75]Babich et al. (2000, 156239); [76]Lee et al. (2005, 155925); [77]Lee et al. (2005, 128139); [78]Anderson and Ogren (1998, 156213); [79]Chung et al. (2001, 156357); [80]Kidwell and Ondov (2004, 155898); [81]Lithgow et al. (2004, 126616); [82]Weber et al. (2003, 157129); [83]Harrison et al. (2004, 136787); [84]Rattigan et al. (2006, 115897); [85]Wittig et al. (2004, 103413); [86]Vaughn et al. (2005, 157089); [87]Chow et al. (2005, 099030); [88]Weber et al (2001, 024640) ; [89]Schwab et al. (2006, 098785); [90]Lim et al. (2003, 037037); [91]Watson and Chow (2002, 037873); [92]Venkatachari et al. (2006, 105918); [93]Bae et al. (2004, 156243); [94]Arhami et al. (2006, 156224); [95]Park et al. (2005, 156843); [96]Bae et al. (2004, 098680); [97]Chow et al. (2006, 156350); [98]Arnott et al. (2005, 156227); [99]Bond et al. (1999, 156281); [100]Virkkula et al. (2005, 157097); [101]Petzold et al. (2002, 156863); [102]Park et al. (2006, 098104); [103]Arnott et al. (1999, 020650); [104]Peters et al. (2001, 016925); [105]Pitchford et al. (1997, 156872); [106]Rees et al. (2004, 097164); [107]Watson et al. (2000, 010354); [108]Lee et al. (2005, 156680); [109]Hering et al. (2004, 155837); [110]Watson et al. (1998, 198805); [111]Chakrabarti et al. (2004, 157426); [112]Mathai et al. (1990, 156741); [113]Kidwell and Ondov (2001, 017092); [114]Stanier et al. (2004, 095955); [115]Khlystov et al. (2005, 156635); [116]Takahama et al. (2004, 157038); [117]Chow et al. (2005, 156348); [118]Zhang et al. (2002, 157181); [119]Subramanian et al. (2004, 081203); [120]Chow et al. (2006, 155207); [121]Birch and Cary (1996, 026004); [122]Birch (1998, 024953); [123]Birch and Cary (1996, 002352); [124]NIOSH (1996, 156810); [125]NIOSH (1999, 156811); [126]Chow et al. (1993, 077459); [127]Chow et al. (2007, 156354); [128]Ellis and Novakov (1982, 156416); [129]Peterson and Richards (2002, 156861); [130]Schauer et al. (2003, 037014); [131]Middlebrook et al. (2003, 042932); [132]Wenzel et al. (2003, 157139); [133]Jimenez et al. (2003, 156611); [134]Phares et al. (2003, 156866); [135]Qin and Prather (2006, 156895); [136]Zhang et al. (2005, 157185); [137]Bein et al. (2005, 156265); [138]Drewnick et al. (2004, 155754); [139]Drewnick et al. (2004, 155755); [140]Lake et al. (2003, 156669); [141]Lake et al. (2004, 088411)

Source: Chow et al. (2008, 156355)

Table A-5. Measurement and analytical specifications for continuous mass and mass surrogate instruments.

Instrument and Measurement Principle	Averaging Time	Analytical Accuracy[a]	Precisionb	MDL	Interferences	Comparability	Data Completeness
INERTIA INSTRUMENTS							
TEOM Air is drawn through a size-selective inlet onto the filter mounted on an oscillating hollow tube. The oscillation frequency changes with mass loading on the filter, which is used to calculate mass concentration by calibrating measured frequency with standards.	10 min-24 h	± 0.75%[c]	± 5 µg/m^3 for 10-min avgc,d ± 1.5 µg/m^3 for 1-h avg[c,d]	0.01 µg, which is 0.06 µg/m^3 for 1-h avg[c]	Loses semi-volatile species at both 30°C and 50°C. SESTEOM, while less sensitive to relative humidity, does not completely eliminate loss of semi-volatile species	Underestimated FRM mass by 20 to 35% [62-64]	99% [65 87]-92% [6]
FDMS TEOM. A self-referencing TEOM with a filter at 4 °C that accounts for volatile species. It is equipped with a diffusion Nafion dryer to remove particle-bound water. The Teflon (PTFE)-coated borosilicate glass-fiber filter that is maintained at 4 °C removes particles during the reference flow cycle. The flow alternates between a base and reference flow every 6 min. If a negative mass is measured during the reference flow, due to loss of volatiles from the filter, it is added to the mass made during the prior particle-laden samples to obtain total $PM_{2.5}$ concentration.	1 h-24 h	± 0.75%[c]	< 10%[65]	0.01 µg, which is 0.06 µg/m^3 for 1-h avg[c]	N/A	9 to 30% higher than FRM mass Within 10% of mass by D-TEOM, PC-BOSS, RAMS and BAM [66,67]	95-99%[65,68] 57-65%[67]
Differential Tapered Element Oscillating Microbalance (D-TEOM) Similar to FDMS, but an electrostatic precipitator is used in place of the glass-fiber filter to remove particles during the 6 min reference flow cycle.	1 h-24 h	± 0.75%[c]	< 10%[e 65,69,70]	0.01 µg, or 0.06 µg/m^3 for 1-h avg[c]	N/A	Within 10% of FDMS-TEOM [65,66]	86%[65]
RAMS. A TEOM with a cyclone inlet, diffusion denuders, and Nafion dryer. Particles are collected on a "sandwich" filter (Teflon followed by carbon-impregnated glass-fiber filter) on the tapered oscillating element. The various denuders remove gas phase organic compounds, nitric acid, sulfur dioxide, nitrogen dioxide, ammonia, and ozone, which could otherwise be adsorbed by the TEOM filter.	10 min-24 h	N/A	< 10%[f 71]	± 1 to 2 µg/m^3 for 30-min avg [72]	N/A	10 to 20% higher than avg [72] FRM mass [73,74]	N/A

Instrument and Measurement Principle	Averaging Time	Analytical Accuracy[a]	Precisionb	MDL	Interferences	Comparability	Data Completeness
PRESSURE DROP INSTRUMENT							
Continuous Ambient Mass Monitor (CAMM) Air is drawn through a Teflon-membrane filter tape and the pressure drop across the filter is monitored continuously. The proportion of pressure drop to aerosol loading is related to the PM concentration. The filter tape advances every 30-60 min to minimize volatilization and adsorption artifacts during sampling.	1 h-24 h	N/A	28.1% for 1-h avg 15.9% for 24-h avg (~3.5 µg/m^3) [75]	< 5 µg/m^3 for 1 h avg [75]	Needs effective sealing for good performance; even slight leaks may result in highly variable baseline. Probably less sensitive than DTEOM or RAMS. [75,77]	Varied performance: within 2% of SES-TEOM and FRM at Houston, TX, while not correlated with D-TEOM or FRM at Rubidoux, CA. [76,77]	N/A
B-ATTENUATION INSTRUMENT							
B Attenuation Monitor (BAM) B rays electrons are passed through a quartz-fiber filter tape on which particles are collected. The loss of electrons (B attenuation) caused by the particle loading on the filter is converted to mass concentration, after subtraction of blank filter attenuation.	1 h-24 h	± 3 µg for 24-h avg concentrations < 100 µg/m^3 and 2% for 100 to 1,000 µg/m^3 ± 8 µg for 1-h concentrations < 100 µg/m^3 and 8% for 100 to 1000 µg/m^3	± 2 µg/m^3 [c,h]	5 µg/m^3 for 1-h avg[1]	Water absorption by particles may result in higher mass measurements; maybe important at RH >85%	Up to 30% higher than FRM mass and within 2% of FDMS TEOM [63,67]	93-99%[6,65,67]
LIGHT-SCATTERING INSTRUMENT							
Nephelometers (including DustTrak) A light source illuminates the sample air and the scattered light is detected at an angle (usually 90°) relative to the source. The signal is related to the concentration of the particles giving an estimate of the particle light-scattering coefficient. Zero air calibrations can be performed using particle-free air.	5 min-24 h	N/A	Nephelometers: < 5% for TSI and NGNi nephelometers [78,79] DustTrak: Greater of 0.1% or 1 µg/m^3 [c,h]	Nephelometer: < 1.5 Mm^{-1} DustTrak: ± 1 µg/m^3 for 24-h avg[j]	Conversion factor to calculate mass concentration from bscat may vary depending on particle size, shape and composition. Light scattering by DustTrak proportional to dp 6 for dp < 0.25 µm 79	Typically good correlation with SES-TEOM and D-TEOM (R^2 >0.80). Comparability depends on conversion factor used.	>80-98% for NGN2, RR-M903 and GreenTek Nephelometers 6 >80% for DustTrak [6 95] to 98% for GRIMM optical particle counter[65]

Instrument and Measurement Principle	Averaging Time	Analytical Accuracy[a]	Precisionb	MDL	Interferences	Comparability	Data Completeness

[a] Accuracy is the ability of analytical methods to quantify the observable of a standard reference material correctly; does not refer to measurement accuracy, since no standards available.
[b] Refers to precision of co-located measurements, unless specified otherwise.
[c] Manufacturer-specified measurement parameter.
[d] Details not available on how the precision was obtained and whether it refers to co-located precision.
[e] Includes a combination of estimates: based on co-located precision and based on regression slopes.
[f] Co-located precision with respect to PC-BOSS reconstructed $PM_{2.5}$ mass.
[g] Using glass-fiber "sandwich" filter.
[h] Specified as "resolution" by the manufacturer.
[i] Co-located precision estimate based on regression slope for NGN nephelometer (slope = 1.01, intercept = -1.64 μg/m^3, R^2 = 0.99).
[j] Specified as "Zero stability" by the manufacturer.
N/A: Not available.

[1]Chow (1995, 077012); [2]Watson and Chow (2001, 157123); [3] Watson et al. (1983, 045084); [4]Fehsenfeld et al. (2004, 157360); [5]Solomon et al. (2001, 157193); [6]Watson et al. (2005, 157124); [7]Mikel (2001, 156762); [8]Watson et al. (1999, 020949); [9]Solomon and Sioutas (2006, 156995); [10]Graney et al. (2004, 053756); [11]Tanaka et al. (1998, 157041); [12]Pancras et al. (2005, 098120); [13]John et al. (1988, 045903); [14]Hering and Cass (1999, 084958); [15]Fitz et al. (1989, 077387); [16]Hering et al. (1988, 036012); [17]Solomon et al. (2003, 156994); [18]Cabada et al. (2004, 148859); [19]Fine et al. (2003, 155775); [20]Hogrefe et al. (2004, 099003); [21]Drewnick et al. (2003, 099160); [22]Watson et al. (2005, 157125); [23]Ho et al. (2006, 156552); [24]Decesari et al. (2005, 144536); [25] Mayol-Bracero et al. (2002, 045010); [26]Yang et al. (2003, 156167); [27]Turšic et al. (2006, 157063); [28]Mader et al.(2004, 156724); [29]Xiao and Liu (2004, 056801); [30]Kiss et al. (2002, 156646); [31]Cornell and Jickells (1999, 156367); [32] Zheng et al. (2002, 026100); [33]Fraser et al. (2002, 140741); [34] Fraser et al. (2003, 042231) [35]Schauer er al. (2000, 012225); [36]Fine et al. (2004, 141283); [37]Yue et al. (2004, 157169); [38]Rinehart et al. (2006, 115184); [39]Wan and Yu (2006, 157104); [40]Poore (2000, 012839); [41]Fraser et al. (2003, 040266); [42]Engling et al. (2006, 156422); [43]Yu et al. (2005, 157167); [44]Tran et al. (2000, 013025); [45]Yao et al. (2004, 102213); [46]Li and Yu (2005, 156692); [47]Henning et al. (2003, 156539); [48]Zhang and Anastasio (2003, 157182); [49]Emmenegger et al. (2007, 156418); [50] Watson et al. (1989, 046318); [51]Greaves et al. (1985, 156494); [52]Waterman et al. (2000, 157116); [53]Waterman et al. (2001, 157117); [54]Falkovich and Rudich (2001, 156427); [55]Chow et al. (2007, 157209); [56]Miguel et al. (2004, 123260); [57]Crimmins and Baker (2006, 097008); [58]Ho and Yu (2004, 156551); [59]Jeon et al. (2001, 016636); [60]Mazzoleni et al. (2007, 098038); [61]Poore (2002, 051444); [62]Butler et al. (2003, 156313); [63]Chow et al. (2006, 146622); [64]Russell et al. (2004, 082453); [65]Grover et al. (2006, 138080); [66]Grover et al. (2005, 090044); [67]Schwab et al. (2006, 098449); [68]Hauck et al. (2004, 156525); [69]Jaques et al. (2004, 155878); [70]Rupprecht and Patashnick (2003, 157207); [71]Pang et al (2002, 030353); [72]Eatough et al. (2001, 010303); [73]Lee et al. (2005, 128139); [74]Lee et al. (2005, 156680); [75]Babich et al. (2000, 156239); [76]Lee et al. (2005, 155925); [77]Lee et al. (2005, 128139); [78]Anderson and Ogren (1998, 156213); [79]Chung et al. (2001, 156357); [80]Kidwell and Ondov (2004, 155898); [81]Lithgow et al. (2004, 126616); [82]Weber et al. (2003, 157129); [83]Harrison et al. (2004, 136787); [84]Rattigan et al. (2006, 115897); [85]Wittig et al. (2004, 103413); [86]Vaughn et al. (2005, 157089); [87]Chow et al. (2005, 099030); [88]Weber et al (2001, 024640) ; [89]Schwab et al. (2006, 098785); [90]Lim et al. (2003, 037037); [91]Watson and Chow (2002, 037873); [92]Venkatachari et al. (2006, 105918); [93]Bae et al. (2004, 156243); [94]Arhami et al. (2006, 156224); [95]Park et al. (2005, 156843); [96]Bae et al. (2004, 098680); [97]Chow et al. (2006, 156350); [98]Arnott et al. (2005, 156227); [99]Bond et al. (1999, 156281); [100]Virkkula et al. (2005, 157097); [101]Petzold et al. (2002, 156863); [102]Park et al. (2006, 098104); [103]Arnott et al. (1999, 020650); [104]Peters et al. (2001, 016925); [105]Pitchford et al. (1997, 156872); [106]Rees et al. (2004, 097164); [107]Watson et al. (2000, 010354); [108]Lee et al. (2005, 156680); [109]Hering et al. (2004, 155837); [110]Watson et al. (1998, 198805); [111]Chakrabarti et al. (2004, 157426); [112]Mathai et al. (1990, 156741); [113]Kidwell and Ondov (2001, 017092); [114]Stanier et al. (2004, 095955); [115]Khlystov et al. (2005, 156635); [116]Takahama et al. (2004, 157038); [117]Chow et al. (2005, 156348); [118]Zhang et al. (2002, 157181); [119]Subramanian et al. (2004, 081203); [120]Chow et al. (2006, 155207); [121]Birch and Cary (1996, 026004); [122]Birch (1998, 024953); [123]Birch and Cary (1996, 002352); [124]NIOSH (1996, 156810); [125]NIOSH (1999, 156811); [126]Chow et al. (1993, 077459); [127]Chow et al. (2007, 156354); [128]Ellis and Novakov (1982, 156416); [129]Peterson and Richards (2002, 156861); [130]Schauer et al. (2003, 037014); [131]Middlebrook et al. (2003, 042932); [132]Wenzel et al. (2003, 157139); [133]Jimenez et al. (2003, 156611); [134]Phares et al. (2003, 156866); [135]Qin and Prather (2006, 156895); [136]Zhang et al. (2005, 157185); [137]Bein et al. (2005, 156265); [138]Drewnick et al. (2004, 155754); [139]Drewnick et al. (2004, 155755); [140]Lake et al. (2003, 156669); [141]Lake et al. (2004, 088411)

Source: Chow et al. (2008, 156355)

Table A-6. Measurement and analytical specifications for continuous elements.

Instrument and Measurement Principle	Averaging Time	Analytical Accuracya	Precision	MDL	Interferences	Comparability	Data Completeness
Semi-continuous Elements in Aerosol System (SEAS) Particles are collected at 30-min interval for subsequent laboratory atomic absorption analysis for elements. Aerosol collection is through condensational growth by direct steam injection. The grown particles are separated from the airstream using virtual impactor. The droplets accumulate in a slurry that is pumped to a separate sample vial for each time period.	15-30 min	± 10%[b] for Mn, Fe, Ni, Cu, Zn, Se, Cd, and Sb ± 20%[b] for Cr, As, and Pb [80]	20-43%c [80]	Al: 440 pg Cr: 6.7 pg Mn: 9.9 pg Fe: 85 pg Ni: 42 pg Cu: 26 pg Zn: 43 pg As: 27 pg Se: 33 pg Cd: 3.2 pg Sb 160 pg Pb: 31 pg[80]	Spectral interferences limit the number of elements detected simultaneously	N/A	N/A
Laser-Induced Breakdown Spectroscopy (LIBS) Used for in-situ single particle analysis. A high-power pulsed laser is projected into particles producing high-temperature plasma. Photons emission from relaxing atoms in the excited states provides characteristics of individual elements.	A few seconds	N/A	N/A	Na: 143 fg Mg: 53 fg Al: 184 fg Ca: 50 fg Cr: 166 fg Mn: 176 fg Cu: 15 fg[81]	N/A	N/A	N/A

[a] Accuracy is the ability of analytical methods to quantify the observable of a standard reference material correctly; does not refer to measurement accuracy, since no standards are available.
[b] Based on analysis of standard reference material (SRM) 1643d from National Institute of Standards and Technology (NIST).
[c] Based on error propagation.
N/A: Not available

[80](Kidwell and Ondov, 2004, 155898); [81](Lithgow et al., 2004, 126616).

Source: Chow et al. (2008, 156355)

Table A-7. Measurement and analytical specifications for continuous NO_3^-.

Instrument and Measurement Principle	Averaging Time	Analytical Accuracy[a]	Precision	MDL	Interferences	Comparability	Data Completion
FLASH VOLATIZATION INSTRUMENTS							
Aerosol Dynamics Inc. continuous nitrate analyzer (ADIN) Particle collection by humidification and impaction followed by flash volatilization and detection of the evolved gases in a chemiluminescent NO_X analyzer.	10 min	N/A	N/A	0.1 µg/m^3 for 10-min avg [82]	N/A	Within 30% of filter and continuous NO_3^-. See Weber et al. [82] for details.	93%[7]
Rupprecht and Patashnick continuous nitrate analyzer (R&P-8400N) Particle collection by impaction followed by flash volatilization and detection of the evolved gases in a chemiluminescent NO_X analyzer. A carbon honeycomb denuder, installed at the inlet to the Nafion humidifier removes nitric acid and ammonia vapor.	10 min	N/A	6.3%-23%[b] [83]	0.17 to 0.3 µg/m^3 for 24-h avg [83,84] 0.24 µg/m^3 to 0.45 µg/m^3 for 10-min avg [83,85]	Conversion and volatilization efficiency appears to depend on ambient composition; extent of underestimation increases with higher concentrations. [84,86]	20 to 45% lower than filter NO_3^- [20,82,85,87]	>80->94%[6,20,83-85]
DENUDER-DIFFERENCE INSTRUMENT							
Atmospheric Research and Analysis nitrate analyzer (ARAN) Sampled air passes through a 350ºC molybdenum (Mo) mesh that converts particulate nitrate into NO. A pre-split stream with a Teflon filter installed upstream of an identical converter (i.e., particle-free air) is used as a reference. NO in both streams is quantified by chemiluminescence and their difference determines the particulate nitrate concentration. The instrument inlet contains a potassium iodide- coated denuder to remove HNO_3 and NO_2.	30 s	N/A	N/A	0.5 µg/m^3 for 30-s avg [82]	N/A	Within 30% of filter and continuous NO_3^-. See Weber et al. [82] for details.	76%[7]
SAMPLE DISSOLUTION FOLLOWED BY IC ANALYSIS INSTRUMENTS							
Energy Research Center of the Netherlands (ECN) IC-based ion analyzer Collects particles into water drops using a steam jet aerosol collector, via cyclone. The combined flow from collected droplets containing dissolved aerosol components and wall steam condensate is directed to an anion IC for analysis of nitrate. Interfering gases are pre-removed by a rotating wet annular denuder system.	1 h	N/A	N/A	0.1 µg/m^3 [82]	N/A	Within 30% of filter and continuous NO_3^-. See Weber et al. [82] for details.	100%[7]
Texas Tech University (TT) ion analyzer Particles in the sample stream are processed through a cyclone and a parallel plate wet denuder, then collected alternatively on one of two 2.5 cm pre-washed glass fiber filters for a period of 15 min. The particles on the freshly sampled filter are automatically extracted for 6.5 min with water and analyzed for nitrate by IC.	15-30 min	N/A	N/A	0.010 µg/m^3 [82]	N/A	Within 30% of filter and continuous NO_3^-. See Weber et al. [82] for details.	97%[7]
Particle into Liquid Sampler-Ion Chromatography (PILS-IC) Ambient particles are mixed with saturated water vapor to produce droplets collected by impaction. The resulting liquid stream is analyzed with an IC to quantify aerosol ionic components.	1 h	N/A	10%-15%[c] [7,82,88]	0.05-0.1 µg/m^3 [20,82,88]	Consistent water quality is essential for good precision.	Within 10% of nylon-filter NO_3^- and 37% higher than R&P-8400N [20]	65-70%[20]

Instrument and Measurement Principle	Averaging Time	Analytical Accuracy[a]	Precision	MDL	Interferences	Comparability	Data Completion
Dionex-IC The gas-denuded air stream enters the annular channel of a concentric nozzle, where deionized water generates a spray that entrains the particles. The flow is then drawn through a 0.5 µm pore size PTFE filter. The remaining solution is aspirated by a peristaltic pump and sent to IC for ion analysis.	1 h	N/A	14%[d 65]	N/A	Consistent water quality is essential for good precision.	Bias of < 10% relative to filter NO_3^- [65]	N/A
Ambient Ion Monitor (AIM; Model 9000) Air is drawn through a size-selective inlet into a liquid diffusion denuder where interfering gases are removed. The stream enters a supersaturation chamber where the resulting droplets are collected through impaction. The collected particles and a fraction of the condensed water are accumulated until the particles can be injected into IC for hourly analysis.	1 h	N/A	N/A	0.1 µg/m^3 for 1-h avg[e]	N/A	N/A	N/A
PARTICLE MASS SPECTROMETER INSTRUMENT							
Aerosol Mass Spectrometer (AMS) Air stream is drawn through an aerodynamic lens and focused into a beam in a vacuum chamber. This aerosol beam is chopped by a mechanical chopper and the flight time of the particles through a particle-sizing chamber is determined by the time-resolved mass spectrometer measurement. The particle impacts onto a 600 °C heated plate where it decomposes and is analyzed by a quadruple mass spectrometer. The nitrate ion, along with other ions, is detected by the mass spectrometer.	A few seconds	N/A	N/A	0.03 µg/m^3 [20]	Subject to interferences from fragments of other species with mass to charge ratio in the same range as fragments of nitrate. Highly refractory materials are not detected.	Within 10% of nylon-filter NO_3^-, and within 15% of PILS-IC and 30% of R&P8400N 20	94-98%[20]

[a] Accuracy is the ability of analytical methods to quantify the observable of a standard reference material correctly; does not refer to measurement accuracy, since no standards are available.
[b] Overall uncertainty estimated by error propagation.
[c] Uncertainty estimated from uncertainties in flow rates and calibrations; does not refer to co-located precision.
[d] Co-located precision with respect to PC-BOSS $PM_{2.5}$ total particulate NO_3 (the sum of the denuded front filter [non-volatilized NO_3-] and HNO_3-absorbing backup filter [volatilized NO_3]).
[e] Manufacturer specified measurement parameter
N/A: Not available.

[1]Chow (1995, 077012); [2]Watson and Chow (2001, 157123); [3] Watson et al. (1983, 045084); [4]Fehsenfeld et al. (2004, 157360); [5]Solomon et al. (2001, 157193); [6]Watson et al. (2005, 157124); [7]Mikel (2001, 156762); [8]Watson et al. (1999, 020949); [9]Solomon and Sioutas (2006, 156995); [10]Graney et al. (2004, 053756); [11]Tanaka et al. (1998, 157041); [12]Pancras et al. (2005, 098120); [13]John et al. (1988, 045903); [14]Hering and Cass (1999, 084958); [15]Fitz et al. (1989, 077387); [16]Hering et al. (1988, 036012); [17]Solomon et al. (2003, 156994); [18]Cabada et al. (2004, 148859); [19]Fine et al. (2003, 155775); [20]Hogrefe et al. (2004, 099003); [21]Drewnick et al. (2003, 099160); [22]Watson et al. (2005, 157125); [23]Ho et al. (2006, 156552); [24]Decesari et al. (2005, 144536); [25] Mayol-Bracero et al. (2002, 045010); [26]Yang et al. (2003, 156167); [27]Turšic et al. (2006, 157063); [28]Mader et al.(2004, 156724); [29]Xiao and Liu (2004, 056801); [30]Kiss et al. (2002, 156646); [31]Cornell and Jickells (1999, 156367); [32] Zheng et al. (2002, 026100); [33]Fraser et al. (2002, 140741); [34] Fraser et al. (2003, 042231) [35]Schauer er al. (2000, 012225); [36]Fine et al. (2004, 141283); [37]Yue et al. (2004, 157169); [38]Rinehart et al. (2006, 115184); [39]Wan and Yu (2006, 157104); [40]Poore (2000, 012839); [41]Fraser et al. (2003, 040266); [42]Engling et al. (2006, 156422); [43]Yu et al. (2005, 157167); [44]Tran et al. (2000, 013025); [45]Yao et al. (2004, 102213); [46]Li and Yu (2005, 156692); [47]Henning et al. (2003, 156539); [48]Zhang and Anastasio (2003, 157182); [49]Emmenegger et al. (2007, 156418); [50] Watson et al. (1989, 046318); [51]Greaves et al. (1985, 156494); [52]Waterman et al. (2000, 157116); [53]Waterman et al. (2001, 157117); [54]Falkovich and Rudich (2001, 156427); [55]Chow et al. (2007, 157209); [56]Miguel et al. (2004, 123260); [57]Crimmins and Baker (2006, 097008); [58]Ho and Yu (2004, 156551); [59]Jeon et al. (2001, 016636); [60]Mazzoleni et al. (2007, 098038); [61]Poore (2002, 051444); [62]Butler et al. (2003, 156313); [63]Chow et al. (2006, 146622); [64]Russell et al. (2004, 082453); [65]Grover et al. (2006, 138080); [66]Grover et al. (2005, 090044); [67]Schwab et al. (2006, 098449); [68]Hauck et al. (2004, 156525); [69]Jaques et al. (2004, 155878); [70]Rupprecht and Patashnick (2003, 157207); [71]Pang et al (2002, 030353); [72]Eatough et al. (2001, 010303); [73]Lee et al. (2005, 128139); [74]Lee et al. (2005, 156680); [75]Babich et al. (2000, 156239); [76]Lee et al. (2005, 155925); [77]Lee et al. (2005, 128139); [78]Anderson and Ogren (1998, 156213); [79]Chung et al. (2001, 156357); [80]Kidwell and Ondov (2004, 155898); [81]Lithgow et al. (2004, 126616); [82]Weber et al. (2003, 157129); [83]Harrison et al. (2004, 136787); [84]Rattigan et al. (2006, 115897); [85]Wittig et al. (2004, 103413); [86]Vaughn et al. (2005, 157089); [87]Chow et al. (2005, 099030); [88]Weber et al (2001, 024640) ; [89]Schwab et al. (2006, 098785); [90]Lim et al. (2003, 037037); [91]Watson and Chow (2002, 037873); [92]Venkatachari et al. (2006, 105918); [93]Bae et al. (2004, 156243); [94]Arhami et al. (2006, 156224); [95]Park et al. (2005, 156843); [96]Bae et al. (2004, 098680); [97]Chow et al. (2006, 156350); [98]Arnott et al. (2005, 156227); [99]Bond et al. (1999, 156281); [100]Virkkula et al. (2005, 157097); [101]Petzold et al. (2002, 156863); [102]Park et al. (2006, 098104); [103]Arnott et al. (1999, 020650); [104]Peters et al. (2001, 016925); [105]Pitchford et al. (1997, 156872); [106]Rees et al. (2004, 097164); [107]Watson et al. (2000, 010354); [108]Lee et al. (2005, 156680); [109]Hering et al. (2004, 155837); [110]Watson et al. (1998, 198805); [111]Chakrabarti et al. (2004, 157426); [112]Mathai et al. (1990, 156741); [113]Kidwell and Ondov (2001, 017092); [114]Stanier et al. (2004, 095955); [115]Khlystov et al. (2005, 156635); [116]Takahama et al. (2004, 157038); [117]Chow et al. (2005, 156348); [118]Zhang et al. (2002, 157181); [119]Subramanian et al. (2004, 081203); [120]Chow et al. (2006, 155207); [121]Birch and Cary (1996, 026004); [122]Birch (1998, 024953); [123]Birch and Cary (1996, 002352); [124]NIOSH (1996, 156810); [125]NIOSH (1999, 156811); [126]Chow et al. (1993, 077459); [127]Chow et al. (2007, 156354); [128]Ellis and Novakov (1982, 156416); [129]Peterson and Richards (2002, 156861); [130]Schauer et al. (2003, 037014); [13]1Middlebrook et al. (2003, 042932); [132]Wenzel et al. (2003, 157139); [133]Jimenez et al. (2003, 156611); [134]Phares et al. (2003, 156866); [135]Qin and Prather (2006, 156895); [136]Zhang et al. (2005, 157185); [137]Bein et al. (2005, 156265); [138]Drewnick et al. (2004, 155754); [139]Drewnick et al. (2004, 155755); [140]Lake et al. (2003, 156669); [141]Lake et al. (2004, 088411)

Source: Chow et al. (2008, 156355)

Table A-8. Measurement and analytical specifications for continuous SO_4^{2-}.

Instrument and Measurement Principle	Averaging Time	Analytical Accuracy[a]	Precision	MDL	Interferences	Comparability	Data Completeness
FLASH VOLATILIZATION INSTRUMENTS							
Aerosol Dynamics, Inc. continuous sulfate analyzer (ADIS) Particle collection by impaction followed by flash volatilization and detection of the evolved gases by a UV-fluorescence SO_2 analyzer.	10 min	N/A	N/A	0.4 µg/m^3 [82]	N/A	Within 15% of filter and continuous SO_4^{2-} See Weber et al. [82] for details.	100%[7]
Rupprecht and Patashnick continuous sulfate analyzer (R&P-8400S) Particle collection by impaction followed by flash volatilization and detection of the evolved gases by a UV-fluorescence SO_2 analyzer. An activated carbon denuder at the inlet to the Nafion humidifier removes SO_2.	10 min	N/A	25% on avg < 15% at conc. >9 µg/m^3 and >30% at conc. < 2 µg/m^3 [b] [84]	0.48 µg/m^3 [85]	SO_4^{2-} to SO_2 conversion and volatilization efficiency appears to depend on ambient composition [84]	10-30% lower than filter SO_4^{2-} [20,21,84]	84- 95%[6,20,21,84,85]
THERMAL REDUCTION INSTRUMENTS							
Continuous Ambient Sulfate Monitor (CASM) Sampled air passes through a Na_2CO_3 coated annular denuder to remove ambient SO_2 and is subsequently split into independent sample and filter flows. The sample flow passes through a quartz tube containing a stainless steel rod maintained at 1000 °C that reduces sulfate to SO_2. The flow then passes through a PTFE filter and into a trace-level SO_2 fluorescence analyzer.	15 min	N/A	N/A	N/A	N/A	Up to 25% lower than filter SO_4^{2-} and within 6% of R&P8400S, PILS-IC and AMS [20,21]	80-98%[20,21]
Thermo Electron Model 5020 sulfate particulate analyzer (TE-5020) The commercial version of CASM, with slight changes in the sample flow path.	15 min	N/A	< 10%[c] [89]	0.3 µg/m^3 for 24-h avg [89] 0.5 µg/m^3 for 15-min avgd	SO_4^{2-} to SO_2 conversion efficiency depends on ambient composition [89]	~20% lower than filter SO_4^{2-} [89]	88-90%[89]
SAMPLE DISSOLUTION FOLLOWED BY IC ANALYSIS INSTRUMENTS							
Energy Research Center of the Netherlands (ECN) IC-based ion analyzer Entrains particles into water drops using the steam jet aerosol collector. The drops are collected using a cyclone and the combined flow from collected droplets containing dissolved aerosol components and wall steam condensate is directed to an anion IC for analysis of sulfate. Interfering gases are pre-removed by a rotating wet annular denuder system.	1 h	N/A	N/A	N/A	N/A	Within 15% of filter and continuous SO_4^{2-} See Weber et al. [82] for details.	100%
Texas Tech University (TT) ion analyzer Particles in the sample stream, after being processed through a cyclone and a parallel plate wet denuder, are collected alternatively on one of two 2.5 cm pre-washed glass fiber filters for a period of 15 min. The particles on the freshly sampled filter are automatically extracted for 6.5 min with water and analyzed for sulfate by IC.	30 min	N/A	N/A	N/A	N/A	Within 15% of filter and continuous SO_4^{2-} See Weber et al. [82] for details.	100%[7]
Particle into Liquid Sampler-Ion Chromatography (PILS-IC) Ambient particles are mixed with saturated water vapor to produce droplets collected by impaction. The resulting liquid stream is analyzed with an IC to quantify aerosol ionic components.	1 h	N/A	10%-15%[e] [7,82,88]	0.1 to 0.18 µg/m^3 [82,88]	Consistent water quality is essential for good precision.	Within 30% of filter and other continuous SO_4^{2-} [20,21]	65-70%[20,21]

Instrument and Measurement Principle	Averaging Time	Analytical Accuracy[a]	Precision	MDL	Interferences	Comparability	Data Completeness
Dionex-IC The gas-denuded air stream enters the annular channel of a concentric nozzle, where deionized water generates a spray that entrains the particles. The flow is then drawn through a 0.5-µm pore size PTFE filter. The remaining solution is aspirated by a peristaltic pump and sent to IC for ion analysis.	1h	N/A	11%[f 65]	N/A	Consistent water quality is essential for good precision.	Within 10% of filter SO_4^{2-} [65]	N/A
Ambient Ion Monitor (AIM; Model 9000) Air is drawn through a size-selective inlet into a liquid diffusion denuder where interfering gases are removed. The stream enters a super saturation chamber where the resulting droplets are collected through impaction. The collected particles and a fraction of the condensed water are accumulated until the particles can be injected into IC for hourly analysis.	1h	N/A	N/A	0.1 µg/m^3 for 1-h avg	N/A	N/A	N/A
PARTICLE MASS SPECTROMETER							
Aerosol Mass Spectrometer (AMS) Airstream is drawn through an aerodynamic lens and focused into a beam in a vacuum chamber. This aerosol beam is chopped by a mechanical chopper and the flight time of the particles through a particle-sizing chamber is determined by the time-resolved mass spectrometer measurement. The particle impacts onto a 600 °C heated plate where it decomposes and is analyzed by a quadruple mass spectrometer. The sulfate ion, along with other ions, is detected by the mass spectrometer.	A few seconds	N/A	N/A	N/A	Subject to interferences from fragments of other species with mass to charge ratio in the same range as fragments of sulfate. Highly refractory materials are not detected.	Up to 30% lower than filter SO_4^{2-} and within 5% of R&P8400S, PILS-IC and CASM [20,21]	93-98%[20,21]

[a] Accuracy is the ability of analytical methods to quantify the observable of a standard reference material correctly; does not refer to measurement accuracy, since no standards available.
[b] Overall uncertainty estimated by error propagation.
[c] Co-located precision estimate based on regression slope (slope = 0.95, intercept = 0.01-0.2, R^2>0.98).
[d] Manufacturer specified measurement parameter.
[e] Uncertainty estimated from uncertainties in flow rates and calibrations; does not refer to co-located precision.
[f] Co-located precision with respect to PC-BOSS $PM_{2.5}$ SO_4^{2-}.
N/A: Not available

[1]Chow (1995, 077012); [2]Watson and Chow (2001, 157123); [3] Watson et al. (1983, 045084); [4]Fehsenfeld et al. (2004, 157360); [5]Solomon et al. (2001, 157193); [6]Watson et al. (2005, 157124); [7]Mikel (2001, 156762); [8]Watson et al. (1999, 020949); [9]Solomon and Sioutas (2006, 156995); [10]Graney et al. (2004, 053756); [11]Tanaka et al. (1998, 157041); [12]Pancras et al. (2005, 098120); [13]John et al. (1988, 045903); [14]Hering and Cass (1999, 084958); [15]Fitz et al. (1989, 077387); [16]Hering et al. (1988, 036012); [17]Solomon et al. (2003, 156994); [18]Cabada et al. (2004, 148859); [19]Fine et al. (2003, 155775); [20]Hogrefe et al. (2004, 099003); [21]Drewnick et al. (2003, 099160); [22]Watson et al. (2005, 157125); [23]Ho et al. (2006, 156552); [24]Decesari et al. (2005, 144536); [25] Mayol-Bracero et al. (2002, 045010); [26]Yang et al. (2003, 156167); [27]Turšic et al. (2006, 157063); [28]Mader et al.(2004, 156724); [29]Xiao and Liu (2004, 056801); [30]Kiss et al. (2002, 156646); [31]Cornell and Jickells (1999, 156367); [32] Zheng et al. (2002, 026100); [33]Fraser et al. (2002, 140741); [34] Fraser et al. (2003, 042231) [35]Schauer er al. (2000, 012225); [36]Fine et al. (2004, 141283); [37]Yue et al. (2004, 157169); [38]Rinehart et al. (2006, 115184); [39]Wan and Yu (2006, 157104); [40]Poore (2000, 012839); [41]Fraser et al. (2003, 040266); [42]Engling et al. (2006, 156422); [43]Yu et al. (2005, 157167); [44]Tran et al. (2000, 013025); [45]Yao et al. (2004, 102213); [46]Li and Yu (2005, 156692); [47]Henning et al. (2003, 156539); [48]Zhang and Anastasio (2003, 157182); [49]Emmenegger et al. (2007, 156418); [50] Watson et al. (1989, 046318); [51]Greaves et al. (1985, 156494); [52]Waterman et al. (2000, 157116); [53]Waterman et al. (2001, 157117); [54]Falkovich and Rudich (2001, 156427); [55]Chow et al. (2007, 157209); [56]Miguel et al. (2004, 123260); [57]Crimmins and Baker (2006, 097008); [58]Ho and Yu (2004, 156551); [59]Jeon et al. (2001, 016636); [60]Mazzoleni et al. (2007, 098038); [61]Poore (2002, 051444); [62]Butler et al. (2003, 156313); [63]Chow et al. (2006, 146622); [64]Russell et al. (2004, 082453); [65]Grover et al. (2006, 138080); [66]Grover et al. (2005, 090044); [67]Schwab et al. (2006, 098449); [68]Hauck et al. (2004, 156525); [69]Jaques et al. (2004, 155878); [70]Rupprecht and Patashnick (2003, 157207); [71]Pang et al (2002, 030353); [72]Eatough et al. (2001, 010303); [73]Lee et al. (2005, 128139); [74]Lee et al. (2005, 156680); [75]Babich et al. (2000, 156239); [76]Lee et al. (2005, 155925); [77]Lee et al. (2005, 128139); [78]Anderson and Ogren (1998, 156213); [79]Chung et al. (2001, 156357); [80]Kidwell and Ondov (2004, 155898); [81]Lithgow et al. (2004, 126616); [82]Weber et al. (2003, 157129); [83]Harrison et al. (2004, 136787); [84]Rattigan et al. (2006, 115897); [85]Wittig et al. (2004, 103413); [86]Vaughn et al. (2005, 157089); [87]Chow et al. (2005, 099030); [88]Weber et al (2001, 024640) ; [89]Schwab et al. (2006, 098785); [90]Lim et al. (2003, 037037); [91]Watson and Chow (2002, 037873); [92]Venkatachari et al. (2006, 105918); [93]Bae et al. (2004, 156243); [94]Arhami et al. (2006, 156224); [95]Park et al. (2005, 156843); [96]Bae et al. (2004, 098680); [97]Chow et al. (2006, 156350); [98]Arnott et al. (2005, 156227); [99]Bond et al. (1999, 156281); [100]Virkkula et al. (2005, 157097); [101]Petzold et al. (2002, 156863); [102]Park et al. (2006, 098104); [103]Arnott et al. (1999, 020650); [104]Peters et al. (2001, 016925); [105]Pitchford et al. (1997, 156872); [106]Rees et al. (2004, 097164); [107]Watson et al. (2000, 010354); [108]Lee et al. (2005, 156680); [109]Hering et al. (2004, 155837); [110]Watson et al. (1998, 198805); [111]Chakrabarti et al. (2004, 157426); [112]Mathai et al. (1990, 156741); [113]Kidwell and Ondov (2001, 017092); [114]Stanier et al. (2004, 095955); [115]Khlystov et al. (2005, 156635); [116]Takahama et al. (2004, 157038); [117]Chow et al. (2005, 156348); [118]Zhang et al. (2002, 157181); [119]Subramanian et al. (2004, 081203); [120]Chow et al. (2006, 155207); [121]Birch and Cary (1996, 026004); [122]Birch (1998, 024953); [123]Birch and Cary (1996, 002352); [124]NIOSH (1996, 156810); [125]NIOSH (1999, 156811); [126]Chow et al. (1993, 077459); [127]Chow et al. (2007, 156354); [128]Ellis and Novakov (1982, 156416); [129]Peterson and Richards (2002, 156861); [130]Schauer et al. (2003, 037014); [13]1Middlebrook et al. (2003, 042932); [132]Wenzel et al. (2003, 157139); [133]Jimenez et al. (2003, 156611); [134]Phares et al. (2003, 156866); [135]Qin and Prather (2006, 156895); [136]Zhang et al. (2005, 157185); [137]Bein et al. (2005, 156265); [138]Drewnick et al. (2004, 155754); [139]Drewnick et al. (2004, 155755); [140]Lake et al. (2003, 156669); [141]Lake et al. (2004, 088411)

Source: Chow et al. (2008, 156355)

Table A-9. Measurement and analytical specifications for ions other than NO_3^- and SO_4^{2-}.

Instrument and Measurement Principle	Averaging Time	Analytical Accuracy[a]	Precision	MDL	Interferences	Comparability	Data Completeness
SAMPLE DISSOLUTION FOLLOWED BY IC ANALYSIS INSTRUMENTS							
NO_2^- by Particle into Liquid Sampler-Ion Chromatography (PILS-IC) Ambient particles are mixed with saturated water vapor to produce droplets collected by impaction. The resulting liquid stream is analyzed with an IC to quantify aerosol ionic components.	1 h	N/A	10%b [88]	0.14 µg/m^3 [3 20]	Consistent water quality is essential for good precision	N/A	N/A
NH_4^+ by Particle into Liquid Sampler-Ion Chromatography (PILS-IC) Ambient particles are mixed with saturated water vapor to produce droplets collected by impaction. The resulting liquid stream is analyzed with an IC to quantify aerosol ionic components.	1 h	N/A	10%[b 88]	[88] 0.05 µg/m^3	Consistent water quality is essential for good precision	~5% lower than all-sampler avg[c] at Atlanta [7]	N/A
Cl^-, Na^+, K^+, Ca^{++} by Particle into Liquid Sampler-Ion Chromatography (PILS-IC) Ambient particles are mixed with saturated water vapor to produce droplets collected by impaction. The resulting liquid stream is analyzed with an IC to quantify aerosol ionic components.	1 h	N/A	10%b [88]	0.1 µg/m^3 [3 88]	Consistent water quality is essential for good precision	N/A	N/A
Cl^-, NO_2^-, NO_3^-, PO_4^{3-}, SO_4^{2-}, NH_4^+, Na^+, Mg^{++}, K^+, Ca^{++} by Ambient Ion Monitor (AIM; Model 9000) Air is drawn through a size-selective inlet into a liquid diffusion denuder where interfering gases are removed. The stream enters a super saturation chamber where the resulting droplets are collected through impaction. The collected particles and a fraction of the condensed water are accumulated until the particles can be injected into IC for hourly analysis.	1 h	N/A	N/A	0.1 µg/m^3 for 1-h avg[d]	N/A	N/A	N/A

[a] Accuracy is the ability of analytical methods to quantify the observable of a standard reference material correctly; does not refer to measurement accuracy, since no standards are available.
[b] Uncertainty estimated from uncertainties in flow rates and calibrations; does not refer to co-located precision.
[c] All-sampler avg appears to include a combination of 10 integrated and 3 continuous samplers, although specific details are missing [7]. Performance evaluations at sites dominated by semi-volatile ammonium nitrate are needed.
[d] Manufacturer specified measurement parameter

[1]Chow (1995, 077012); [2]Watson and Chow (2001, 157123); [3] Watson et al. (1983, 045084); [4]Fehsenfeld et al. (2004, 157360); [5]Solomon et al. (2001, 157193); [6]Watson et al. (2005, 157124); [7]Mikel (2001, 156762); [8]Watson et al. (1999, 020949); [9]Solomon and Sioutas (2006, 156995); [10]Graney et al. (2004, 053756); [11]Tanaka et al. (1998, 157041); [12]Pancras et al. (2005, 098120); [13]John et al. (1988, 045903); [14]Hering and Cass (1999, 084958); [15]Fitz et al. (1989, 077387); [16]Hering et al. (1988, 036012); [17]Solomon et al. (2003, 156994); [18]Cabada et al. (2004, 148859); [19]Fine et al. (2003, 155775); [20]Hogrefe et al. (2004, 099003); [21]Drewnick et al. (2003, 099160); [22]Watson et al. (2005, 157125); [23]Ho et al. (2006, 156552); [24]Decesari et al. (2005, 144536); [25] Mayol-Bracero et al. (2002, 045010); [26]Yang et al. (2003, 156167); [27]Turšic et al. (2006, 157063); [28]Mader et al.(2004, 156724); [29]Xiao and Liu (2004, 056801); [30]Kiss et al. (2002, 156646); [31]Cornell and Jickells (1999, 156367); [32] Zheng et al. (2002, 026100); [33]Fraser et al. (2002, 140741); [34] Fraser et al. (2003, 042231) [35]Schauer er al. (2000, 012225); [36]Fine et al. (2004, 141283); [37]Yue et al. (2004, 157169); [38]Rinehart et al. (2006, 115184); [39]Wan and Yu (2006, 157104); [40]Poore (2000, 012839); [41]Fraser et al. (2003, 040266); [42]Engling et al. (2006, 156422); [43]Yu et al. (2005, 157167); [44]Tran et al. (2000, 013025); [45]Yao et al. (2004, 102213); [46]Li and Yu (2005, 156692); [47]Henning et al. (2003, 156539); [48]Zhang and Anastasio (2003, 157182); [49]Emmenegger et al. (2007, 156418); [50] Watson et al. (1989, 046318); [51]Greaves et al. (1985, 156494); [52]Waterman et al. (2000, 157116); [53]Waterman et al. (2001, 157117); [54]Falkovich and Rudich (2001, 156427); [55]Chow et al. (2007, 157209); [56]Miguel et al. (2004, 123260); [57]Crimmins and Baker (2006, 097008); [58]Ho and Yu (2004, 156551); [59]Jeon et al. (2001, 016636); [60]Mazzoleni et al. (2007, 098038); [61]Poore (2002, 051444); [62]Butler et al. (2003, 156313); [63]Chow et al. (2006, 146622); [64]Russell et al. (2004, 082453); [65]Grover et al. (2006, 138080); [66]Grover et al. (2005, 090044); [67]Schwab et al. (2006, 098449); [68]Hauck et al. (2004, 156525); [69]Jaques et al. (2004, 155878); [70]Rupprecht and Patashnick (2003, 157207); [71]Pang et al (2002, 030353); [72]Eatough et al. (2001, 010303); [73]Lee et al. (2005, 128139); [74]Lee et al. (2005, 156680); [75]Babich et al. (2000, 156239); [76]Lee et al. (2005, 155925); [77]Lee et al. (2005, 128139); [78]Anderson and Ogren (1998, 156213); [79]Chung et al. (2001, 156357); [80]Kidwell and Ondov (2004, 155898); [81]Lithgow et al. (2004, 126616); [82]Weber et al. (2003, 157129); [83]Harrison et al. (2004, 136787); [84]Rattigan et al. (2006, 115897); [85]Wittig et al. (2004, 103413); [86]Vaughn et al. (2005, 157089); [87]Chow et al. (2005, 099030); [88]Weber et al (2001, 024640) ; [89]Schwab et al. (2006, 098785); [90]Lim et al. (2003, 037037); [91]Watson and Chow (2002, 037873); [92]Venkatachari et al. (2006, 105918); [93]Bae et al. (2004, 156243); [94]Arhami et al. (2006, 156224); [95]Park et al. (2005, 156843); [96]Bae et al. (2004, 098680); [97]Chow et al. (2006, 156350); [98]Arnott et al. (2005, 156227); [99]Bond et al. (1999, 156281); [100]Virkkula et al. (2005, 157097); [101]Petzold et al. (2002, 156863); [102]Park et al. (2006, 098104); [103]Arnott et al. (1999, 020650); [104]Peters et al. (2001, 016925); [105]Pitchford et al. (1997, 156872); [106]Rees et al. (2004, 097164); [107]Watson et al. (2000, 010354); [108]Lee et al. (2005, 156680); [109]Hering et al. (2004, 155837); [110]Watson et al. (1998, 198805); [111]Chakrabarti et al. (2004, 157426); [112]Mathai et al. (1990, 156741); [113]Kidwell and Ondov (2001, 017092); [114]Stanier et al. (2004, 095955); [115]Khlystov et al. (2005, 156635); [116]Takahama et al. (2004, 157038); [117]Chow et al. (2005, 156348); [118]Zhang et al. (2002, 157181); [119]Subramanian et al. (2004, 081203); [120]Chow et al. (2006, 155207); [121]Birch and Cary (1996, 026004); [122]Birch (1998, 024953); [123]Birch and Cary (1996, 002352); [124]NIOSH (1996, 156810); [125]NIOSH (1999, 156811); [126]Chow et al. (1993, 077459); [127]Chow et al. (2007, 156354); [128]Ellis and Novakov (1982, 156416); [129]Peterson and Richards (2002, 156861); [130]Schauer et al. (2003, 037014); [131]Middlebrook et al. (2003, 042932); [132]Wenzel et al. (2003, 157139); [133]Jimenez et al. (2003, 156611); [134]Phares et al. (2003, 156866); [135]Qin and Prather (2006, 156895); [136]Zhang et al. (2005, 157185); [137]Bein et al. (2005, 156265); [138]Drewnick et al. (2004, 155754); [139]Drewnick et al. (2004, 155755); [140]Lake et al. (2003, 156669); [141]Lake et al. (2004, 088411)

Source: Chow et al. (2008, 156355)

Table A-10. Measurement and analytical specifications for continuous carbon.

Instrument and Measurement Principle	Averaging Time	Analytical Accuracy[a]	Precision	MDL	Interferences	Comparability	Data Completeness
PARTICLE COLLECTION ON IMPACTOR FOLLOWED BY FLASH VOLATILIZATION INSTRUMENT							
Aerosol Dynamic Inc. continuous carbon analyzer (ADI-C) Particle collection by impaction followed by flash oxidation and detection of the evolved gases by a non-dispersive infrared CO_2 analyzer. OC is estimated as twice the oxidizable carbon. EC is not quantified.	10 min	N/A	N/A	OC: 2 µg/m^3 EC, TC: not applicable, since it measures only OC [90]	N/A	15-22% lower OC than that by R&P-5400 and RU-OGI	83%[7]
PARTICLE COLLECTION ON FILTER / IMPACTOR FOLLOWED BY HEATING/ANALYSIS INSTRUMENTS							
Rupprecht and Patashnick 5400 continuous ambient carbon analyzer (R&P-5400) Particles collected on an impactor, which is heated to 275 °C to 350 °C, then to 700 °C after sample collection is complete. Evolved CO_2 is measured by an infrared detector. OC is defined as the carbon measured at the lower temperature, and EC is the remaining carbon measured at the higher temperature.	1 h	N/A	N/A	OC: 0.5 µg/m^3 EC: 0.5 µg/m^3 TC: 0.5 µg/m^3 [90]	N/A	20 to 60% lower TC than filter TC by TOR or TOT.[91,92]	56-60%[6,91]
Rutgers University-Oregon Graduate Institute (RU-OGI) in-situ thermal/optical transmittance carbon analyzer. Air is sampled through a quartz-fiber filter for 1 h and then analyzed by heating through different temperature steps to determine OC and EC. Sample flow is pre-split into two identical systems that alternate every hour between sampling and analysis mode to achieve continuous measurements.	30 min	N/A	3%[b,7]	OC: 0.3 µg/m^3 EC: 0.5 µg/m^3 TC: 0.4 µg/m^3 [90]	N/A	8% higher OC and 20% lower EC than R&P-5400 [90]	86%[7]
Sunset semi-continuous realtime carbon aerosol analysis instrument (Sunset OCEC) Particles collected on a quartz-fiber filter are subject to heating temperature ramps following the NIOSH 5040 TOT protocol and the resulting CO_2 is analyzed by nondispersive infrared (NDIR) detector to quantify OC and EC. Instrument is alternated between sampling and analytical mode.	1 h	N/A	OC: 10%[c] EC: 20%[c] TC: 10%[c] [93,94]	OC: N/A EC: N/A TC: 0.4 µg/m^3 (1-h avg)[95]	N/A	Within 7 to 25% of filter OC and EC and within 15% for TC. Wide variation due to differences in temperature and analysis protocols. [92,95,96]	80-89%[6,95]
LIGHT ABSORPTION INSTRUMENTS							
Aethalometer (AE-16, AE-21, AE-31) Attenuation of light transmitted through a quartz-fiber filter tape that continuously samples aerosol is measured and converted to a BC mass concentration using σ_{abs} of 14625/λ (m^2/g).	5 min	N/A	5 to 10%[d,7,97]	BC[e]: 0.1 µg/m^3 [90]	Subject to multiple scattering effects by particle and filter matrix resulting in absorption enhancement. Empirical corrections have been proposed 98 that can correct for such effects.	Within ± 25% of RU-OGI, Sunset and filter EC by TOR/TOT.[90-92]	75-90%[6]

Instrument and Measurement Principle	Averaging Time	Analytical Accuracy[a]	Precision	MDL	Interferences	Comparability	Data Completeness
Particle Soot Absorption Photometer (PSAP) Attenuation of light transmitted through a glass-fiber filter that continuously samples aerosol is measured to quantify light absorption (b_{abs}).	1 min	N/A	6 to 8%[99,100]	BC[f]: 0.1 µg/m^3 [90]	Instrument includes an empirical correction for scattering and loading effects 99 and adjustments have been proposed for the three wavelength model 100	~50% lower than AE-16, RU-OGI and R&P-5400 EC.[90]	N/A
Multi-Angle Absorption Photometer (MAAP) Light transmittance at 0° and reflectance from a glass-fiber filter at 130° and 165° from the illumination direction are used in a radiative transfer model to estimate babs and is converted to BC using σ_{abs} of 6.6 m_2/g.	1 min	N/A	12%[9,101]	BC[h]: 0.05 µg/m^3 (or b_{abs} = 0.33 Mm^{-1} for 10-min avg) 0.02 µg/m^3 (or b_{abs} = 0.13 Mm^{-1} for 30-min avg)[101]	The instrument is designed to minimize multiple scattering and loading effects by measuring both transmittance and reflectance and using a two-stream approximation radiative transfer model to calculate b_{abs}.	Within 18% of filter EC by IMPROVE_TOR (R^2 = 0.96) and up to 40% higher than Sunset EC. [102]	N/A
DRI Photoacoustic Analyzer (DRI-PA) Light absorption by particles in air results in a heating of the surrounding air. The expansion of the heated air produces an acoustic (sound wave) signal which is detected by a microphone to determine babs, which is converted to BC using σ_{abs}s = 5 m^2/g for the 1047 nm instrument and σ_{abs} = 10 m2/g for the 532 nm instrument.	5 s	N/A	N/A	BC[i]: 0.04 µg/m^3 (or b_{abs} = 0.4 Mm^{-1} for 10-min avg) at 532 nm[103]	At 532 nm, absorbance by NO_2 interferes with that by particles. Accounted by either removing NO_2 from sample line using denuders or by doing a periodic background (particle-free air) subtraction.	Good correlation (R^2 >0.80), but more than 40% lower than aethalometer, MAAP and filter IMPROVE_TOR EC. Suggests need for a different σ_{abs}. [102]	N/A
PHOTO-IONIZATION INSTRUMENTS							
Photoionization monitor for polycyclic aromatic hydrocarbons (PAS-PAH) The air stream is exposed to UV radiation, which ionizes the particle-bound PAH molecules. The charged particles are collected on a filter element and the piezoelectric current is proportional to the particle-bound PAH.	5 min	N/A	N/A	~3 ng/m^3 [j,k]	N/A	N/A	>91%[6]

Instrument and Measurement Principle	Averaging Time	Analytical Accuracy[a]	Precision	MDL	Interferences	Comparability	Data Completeness

[a] Accuracy is the ability of analytical methods to quantify the observable of a standard reference material correctly; does not refer to measurement accuracy, since no standards are available.
[b] No specific details on how the precision was estimated; appears to be based on replicate analysis, may not represent overall co-located measurement precision
[c] Co-located precision estimates based on variation in avg ratios of replicate analysis using laboratory instrument and regression slopes (Slopes for OC = 1.01, EC = 0.82, TC = 0.94; R^2 = 0.97-0.99) of co-located field measurements.
[d] Estimated using co-located AE-21 and AE-31 BC measurements at Fresno, CA.97
[e] While the default manufacturer recommended conversion factor (or mass absorption efficiency, σabs) is 16.6 m2/g at 880 nm, Lim et al. (2003, 037037) assumed a value of 12.6 m^2/g.
[f] Assuming a σabs of 10 m^2/g.
[g] Co-located precision estimate based on the variability of the avg ratio (0.99 ± 0.12).
[h] Assuming a σabs of 6.5 m^2/g.
[i] Assuming a σabs of 10 m^2/g at 532 nm and 5 m^2/g at 1047 nm.
[j] Specified by manufacturer as "lower threshold"; needs to be calibrated with site-specific PAH. Typically used as a relative measure in terms of electrical output in femtoamps.
[k] Manufacturer specified measurement parameter
N/A: Not available.

[1]Chow (1995, 077012); [2]Watson and Chow (2001, 157123); [3] Watson et al. (1983, 045084); [4]Fehsenfeld et al. (2004, 157360); [5]Solomon et al. (2001, 157193); [6]Watson et al. (2005, 157124); [7]Mikel (2001, 156762); [8]Watson et al. (1999, 020949); [9]Solomon and Sioutas (2006, 156995); [10]Graney et al. (2004, 053756); [11]Tanaka et al. (1998, 157041); [12]Pancras et al. (2005, 098120); [13]John et al. (1988, 045903); [14]Hering and Cass (1999, 084958); [15]Fitz et al. (1989, 077387); [16]Hering et al. (1988, 036012); [17]Solomon et al. (2003, 156994); [18]Cabada et al. (2004, 148859); [19]Fine et al. (2003, 155775); [20]Hogrefe et al. (2004, 099003); [21]Drewnick et al. (2003, 099160); [22]Watson et al. (2005, 157125); [23]Ho et al. (2006, 156552); [24]Decesari et al. (2005, 144536); [25] Mayol-Bracero et al. (2002, 045010); [26]Yang et al. (2003, 156167); [27]Turšic et al. (2006, 157063); [28]Mader et al.(2004, 156724); [29]Xiao and Liu (2004, 056801); [30]Kiss et al. (2002, 156646); [31]Cornell and Jickells (1999, 156367); [32] Zheng et al. (2002, 026100); [33]Fraser et al. (2002, 140741); [34] Fraser et al. (2003, 042231) [35]Schauer er al. (2000, 012225); [36]Fine et al. (2004, 141283); [37]Yue et al. (2004, 157169); [38]Rinehart et al. (2006, 115184); [39]Wan and Yu (2006, 157104); [40]Poore (2000, 012839); [41]Fraser et al. (2003, 040266); [42]Engling et al. (2006, 156422); [43]Yu et al. (2005, 157167); [44]Tran et al. (2000, 013025); [45]Yao et al. (2004, 102213); [46]Li and Yu (2005, 156692); [47]Henning et al. (2003, 156539); [48]Zhang and Anastasio (2003, 157182); [49]Emmenegger et al. (2007, 156418); [50] Watson et al. (1989, 046318); [51]Greaves et al. (1985, 156494); [52]Waterman et al. (2000, 157116); [53]Waterman et al. (2001, 157117); [54]Falkovich and Rudich (2001, 156427); [55]Chow et al. (2007, 157209); [56]Miguel et al. (2004, 123260); [57]Crimmins and Baker (2006, 097008); [58]Ho and Yu (2004, 156551); [59]Jeon et al. (2001, 016636); [60]Mazzoleni et al. (2007, 098038); [61]Poore (2002, 051444); [62]Butler et al. (2003, 156313); [63]Chow et al. (2006, 146622); [64]Russell et al. (2004, 082453); [65]Grover et al. (2006, 138080); [66]Grover et al. (2005, 090044); [67]Schwab et al. (2006, 098449); [68]Hauck et al. (2004, 156525); [69]Jaques et al. (2004, 155878); [70]Rupprecht and Patashnick (2003, 157207); [71]Pang et al (2002, 030353); [72]Eatough et al. (2001, 010303); [73]Lee et al. (2005, 128139); [74]Lee et al. (2005, 156680); [75]Babich et al. (2000, 156239); [76]Lee et al. (2005, 155925); [77]Lee et al. (2005, 128139); [78]Anderson and Ogren (1998, 156213); [79]Chung et al. (2001, 156357); [80]Kidwell and Ondov (2004, 155898); [81]Lithgow et al. (2004, 126616); [82]Weber et al. (2003, 157129); [83]Harrison et al. (2004, 136787); [84]Rattigan et al. (2006, 115897); [85]Wittig et al. (2004, 103413); [86]Vaughn et al. (2005, 157089); [87]Chow et al. (2005, 099030); [88]Weber et al (2001, 024640) ; [89]Schwab et al. (2006, 098785); [90]Lim et al. (2003, 037037); [91]Watson and Chow (2002, 037873); [92]Venkatachari et al. (2006, 105918); [93]Bae et al. (2004, 156243); [94]Arhami et al. (2006, 156224); [95]Park et al. (2005, 156843); [96]Bae et al. (2004, 098680); [97]Chow et al. (2006, 156350); [98]Arnott et al. (2005, 156227); [99]Bond et al. (1999, 156281); [100]Virkkula et al. (2005, 157097); [101]Petzold et al. (2002, 156863); [102]Park et al. (2006, 098104); [103]Arnott et al. (1999, 020650); [104]Peters et al. (2001, 016925); [105]Pitchford et al. (1997, 156872); [106]Rees et al. (2004, 097164); [107]Watson et al. (2000, 010354); [108]Lee et al. (2005, 156680); [109]Hering et al. (2004, 155837); [110]Watson et al. (1998, 198805); [111]Chakrabarti et al. (2004, 157426); [112]Mathai et al. (1990, 156741); [113]Kidwell and Ondov (2001, 017092); [114]Stanier et al. (2004, 095955); [115]Khlystov et al. (2005, 156635); [116]Takahama et al. (2004, 157038); [117]Chow et al. (2005, 156348); [118]Zhang et al. (2002, 157181); [119]Subramanian et al. (2004, 081203); [120]Chow et al. (2006, 155207); [121]Birch and Cary (1996, 026004); [122]Birch (1998, 024953); [123]Birch and Cary (1996, 002352); [124]NIOSH (1996, 156810); [125]NIOSH (1999, 156811); [126]Chow et al. (1993, 077459); [127]Chow et al. (2007, 156354); [128]Ellis and Novakov (1982, 156416); [129]Peterson and Richards (2002, 156861); [130]Schauer et al. (2003, 037014); [13]1Middlebrook et al. (2003, 042932); [132]Wenzel et al. (2003, 157139); [133]Jimenez et al. (2003, 156611); [134]Phares et al. (2003, 156866); [135]Qin and Prather (2006, 156895); [136]Zhang et al. (2005, 157185); [137]Bein et al. (2005, 156265); [138]Drewnick et al. (2004, 155754); [139]Drewnick et al. (2004, 155755); [140]Lake et al. (2003, 156669); [141]Lake et al. (2004, 088411)

Source: Chow et al. (2008, 156355)

Table A-11. Summary of mass measurement comparisons.

Site / Period / Sampler / Configuration	Summary of Findings

1. Birmingham, AL (11/04/96 To 11/23/96)
2. Denver-Adams City, CO (12/11/96 To 1/7/97)
3. Bakersfield, CA (1/21/97 To 3/19/97)
4. Denver-Welby, Co (12/12/96 To 12/21/96)
5. Phoenix, AZ (12/06/96 To 12/21/96)
6. Azusa, CA (3/25/97 To 5/19/97)
7. Research Triangle Park (RTP), NC (1/17/97 To 8/14/97)
8. Rubidoux, CA (1/6/99 To 2/26/99)
9. Atlanta, GA (8/3/99 To 8/31/99)

Sampler	Flow Rate (L/Min)	Filter Type[a]	Denuder[b]
RAAS2.5-100 $PM_{2.5}$ FRM	16.7	Teflon (N/A)	None
RAAS2.5-300 $PM_{2.5}$ FRM	16.7	Teflon (N/A)	None
RAAS2.5-200 $PM_{2.5}$ FRM	16.7	Teflon (N/A)	None
R&P Partisol 2000 $PM_{2.5}$ FRM	16.7	Teflon (N/A)	None
R&P Partisol-plus 2025 $PM_{2.5}$ FRM	16.7	Teflon (N/A)	None
BGI PQ200 $PM_{2.5}$ FRM	16.7	Teflon (N/A)	None
Sierra Instruments SA-244 Dichot	16.7	Teflon (N/A)	None
IMPROVE $PM_{2.5}$	22.8	Teflon (N/A)	None
Harvard $PM_{2.5}$ Impactor	10	Teflon (N/A)	None
Airmetrics battery powered $PM_{2.5}$ MiniVol	5	Teflon (N/A)	None

Peters et al. (2001, 017108)[104]: Pitchford et al. (1997, 156872)[105] dataset

Co-located precision (CV) for the RAAS2.5-100 samplers ranged from 1.5% at Bakersfield to 6.2% at Birmingham.

In Birmingham, CV for two co-located Harvard Impactor was 1% and for three Dichots was 6.2%. The IMPROVE samplers had greater variability, with a CV of 11.3% (Denver-Adam City) and 10.8% (Bakersfield).

Partisol and RAAS showed the strongest pairwise comparison (slope = 1.0 ± 0.06, intercept = 0.26 ± 1.81, and correlation = 1.0), within the EPA equivalency criteria. Strong relationships (correlation >0.96; slope = 0.9-1.12, intercept < 3σ) were observed for other samplers in reference to the RAAS.

At Denver-Welby, 6 RAAS samplers were deployed (3 with and 3 without temperature compensation for flow control). The units with temperature compensation had a positive bias relative to the non-temperature compensated units.

Non-FRM samplers did not meet the EPA equivalency criteria, despite strong linear relationships with the FRM sampler.

Peters et al. (2001, 016925)[104]: RTP [97] dataset

CV was 1.7%, 2.3%, 3.4%, 6.4% for the PQ200, Partisol 2000, RAAS2.5100, and Dichot, respectively. Dichot flows were valve controlled and set visually by the operator using rotameters.

Good one-to-one correspondence was observed for FRM comparisons. The FRM averages were within -1.2% to 3.2%, within the acceptable ± 10% range

Peters et al. (2001, 016925)[104]: Rubidoux 99 and Atlanta 99 dataset

In Rubidoux, the precision for PQ200 was 6.1%, higher than at RTP [97]. In Atlanta, the grouped data from PQ200, RAAS2.5-300, and Partisol yielded a precision of 1.7%.

Linear regression results met the EPA equivalency criteria for all FRMs.

Atlanta Supersite, GA: 8/3/99 to 9/1/99
Four km NW of downtown, within 200 m of a bus maintenance yard and several warehouse facilities, representative of a mixed commercial-residential neighborhood.

Sampler	Flow Rate (L/Min)	Filter Type[a]	Denuder[b]
R&P-2000 FRM	16.7	Teflon (P)	None
RAAS-100 FRM	16.7	Teflon (P)	None
RAAS-400	24	Teflon (P)	None
SASS	6.7	Teflon (P)	None
MASS-400	16.7	Teflon (P)	Na_2CO_3
R&P-2300	10	Teflon (P)	None
R&P-2025 Dichot:			
$PM_{2.5}$	15	Teflon (P)	None
$PM_{10\text{-}2.5}$	1.67	Polycarbonate	None Na_2CO_3/Citric
URG-PCM	16.7	Teflon (P)	Acid
ARA-PCM	16.7	Teflon (N/A)	Na_2CO_3/Citric acid
PC-BOSS (operated by TVA)	105	Teflon (W)	CIF

Solomon et al. (2003, 156994)[17]

$PM_{2.5}$ mass from individual samplers was compared to all-sampler avgs, called the filter relative reference (filter RR) value. Overall agreements were within ± 20% of filter RR.

FRM samplers were within 3.5% of filter RR.

Avg mass measured by RAAS-400, SASS and URG-PCM were within ± 10% of filter RR. Avg mass measured by MASS-400, R&P-2300 and R&P-2025 dichot were greater than filter RR but within ± 20%. Avg mass measured by PC-BOSS (BYU) and ARA-PCM were lower than filter RR within ± 10%.

All samplers except PC-BOSS (TVA) had R^2 >0.80, relative to filter RR.

While avg mass for each sampler was within 20%, daily variability was >50% of filter RR.

Glycerol in the Na_2CO_3 denuder may have contaminated the filter in the MASS-400 sampler resulting in higher $PM_{2.5}$ values.

PC-BOSS samplers removed particles < 0.1 µm aerodynamic diameter from $PM_{2.5}$ measurements. Corrections were made using sulfate (SO_4^{2-}) concentrations in the major flow or immediately after the $PM_{2.5}$ inlet, but before the flow split-up. This was insufficient to bring PC-BOSS mass close to filter RR. PC-BOSS was also equipped with upstream denuders ahead of the filters, which may have enhanced loss of semi-volatile components, resulting in a lower mass on the filter.

Site / Period / Sampler / Configuration					Summary of Findings
PC-BOSS (operated by BYU)	150	Teflon (W)		CIF	**Butler et al. (2003, 156313)[62]** The sum of individual species accounted for ~78% of the RAAS-100 FRM $PM_{2.5}$ mass concentration. TEOM explained ~82 to 92% of the species sum of RAAS with R^2 = 0.86.
$PM_{2.5}$ Continuous Sampler	**Flow Rate (L/Min)**	**Inlet Temperature**	**Dryer**	**Other**	
TEOM	16.7	30 °C	Nafion	$PM_{2.5}$	
Atlanta Supersite, GA: 11/21/01 to 12/23/01					**Lee et al. (2005, 128139)[73]** RAMS $PM_{2.5}$ adjusted using particle concentrator efficiency of 0.5. Good correlation between SES-TEOM and Radiance Research M903s (R^2 = 0.80), while medium correlation was found between CAMM and Radiance Research M903 (R^2 = 0.64) or RAMS and Radiance Research M903 (R^2 = 0.63). CAMM = (0.75 ± 0.03) SES-TEOM + (2.51 ± 0.51); R^2 = 0.78; N = 196 RAMS = (0.85 ± 0.06) SES-TEOM + (5.34 ± 1.04); R^2 = 0.52; N = 96 RAMS = (0.91 ± 0.07) CAMM + (5.71 ± 1.20); R^2 = 0.43; N = 196 Semi-volatile material explains the difference between RAMS and SES TEOM. CAMM = (0.75 ± 0.08) R&P-2025 FRM + (2.47 ± 1.02); R^2 = 0.76; N = 31 RAMS = (0.97 ± 0.22) R&P-2025 FRM + (2.39 ± 3.42); R^2 = 0.64; N = 13 SES-TEOM = (1.07 ± 0.05) R&P-2025 FRM + (-1.34 ± 0.71); R^2 = 0.95; N = 26 CAMM vs. FRM yielded lower slopes (0.75) with high intercepts.
$PM_{2.5}$ Sampler	**Flow Rate (L/Min)**	**Filter Type[a]**		**Denuder[b]**	
R&P-2025 FRM	16.7	Teflon (N/A)		None	
$PM_{2.5}$ Continuous Sampler	**Flow Rate (L/Min)**	**Inlet Temperature**	**Dryer**	**Other**	
TEOM	16.7	30 °C	Nafion	$PM_{2.5}$	
SES-TEOM	16.7	30 °C	Nafion	$PM_{2.5}$	
CAMM	0.3	N/A	Nafion	$PM_{2.5}$	
RAMS	16.7	30 °C	Nafion	$PM_{2.5}$ TEA & CIF denuders With particle concentrator	
Radiance Research M903	N/A	N/A	Nafion	bscat	
Radiance Research M903	N/A	N/A	None	bscat	
PITTSBURGH SUPERSITE, PA: 7/1/01 to 6/1/02 6 km east of downtown in a park on the top of a hill					**Cabada et al. (2004, 148859)[18]: Rees et al. (2004, 097164)[106]** MOUDI PM_{10} = 0.80 Dichot PM_{10}, R^2 = 0.85 MOUDI $PM_{2.5}$ = 1.03 Dichot $PM_{2.5}$, R^2 = 0.78 MOUDI $PM_{2.5}$ = 1.01 FRM $PM_{2.5}$, R^2 = 0.78 Dichot $PM_{2.5}$ = 0.97 FRM $PM_{2.5}$ + 0.02; R^2 = 0.94 Good agreement for $PM_{2.5}$ FRM, Dichot, and MOUDI. Lower slope for PM_{10} suggests loss of coarse particles in the MOUDI sampler. Ultrafine (< 100 nm) mass (PM_{0-10}) measurements had high uncertainties (~30%) Ultrafine mass by MOUDI showed no correlation with ultrafine volume (V0.10) by DAASS. Ratio of $PM_{0.10}/PM_{2.5}$ mass ratio showed reasonable agreement with volume ratio (V0.10/V2.5, R^2 = 0.55, slope = 0.76). Bounce of large particles to smaller stages in MOUDI was small, since mass ratio ($PM_{0.10}/PM_{2.5}$) did not exceed volume ratio (V0.10/V2.5). Low correlation between ultrafine mass and volume could be due to the ultrafine mass measurement uncertainty or due to fundamental differences in the measurement methods employed by MOUDI and DAASS. Ambient conditions and characteristics of the aerosols (such as non-spherical shapes of fresh particles) could also influence these estimates. **Rees et al. (2004, 097164)[106]** SES-TEOM $PM_{2.5}$ = 1.02 FRM $PM_{2.5}$ + 0.65; R^2 = 0.95 Volatilization did not affect SES-TEOM performance when $PM_{2.5}$ mass >20-30 µg/m^3. When ambient temperature was < -6 °C, and when mass was low, SES-TEOM was lower (up to 50%) than FRM or Dichot.
Sampler	**Flow Rate (L/Min)**	**Filter Type[a]**		**Denuder**	
MOUDI-110	30	Teflon (P,d)		None	
And-241 Dichot	16.7	Teflon (P		None	
R&P-2000 $PM_{2.5}$ FRM	16.7	Teflon (W)		None	
$PM_{2.5}$ Continuous Sampler	**Flow Rate (L/Min)**	**Inlet Temperature**	**Dryer**	**Other**	
SES-TEOM	16.7	30 °C	Nafion	$PM_{2.5}$	
DAASS	N/A	30 °C	Nafion or None	$PM_{2.5}$	

Site / Period / Sampler / Configuration	Summary of Findings

FRESNO SUPERSITE, CA and other CRPAQS sites; 12/2/99 to 2/3/01. Some comparisons included data till 12/29/03 . Fresno Supersite was located 5.5 km northeast of downtown in a mixed residential-commercial neighborhood. [107]

Sampler	Flow Rate (L/Min)	Filter Type[a]	Denuder
RAAS-100 $PM_{2.5}$ FRM	16.7	Teflon (P)	None
RAAS-300 $PM_{2.5}$ FRM	16.7	Teflon (P)	None
R&P-2000 $PM_{2.5}$ FRM	16.7	Teflon (P)	None
R&P-2025 $PM_{2.5}$ FRM	16.7	Teflon (P)	None
RAAS-400 $PM_{2.5}$	24	Teflon (P)	None
SASS $PM_{2.5}$	6.7	Teflon (P)	None
And-246 Dichot			
$PM_{2.5}$	15	Teflon (P)	None
$PM_{10-2.5}$	1.67	Teflon (P)	None
DRI-SFS $PM_{2.5}$	113	Teflon (P)	None
MiniVol $PM_{2.5}$	5	Teflon (P)	None
MOUDI-100	30	FEPb Teflon (P)	None
And-hIVOL PM_{10} FRM	1130	Teflon (P)	None

Chow et al. (2006, 146622)[63]

$PM_{2.5}$ measurements from the 11 filter samplers were within ~20% of each other, except for MiniVols, which were 20 to 30% lower than RAAS-300 FRM.

All the FRM samplers were within ± 10% of each other.

All the filter samplers were well correlated with each other (R^2 >0.90).[e]

DRI-SFS (with HNO_3 denuder) and And-246 Dichot $PM_{2.5}$ were lower (~5% and 7%, respectively, on avg) than FRM, possibly due to nitrate (NO_3^- volatilization.

Poor correlation (R^2) found between TEOM $PM_{2.5}$ concentrations and RAAS-100 FRM. TEOM $PM_{2.5}$ was lower than RAAS-100 FRM by 22%. Heating of TEOM inlet to 50 °C resulted in loss of semi-volatile components such as ammonium nitrate (NH_4NO_3) and possibly some semi-volatile organic compounds.

TEOM PM_{10} concentrations were 28% lower than the And-hIVOL10 FRM on avg, ranging from 13% in summer to 43% in winter.

TEOM was neither equivalente nor comparablee to the FRM sampler for $PM_{2.5}$ or PM_{10}.

BAM $PM_{2.5}$ concentrations showed high correlation (R^2 >0.90) with the RAAS-100 and RAAS-300 FRM samplers, with slopes ranging from 0.92 to 0.97. BAM $PM_{2.5}$ was typically higher than FRM (17 to 30%) except at Bakersfield, CA, where it was 21% lower, suggesting a BAM calibration difference between Bakersfield and other sites.

BAM PM_{10} concentrations were 26% higher than And-hIVOL PM_{10} FRM concentration on avg (R^2 >0.92).

Higher BAM measurements were attributed to water absorption by hygroscopic particles. BAM $PM_{2.5}$ and PM_{10} deviations were larger for concentrations < 25 µg/m^3.

Grover et al. (2006, 138080) [65]

PC-BOSS $PM_{2.5}$ = (0.88 ± 0.04) FDMS-TEOM + (6.7 ± 4.3); R^2 = 95; n = 29

PC-BOSS $PM_{2.5}$ = (1.11 ± 0.07) D-TEOM + (7.5 ± 6.1); R^2 = 0.90; n = 29

TEOM50C $PM_{2.5}$ = (0.80 ± 0.01) TEO$m^3$0C + (1.1 ± 3.1); R^2 = 0.91; n = 507

TEO$m^3$0C $PM_{2.5}$ = (0.50 ± 0.01) FDMS-TEOM -(1.7 ± 6.9); R^2 = 0.68; n = 516

Heated GRIMM PM concentrations were lower than FDMS-TEOM and ambient temperature GRIMM, suggesting loss of semi-volatile matter.

Data recovery was greater than 95% for all continuous instruments, except for D-TEOM, which had 86% recovery.

Reasonable agreement was seen between FDMS-TEOM, D-TEOM, BAM, and GRIMM $PM_{2.5}$ when semi-volatile matter was dominated by NH_4NO_3. However, the FDMS-TEOM was higher than the other instruments during high concentration periods, associated with days with a high fraction of semi-volatile organic compounds (SVOCs). Possible differences in SVOCs may have contributed to the differences between FDMS and other instruments.

Continuous Sampler	Flow Rate (L/Min)	Inlet Temperature	Dryer	Other
TEOM	16.7	50 °C	None	$PM_{2.5}$ and PM_{10}
BAM	16.7	Ambient	None	$PM_{2.5}$ and PM_{10}
Sampler	**Flow Rate (L/Min)**	**Filter Type[a]**		**Denuder[b]**
PC-BOSS $PM_{2.5}$	150	Teflon (W)		CIF

Site / Period / Sampler / Configuration					Summary of Findings
Continuous Sampler	**Flow Rate (L/Min)**	**Inlet Temperature**	**Dryer**	**Other**	
TEOM	16.7	50 °C	None	$PM_{2.5}$	
TEOM	16.7	30 °C	None	$PM_{2.5}$	
FDMSTEOM	16.7	30 °C	Nafion	$PM_{2.5}$	
D-TEOM	16.7	30 °C	Nafion	$PM_{2.5}$	
GRIMM1100	1.2	Ambient	None	bscat	
GRIMM1100	1.2	80 °C heater, resulting in aerosol temperature	Heater	bscat	
BAM	16.7	Ambient	None	$PM_{2.5}$	
HOUSTON SUPERSITE, TX; 1/1/00 to 2/28/02 The Houston Supersite included three sites located in southeast Texas including one on the grounds of a municipal airport at the edge of a small community, one adjacent to the highly industrial ship channel and one on the grounds of a middle school in a suburban community.					**Russell et al. (2004, 082453)[64]; Lee et al. (2005, 156680)[108]** Good correlations between 24-h SES-TEOM $PM_{2.5}$ and R&P-2025 FRM mass. CAMM = (0.93 ± 0.03) RAMS + (3.14 ± 0.74); R^2 = 0.81 SES-TEOM = (0.92 ± 0.03) RAMS + (1.52 ± 0.77); R^2 = 0.80 SES-TEOM = (1.01 ± 0.03) CAMM + (-1.91 ± 0.79); R^2 = 0.83 Correlation of Radiance Research M903 and SES-TEOM was good (R^2 = 0.95), while that of Radiance Research M903 with CAMM or RAMS was poor (R^2 ~ 0.4). RAMS >SES-TEOM at high temperature and low RH (< 60%), suggesting loss of water and particulate NO_3^- from SES-TEOM. CAMM = (1.02 ± 0.08) R&P-2025 + (1.62 ± 1.35); R^2 = 0.89 RAMS = (1.10 ± 0.08) R&P-2025 + (0.68 ± 1.28); R^2 = 0.89 SES-TEOM = (1.09 ± 0.07) R&P-2025 + (0.21 ± 1.27); R^2 = 0.94 Integrated mass < Continuous $PM_{2.5}$ mass. Difference possibly related to loss of SVOCs and NO_3^- from integrated sampler
$PM_{2.5}$ Sampler	**Flow Rate (L/Min)**	**Filter Type[a]**		**Denuder**	
R&P-2025 FRM	16.7	Teflon (N/A)		None	
Continuous Sampler	**Flow Rate (L/Min)**	**Inlet Temperature**	**Dryer**	**Other[b]**	
TEOM	16.7	50 °C	None	$PM_{2.5}$	
SES-TEOM	16.7	30 °C	Nafion	$PM_{2.5}$ Aug-Sep '00	
CAMM	0.3	Ambient	Nafion	$PM_{2.5}$ Aug-Sep '00	
RAMS	16.7	30 °C	Nafion	$PM_{2.5}$ TEA & CIF denuders; Aug-Sep '00	
Radiance Research M903	N/A	N/A	Nafion	Bscat Aug-Sep '00	
LOS ANGELES SUPERSITE, CA; 9/01 to 8/02 The Los Angeles Supersite consisted of multiple sampling locations in the South Coast Air Basin to provide wide geographical and seasonal coverage, including urban "source" sites and downwind "receptor" sites.					**Jaques et al. (2004, 155878)[69]; Hering et al. (2004, 155837)[109]** Dichot $PM_{2.5}$ = 0.83 MOUDI + 1.23; R^2 = 0.83 (n = 37) Dichot $PM_{2.5}$ showed higher NO_3^- loss than MOUDI, consistent with anodized aluminum surfaces serving as efficient denuders that remove volatilized NO_3^- 2,110. D-TEOM $PM_{2.5}$ = 1.18 MOUDI – 1.28; R^2 = 0.86 (n = 20) Over-estimation of D-TEOM may be due to particle losses in the MOUDI. $PM_{2.5}$ by D-TEOM during ESP-off phase (net artifact effect) tracked well with the NO_3^- concentrations. NO_3^- vaporization from the TEOM was caused by the temperature of the TEOM filter (~30-50 °C) rather than the pressure drop across the filter. Vaporization from the TEOM had a time constant between 10 and 100 min depending on ambient and TEOM filter temperatures, the vapor pressure, and
Sampler	**Flow Rate (L/Min)**	**Filter Type[a]**		**Denuder[b]**	
R&P-2025 Dichot					
$PM_{2.5}$	15	Teflon (P)		None	
$PM_{10-2.5}$	16.7	N/A		None	
MOUDI-110	30	Teflon (P		None	
HEADS $PM_{2.5}$	10	Teflon (N/A)		$NaHCO_3$	
Continuous Sampler	**Flow Rate (L/Min)**	**Inlet Temperature**	**Dryer**	**Other**	
D-TEOM	16.7	30 °C	Nafion	$PM_{2.5}$	
Nano-BAM (BAM-1020 with d50 148 ± 10 nm inlet)	16.7	Ambient	None	~150 nm cut-point at 16.7 L/min	

Site / Period / Sampler / Configuration					Summary of Findings
					the extent of vapor saturation upstream and downstream of the TEOM filter. The mass measured during 5-min periods (ESP-on and off cycle in D-TEOM) provides an estimate of the dynamic vaporization losses.
SMPS-3936	0.3	Ambient	None	Number to mass assuming spherical particles of 1.6 g/cc density	**Chakrabarti et al. (2004, 157426)[111]** Good agreement between MOUDI $PM_{0.15}$ and Nano-BAM $PM_{0.15}$ (MOUDI PM0.15 = 0.97 Nano-BAM $PM_{0.15}$ + 0.60; R^2 = 0.92; n = 24) Nano-BAM captured peak $PM_{0.15}$ concentrations not quantified by SMPS. Potential particle agglomeration (with resulting high surface areas) caused SMPS to include particles in the accumulation- rather than ultrafine-mode, since mobility diameter is a function of surface area.

RUBIDOUX, CA; 08/15/01 to 09/07/01, 07/01/03 to 07/31/03. Rubidoux is located in the eastern section of the South Coast Air Basin (SoCAB) in the northwest corner of Riverside County, 78 km downwind of the central Los Angeles metropolitan area and in the middle of the remaining agricultural production area in SoCAB.

Sampler	Flow Rate (L/Min)	Filter Type[a]		Denuder[b]
PC-BOSS $PM_{2.5}$	150	Teflon (W)		CIF
R&P-2025 $PM_{2.5}$ FRM	16.7	Teflon (N/A)		None
Continuous Sampler	**Flow Rate (L/Min)**	**Inlet Temperature**	**Dryer**	**Other**
TEOM	16.7	50 °C	None	$PM_{2.5}$
FDMS-TEOM	16.7	30 °C	Nafion	$PM_{2.5}$
D-TEOM	16.7	30 °C	Nafion	$PM_{2.5}$
RAMS	16.7	30 °C	Nafion	$PM_{2.5}$ Denuders used
CAMM	0.3	N/A	None	$PM_{2.5}$
Radiance Research M903	N/A	N/A	Nafion	bscat
Radiance Research M903	N/A	N/A	None	bscat

Grover et al. (2005, 090044)[66] (2003 measurements):

D-TEOM = (0.98 ± 0.02) FDMS-TEOM + (-0.6 ± 5.3); R^2=0.85; n = 426; excludes 38 data points when FDMS-TEOM $PM_{2.5}$ was higher than D-TEOM $PM_{2.5}$ by ~21 µg/m^3.

RAMS = (0.93 ± 0.02) FDMS-TEOM + (2.4 ± 8.2); R^2 = 0.81; n = 337

FDMS-TEOM = (0.96 ± 0.06) PC-BOSSconstructed mass + (-0.3 ± 3.9); R^2 = 0.90; n = 33

R&P-2025 FRM = (0.96 ± 0.06) FDMS-TEOM + (-9.3 ± 3.9); R^2 = 0.90; n = 29

The R&P-2025 FRM $PM_{2.5}$ was, on avg, ~32% lower than FDMSTEOM. Losses of NH_4NO_3 and organics can account for the difference.

TEOM @ 50 °C $PM_{2.5}$ was consistently lower than FDMS-TEOM, DTEOM or RAMS and was, on avg, ~ 50% lower than FDMS-TEOM. This difference is due to loss of semi-volatile NO_{3-} and organics from the heated TEOM.

FDMS-TEOM and D-TEOM needed little attention from site operators.

Lee et al. (2005, 155925)[76] (2001 measurements)

D-TEOM $PM_{2.5}$ and Radiance Research M903s light scattering (with and without dryers) showed good correlation.

D-TEOM = (3.69 ± 0.09) Radiance Research M903no-dryer + (2.74 ± 0.89); R^2 = 0.84; n = 299

D-TEOM = (3.79 ± 0.10) Radiance Research M903dryed + (4.08 ± 0.84); R^2 = 0.83; n = 312

Radiance Research M903no-dryer = (1.03 ± 0.01) Radiance Research M903dryed + (0.34 ± 0.05); R^2 = 0.98; n = 513; absorbed water did not affect relationship to $PM_{2.5}$.

CAMM and RAMS compared poorly (R^2 = 0 to 0.25) with D-TEOM, Radiance Research M903s and among themselves.

RAMS correlated well with D-TEOM for $PM_{2.5}$ >30 µg/m^3 due to RAMS's efficient particle collection of larger particle sizes (historically associated with high mass loadings at this site) in the $PM_{2.5}$ size range.

D-TEOM $PM_{2.5}$ correlated well with ADI-N sized NO_3 (R^2 = 0.62) and OC by Sunset OCEC (R^2 = 0.61) suggesting that D-TEOM measured $PM_{2.5}$ mass with minimum loss of SVOCs. RAMS showed R^2 of 0.20 (NO_3^-) to 0.30 (OC), while CAMM showed no correlation.

Site / Period / Sampler / Configuration					Summary of Findings
LINDON, UT; 01/29/03 to 02/12/03					**Grover et al. (2005, 090044)**[66]
Sampler	**Flow Rate (L/Min)**	**Filter Type**[a]		**Denuder**[b]	RAMS required regular maintenance.
PC-BOSS $PM_{2.5}$	150	Teflon (W)		CIF	RAMS = (0.92 ± 0.03) FDMS-TEOM + (1.3 ± 3.9); R^2 = 0.69; n = 332
CONTINUOUS SAMPLER	**FLOW RATE (L/MIN)**	**INLET TEMPERATURE**	**DRYER**	**OTHER**	PC-BOSS constructed mass = (0.89 ± 0.21) FDMS-TEOM + (1.8 ± 2.8); R^2 = 0.66; n = 11
TEOM	16.7	30 °C	None	$PM_{2.5}$	TEOM @ 30 °C $PM_{2.5}$ was consistently lower than FDMS-TEOM and the difference was consistent with concentrations SVOCs and NH_4NO_3 measured by PC-BOSS.
FDMS-TEOM	16.7	30 °C	Nafion	$PM_{2.5}$	
RAMS	16.7	30 °C	Nafion	$PM_{2.5}$ Denuder used	
PHILADELPHIA, PA; 07/02/01 to 08/01/01 At water treatment center in a grassy field surrounded by mixed deciduous and pine trees on three sides and a river on the other. Within 0.5 km of Interstate I-95 and within 30 km from downtown Philadelphia.					**Lee et al. (2005, 128139)**[73]
Sampler	**Flow Rate (L/Min)**	**Filter Type**[a]		**Denuder**[b]	Radiance Research M903dryer = (0.78 ± 0.01) Radiance Research M903no dryer + (0.30 ± 0.03); R^2 = 0.95
Harvard Impactor $PM_{2.5}$	10	Teflon (N/A)		N/A	Radiance Research M903s vs. CAMM, R^2 = 0.78
Continuous Sampler	**Flow Rate (L/Min)**	**Inlet Temperature**	**Dryer**	**Other**	Radiance Research M903s vs. RAMS, R^2 = 0.63
SES-TEOM	16.7	35 °C	Nafion	$PM_{2.5}$	Radiance Research M903s vs. SES-TEOM, R^2 = 0.72
CAMM	0.3	N/A	Nafion	$PM_{2.5}$	CAMM = (0.60 ± 0.03) SES-TEOM + (2.0 ± 0.42); R^2 = 0.71; N = 185
RAMS	16.7	30 °C	Nafion	$PM_{2.5}$ TEA & CIF denuders With particle concentrator	RAMS = (0.71 ± 0.04) SES-TEOM + (2.51 ± 0.59); R^2 = 0.63; N = 185
Radiance Research M903	N/A	N/A	Nafion	bscat	RAMS = (0.93 ± 0.06) CAMM + (2.44 ± 0.68); R^2 = 0.55; N = 185
Radiance Research M903	N/A	N/A	None	bscat	Both RAMS and CAMM under-measured ambient $PM_{2.5.}$ CAMM = (0.70 ± 0.06) HI + (0.16 ± 0.96); R^2 = 0.87; N = 22 SES-TEOM = (1.0 ± 0.10) HI + (-0.68 ± 1.74); R^2 = 0.89; N = 15
BALTIMORE SUPERSITE, MD; 05/17/01 to 06/11/01. Located near a freeway and bus yard.					**Lee et al. (2005, 128139)**[73]
Sampler	**Flow Rate (L/Min)**	**Filter Type**		**Denuder**	Radiance Research M903dryed = (0.65 ± 0.02) Radiance Research M903no dryer + (1.80 ± 0.20); R^2 = 0.75, suggesting influence from particle-bound water.
RAAS-100 $PM_{2.5}$ FRM	16.7	Teflon		None	High correlation (R^2 = 0.75) between Radiance Research M903s.
Continuous Sampler	**Flow Rate (L/Min)**	**Inlet Temperature**	**Dryer**	**Other**	Poor correlation among the continuous instruments.
SES-TEOM	16.7	35 °C	Nafion	$PM_{2.5}$	Radiance Research M903s did not follow $PM_{2.5}$ concentrations measured by other continuous instruments.
CAMM	0.3	N/A	Nafion	$PM_{2.5}$	CAMM = (0.32 ± 0.07) SES-TEOM + (9.45 ± 1.61); R^2 = 0.14; N = 120
RAMS	16.7	30 °C	Nafion	$PM_{2.5}$ TEA & CIF denuders; No particle	RAMS = (0.82 ± 0.10) SES-TEOM + (6.41 ± 2.09); R^2 = 0.38; N = 120
Radiance Research M903	N/A	N/A	Nafion	bscat	RAMS = (0.71 ± 0.12) CAMM + (11.3 ± 2.23); R^2 = 0.21; N = 120
Radiance Research M903	N/A	N/A	None	bscat	CAMM = (0.80 ± 0.29) RAAS-100 FRM + (-0.83 ± 5.85); R^2 = 0.60; N = 7 RAMS = (1.05 ± 0.12) RAAS-100 FRM + (4.80 ± 2.60); R^2 = 0.90; N = 11 SES-TEOM = (0.86 ± 0.10) RAAS-100 FRM + (2.96 ± 1.99); R^2 = 0.90; N = 10

Site / Period / Sampler / Configuration					Summary of Findings
SEATTLE, WA; 01/28/01 to 02/21/01 Urban area near major highway and interstate, 8 km southeast of downtown.					**Lee et al. (2005, 156680)**[108] Radiance Research M903dryed = 0.94 ± 0.00 Radiance Research M903no dryer; R^2 = 1.0. Correlation of Radiance Research M903 vs. SES-TEOM, R^2 = 0.80, while that of Radiance Research M903 with CAMM was R^2 = 0.84 and with RAMS was R^2 = 0.72. CAMM = (1.07 ± 0.05) RAMS + (1.03 ± 0.55); R^2 = 0.61 SES-TEOM = (0.95 ± 0.03) RAMS + (1.24 ± 0.38); R^2 = 0.72 SES-TEOM = (0.87 ± 0.03) CAMM + (0.55 ± 0.37); R^2 = 0.74 SES-TEOM likely lost semi-volatile organic matter. Continuous $PM_{2.5}$ samplers were similar to filter $PM_{2.5}$ sampler. Number of samples was small (~7). Some SES-TEOM mass values were less than MASS filter values suggesting that loss of mass is likely for a SES-TEOM at 30°C, particularly during the cold season.
SAMPLER	**FLOW RATE (L/MIN)**	**FILTER TYPE**[a]		**DENUDER**[b]	
MASS $PM_{2.5}$	16.7	Teflon (N/A)		Na_2CO_3	
Continuous Sampler	**Flow Rate (L/Min)**	**Inlet Temperature**	**Dryer**	**Other**	
SES-TEOM	16.7	30 °C	Nafion	$PM_{2.5}$	
CAMM	0.3	Ambient	Nafion	$PM_{2.5}$	
RAMS	16.7	30 °C	Nafion	$PM_{2.5}$ TEA & CIF denuders	
Radiance Research M903	N/A	N/A	Nafion	bscat	
Radiance Research M903	N/A	N/A	None	bscat	
NEW YORK SUPERSITE, NY; 01/01/03 to 12/31/04 Urban site located at Queens College, NY, about 14 km west of Manhattan, within 2 km of freeways, and within 12 km of international airports. A rural site was located at Pinnacle State Park surrounded by golf course, picnic areas, undeveloped forest lands, and no major cities within 15 km.					**Schwab et al. (2006, 098449)**[67] FDMS-TEOM had operational difficulties resulting in low data capture (65% at urban site and 57% at rural site). BAM had data captures greater than 95% at both sites. Urban site: BAM = (1.02 ± 0.02) FDMS-TEOM + 1.72; R^2 = 0.93; n = 244 FDMS-TEOM = (1.25 ± 0.02) FRM – (0.63 ± 0.26); R^2 = 0.95; n = 238 BAM = (1.28 ± 0.03) FRM + (1.27 ± 0.38); R^2 = 0.88; n = 320 Rural site: FDMS-TEOM = (1.09 ± 0.02) FRM – (0.004 ± 0.18); R^2 = 0.95; n = 349 $PM_{2.5}$ FDMS-TEOM >FRM >TEOM50°C, suggesting that FRM captured a fraction, but not all, of the volatile components. TEOM50°C volatilizes $PM_{2.5}$, particularly during winter.
Sampler	**Flow Rate (L/Min)**	**Filter Type**[a]		**Denuder**[b]	
R&P-2025 $PM_{2.5}$ FRM	16.7	Teflon (N/A)		None	
R&P-2300 $PM_{2.5}$	16.7	Teflon (N/A)		None	
Continuous Sampler	**Flow Rate (L/Min)**	**Inlet Temperature**	**Dryer**	**Other**	
TEOM	16.7	50 °C	None	$PM_{2.5}$	
FDMS-TEOM	16.7	30 °C	Nafion	$PM_{2.5}$	
BAM	16.7	"smart" heater on @ RH >44%		$PM_{2.5}$	

Site / Period / Sampler / Configuration	Summary of Findings

[a]Filter Manufacturer in parentheses - W: Whatman, Clifton, NJ; P: Pall-Gelman, Ann Arbor, MI; S: Schleicher & Schnell. Keene, NH; N/A: not available or not reported.
[b]Na_2CO_3: Sodium carbonate; $NaHCO_3$: Sodium bicarbonate CIF: Charcoal Impregnated Filter; FEP: Fluorinated Ethylene Propylene copolymer; TEA: Triethanolamine; TSP: Total Suspended PM.
[c]37 mm filter.
[d]37 mm after-filter for stages smaller than 0.16 µm and 47-mm for higher stages.
[e]Equivalence requires correlation coefficient (r) ≥ 0.97, linear regression slope 1.0 ± 0.05 and an intercept 0 ± 1 µg/m^3; Comparability requires r>0.9 and linear regression slope equal 1 within 3 standard errors and intercept equal zero within 3 standard errors; Predictability requires r>0.9. 91, 112

[1]Chow (1995, 077012); [2]Watson and Chow (2001, 157123); [3] Watson et al. (1983, 045084); [4]Fehsenfeld et al. (2004, 157360); [5]Solomon et al. (2001, 157193); [6]Watson et al. (2005, 157124); [7]Mikel (2001, 156762); [8]Watson et al. (1999, 020949); [9]Solomon and Sioutas (2006, 156995); [10]Graney et al. (2004, 053756); [11]Tanaka et al. (1998, 157041); [12]Pancras et al. (2005, 098120); [13]John et al. (1988, 045903); [14]Hering and Cass (1999, 084958); [15]Fitz et al. (1989, 077387); [16]Hering et al. (1988, 036012); [17]Solomon et al. (2003, 156994); [18]Cabada et al. (2004, 148859); [19]Fine et al. (2003, 155775); [20]Hogrefe et al. (2004, 099003); [21]Drewnick et al. (2003, 099160); [22]Watson et al. (2005, 157125); [23]Ho et al. (2006, 156552); [24]Decesari et al. (2005, 144536); [25] Mayol-Bracero et al. (2002, 045010); [26]Yang et al. (2003, 156167); [27]Turšic et al. (2006, 157063); [28]Mader et al.(2004, 156724); [29]Xiao and Liu (2004, 056801); [30]Kiss et al. (2002, 156646); [31]Cornell and Jickells (1999, 156367); [32] Zheng et al. (2002, 026100); [33]Fraser et al. (2002, 140741); [34] Fraser et al. (2003, 042231) [35]Schauer er al. (2000, 012225); [36]Fine et al. (2004, 141283); [37]Yue et al. (2004, 157169); [38]Rinehart et al. (2006, 115184); [39]Wan and Yu (2006, 157104); [40]Poore (2000, 012839); [41]Fraser et al. (2003, 040266); [42]Engling et al. (2006, 156422); [43]Yu et al. (2005, 157167); [44]Tran et al. (2000, 013025); [45]Yao et al. (2004, 102213); [46]Li and Yu (2005, 156692); [47]Henning et al. (2003, 156539); [48]Zhang and Anastasio (2003, 157182); [49]Emmenegger et al. (2007, 156418); [50] Watson et al. (1989, 046318); [51]Greaves et al. (1985, 156494); [52]Waterman et al. (2000, 157116); [53]Waterman et al. (2001, 157117); [54]Falkovich and Rudich (2001, 156427); [55]Chow et al. (2007, 157209); [56]Miguel et al. (2004, 123260); [57]Crimmins and Baker (2006, 097008); [58]Ho and Yu (2004, 156551); [59]Jeon et al. (2001, 016636); [60]Mazzoleni et al. (2007, 098038); [61]Poore (2002, 051444); [62]Butler et al. (2003, 156313); [63]Chow et al. (2006, 146622); [64]Russell et al. (2004, 082453); [65]Grover et al. (2006, 138080); [66]Grover et al. (2005, 090044); [67]Schwab et al. (2006, 098449); [68]Hauck et al. (2004, 156525); [69]Jaques et al. (2004, 155878); [70]Rupprecht and Patashnick (2003, 157207); [71]Pang et al (2002, 030353); [72]Eatough et al. (2001, 010303); [73]Lee et al. (2005, 128139); [74]Lee et al. (2005, 156680); [75]Babich et al. (2000, 156239); [76]Lee et al. (2005, 155925); [77]Lee et al. (2005, 128139); [78]Anderson and Ogren (1998, 156213); [79]Chung et al. (2001, 156357); [80]Kidwell and Ondov (2004, 155898); [81]Lithgow et al. (2004, 126616); [82]Weber et al. (2003, 157129); [83]Harrison et al. (2004, 136787); [84]Rattigan et al. (2006, 115897); [85]Wittig et al. (2004, 103413); [86]Vaughn et al. (2005, 157089); [87]Chow et al. (2005, 099030); [88]Weber et al (2001, 024640) ; [89]Schwab et al. (2006, 098785); [90]Lim et al. (2003, 037037); [91]Watson and Chow (2002, 037873); [92]Venkatachari et al. (2006, 105918); [93]Bae et al. (2004, 156243); [94]Arhami et al. (2006, 156224); [95]Park et al. (2005, 156843); [96]Bae et al. (2004, 098680); [97]Chow et al. (2006, 156350); [98]Arnott et al. (2005, 156227); [99]Bond et al. (1999, 156281); [100]Virkkula et al. (2005, 157097); [101]Petzold et al. (2002, 156863); [102]Park et al. (2006, 098104); [103]Arnott et al. (1999, 020650); [104]Peters et al. (2001, 016925); [105]Pitchford et al. (1997, 156872); [106]Rees et al. (2004, 097164); [107]Watson et al. (2000, 010354); [108]Lee et al. (2005, 156680); [109]Hering et al. (2004, 155837); [110]Watson et al. (1998, 198805); [111]Chakrabarti et al. (2004, 157426); [112]Mathai et al. (1990, 156741); [113]Kidwell and Ondov (2001, 017092); [114]Stanier et al. (2004, 095955); [115]Khlystov et al. (2005, 156635); [116]Takahama et al. (2004, 157038); [117]Chow et al. (2005, 156348); [118]Zhang et al. (2002, 157181); [119]Subramanian et al. (2004, 081203); [120]Chow et al. (2006, 155207); [121]Birch and Cary (1996, 026004); [122]Birch (1998, 024953); [123]Birch and Cary (1996, 002352); [124]NIOSH (1996, 156810); [125]NIOSH (1999, 156811); [126]Chow et al. (1993, 077459); [127]Chow et al. (2007, 156354); [128]Ellis and Novakov (1982, 156416); [129]Peterson and Richards (2002, 156861); [130]Schauer et al. (2003, 037014); [131]Middlebrook et al. (2003, 042932); [132]Wenzel et al. (2003, 157139); [133]Jimenez et al. (2003, 156611); [134]Phares et al. (2003, 156866); [135]Qin and Prather (2006, 156895); [136]Zhang et al. (2005, 157185); [137]Bein et al. (2005, 156265); [138]Drewnick et al. (2004, 155754); [139]Drewnick et al. (2004, 155755); [140]Lake et al. (2003, 156669); [141]Lake et al. (2004, 088411)

Source: Chow et al. (2008, 156355)

Table A-12. Summary of element and liquid water content measurement comparisons.

SITE / PERIOD / SAMPLER	SUMMARY OF FINDINGS
College Park, MD; 11/18/1999 to 11/19/1999, 11/22/1999 Adjacent to a parking lot in the University of Maryland campus, influenced by motor vehicles, coal-fired power plants and incinerators ~21 km southwest of site and regionally transported material. **Concentrated Slurry/Graphite Furnace Atomic Absorption Spectrometry (GFAAS) (collectively known as Semi-Continuous Elements in Aerosol Sampler, SEAS)** Ambient air is pulled in at a flow rate of 170 L/min. Particles are grown using steam injection to about 3 to 4 µm in diameter, which are then concentrated and separated from the air stream in the form of a slurry using impactors. The slurry is collected in glass sample vials, which are subsequently analyzed by GFAAS in the laboratory.	**Kidwell and Ondov (2001, 017092; 2004, 155898)** Overall collection efficiency (of the entire system) measured using latex particles was 40% for particles initially 0.1 to 0.5 µm in diameter, increasing with size to 68% for particles 3 µm in diameter. Major losses were in the virtual impactor major flow channel and in the condensers. Six elements were detected simultaneously, limited by spectral interference and the minimum detectable limit (MDL). Twelve elements (Al, Cr, Mn, Fe, Ni, Cu, Zn, As, Se, Cd, Sb, and Pb) were measured. MDLs ranged from 3.2 picogram (pg = 10^{-12} gram) to 440 pg. Comparison with NIST standards showed good agreement, except for Al, Cr and Fe, due to poor atomization. The method was valid for dissolved solutions, but not for large particles (>10 µm). Overall avg relative standard deviation (RSD) was 20 to 43% by error propagation, mainly due to the collection and analytical efficiencies. There were possible memory effects due to particle adhesion to impactor collection surfaces. Lower MDLs may be possible through redesign and introduction of a wash cycle between samples. A 2.5 µm inlet might improve analytical efficiency by removing coarse particles.
Pittsburgh Supersite, PA; 08/26/2002 to 09/02/2002 6 km east of downtown in a park on the top of a hill. **Laser Induced Breakdown Spectroscopy (LIBS)** Ambient air was concentrated using a $PM_{2.5}$ inlet and a virtual impactor. The concentrated stream was transported through a Teflon tube to the sample cell of the LIBS system. The sample cell was excited using a Nd: YAG laser. The resulting plasma was collected and focused into a spectrometer, generating spectra characteristic of different elements.	**Lithgow et al. (2004, 126616)** Calibration was done by sampling particle-laden streams with known metal concentrations. Good linear fits with correlation coefficients 0.97 to 0.99 Seven metals (Na, Mg, Al, Ca, Cr, Mn, and Cu) were analyzed. The MDLs were in the order of femtograms (fg = 10^{-15} gram) per sample. This system has the capability of identifying the components, quantifying them and also giving a particle size distribution. Mass was underestimated because of missing small particles.
Pittsburgh Supersite, PA; 07/01/2001 to 08/31/2001, 01/01/2002 to 07/01/2002. 6 km east of downtown in a park on the top of a hill. **Dry Ambient Aerosol Size Spectrometer (DAASS)** Measures the aerosol size distribution (using nano-SMPS, SMPS and APS) alternatively, at ambient relative humidity (RH) (ambient channel) and at low RH (18 ± 6%) (dry channel). A comparison of the two size distributions provides information on the water absorption and change in size due to RH.	**Stanier et al. (2004, 095955); Khlystov et al. (2005, 156635)** Measured water content ranging from less than 1 µg/m^3 to 30 µg/m^3, constituting < 5% to 100% of the dry aerosol mass. Small differences between dry and ambient channels of the DAASS. Number concentrations were within 5% of each other. Additional sources of error are associated with temperature differences between measured outdoor ambient temperature and the temperature at which the ambient measurement channel was maintained. Although the measurement system was placed in a ventilated enclosure, it was ~4 °C higher than ambient temperature during July 2001. During winter, the system was maintained at a minimum temperature of 9 °C, while the outdoor temperature dropped to -5 °C. This caused differences in RH sensed by the system in the ambient channel versus the actual outdoor RH. RH differences cause underestimation of the particle number at sizes < 200 nm and an overestimation at sizes >200 nm. This causes the volume growth factor to be higher by 2 to 14%, with the highest bias occurring at high RH and low temperature (92% outside RH and -5 °C). The difference in temperature might also lead to evaporation of semi-volatile components such as NH_4NO_3. For the winter period, it was estimated that, for the worst case, the volume growth factor would be underestimated by about 10% for 60-90% RH. Insufficient purging of dry air between the dry and ambient cycles (implying the need for supplemental vacuum power during the vent stages) causes uncertainties in estimated growth factors. Correction factors were between 0.97 and 1.03. Water content estimated by DAASS can be used to evaluate the thermodynamic models. For the Pittsburgh study, the models underestimated the water content by 37%. Data from DAASS showed that the aerosol was wet even at ambient RH less than 30%.

Source: Chow et al. (2008, 156355)

Table A-13. Summary of $PM_{2.5}$ NO_3^- measurement comparisons.

SITE / PERIOD / SAMPLER / CONFIGURATION				SUMMARY OF FINDINGS
ATLANTA SUPERSITE, GA: 8/3/99 to 9/1/99 Four km NW of downtown, within 200 m of a bus maintenance yard and several warehouse facilities, representative of a mixed commercial-residential neighborhood.				**Solomon et al.(2003, 156994)**[17]
Sampler	**Flow Rate (L/Min)**	**Filter Type**[a]	**Denuder**[b]	$PM_{2.5}$ NO_3^- from each sampler was compared to the all-sampler avgs, called the filter relative reference (filter RR) value. Overall agreements were within 30-35% of filter RR.
R&P-2000 FRM	16.7	Quartz (P)	None	Wide scatter from paired comparisons, possibly due to volatilized NO_3^-, differences in denuder design and filter types, and low concentrations (close to analytical uncertainty).
RAAS-400	24	Nylon (P)	MgO	
SASS	6.7	Nylon (P)	MgO	A small positive artifact (few tenths of $\mu g/m^3$) might be present when using Na_2
MASS-400	16.7	Teflon (P)-Nylon (P	Na_2CO_3	
MASS-450	16.7	Quartz (P)	None	CO_3 impregnated filters, due to possible collection (and subsequent oxidation) of HONO and NO_2 on carbonate-impregnated filters. In addition, glycerol in Na_2CO_3 coated denuders may contaminate the filters downstream.
R&P-2300	10	Nylon (P)	Na_2CO_3	
VAPS	15	Polycarbonatec (front & back-up)	Na_2CO_3	$PM_{2.5}$ NO_3- R&P-2000 FRM and MOUDI-100 samplers are consistently lower than other samplers.
URG-PCM	16.7	Teflon (P)-Cellulose-fiber (W	Na_2CO_3	**Weber et al. (2003, 157129)**[82]
ARA-PCM	16.7	Teflon (N/A)-Nylon (N/A)	Na_2CO_3/Citric acid	Hourly $PM_{2.5}$ NO_3-were compared to all-sampler averages (continuous RR), similar to the approach used for integrated filter samplers. Overall agreements were within ± 20-30% (or ± 0.2 $\mu g/m^3$) except for ARA-N.
PC-BOSS (TVA)	105	Teflon (W)-Nylon (P)	CIF	
PC-BOSS (BYU)	150	Teflon (W)-Nylon (P)	CIF	Except for ARA-N, good correlations (R^2 = 0.70 to 0.90) were found during the second half of the study. The poor performance of ARA-N was probably due to an inefficient denuder (25-60% efficient) resulting in high background.
PC-BOSS (BYU)	150	Quartz (P)-CIF (S)	CIF	
MOUDI-100	30	Teflon (N/A-Quartz (N/A	None	
Continuous Sampler	**Flow Rate (L/Min)**	**Denuder**	**Analysis Method**[b]	Large discrepancies between continuous and filter RR, probably due to low ambient concentrations (study avg = 0.5 $\mu g/m^3$) near the detection limit (~0.1 $\mu g/m^3$, except for ARA-N, which had 0.5 $\mu g/m^3$).
ADI-N	1	Activated Carbon	NO_X Chemiluminescence	
ARA-N	3	Potassium iodide (KI) and dual sodium chlorite ($NaClO_2$)	NO_X Chemiluminescence	The ARA-N was within 13%, ADI-N, ECN and PILS-IC within 18% and TT within 26% of filter RR (all <0.2 $\mu g/m^3$ difference).
PILS-IC	5	Two URG annular glass denuders in series containing citric acid and $CaCO_3$	IC	
ECN	16.7	Rotating annular wet denuder system	IC	Filter samples showed more variability (Relative Standard Deviation, RSD = 22%) than continuous measurements (RSD = 13%). This is probably due to sampling artifacts in filter samples; NO_3-volatilization in continuous monitors is expected to be minimal due to shorter averaging times and rapid stabilization in solutions.
TT	5	Wet parallel plate denuder	IC	

SITE / PERIOD / SAMPLER / CONFIGURATION				SUMMARY OF FINDINGS
PITTSBURGH SUPERSITE, PA; 7/1/01 to 8/1/02 6km east of downtown in a park on the top of a hill				**Cabada et al. (2004, 148859)[18]; Takahama et al. (2004, 157038)[116]**
Sampler	**Flow Rate (L/Min)**	**Filter Type[a]**	**Denuder[b]**	More than 70% (~0.5 µg/m^3) of NO_3 mass was lost from MOUDI samplers during summer.
MOUDI-110	30	Teflon (W) Teflon (W)	None	MOUDI NO_3 = 0.27 CMU; R^2 = 0.40; Summer MOUDI NO_3 = 0.99 CMU; R^2 = 0.49; winter
CMU	16.7	Nylon (W)	MgO/Citric acid	**Wittig et al. (2004, 103413)[85]**
R&P-2000 FRM	16.7	Teflon (W)	None	Avg conversion efficiency to NO_X (tested using NH_4NO_3 solution) was 0.85 ± 0.08. Gas analyzer efficiency was stable at 0.99 ± 0.04.
				Corrections were made for instrument offset, software calculation error, conversion efficiency, gas analyzer efficiency, vacuum drift, and sample flow drift. The overall avg correction was 8%, ranging from -62% to 93%.
				Data Recovery >80%. Data loss was associated with vacuum pump failures and excessive flash strip breakage.
				R&P-8400N = 0.83 CMU + 0.20 µg/m^3; R^2 = 0.84
				Underestimation in the R&P-8400N could be due to incomplete particle collection or incomplete conversion of various forms of NO_3^-.
				Used co-located filter measurements for final calibration.
FRESNO SUPERSITE, CA and other CRPAQS sites; 12/2/99 to 2/3/01 Located 5.5 km northeast of downtown in a mixed residential-commercial neighborhood. [107]				**Chow et al. (2005, 099030)[87]**
Sampler	**Flow Rate (L/Min)**	**Filter Type[a]**	**Denuder[b]**	Maximum NO_3- volatilization was observed during summer (Jun-Aug), while the lowest volatilization was observed during winter (Dec-Feb).
DRI-SFS	113	Quartz (Pellulose	Al_2O_3	Seasonal avg volatilized NO_3- in particulate NO_3^- (PNO_3^-, the sum of non-volatilized and volatilized NO_3^-) ranged from less than 10% during winter to more than 80% during summer.
RAAS-400	24	Quartz (P)-Nylon (P)	Na_2CO_3	
RAAS-400	24	Quartz (P)-Quartz (P)	None	Volatilized NH_4NO_3 accounted for 44% of actual $PM_{2.5}$ mass (i.e., measured mass plus volatilized NH_4NO_3) in Fresno during summer.
RAAS-100 FRM	16.7	Quartz (P)	None	
Continuous Sampler	**Flow Rate (L/Min)**	**Denuder**	**Analysis Method[b]**	Front-quartz non-volatilized NO_3- concentrations were similar for DRISFS (0.52 ± 0.26 µg/m^3) and RAAS-100 FRM (0.81 ± 0.33 µg/m^3) for warm months (May-Sep). With preceding denuders, the DRI-SFS PNO_3 concentration (3 ± 1.9 µg/m^3) was much higher than the RAAS100 FRM NO_3^-, suggesting that the FRM sampler removed gaseous nitric acid (HNO_3) resulting in NO_3- volatilization. FRM Teflon-membrane filters are subject to similar NO_3^- losses.
R&P-8400N	5	Activated Carbon	NO_X Chemiluminescence	
Sampler	**Flow Rate (L/Min)**	**Filter Type[a]**	**Denuder[b]**	**Chow et al. (2005, 156348)[117]**
PC-BOSS	150	Teflon (W)- Nylon (P)	CIF	
Continuous Sampler	**Flow Rate (L/Min)**	**Denuder**	**Analysis Method[b]**	
R&P-8400N	5	Activated Carbon	NO_X Chemiluminescence	
Dionex-IC	5	Parallel plate wet denuder	IC	

SITE / PERIOD / SAMPLER / CONFIGURATION	SUMMARY OF FINDINGS
	High correlation (R^2 >0.90) between 24-h avg R&P-8400N NO_3 and SFS filter NO_3^- concentrations, but R&P-8400N NO_3- was 7 to 25% lower than filter NO_3-.
	Limited comparison (n < 15) with filter samples at Bakersfield showed that the slopes were close to unity during early morning hours, while they decreased during the afternoon hours, indicating possible loss of NO_3^- by the R&P-8400N instrument.
	The R&P-8400N required substantial maintenance and careful operation.
	Grover et al. (2006, 138080)[65]
	Dionex-IC NO_3 = (0.71 ± 0.04) PC-BOSS NO_3 + (3.2 ± 1.1); R^2 = 0.91; n = 29
	R&P-8400N = (1.10 ± 0.06) PC-BOSS NO_3 - (0.8 ± 1.8); R^2 = 0.93; n = 29
	R&P-8400N = (0.55 ± 0.01) Dionex-IC + (1.4 ± 1.8); R^2 = 0.75; n = 493
	R&P-8400N measured less than Dionex-IC, particularly at high RH. R&P-8400N may suffer incomplete flash vaporization under conditions of high RH.

SITE / PERIOD / SAMPLER / CONFIGURATION	SUMMARY OF FINDINGS
BALTIMORE SUPERSITE, MD; 2/14/02 to 11/30/02 Adjacent to a parking lot in the University of Maryland campus, influenced by motor vehicles, coal-fired power plants and incinerators ~21 km southwest of site and regionally transported material. **Sampler** / **Flow Rate (L/Min)** / **Filter Type**[a] / **Denuder**[b] SASS / 6.7 / Nylon (N/A) / MgO **Continuous Sampler** / **Flow Rate (L/Min)** / **Denuder** / **Analysis Method**[b] R&P-8400N / 5 / Activated Carbon / NO_X Chemiluminescence	**Harrison et al. (2004, 136787)**[83] Corrections were made to R&P-8400N data for software calculation error, conversion efficiency, gas analyzer efficiency, vacuum drift and sample flow drift. The relative uncertainty of R&P-8400N measurements averaged 8.7%, ranging from 6.3% to 23%. Data capture >95%. R&P-8400N underestimated SASS filter NO_3^- by ~33%, attributed to variations in conversion efficiency, matrix effects, and impaction efficiency. This suggested a true conversion efficiency of 68% as compared to an avg conversion efficiency of R&P-8400N to NO_X (tested using potassium nitrate solution) of 0.90 ± 0.04. Large errors occurred when the concentrations were near the detection limit, when the temperature difference (between instrument and ambient) was large, and when the ambientRH was < 40%. Ridged flash strips produced lower dissociation losses than flat strips. Reliable measurements were obtained when the instrument-outdoor temperature differences were minimal and when grooved/ridged flash strips were used. A co-located filter measurement was used for final corrections.
NEW YORK SUPERSITE, NY; 06/29/01 to 08/05/01 and 07/09/02 to 08/07/02 Urban site located at Queens College, NY, about 14 km west of Manhattan, within 2 km of freeways, and within 12 km of international airports. Rural site located at Whiteface mountain, 600 m above sea level, in a clearing surrounded by deciduous and evergreen trees and no major cities within 20 km of the site. **Sampler** / **Flow Rate (L/Min)** / **Filter Type**[a] / **Denuder**[b] R&P-2300 / 10 / Nylon (N/A) / Na_2CO_3 **Continuous Sampler** / **Flow Rate (L/Min)** / **Denuder** / **Analysis Method**[b] R&P-8400N / 5 / Activated Carbon / NO_X Chemiluminescence PILS-IC / 5 / Na_2CO_3 and citric acid / IC AMS / 0.1 / None / Mass Spectrometry	**Hogrefe et al. (2004, 099003)**[20] Data completeness: 86-88% for R&P-8400N, 94 - 98% for AMS, and 65-70% for PILS-IC. Some PILS measurements were invalidated owing to larger aqueous flow caused by bigger tubing. Larger aqueous flow and inconsistent water quality affected NO_3^- concentrations. R&P-8400N NO_{3-} was lower than R&P-2300 filter NO_3^-. PILS-IC was within 5% of R&P-2300 filter NO_{3-} concentrations. At the urban site, AMS was within 10% of the filter NO_3 concentration. At the rural site, AMS had a slope of 0.51 and R^2 of 0.46, compared with filter NO_3^-.
NEW YORK SUPERSITE, NY; 10/01 to 07/05 (urban), 07/02 to 07/05 (rural) Urban site located at a school in South Bronx, NY in a residential area, within a few kilometers away from major highways and a freight yard (experiencing significant truck traffic). Rural site located at Whiteface mountain, 600 m above sea level, in a clearing surrounded by deciduous and evergreen trees and no major cities within 20 km of the site. **Sampler** / **Flow Rate (L/Min)** / **Filter Type**[a] / **Denuder**[b] R&P-2300 / 10 / Nylon (N/A) / Na_2CO_3 TEOM-ACCU / 16.7 / Zefluor / None **Continuous Sampler** / **Flow Rate (L/Min)** / **Denuder** / **Analysis Method**[b] R&P-8400N / 5 / Activated Carbon / NO_X Chemiluminescence	**Rattigan et al. (2006, 115897)**[84] Data capture was more than 94%. Data were adjusted for span and zero drifts, conversion efficiency, flow drift, and blanks. R&P-8400N NO_3^- was systematically lower than R&P-2300 filter NO_3 over all concentration ranges, except at <1 µg/m^3. Urban: R&P-8400N = 0.59 R&P-2300 NO_3 + 0.28; R^2 = 0.88; n = 305 Rural: R&P-8400N = 0.73 R&P-2300 NO_3 + 0.01; R^2 = 0.90; n~161; however concentrations were low with 95% of data < 1 µg/m^3. Required weekly or biweekly maintenance by trained personnel.
LOS ANGELES SUPERSITE, CA; 7/13/01 to 9/15/01 (Rubidoux) and 9/15/01 to 2/10/02 (Claremont) Multiple sampling locations in the South Coast Air Basin (SoCAB), including urban "source" sites and downwind "receptor" sites. **Sampler** / **Flow Rate (L/Min)** / **Filter Type**[a] / **Denuder**[b]	**Fine et al. (2003, 155775)**[19] MOUDI = 0.68 HEADS; R^2 = 0.88 ADI-N Sized = 0.80 HEADS; R^2 = 0.79

SITE / PERIOD / SAMPLER / CONFIGURATION				SUMMARY OF FINDINGS
MOUDI	30	Teflon (P)	None	ADI-N Sized = 1.12 MOUDI; R^2 = 0.53 ADI-N NO_{3^-} showed better agreement with HEADS at lower concentrations, the ADI-N deviated (biased low) from the HEADS concentrations at higher NO_3^- concentrations. This deviation was attributed to NO_{3^-} vaporization, loss of NO_3^- associated with particles less than 0.1 µm not collected by the ADI-N sampler, or loss of particles in the ADI-N inlet tubing. The underestimation of NO_{3^-} by MOUDI compared to HEADS may be due to NO_3^- volatilization from MOUDI stages, since SO_4^{2-} comparisons showed MOUDI to explain 85% of HEADS SO_4^{2-}. ADI-N and MOUDI showed better correlation (R^2 = 0.67) for the 1-2 µm size range NO_3 relative to other size ranges (R^2 < = 0.56). This is possibly due to NO_3^- in the form of non-volatilized sodium nitrate ($NaNO_3$) than volatilized NH_4NO_3 in the 1-2 µm size range. Single particle analysis also indicated this possibility of $NaNO_3$ in the 1-2 µm range.
HEADS	10	Teflon (N/A) -GF--GF	Carbonate	
Continuous Sampler	**Flow Rate (L/Min)**	**Denuder**	**Analysis Method**[b]	
ADI-N Sized	0.9	Activated Carbon	NO_X Chemiluminescence	
RUBIDOUX, CA; 07/01/03 to 07/31/03 Located in the eastern section of SoCAB in the northwest corner of Riverside County, 78 km downwind of the central Los Angeles metropolitan area and in the middle of the remaining agricultural production area in SoCAB.				**Grover et al. (2005, 090044)**[66] R&P-8400N = (0.65 ± 0.07) PC-BOSS + (3.3 ± 2.4); R^2 = 0.73; n = 31 At higher concentrations (no numerical value reported), R&P-8400N $NO_{3^-}$was lower than PC-BOSS NO_{3^-}, possibly due to incomplete volatilization of NH_4NO_3 in R&P-8400N at higher concentrations (and higher relative humidity). At the urban site, the continuous instruments correlated well with filter NO_3^- measurements and among themselves (R^2 ≥ 0.89). At the rural site, R^2 ranged from 0.61 to 0.83, except for the AMS versus R&P2300 comparison, with an R^2 of 0.46.
Sampler	**Flow Rate (L/Min)**	**Filter Type**[a]	**Denuder**[b]	
PC-BOSS	150	Teflon (W)-Nylon (P)	CIF	
Continuous Sampler	**Flow Rate (L/Min)**	**Denuder**	**Analysis Method**[b]	
R&P-8400N	5	Activated Carbon	NO_X Chemiluminescence	
R&P-8400N	5	Activated Carbon	NO_X Chemiluminescence	
PILS-IC	5	Na_2CO_3 and Citric acid	IC	
AMS	0.1	None	Mass Spectrometry	

SITE / PERIOD / SAMPLER / CONFIGURATION	SUMMARY OF FINDINGS

[a]Filter Manufacturer in parenthesis - W: Whatman, Clifton, NJ; P: Pall-Gelman, Ann Arbor, MI; S: Schleicher & Schnell. Keene, NH; N/A: not available or not reported.
[b]Al_2O_3: Aluminum oxide; GF: Na_2CO_3 impregnated Glass Fiber Filters; IC: Ion chromatography; MgO: Magnesium oxide; Na_2CO_3: Sodium carbonate; $NaHCO_3$: Sodium bicarbonate NO_X: Oxides of nitrogen; CIF: Charcoal Impregnated Filter; FEP: Fluorinated Ethylene Propylene copolymer; TEA: Triethanolamine; TSP: Total Suspended PM.
[c]Na_2CO_3 impregnated.
[d]37 mm filter.

[1]Chow (1995, 077012); [2]Watson and Chow (2001, 157123); [3] Watson et al. (1983, 045084); [4]Fehsenfeld et al. (2004, 157360); [5]Solomon et al. (2001, 157193); [6]Watson et al. (2005, 157124); [7]Mikel (2001, 156762); [8]Watson et al. (1999, 020949); [9]Solomon and Sioutas (2006, 156995); [10]Graney et al. (2004, 053756); [11]Tanaka et al. (1998, 157041); [12]Pancras et al. (2005, 098120); [13]John et al. (1988, 045903); [14]Hering and Cass (1999, 084958); [15]Fitz et al. (1989, 077387); [16]Hering et al. (1988, 036012); [17]Solomon et al. (2003, 156994); [18]Cabada et al. (2004, 148859); [19]Fine et al. (2003, 155775); [20]Hogrefe et al. (2004, 099003); [21]Drewnick et al. (2003, 099160); [22]Watson et al. (2005, 157125); [23]Ho et al. (2006, 156552); [24]Decesari et al. (2005, 144536); [25] Mayol-Bracero et al. (2002, 045010); [26]Yang et al. (2003, 156167); [27]Turšic et al. (2006, 157063); [28]Mader et al.(2004, 156724); [29]Xiao and Liu (2004, 056801); [30]Kiss et al. (2002, 156646); [31]Cornell and Jickells (1999, 156367); [32] Zheng et al. (2002, 026100); [33]Fraser et al. (2002, 140741); [34] Fraser et al. (2003, 042231) [35]Schauer er al. (2000, 012225); [36]Fine et al. (2004, 141283); [37]Yue et al. (2004, 157169); [38]Rinehart et al. (2006, 115184); [39]Wan and Yu (2006, 157104); [40]Poore (2000, 012839); [41]Fraser et al. (2003, 040266); [42]Engling et al. (2006, 156422); [43]Yu et al. (2005, 157167); [44]Tran et al. (2000, 013025); [45]Yao et al. (2004, 102213); [46]Li and Yu (2005, 156692); [47]Henning et al. (2003, 156539); [48]Zhang and Anastasio (2003, 157182); [49]Emmenegger et al. (2007, 156418); [50] Watson et al. (1989, 046318); [51]Greaves et al. (1985, 156494); [52]Waterman et al. (2000, 157116); [53]Waterman et al. (2001, 157117); [54]Falkovich and Rudich (2001, 156427); [55]Chow et al. (2007, 157209); [56]Miguel et al. (2004, 123260); [57]Crimmins and Baker (2006, 097008); [58]Ho and Yu (2004, 156551); [59]Jeon et al. (2001, 016636); [60]Mazzoleni et al. (2007, 098038); [61]Poore (2002, 051444); [62]Butler et al. (2003, 156313); [63]Chow et al. (2006, 146622); [64]Russell et al. (2004, 082453); [65]Grover et al. (2006, 138080); [66]Grover et al. (2005, 090044); [67]Schwab et al. (2006, 098449); [68]Hauck et al. (2004, 156525); [69]Jaques et al. (2004, 155878); [70]Rupprecht and Patashnick (2003, 157207); [71]Pang et al (2002, 030353); [72]Eatough et al. (2001, 010303); [73]Lee et al. (2005, 128139); [74]Lee et al. (2005, 156680); [75]Babich et al. (2000, 156239); [76]Lee et al. (2005, 155925); [77]Lee et al. (2005, 128139); [78]Anderson and Ogren (1998, 156213); [79]Chung et al. (2001, 156357); [80]Kidwell and Ondov (2004, 155898); [81]Lithgow et al. (2004, 126616); [82]Weber et al. (2003, 157129); [83]Harrison et al. (2004, 136787); [84]Rattigan et al. (2006, 115897); [85]Wittig et al. (2004, 103413); [86]Vaughn et al. (2005, 157089); [87]Chow et al. (2005, 099030); [88]Weber et al (2001, 024640) ; [89]Schwab et al. (2006, 098785); [90]Lim et al. (2003, 037037); [91]Watson and Chow (2002, 037873); [92]Venkatachari et al. (2006, 105918); [93]Bae et al. (2004, 156243); [94]Arhami et al. (2006, 156224); [95]Park et al. (2005, 156843); [96]Bae et al. (2004, 098680); [97]Chow et al. (2006, 156350); [98]Arnott et al. (2005, 156227); [99]Bond et al. (1999, 156281); [100]Virkkula et al. (2005, 157097); [101]Petzold et al. (2002, 156863); [102]Park et al. (2006, 098104); [103]Arnott et al. (1999, 020650); [104]Peters et al. (2001, 016925); [105]Pitchford et al. (1997, 156872); [106]Rees et al. (2004, 097164); [107]Watson et al. (2000, 010354); [108]Lee et al. (2005, 156680); [109]Hering et al. (2004, 155837); [110]Watson et al. (1998, 198805); [111]Chakrabarti et al. (2004, 157426); [112]Mathai et al. (1990, 156741); [113]Kidwell and Ondov (2001, 017092); [114]Stanier et al. (2004, 095955); [115]Khlystov et al. (2005, 156635); [116]Takahama et al. (2004, 157038); [117]Chow et al. (2005, 156348); [118]Zhang et al. (2002, 157181); [119]Subramanian et al. (2004, 081203); [120]Chow et al. (2006, 155207); [121]Birch and Cary (1996, 026004); [122]Birch (1998, 024953); [123]Birch and Cary (1996, 002352); [124]NIOSH (1996, 156810); [125]NIOSH (1999, 156811); [126]Chow et al. (1993, 077459); [127]Chow et al. (2007, 156354); [128]Ellis and Novakov (1982, 156416); [129]Peterson and Richards (2002, 156861); [130]Schauer et al. (2003, 037014); [131]Middlebrook et al. (2003, 042932); [132]Wenzel et al. (2003, 157139); [133]Jimenez et al. (2003, 156611); [134]Phares et al. (2003, 156866); [135]Qin and Prather (2006, 156895); [136]Zhang et al. (2005, 157185); [137]Bein et al. (2005, 156265); [138]Drewnick et al. (2004, 155754); [139]Drewnick et al. (2004, 155755); [140]Lake et al. (2003, 156669); [141]Lake et al. (2004, 088411)

Source: Chow et al. (2008, 156355)

Table A-14. Summary of $PM_{2.5}$ SO_4^{2-} measurement comparisons

SITE/PERIOD/SAMPLER/ CONFIGURATION				SUMMARY OF FINDINGS
ATLANTA SUPERSITE, GA: 08/03/99 to 09/01/99 Four km NW of downtown, within 200 m of a bus maintenance yard and several warehouse facilities, representative of a mixed commercial-residential neighborhood.				**Solomon et al. (2003, 156994)[17]**
Sampler	**Flow Rate (L/Min)**	**Filter Type[a]**	**Denuder[b]**	$PM_{2.5}$ SO_4^{2-} from each sampler was compared to all-sampler averages, called the filter relative reference (filter RR) value. The samplers agreed to within 10% of filter RR, except for the PC-BOSS (TVA) and MOUDI-100.
R&P-2000 FRM	16.7	Quartz (P)	None	
RAAS-400	24	Teflon (P)	None	
SASS	6.7	Teflon (P)	None	While avg mass was within 10%, daily variability was >50% of filter RR.
MASS-450	16.7	Quartz (P)	None	
R&P-2300	10	Quartz (P)	None	All samplers, except for the PC-BOSS (TVA), correlated well (R^2 >0.90) with daily filter RR.
VAPS	15	Quartz (P)	XAD-4	PC-BOSS (TVA) had instrument leaks.
URG-PCM	16.7	Teflon (P)-Cellulose-fiber (W)		The R&P-2000 FRM, on avg, agreed within 1% of filter RR.
ARA-PCM	16.7	Teflon (N/A)	Na_2CO_3/Citric acid	MOUDI-100 was ~13% low compared to filter RR.
ARA-PCM	16.7	Nylon (N/A)	Na_2CO_3/Citric acid	**Weber et al. (2003, 157129)[82]; Zhang et al. (2002, 157181)[118]**
PC-BOSS (TVA)	105	Teflon (W)	CIF	Hourly $PM_{2.5}$ SO_4^{2-} were compared to all-sampler averages (continuous RR), similar to the approach used for filter samplers. Overall agreement was within 16% or 2 µg/m^3.
PC-BOSS (TVA)	105	Quartz (P)	CIF	
PC-BOSS (BYU)	150	Teflon (W)	CIF	Good correlations (R^2 = 0.76 to 0.94) were found during the second half of the study, except for TT versus ADI.
PC-BOSS (BYU)	150	Quartz (P)	CIF	
MOUDI-100	30	Teflon (N/A) Quartz (N/A)	None	
Continuous Sampler	**Flow Rate (L/Min)**	**Denuder**	**Analysis Method[b]**	Good correlation (R^2 = 0.84) was found between continuous and filter-based SO_4^{2-}
ADI-S	2.7	Activated Carbon	SO_2, UV Fluorescence	Continuous RR = (1.15 ± 0.15), Filter RR + (0.41 ± 1.73)
PILS-IC	5	Two URG annular glass denuders in series containing citric acid & $CaCO_3$	IC	Variability among continuous SO_4^{2-} instruments (RSD = 13%) was similar to that for NO_3^- instruments. Filter sample variability was low (RSD = 8%) indicating more uniformity among samplers.
ECN	16.7	Rotating annular wet denuder system	IC	
TT	5	Wet parallel plate denuder	IC	The ECN and TT instruments were within 15%, PILS-IC was within 20% and ADI-S was within 26% of filter RR.
PITTSBURGH SUPERSITE, PA; 070/1/01 to 08/01/02 6 km east of downtown in a park on the top of a hill				**Cabada et al. (2004, 148859)[18]; Takahama et al. (2004, 157038)[116]**
Sampler	**Flow Rate (L/Min)**	**Filter Type[a]**	**Denuder[b]**	MOUDI SO_4^{2-} 0.80 CMU; R^2 = 0.95; Summer
MOUDI-110	30	Teflon (W)	None	MOUDI SO_4^{2-} 0.97 CMU; R^2 = 0.48; winter
CMU	16.7	Teflon (W)	MgO/Citric acid	**Wittig et al. (2004, 103413)[85]**

SITE/PERIOD/SAMPLER/ CONFIGURATION				SUMMARY OF FINDINGS
R&P-2000 FRM	16.7	Teflon (W)	None	Avg conversion efficiency to SO_2 (tested using ammonium sulfate [$(NH_4)_2SO_4$] solution) was 0.65 ± 0.07. Gas analyzer efficiency was stable at 0.99 ± 0.06.
Continuous Sampler	**Flow Rate (L/Min)**	**Denuder**	**Analysis Method[b]**	Corrections were made for instrument offset, software calculation error, conversion efficiency, gas analyzer efficiency, vacuum drift, and sample flow drift. The overall correction was, on avg, -1% and ranged from -90% to 100% for individual samples.
R&P-8400S	5	Activated Carbon	SO_2 UV Fluorescence	Data Recovery >90%. Data loss was associated with vacuum pump failures or excessive flash strip breakage.
				R&P-8400S (SO_4^{2-}) = 0.71 CMU + 0.42 µg/m^3; R^2 = 0.83
				Underestimation is attributed to incomplete particle collection or incomplete conversion of various forms of SO_4^{2-}.
				Used co-located filter measurements for final calibration.
LOS ANGELES SUPERSITE, CA; 07/13/01 to 09/15/01 (Rubidoux) and 09/15/01 to 02/10/02 (Claremont) Multiple sampling locations in the South Coast Air Basin (SoCAB), including urban "source" sites and downwind "receptor" sites.				**Fine et al. (2003, 155775)[19]** MOUDI explained 85% of HEADS SO_4^{2-} (R^2 = 0.89; n = 40)
Sampler	**Flow Rate (L/Min)**	**Filter Type[a]**	**Denuder[b]**	
MOUDI	30	Teflon (P)	None	
HEADS	10	Teflon (N/A) GF-GF[c]	Carbonate	
NEW YORK SUPERSITE, NY; 06/29/01 to 08/05/01 and 07/09/02 to 08/07/02 Urban site located at Queens College, NY, about 14 km west of Manhattan, within 2 km of freeways, and within 12 km of international airports. Rural site located at Whiteface mountain, 60m above sea level, in a clearing surrounded by deciduous and evergreen trees and no major cities within 20 km of the site.				**Drewnick et al. (2003, 099160)[21]; Hogrefe et al. (2004, 099003)[20]** Data completeness: 89-93% for R&P-8400S, 94-98% for AMS, 81-98% for CASM, and 65-70% for PILS-IC.
Sampler	**Flow Rate (L/Min)**	**Filter Type[a]**	**Denuder[b]**	
R&P-2300	10	Nylon (N/A)	Na_2CO_3	
SCS	42	Zefluor (N/A)	None	
TEOM-ACCU	16.7	Zefluor (N/A)	None	
Continuous Sampler	**Flow Rate (L/Min)**	**Denuder**	**Analysis Method[b]**	
R&P-8400S	5	Activated Carbon	SO_2 UV Fluorescence	
PILS-IC	5	Na_2CO_3 and Citric acid	IC	
AMS	0.1	None	Mass Spectrometry	
CASM	5	Na_2CO_3 and Carbon and a Nafion dryer	SO_2 UV Fluorescence	The urban site data showed good correlations (R^2 = 0.87 to 0.94) with slopes ranging from 0.97 to 1.01. At the rural site, the variability was large (R^2 = 0.73 to 0.91) with slopes ranging from 0.76 to 1.32. SO_4 from PILS-IC was overestimated by ~25% when compared to the AMS at the rural site.
				Filter samples were within 5% of each other, except for comparison of ACCU with R&P-2300 at the rural site, with high correlations (R^2 = 0.97 to 1.0). ACCU underestimated SO_4^{2-} by ~15%.
				Continuous versus 6-h SCS filter comparisons showed high R^2 (0.91 to 0.95) at the urban site. Continuous instruments consistently measured lower SO_4^{2-} concentrations compared to the SCS filter measurements (slopes 0.68 to 0.73)
				On avg, 85% of the filter-based SO_4^{2-} was measured by the continuous instruments with consistent relationships. At the rural site, PILS-IC overestimated SO_4^{2-} concentrations (slopes 1.11 to 1.15), AMS and R&P-8400S showed slopes of 0.71-0.74 against SCS and ACCU, while it ranged from 0.53- 0.68 against R&P-2300.
				Error estimates:
				Sampling losses: 2-3% for AMS and PILS-IC, 5-10% for R&P-8400S and none for CASM.
				Continuous instruments probably experienced more inlet transport losses (~

SITE/PERIOD/SAMPLER/ CONFIGURATION	SUMMARY OF FINDINGS
	25%) than filter samplers due to longer inlet lines. Small (< 2%) positive artifact was found in filters.
NEWYORK SUPERSITE, NY; 10/01 to 07/05 (urban), 07/02 to 07/05 (rural) Urban site located at a school in South Bronx, NY in a residential area, within a few kilometers from major highways and a freight yard (experiencing significant truck traffic). Rural site located at Whiteface mountain, 600m above sea level, in a clearing surrounded by deciduous and evergreen trees and no major cities within 20 km of the site. The study by Schwab et al.89 was based at a rural site located at Pinnacle State Park surrounded by golf course, picnic areas and undeveloped forest lands and no major cities within 15 km.	**Rattigan et al. (2006, 115897)**[84] Data capture was above 85%. Data loss was primarily due to frequent flash strip failures, every 2 wk and without warning. Data were adjusted for span and zero drifts, measured conversion efficiency, flow drift, and blanks. Calibrations used aqueous standards of $(NH_4)_2SO_4$ and oxalic acid solution in 1:4 ratio. Lower fractions of oxalic acid showed lower conversion efficiencies. Urban South Bronx site: R&P-8400S = 0.82 TEOM-ACCU + 1.15; R^2 = 0.84; n = 513 R&P-8400S = 0.74 R&P-2300 + 1.14; R^2 = 0.81; n = 322 Rural Whiteface mountain: R&P-8400S = 0.75 TEOM-ACCU + 0.22; R^2 = 0.95; n = 207 R&P-8400S = 0.78 R&P-2300 + 0.17; R^2 = 0.85; n = 198 Required weekly or biweekly maintenance by trained personnel **Schwab et al. (2006, 098785)**[89] TE-5020 = 0.78 ACCU – 0.2; R^2 = 0.94 Similar studies at St. Louis, MO, show slopes near unity. This suggests that the instrument is sensitive to aerosol composition. Low maintenance and calibration requirements for TE-5020 compared to PILS-IC and R&P-8400S.

Integrated Sampler	Flow Rate (L/Min)	Filter Type[a]	Denuder[b]
R&P-2300	10	Nylon (N/A)	Na_2CO_3
TEOM-ACCU	16.7	Zefluor	None

Continuous Sampler	Flow Rate (L/Min)	Denuder	Analysis Method[b]
R&P-8400S	5	Activated Carbon	SO_2 pulsed fluorescence
TE-5020 (07/14/04 to 11/01/04)	5	Na_2CO_3	SO_2 pulsed fluorescence

FRESNO SUPERSITE,CA; 12/01/03 to 12/23/03 Located 5.5 km northeast of downtown in a mixed residential-commercial neighborhood. Flow Sampler (L/min) Filter Typea Denuderb	**Grover et al. (2006, 138080)**[65] Dionex-IC SO_4^{2-} (1.03 ± 0.03) PC-BOSS SO_4 + (0.2 ± 0.3); R^2 = 0.98; n = 27 R&P-8400S SO_4^{2-} (0.95 ± 0.05) Dionex-IC SO_4 + (0.3 ± 0.6); R^2 = 0.68; n = 195

Sampler	Flow Rate (L/Min)	Filter Type[a]	Denuder[b]
PC-BOSS	150	Teflon (W)-Nylon (P)	CIF

Continuous Sampler	Flow Rate (L/Min)	Denuder	Analysis Method[b]
R&P-8400S	5	Activated Carbon	SO_2 pulsed fluorescence
Dionex-IC	5	Parallel plate wet denuder	IC

SITE/PERIOD/SAMPLER/ CONFIGURATION	SUMMARY OF FINDINGS

[a]Filter Manufacturer in parentheses - W: Whatman, Clifton, NJ; P: Pall-Gelman, Ann Arbor, MI; S: Schleicher & Schnell. Keene, NH; N/A: not available.
[b]Al_2O_3: Aluminum oxide; IC: Ion chromatography; CIF: Charcoal Impregnated Filter; FEP: Fluorinated Ethylene Propylene copolymer; MgO: Magnesium oxide; Na_2CO_3: Sodium carbonate; $NaHCO_3$: Sodium bicarbonate NO_x: Oxides of nitrogen; SO_2: Sulfur dioxide; TEA: Triethanolamine; TSP: Total Suspended PM; UV: Ultraviolet; XAD-4: Hydrophobic, non-polar polyaromatic resin.
[c]Na_2CO_3 impregnated.
[d]37 mm filter.

[1]Chow (1995, 077012); [2]Watson and Chow (2001, 157123); [3] Watson et al. (1983, 045084); [4]Fehsenfeld et al. (2004, 157360); [5]Solomon et al. (2001, 157193); [6]Watson et al. (2005, 157124); [7]Mikel (2001, 156762); [8]Watson et al. (1999, 020949); [9]Solomon and Sioutas (2006, 156995); [10]Graney et al. (2004, 053756); [11]Tanaka et al. (1998, 157041); [12]Pancras et al. (2005, 098120); [13]John et al. (1988, 045903); [14]Hering and Cass (1999, 084958); [15]Fitz et al. (1989, 077387); [16]Hering et al. (1988, 036012); [17]Solomon et al. (2003, 156994); [18]Cabada et al. (2004, 148859); [19]Fine et al. (2003, 155775); [20]Hogrefe et al. (2004, 099003); [21]Drewnick et al. (2003, 099160); [22]Watson et al. (2005, 157125); [23]Ho et al. (2006, 156552); [24]Decesari et al. (2005, 144536); [25] Mayol-Bracero et al. (2002, 045010); [26]Yang et al. (2003, 156167); [27]Turšic et al. (2006, 157063); [28]Mader et al.(2004, 156724); [29]Xiao and Liu (2004, 056801); [30]Kiss et al. (2002, 156646); [31]Cornell and Jickells (1999, 156367); [32] Zheng et al. (2002, 026100); [33]Fraser et al. (2002, 140741); [34] Fraser et al. (2003, 042231) [35]Schauer er al. (2000, 012225); [36]Fine et al. (2004, 141283); [37]Yue et al. (2004, 157169); [38]Rinehart et al. (2006, 115184); [39]Wan and Yu (2006, 157104); [40]Poore (2000, 012839); [41]Fraser et al. (2003, 040266); [42]Engling et al. (2006, 156422); [43]Yu et al. (2005, 157167); [44]Tran et al. (2000, 013025); [45]Yao et al. (2004, 102213); [46]Li and Yu (2005, 156692); [47]Henning et al. (2003, 156539); [48]Zhang and Anastasio (2003, 157182); [49]Emmenegger et al. (2007, 156418); [50] Watson et al. (1989, 046318); [51]Greaves et al. (1985, 156494); [52]Waterman et al. (2000, 157116); [53]Waterman et al. (2001, 157117); [54]Falkovich and Rudich (2001, 156427); [55]Chow et al. (2007, 157209); [56]Miguel et al. (2004, 123260); [57]Crimmins and Baker (2006, 097008); [58]Ho and Yu (2004, 156551); [59]Jeon et al. (2001, 016636); [60]Mazzoleni et al. (2007, 098038); [61]Poore (2002, 051444); [62]Butler et al. (2003, 156313); [63]Chow et al. (2006, 146622); [64]Russell et al. (2004, 082453); [65]Grover et al. (2006, 138080); [66]Grover et al. (2005, 090044); [67]Schwab et al. (2006, 098449); [68]Hauck et al. (2004, 156525); [69]Jaques et al. (2004, 155878); [70]Rupprecht and Patashnick (2003, 157207); [71]Pang et al (2002, 030353); [72]Eatough et al. (2001, 010303); [73]Lee et al. (2005, 128139); [74]Lee et al. (2005, 156680); [75]Babich et al. (2000, 156239); [76]Lee et al. (2005, 155925); [77]Lee et al. (2005, 128139); [78]Anderson and Ogren (1998, 156213); [79]Chung et al. (2001, 156357); [80]Kidwell and Ondov (2004, 155898); [81]Lithgow et al. (2004, 126616); [82]Weber et al. (2003, 157129); [83]Harrison et al. (2004, 136787); [84]Rattigan et al. (2006, 115897); [85]Wittig et al. (2004, 103413); [86]Vaughn et al. (2005, 157089); [87]Chow et al. (2005, 099030); [88]Weber et al (2001, 024640) ; [89]Schwab et al. (2006, 098785); [90]Lim et al. (2003, 037037); [91]Watson and Chow (2002, 037873); [92]Venkatachari et al. (2006, 105918); [93]Bae et al. (2004, 156243); [94]Arhami et al. (2006, 156224); [95]Park et al. (2005, 156843); [96]Bae et al. (2004, 098680); [97]Chow et al. (2006, 156350); [98]Arnott et al. (2005, 156227); [99]Bond et al. (1999, 156281); [100]Virkkula et al. (2005, 157097); [101]Petzold et al. (2002, 156863); [102]Park et al. (2006, 098104); [103]Arnott et al. (1999, 020650); [104]Peters et al. (2001, 016925); [105]Pitchford et al. (1997, 156872); [106]Rees et al. (2004, 097164); [107]Watson et al. (2000, 010354); [108]Lee et al. (2005, 156680); [109]Hering et al. (2004, 155837); [110]Watson et al. (1998, 198805); [111]Chakrabarti et al. (2004, 157426); [112]Mathai et al. (1990, 156741); [113]Kidwell and Ondov (2001, 017092); [114]Stanier et al. (2004, 095955); [115]Khlystov et al. (2005, 156635); [116]Takahama et al. (2004, 157038); [117]Chow et al. (2005, 156348); [118]Zhang et al. (2002, 157181); [119]Subramanian et al. (2004, 081203); [120]Chow et al. (2006, 155207); [121]Birch and Cary (1996, 026004); [122]Birch (1998, 024953); [123]Birch and Cary (1996, 002352); [124]NIOSH (1996, 156810); [125]NIOSH (1999, 156811); [126]Chow et al. (1993, 077459); [127]Chow et al. (2007, 156354); [128]Ellis and Novakov (1982, 156416); [129]Peterson and Richards (2002, 156861); [130]Schauer et al. (2003, 037014); [13]1Middlebrook et al. (2003, 042932); [132]Wenzel et al. (2003, 157139); [133]Jimenez et al. (2003, 156611); [134]Phares et al. (2003, 156866); [135]Qin and Prather (2006, 156895); [136]Zhang et al. (2005, 157185); [137]Bein et al. (2005, 156265); [138]Drewnick et al. (2004, 155754); [139]Drewnick et al. (2004, 155755); [140]Lake et al. (2003, 156669); [141]Lake et al. (2004, 088411)

Source: Chow et al. (2008, 156355)

Table A-15. Summary of $PM_{2.5}$ carbon measurement comparisons.

SITE/PERIOD/SAMPLER/ CONFIGURATION						SUMMARY OF FINDINGS
ATLANTA SUPERSITE, GA: 08/03/99 to 09/01/99 Four km NW of downtown, within 200 m of a bus maintenance yard and several warehouse facilities, representative of a mixed commercial-residential neighborhood.						**Solomon et al. (2003, 156994)[17]** **Organic Carbon (OC);** $PM_{2.5}$ OC from each sampler was compared to the all-sampler avg, called the relative reference (RR) value. The samplers agreed to within 20 to 50% of RR. Only front filter OC is reported without artifact correction. Denuded samplers showed lower OC (20 to 35%) than RR, while non-denuded sampler OC was higher (5 to 35%). Among non-denuded samplers, as filter face velocity decreased, OC increased, with the exception of R&P-2300. OC positive artifacts ranged from 2 to 4 µg/m^3 **EC:** $PM_{2.5}$ EC from each sampler was compared to the all-sampler avg, called the relative reference (RR) value. The samplers agreed to within 20 to 200% of RR. TOT samples showed less EC than RR by 15 to 30%, while TOR samples showed more EC than RR by 40 to 90%. PCBOSS (BYU) >RR value by 140%. EC by TOR is ~twice EC by TOT. Major difference in EC is due to the carbon analysis protocol and optical monitoring correction (i.e., transmittance, reflectance). **Lim et al. (2003, 037037)[90]**
Sampler	**Flow Rate (L/Min)**	**Filter Type[a]**	**Denuder[b]**		**Analysis Method[c]**	
R&P-2000 FRM	16.7	Quartz (P)	None		NIOSH 5040-TOT	
RAAS-400	24	Quartz (P)	None		NIOSH 5040-TOT	
SASS	6.7	Quartz (P)-Quartz (P)	None		NIOSH 5040-TOT	
MASS-450	16.7	Quartz (P)	None		NIOSH 5040-TOT	
R&P-2300	10	Quartz (P)-Quartz (P)	None		NIOSH 5040-TOT	
VAPS	15	Quartz (P)	XAD-4		NIOSH 5040-TOT	
URG-PCM	16.7	Quartz (P)-Quartz (P)	XAD-4		Front: NIOSH 5040-TOT; Backup: custom-TOTd	
ARA-PCM	16.7	Quartz (N/A)-Quartz (N/A)	CIF		IMPROVE_TOR	
PC-BOSS (TVA)	150	Quartz (P)-CIF (N/A)	CIF		Front: IMPROVE_TOR; Backup: TPV	
PC-BOSS (BYU)	150	Quartz (P)-CIF (S)	CIF		TPB	
MOUDI-100	30	Al Foil-Quartz (N/A)[f]	None		Custom-TOR to suit Al[e]	
Continuous Sampler	**Flow Rate (L/Min)**	**Denuder**	**OC**	**EC**	**Comments**	

SITE/PERIOD/SAMPLER/ CONFIGURATION						SUMMARY OF FINDINGS
ADI-C	2.7	Activated Carbon	Not known	N/A	Part of SO_4^{2-} instrument w/CO_2 non-dispersive infrared (NDIR) analyzer; data corrected for avg field blank; OC = 2 oxidized OC	TC concentrations measured by the RU-OGI and R&P-5400 correlated reasonably well (R^2 = 0.83), with a slope of 0.96. The ratio of the mean RU-OGI to mean R&P-5400 TC was 1.02.
RU-OGI	16.1	None	700 in He	850 in 2% O_2	TOT; Dynamic blank for adsorption correction	R&P-5400 OC was 8% lower than the RU-OGI (R^2 = 0.73), while the R&P-5400 EC was 20% higher than RU-OGI (R^2 = 0.74).
R&P-5400	16.7	None	275 in air	750 in air	No pyrolysis correction	OC measured by ADI-C was lower than R&P-5400 and RUOGI by 15% and 22%, respectively.
PSAP	1.26	None		b_{abs}@ 565 nm	10m^2/g factor	EC from PSAP and AE-16 correlated well (R^2 = 0.97). PSAP was lower by ~50%, compared with AE-16, R&P-5400 and RU-OGI.
AE-16	4	None		b_{abs}@ 880 nm	12.6 m^2/g factor	EC measured by AE-16 was ~12% higher than RU-OGI. Calibration factors for the light absorption instruments need to be adjusted for better correlation.
						Calibration factor might be non-linear over the range of absorbance measured.
						The mean OC from R&P-5400 and RU-OGI were within 10% of filter RR values. Mean ADI-C OC was 14% lower than filter RR OC.
						EC from continuous instruments was 2-2.5 times filter RR EC; continuous TC was also greater than filter RR TC by 17% (R&P-400) to 27% (RU-OGI).

SITE/PERIOD/SAMPLER/ CONFIGURATION						SUMMARY OF FINDINGS
PITTSBURGH SUPERSITE, PA; 06/01/01 to 07/31/02 Six km east of downtown in a park on the top of a hill.						**Subramanian et al. (2004, 081203)**[119] Particulate OC (POC) was estimated from denuded sample (Quartz OC + CIG OC) after subtracting DYN POC. Denuder efficiency (1-DYN POC/UDB POC) was 94 ± 3%. No seasonal variability or deterioration in denuder performance was observed. Positive artifact due to denuder breakthrough was 18.3 ± 12.5% of the denuded sample POC. Negative artifact (CIGsample-CIGDYN) was, on avg, 6.3 ± 6.2% of POC. Positive artifact was 34 ± 10% from QBT, and was 13 ± 5% from QBQ. QBT >>QBQ. QBT over-corrected the positive artifact by 20%. OC volatilization from the front Teflon filter that subsequently adsorbed on the back-up quartz filter, resulted in an overestimation of the positive artifact. Non-denuded QBQ provided a more representative estimate of the positive artifact on the non-denuded front quartz filter for 24-h samples. However, it was not suitable for 4- to 6-h samples, because the filters were not in equilibrium with the air stream. Positive artifact dominated when sampling with a non-denuded quartz filter. Comparison of 24-h avg non-denuded front quartz OC versus denuded POC over the year showed an intercept of 0.53 μg/m^3, indicative of a positive artifact on quartz filter samples. The artifacts were higher in summer on an absolute basis; however, they showed no seasonal variation when expressed as a fraction of POC.
Sampler	**Flow**	**Filter Type/Pack**[a]		**Denuder**	**Analysis Method**[c]	
CMU Custom-1	16.7	*Non-denuded sample*	Teflon (P/W)-Quartz (P) (QBT)	None	NIOSH 5040-TOT	
	16.7	*Non-denuded sample*	Quartz (P)-Quartz (P) (QBQ)	None	NIOSH 5040-TOT	
CMU Custom-2	16.7	*Denuded sample*	Denuder-Quartz (P)-CIG (S)	Activated Carbon	NIOSH 5040-TOT	
	16.7	*Dynamic blank (DYN)*	Teflon (P/W)-Denuder-Quartz (P)-CIG (S)	Activated Carbon	NIOSH 5040-TOT	
	16.7	Non-denuded blank (UDB)	Teflon (P/W)-Quartz (P)-CIG (S)	None	NIOSH 5040-TOT	
ST. LOUIS SUPERSITE, IL, MO; 01/01/02 to 12/31/02 Three km east of St. Louis, MO City center, also impacted by industrial sources, and located in a mixed residential light commercial neighborhood.						**Bae et al. (2004, 156243)**[93]**; Bae et al. (2004, 098680)**[96] Denuder breakthrough was 0.17 ± 0.15 μg/m^3, and constituted less than 5% of annual avg OC concentration. Non-denuded OC = (1.06 ± 0.02) × denuded OC + (0.34 ± 0.10) Equivalence of OC intercept and denuder breakthrough implies that the low-level artifact is caused by denuder breakthrough. Non-denuded EC = (1.04 ± 0.03) × denuded EC + (0.07 ± 0.03), indicating negligible EC artifact. Results suggested higher summertime OC artifact, on an absolute basis.
Sampler	**Flow Rate (Lmin)**	**Filter Type/Pack**[a]	**Denuder**[b]		**Analysis Method**[c]	
University of Wisconsin Custom-1	24	Quartz (P)	None		ACE Asia TOT	
		Denuder-Quartz (P)	CIF		ACE Asia TOT	
University of Wisconsin Custom-2	24	Denuder-Quartz (P)	CIF		ACE Asia TOT	
		Teflon (N/A)-Denuder-Quartz (P)	CIF		ACE Asia TOT	
Continuous Sampler	**Flow Rate (L/Min)**	**Denuder**	**OC**	**EC**	**Comments**	

SITE/PERIOD/SAMPLER/ CONFIGURATION						SUMMARY OF FINDINGS
Sunset OCEC	8	CIF	340, 500, 615, 870°C in 100% He	550, 625, 700, 775, 850, 900 °C in 2% O2, 98% He	ACE Asia TOT; CH4 FID detector	Comparison of continuous Sunset TC and OC with 24-h filter samples showed good correlations (R^2) of 0.89 and 0.90, respectively. Continuous Sunset TC in $\mu g/m^3$ = (0.97 ± 0.02) × filter TC + (0.83 ± 0.11), indicating comparability with the filter measurements. Continuous Sunset OC = (0.93 ± 0.02) × filter OC + (0.94 ± 0.09) Positive intercept was interpreted to be a blank correction for the continuous measurements. EC comparison was poor with large scatter in data (R^2 = 0.60), probably due to low EC concentrations (avg = 0.70 $\mu g/m^3$), close to the detection limit (0.5 $\mu g/m^3$).

FRESNO SUPERSITE, CA and other CRPAQS sites; 12/02/99 to 02/03/01, 12/1/03 to 11/30/04
Fresno Supersite was located 5.5 km northeast of downtown in a mixed residential-commercial neighborhood.

Sampler	Flow Rate (Lmin)	Filter Type/Pack[a]	Denuder[b]	Analysis Method[c]
DRI-SFS	113	Quartz (P)	None	IMPROVE_TOR
		Teflon (P)-Quartz (P) (QBT)	None	IMPROVE_TOR
RAAS-400	24	(P) (QBT) Quartz (P)-Quartz (P) (QBQ)	None	IMPROVE_TOR
RAAS-400	24	Quartz (P)-Quartz (P) (QBQ)	XAD-4 / CIF	IMPROVE_TOR
RAAS-100 FRM	16.7	Quartz (P)	None	IMPROVE_TOR

Continuous Sampler	Flow Rate (L/Min)	Denuder	OC	EC	Comments
R&P-5400	16.7	None	275°C in air	750°C in air	No pyrolysis correction
Sunset OCEC	8.5	CIG	250, 500, 650, 850°C in He	650, 750, 850, 940°C in 2% O_2 in He	Transmittance
MAAP	16.7	None		b_{abs} @ 670 nm	Transmittance 6.5 m^2/g factor
AE-16	6.8	None		b_{abs} @ 880 nm	Transmittance 14625/λ m^2/g factor, where λ is in nm
AE-21	6.8	None		b_{abs} @ 370, 880 nm	
AE-31	6.8	None		b_{abs} @ 370, 470, 520, 590, 660, 880 and 950 nm	
DRI-PA	3	None		b_{abs} @ 1047 nm	Absorption, 5 m^2/g factor

Sampler	Flow Rate (Lmin)	Filter Type/Pack[a]	Denuder[b]	Analysis Method[c]

Watson and Chow (2002, 037873)[91]; Chow et al. (2005, 156348)[117]; Chow et al. (2006, 155207)[120]; Watson et al. (2005, 157124)[6]; Park et al. (2006, 098104)[102]

Non-denuded RAAS-400 and RAAS-100 FRM measured equivalent TC. DRI-SFS, RAAS-400 and RAAS-100 FRM samplers showed comparability for front filter TC, OC and EC measurements.

Positive OC artifact was 1.62 ± 0.58 $\mu g/m^3$ (~24% of non-denuded front quartz OC) from QBT, and 1.12 ± 0.91 $\mu g/m^3$ (~17% of non-denuded front quartz OC) from QBQ. QBT >>QBQ

Results from CRPAQS showed, on avg, a positive OC artifact of 34% (of the non-denuded front quartz OC) from QBT and 17.5% (of the non-denuded front quartz OC) from QBQ.

Positive artifact was higher during summer than winter.

Negative artifact was, on avg, 0.61 ± 0.58 $\mu g/m^3$ (~10% of POC) at Fresno. Over all the CRPAQS sites, it ranged from 2.3% in winter to 11% in summer, with an avg of 4.9%.

Positive artifact is estimated to be 0.5 $\mu g/m^3$.

No difference in denuded quartz backup OC was found between using XAD and CIF denuders.

Comparison of R&P-5400 TC, OC, and EC against filter samples showed poor correlation (R^2 < 0.55).

TC from R&P-5400 was 40-60% higher than filter TC by TOR. None of the R&P-5400 versus TOR filter comparisons were comparable or predictable, due to several frequent instrument malfunctions during the experiment and the small data set (~35 data points).

IMPROVE_TOR EC was consistently 20-25% higher than aethalometer BC.

IMPROVE_TOR EC was comparable to MAAP BC.

Comparison of light absorption (babs) from DRI-PA (1047 nm), MAAP (670 nm), and AE

SITE/PERIOD/SAMPLER/ CONFIGURATION						SUMMARY OF FINDINGS
PC-BOSS	150	Quartz (P)-CIG (S)†	CIF		TPV	(880 nm) analyzers with the filter IMPROVE_TOR EC, gave a σ_{abs} of 2.3, 5.5 and 10 m^2/g, differing from the default conversion factors of 5, 6.5, and 16.6 m^2/g used for each instrument at the specified wavelength.
Continuous Sampler	**Flow Rate (L/Min)**	**Denuder**	**OC**	**EC**	**Comments**	
R&P-5400	16.7	None	375°C in air	750°C in air	No pyrolysis	**Grover et al. (2006, 138080)**[65]
Sunset OCEC	8.0	CIG	250, 500, 650, 850°C in He	650, 750, 850°C in 2% O_2 & 98% He	NIOSH 5040_TOT NDIR CO_2 detector	R&P-5400 TC = (0.50 ± 0.01) Sunset TC + (3.6 ± 1.5); R^2 = 0.73; n = 480 Sunset TC = (0.63 ± 0.05) PC-BOSS TC + (4.1 ± 3.2); R^2 = 0.86; n = 29 R&P-5400 TC = (0.41 ± 0.02) PC-BOSS TC + (6.7 ± 1.6); R^2 = 0.91; n = 29

SITE/PERIOD/SAMPLER/ CONFIGURATION	SUMMARY OF FINDINGS

BALTIMORE SUPERSITE, MD; 02/15/2002 to 11/30/2002
East of downtown in an urban residential area. Within 91 m of bus maintenance facility.

Sampler	Flow Rate (L/Min)	Filter Type/Pack[a]	Denuder[b]		Analysis Method[c]
SASS	6.7	Quartz (P)-Quartz (P)	None		STN_TOT
Continuous Sampler	**Flow Rate (L/Min)**	**Denuder[b]**	**OC**	**EC**	**Comments**
Sunset OCEC	8	Carbon	600°C, then 870°C in He	870°C in 2% O_2 in He	TOT; CH4 FID detector; Denuder breakthrough ~ 0.5-1 µg C/m^3; Used 0.5 to correct OC concentrations

Park et al. (2005, 156843)[95]

Data capture 93.8%

Compared to SASS, Sunset underestimated OC and EC by 22% and ~11.5%, respectively.

Higher OC in SASS was attributed to the absence of a denuder (i.e., positive artifact by gaseous adsorption) and to temperature differences between the STN_TOT and Sunset_TOT carbon analysis temperature protocols.

EC discrepancy was probably related to the differences in temperature protocol.

RUBIDOUX, CA; 07/13/03 to 07/26/03
Rubidoux is located in the eastern section of the South Coast Air Basin (SoCAB) in the northwest corner of Riverside County, 78 km downwind of the central Los Angeles metropolitan area and in the middle of the remaining agricultural production area in SoCAB.

Sampler	Flow Rate (L/Min)	Filter Type/Pack[a]	Denuder[b]		Analysis Method[c]
PC-BOSS	150	Quartz (P)-CIG (S)	CIF		TPB (CIG heated to 450 °C in N2)
Continuous Sampler	**Flow Rate (L/Min)**	**Denuder[b]**	**OC**	**EC**	**Comments**
Sunset OCEC	8	CIF	N/A	N/A	TOT; NDIR detector; NIOSH 5040 protocol
Sunset OCEC	8	CIF	N/A	Not meas-ured	TOT; has blank quartz filter before entering analyzer. Used as "blank" stream for quantifying OC artifacts; 3-step analysis only in He.

Grover et al. (2005, 090044)[66]

Sunset OCEC TC = (0.90 ± 0.06) PC-BOSS + (2.0 ± 2.1); R^2 = 0.93; n = 21

Sunset TC was adjusted for carbon artifacts measured by second (blank) instrument.

NEW YORK SUPERSITE, NY; 01/12/04 to 02/05/04
Urban site located at Queens College, NY, about 14 km west of Manhattan, within 2 km of freeways, and within 12 km of international airports.

Integrated Sampler	Flow Rate (L/Min)	Filter Type/Pack[a]	Denuder[b]		Analysis Method[c]
R&P-2300	10	Quartz	None		STN_TOT
Continuous Sampler	**Flow Rate (L/Min)**	**Denuder[b]**	**OC**	**EC**	**Comments**
R&P-5400	16.7	None	340 °C in air	750 °C in air	No pyrolysis correction
Sunset OCEC	N/A	CIF	600, 870 °C in He	870 °C at 10% O_2 in He	Transmittance
AE-20	N/A	None		b_{abs} @ 370, 880 nm	Transmittance, 14625 λ m^2/g factor, where λ is in nm
AMS	N/A	None	N/A	N/A	~ 1 µm cut-point

Venkatachari et al. (2006, 105918)[92]

Regression of OC from Sunset OCEC against $PM_{2.5}$ mass concentration yielded an intercept of 1.14 µg/m^3, which was used as a measure of the positive artifact on the Sunset data. The Sunset OC data was corrected for this artifact.

AE-20 BC concentrations were ~86% of Sunset EC and R&P2300 filter EC concentrations.

AE-20 versus R&P-5400 showed high scatter.

Sunset Optical EC = 0.58 ± 0.05 Sunset Thermal EC; R^2 = 0.86; n = 506

Sunset Optical EC = 0.62 ± 0.05 AE-20 BC; R^2 = 0.96; n = 539

R&P-5400 TC tracked filter TC closely, but differed widely for OC and EC.

Sunset OC = (0.75 ± 0.76) R&P-2300 OC + (0.08 ± 0.36); R^2 = 0.67; n = 16

Sunset OC = (0.98 ± 0.11) R&P-5400 OC - (0.47 ± 0.17); R^2 = 0.44; n = 327

SITE/PERIOD/SAMPLER/ CONFIGURATION	SUMMARY OF FINDINGS
	R&P-5400 OC = (0.60 ± 0.47) R&P-2300 OC + (0.58 ± 0.82); R^2 = 0.58; n = 17 Organic matter measurements by AMS showed reasonable correlation (R^2 = 0.76) with filter (R&P-2300) OC, while being poorly correlated with continuous OC by Sunset (R^2 = 0.32) and R&P-5400 (R^2 = 0.36) Sunset EC = (1.21 ± 0.44) R&P-2300 EC – (0.03 ± 0.13); R^2 = 0.94; n = 16 Sunset EC = (1.35 ± 0.12) R&P-5400 EC + (0.06 ± 0.04); R^2 = 0.61; n = 327 R&P-5400 EC = (0.49 ± 0.46) R&P-2300 EC + (0.09 ± 0.26); R^2 = 0.77; n = 15 Sunset TC = (0.86 ± 0.39) R&P-2300 TC – (0.06 ± 0.69); R^2 = 0.77; n = 16 Sunset TC = (1.31 ± 0.10) R&P-5400 TC – (1.15 ± 0.15); R^2 = 0.59; n = 327 R&P-5400 TC = (0.77 ± 0.58) R&P-2300 TC + (0.35 ± 1.37); R^2 = 0.83; n = 16

[a]Filter Manufacturer in parentheses - W: Whatman, Clifton, NJ; P: Pall-Gelman, Ann Arbor, MI; S: Schleicher & Schnell. Keene, NH; N/A: not available. QBT: quartz backup filter behind Teflon front filter. QBQ: quartz backup filter behind Quartz front filter.

[b]Al_2O_3: Aluminum oxide; IC: Ion chromatography; CIF: Charcoal Impregnated Filter; CIG: Charcoal Impregnated Glass-Fiber Filter; FEP: Fluorinated Ethylene Propylene copolymer; MgO: Magnesium oxide; Na_2CO_3: Sodium carbonate; $NaHCO_3$: Sodium bicarbonate NO_X: Oxides of nitrogen; SO_2: Sulfur dioxide; TEA: Triethanolamine; TSP: Total Suspended PM; UV: Ultraviolet; XAD-4: (hydrophobic, non-polar polyaromatic resin.

[c]NIOSH 5040_TOT: National Institute of Occupational Safety and Health Method 5040 Thermal Optical Transmittance Protocol. [121, 122, 123, 124, 125] OC: 250, 500, 650, 850 °C for OC1, OC2, OC3, and OC4 fractions, respectively, for 60, 60, 60, 90 sec respectively, in 100% He atmosphere. EC: 650, 750, 850, 940 °C for EC1, EC2, EC3, and EC4 fractions, respectively, 30, 30, 30, >120 sec respectively, in 98% He and 2% O_2 atmosphere. OPT: Pyrolysis correction by transmittance. IMPROVE_TOR: Interagency Monitoring of Protected Visual Environments Thermal Optical Reflectance Protocol [126] OC fractions: 120, 250, 450, 550 °C for OC1, OC2, OC3, and OC4 fractions, respectively, until a well defined peak has evolved at each step, with a time limit of min 80 sec and max of 580 sec, in 100% He atmosphere. EC fractions: 550, 700, 800 °C for EC1, EC2, and EC3 fractions, respectively, until a well defined peak has evolved at each step, with a time limit of min 80 sec and max of 580 sec, in 2% O2 and 98% He atmosphere. OPR: Pyrolysis correction for pyrolyzed organic carbon (OP) by reflectance. OC = OC1+OC2+OC3+OC4+OP EC = EC1+EC2+EC3-OP TC = OC+EC. IMPROVE_A TOR: 127 Note that as of May, 2007, the U.S. EPA is switching samples from the Speciation Trends Network thermal optical transmittance protocol to the IMPROVE_A protocol. OC: 140, 280, 480, 580 °C for OC1, OC2, OC3, and OC4, fractions, respectively, until a well defined peak has evolved at each step, with a time limit of 80 sec and max of 580 sec, in 100% He atmosphere EC: 580, 740, 840 °C for EC1, EC2, and EC3 fractions, respectively, until a well defined peak has evolved at each step, with a time limit of min 80 sec and max of 580 sec, in 2% O_2 and 98% He atmosphere. OPR: Pyrolysis correction for pyrolyzed organic carbon (OP) by reflectance. OPT: Pyrolysis correction by transmittance. TPV: Temperature Programmed Volatilization [17, 81, 128] For CIF Filters: Heated from 50 °C to 300 °C at a ramp rate of 10 °C/min in N2. For Quartz filters: Heated from 50 °C to 800 °C at a ramp rate of 28 °C/min in 70% N2 and 30% O2; EC estimated from high temperature peak (>450 °C) on thermogram obtained from quartz-fiber filter analysis; No pyrolysis correction. STN_TOT: Speciation Trends Network Thermal Optical Transmittance Protocol.129 OC: 310, 480, 615, 920 °C for 60, 60, 60, 90 sec respectively, in 100% He atmosphere. EC: 600, 675, 750, 825, 920 °C for 45, 45, 45, 45, 120 sec respectively, in 98% He and 2% O_2 atmosphere. ACE Asia TOT: Aerosol Characterization Experiments in Asia Thermal Optical Transmittance Protocol. 130 OC: 340, 500, 615, 870 °C for 60, 60, 60, 90 sec respectively, in 100% He atmosphere. EC: 550, 625, 700, 775, 850, 900 °C for45, 45, 45, 45, 45, 120 sec respectively, in 98% He, 2% O_2. Pyrolysis correction by transmittance.

[d]Custom TOT: XAD-4 impregnated quartz, analyzed in He-only atmosphere with a maximum temperature 176 °C; EC is not measured.

[e]Custom TOR to suit Al substrate; details not reported.

[f]37 mm filter

[1]Chow (1995, 077012); [2]Watson and Chow (2001, 157123); [3] Watson et al. (1983, 045084); [4]Fehsenfeld et al. (2004, 157360); [5]Solomon et al. (2001, 157193); [6]Watson et al. (2005, 157124); [7]Mikel (2001, 156762); [8]Watson et al. (1999, 020949); [9]Solomon and Sioutas (2006, 156995); [10]Graney et al. (2004, 053756); [11]Tanaka et al. (1998, 157041); [12]Pancras et al. (2005, 098120); [13]John et al. (1988, 045903); [14]Hering and Cass (1999, 084958); [15]Fitz et al. (1989, 077387); [16]Hering et al. (1988, 036012); [17]Solomon et al. (2003, 156994); [18]Cabada et al. (2004, 148859); [19]Fine et al. (2003, 155775); [20]Hogrefe et al. (2004, 099003); [21]Drewnick et al. (2003, 099160); [22]Watson et al. (2005, 157125); [23]Ho et al. (2006, 156552); [24]Decesari et al. (2005, 144536); [25] Mayol-Bracero et al. (2002, 045010); [26]Yang et al. (2003, 156167); [27]Turšic et al. (2006, 157063); [28]Mader et al.(2004, 156724); [29]Xiao and Liu (2004, 056801); [30]Kiss et al. (2002, 156646); [31]Cornell and Jickells (1999, 156367); [32] Zheng et al. (2002, 026100); [33]Fraser et al. (2002, 140741); [34] Fraser et al. (2003, 042231) [35]Schauer er al. (2000, 012225); [36]Fine et al. (2004, 141283); [37]Yue et al. (2004, 157169); [38]Rinehart et al. (2006, 115184); [39]Wan and Yu (2006, 157104); [40]Poore (2000, 012839); [41]Fraser et al. (2003, 040266); [42]Engling et al. (2006, 156422); [43]Yu et al. (2005, 157167); [44]Tran et al. (2000, 013025); [45]Yao et al. (2004, 102213); [46]Li and Yu (2005, 156692); [47]Henning et al. (2003, 156539); [48]Zhang and Anastasio (2003, 157182); [49]Emmenegger et al. (2007, 156418); [50] Watson et al. (1989, 046318); [51]Greaves et al. (1985, 156494); [52]Waterman et al. (2000, 157116); [53]Waterman et al. (2001, 157117); [54]Falkovich and Rudich (2001, 156427); [55]Chow et al. (2007, 157209); [56]Miguel et al. (2004, 123260); [57]Crimmins and Baker (2006, 097008); [58]Ho and Yu (2004, 156551); [59]Jeon et al. (2001, 016636); [60]Mazzoleni et al. (2007, 098038); [61]Poore (2002, 051444); [62]Butler et al. (2003, 156313); [63]Chow et al. (2006, 146622); [64]Russell et al. (2004, 082453); [65]Grover et al. (2006, 138080); [66]Grover et al. (2005, 090044); [67]Schwab et al. (2006, 098449); [68]Hauck et al. (2004, 156525); [69]Jaques et al. (2004, 155878); [70]Rupprecht and Patashnick (2003, 157207); [71]Pang et al (2002, 030353); [72]Eatough et al. (2001, 010303); [73]Lee et al. (2005, 128139); [74]Lee et al. (2005, 156680); [75]Babich et al. (2000, 156239); [76]Lee et al. (2005, 155925); [77]Lee et al. (2005, 128139); [78]Anderson and Ogren (1998, 156213); [79]Chung et al. (2001, 156357); [80]Kidwell and Ondov (2004, 155898); [81]Lithgow et al. (2004, 126616); [82]Weber et al. (2003, 157129); [83]Harrison et al. (2004, 136787); [84]Rattigan et al. (2006, 115897); [85]Wittig et al. (2004, 103413); [86]Vaughn et al. (2005, 157089); [87]Chow et al. (2005, 099030); [88]Weber et al (2001, 024640) ; [89]Schwab et al. (2006, 098785); [90]Lim et al. (2003, 037037); [91]Watson and Chow (2002, 037873); [92]Venkatachari et al. (2006, 105918); [93]Bae et al. (2004, 156243); [94]Arhami et al. (2006, 156224); [95]Park et al. (2005, 156843); [96]Bae et al. (2004, 098680); [97]Chow et al. (2006, 156350); [98]Arnott et al. (2005, 156227); [99]Bond et al. (1999, 156281); [100]Virkkula et al. (2005, 157097); [101]Petzold et al. (2002, 156863); [102]Park et al. (2006, 098104); [103]Arnott et al. (1999, 020650); [104]Peters et al. (2001, 016925); [105]Pitchford et al. (1997, 156872); [106]Rees et al. (2004, 097164); [107]Watson et al. (2000, 010354); [108]Lee et al. (2005, 156680); [109]Hering et al. (2004, 155837); [110]Watson et al. (1998, 198805); [111]Chakrabarti et al. (2004, 157426); [112]Mathai et al. (1990, 156741); [113]Kidwell and Ondov (2001, 017092); [114]Stanier et al. (2004, 095955); [115]Khlystov et al. (2005, 156635); [116]Takahama et al. (2004, 157038); [117]Chow et al. (2005, 156348); [118]Zhang et al. (2002, 157181); [119]Subramanian et al. (2004, 081203); [120]Chow et al. (2006, 155207); [121]Birch and Cary (1996, 026004); [122]Birch (1998, 024953); [123]Birch and Cary (1996, 002352); [124]NIOSH (1996, 156810); [125]NIOSH (1999, 156811); [126]Chow et al. (1993, 077459); [127]Chow et al. (2007, 156354); [128]Ellis and Novakov (1982, 156416); [129]Peterson and Richards (2002, 156861); [130]Schauer et al. (2003, 037014); [131]Middlebrook et al. (2003, 042932); [132]Wenzel et al. (2003, 157139); [133]Jimenez et al. (2003, 156611); [134]Phares et al. (2003, 156866); [135]Qin and Prather (2006, 156895); [136]Zhang et al. (2005, 157185); [137]Bein et al. (2005, 156265); [138]Drewnick et al. (2004, 155754); [139]Drewnick et al. (2004, 155755); [140]Lake et al. (2003, 156669); [141]Lake et al. (2004, 088411)

Source: Chow et al. (2008, 156355)

Table A-16. Summary of particle mass spectrometer measurement comparisons.

ATLANTA SUPERSITE, GA: 08/03/99 to 09/01/99
Four km NW of downtown, within 200 m of a bus maintenance yard and several warehouse facilities, representative of a mixed commercial-residential neighborhood.

Spectrometer	Inlet Characteristics (Flow Rate [L/Min]; Size Inlet; Dryer Aerodynamic Diameter, µm; Particle Sizing Method)	Volatilization/ Ionization Method[a]	Hit Rates[b]	Mass Spectrometer[c]	Particle Analysis/ Classification	Other
PALMS	N/A $PM_{2.5}$ cyclone Nafion (17 days) / None (4 days) 0.35-2.5 Light scattering	LDI, ArF 193 nm $2x10^9$ to $5x10^9$ W/cm^2	14 to 100%, overall 87%	Single TOF reflectron; Ion polarity needs to be pre-selected	Peak ID/regression tree analysis	Pure sulfuric acid (H_2SO_4), $(NH_4)_2SO_4$, and water (H_2O) have relatively high ionization thresholds (i.e. difficult to ionize). Fraction of molecules ionized in the particles is on the order of 10^{-5} to 10^{-6}.
ATOFMS	1 None None 0.2-2.5 Aerosol TOF	LDI, Nd: YAG 266 nm laser ~ $1x10^8$ W/cm^2	25-30%, occasionally as low as 5%	Dual TOF reflectron; Detects both positive and negative ions	Aerosol TOF	
RSMS-II	N/A None Nafion 0.015-1.3 Aerodynamic focusing; Need to pre-select sizes to be analyzed	LDI, Arf laser, 193 nm $1x10^8$ to $2x10^8$ W/cm^2	N/A	Single linear TOF; Ion polarity needs to be pre-selected	Peak ID/artificial neural network	
AMS	N/A $PM_{2.5}$ cyclone None 0.05-2.5 Aerosol TOF	T~550°C/ EI	N/A	Quadrupole; Mass weighted size distributions on pre-selected positive ions only.	ID using standard EI ionization databases	Does not detect/ analyze highly refractory materials such as metals, sea salt, soot etc. Fraction of molecules ionized in the particles is on the order of 10^{-6} to 10^{-7}

Middlebrook et al. (2003, 042932)[131]; Wenzel et al. (2003, 157139)[132]; Jimenez et al. (2003, 156611)[133]

Particle sizing is approximate in PALMS, while ATOFMS, RSMS-II and AMS provide relatively accurate particle sizing.

Particle transmission in AMS is ~100% (i.e., it uses all particles in the sampled air) between 60 and 600 nm, while that for PALMS, ATOFMS and RSMS-II range from 10-6 for submicron particles to 2% for supermicron (>0.8 µm) particles.

AMS has fewer matrix effects (due to separate volatilization and ionization steps) compared to single-step LDI instruments.

While four major particle classifications (organic/SO_4^{2-}, sodium/potassium sulfate, soot/hydrocarbon and mineral) were observed by all three laser instruments, they differed in the classification frequencies. Differences in frequencies that are detected and grouped are related to the differences in the laser ionization conditions (e.g., wavelength), particle transmission, sizing method and the way the spectra were classified.

Shorter ionization wavelengths are able to produce ions more easily than longer ones.

Low hit rates in ATOFMS corresponded to periods of high SO_4^{2-} concentrations. Low hit rates in PALMS were related to a variety of factors including high SO_4^{2-} concentrations, differing laser fluence and laser position relative to particle beam. Use of a dryer in PALMS enhanced ionization of particles that were difficult to ionize at high ambient RH.

The RSMS-II and ATOFMS were less sensitive to SO_4^{2-} and hence may have fewer organic/SO_4^{2-} particles (i.e., underestimate SO_4^{2-} , pure sulfuric acid etc.).

The PALMS, ATOFMS and RSMS (laser based instruments) are qualitative, while the AMS can be quantitative. The relative ratio of ion intensities from the laser instruments, however, may be indicative of relative concentrations, thus giving semi-quantitative information.

Comparison of the ratio of NO_3 to SO_4 peaks with the results from the semi continuous instruments showed better correlation with the AMS (R^2 = 0.93) than PALMS (R^2 = 0.65 for non-dry particles to 0.70 for dry particles). While reasonable correlations between the PALMS and the composite semi-continuous data indicate the possibility for calibration of laser-based data for certain ions, the calibration factors may vary depending on the particle matrix, water content and laser ionization parameters, and averaging the spectra according to these factors may minimize these effects.

Comparison of AMS SO_4 with PILS SO_4 showed good correlation (R^2 = 0.79), and the data uniformly scattered around a 1:1 line. NO_3 comparison was poor (R^2 = 0.49) because of the low signal to noise ratio at low concentrations

The continuum between particle classifications indicates that the particles were not adequately represented by non-overlapping classifications.

ATLANTA SUPERSITE, GA: 08/03/99 to 09/01/99
Four km NW of downtown, within 200 m of a bus maintenance yard and several warehouse facilities, representative of a mixed commercial-residential neighborhood.

HOUSTON SUPERSITE, TX; 08/23/00 to 09/18/00
Houston Regional Monitoring Site was located < 1.0 km north of the Houston ship channel, where chemical and other industries are present. The site was located between a railway to the south and a chemical plant to the north. Major freeways were located just to the north and east of the sampling site.

Spectrometer	Inlet Characteristics (Flow Rate [L/Min]; Size Inlet; Dryer Aerodynamic Diameter, µm; Particle Sizing Method)	Volatilization/ Ionization Method[a]	Hit Rates[b]	Mass Spectrometer[c]	Particle Analysis/ Classification	Other
RSMS-II	N/A None Nafion 0.035-1.14 Aerodynamic focusing; Need to pre-select sizes to be analyzed	LDI, ArF laser, 193 nm	N/A	Single linear TOF; Ion polarity needs to be pre-selected	Peak ID/artificial neural network	At each size point, aerosol was sampled in each cycle for either 10 min or until mass spectra for 30 particles per major class were collected, whichever came first.

Phares et al. (2003, 156866)[134]

27,000 spectra were classified using a neural network into 15 particle types

Fifteen particle type mass spectra were presented along with their size distribution, avg time of day occurrence, and wind direction dependence

Major classes were a K^+ dominant, Si/Silicon Oxide, Carbon, Sea Salt, Fe, Zn, Amines, Lime, Vanadium, Organic Mineral, Pb and K, Al, and a Pb salt particle type.

FRESNO SUPERSITE, CA: 11/30/00 to 2/4/01
Urban location in a residential neighborhood.

Spectrometer	Inlet Characteristics (Flow Rate [L/Min]; Size Inlet; Dryer Aerodynamic Diameter, µm; Particle Sizing Method)	Volatilization/ Ionization Method[a]	Hit Rates[b]	Mass Spectrometer[c]	Particle Analysis/ Classification	Other
ATOFMS	1 None None 0.3-2.5 Aerodynamic	LDI, ND: YAG 266 nm	N/A	Dual reflectron TOF	Peak ID/artificial neural network	ATOFMS unscaled detected particles tracked β attenuation monitor $PM_{2.5}$ mass concentration

Qin and Prather (2008, 156985)[135]

Biomass burning particles reached a maximum at night and a minimum during the day. These particles were less than 1 µm in diameter and accounted for more than 60% of the particles detected at night.

Another particle class characterized by high mass carbon fragments had a similar diurnal pattern. These particles were larger than 1 µm and were interpreted as biomass particles that have undergone gas to particle conversion of semi-volatile species followed by dissolution in a water droplet.

PITTSBURGH SUPERSITE, PA; 09/07/02 TO 09/22/02 FOR AMS; 09/20/01 to 09/26/02 for RSMS-III
6 km east of downtown in a park on the top of a hill

Spectrometer	Inlet Characteristics (Flow Rate [L/Min]; Size Inlet; Dryer Aerodynamic Diameter, µm; Particle Sizing Method)	Volatilization/ Ionization Method[a]	Hit Rates[b]	Mass Spectrometer[c]
AMS	1.4 cc/s $PM_{2.5}$ cyclone None 0.05-1.0 Aerosol TOF	T - 600°C/ EI	Quadrupole; Mass weighted size distributions on pre-selected positive ions only.	Particle size-cut of ~1 µm
RSMS-III	N/A None Nafion 0.03-1.1 Aerodynamic focusing; Need to pre-select sizes to be analyzed.	LDI, ArF laser, 193 nm	Dual TOF feflectron; Detects both positive and negative ions	At each size point, aerosol was sampled in each cycle for either 10 min or until mass spectra for 30 particles per major class were collected, whichever came first

ATLANTA SUPERSITE, GA: 08/03/99 to 09/01/99
Four km NW of downtown, within 200 m of a bus maintenance yard and several warehouse facilities, representative of a mixed commercial-residential neighborhood.

Zhang et al. (2005, 157185)[136]; Bein et al. (2005, 156265)[137]

The AMS observed 75% of the SO_4^{2-} measured by R&P-8400S (R^2 = 0.69).

Collection efficiency (CE) of 0.5 used for SO_4^{2-}, NO_3 and NH_4^+ and 0.7 for organics to correct mass concentrations for incomplete detection. Use of a constant CE irrespective of size and shape may overestimate accumulation mode (mostly, oxygenated) organics (true CE ~ 0.5) and underestimate smaller mode (primary) organics (true CE ~ 1.0).

Comparison of AMS organics (organic matter, OM) with OC measured by a continuous Sunset OCEC instrument showed good correlation (R^2 = 0.88) with a slope of 1.69. A 24-h avg comparison, showed a slope of 1.45. These values are in the typical range of 1.2 to 2.0 for OM/OC ratios.

AMS could be used along with the SMPS to estimate particle density. The AMS did not always agree with SMPS, probably due to non-spherical particles (irregular) such as soot from fresh traffic emissions, whose mass may be overestimated by the SMPS.

Comparison of AMS mass with the MOUDI, showed differences for aerodynamic diameters >600 nm, probably due to the AMS transmission being less than unity for particles larger than 600 nm.

For RSMS-III, 54% of the detected particles were assigned to one class (carbonaceous ammonium nitrate). This class was preferentially detected during the colder months and was detected from many different wind directions.

The next largest RSMS-III class was EC/OC/K class at 11%, and is believed to be from biomass burning.

An unidentified organic carbon RSMS-III class (3.3% of all detected particles) was seen to be highly dependent on wind direction dependence and was primarily detected during August and September of 2002. These particles likely originated from a landfill.

NEW YORK SUPERSITE; 06/30/01 to 08/05/01 (urban); 07/09/02 to 08/07/02: (rural)
Urban Site: Queens College, Queens, New York, located at the edge of a parking lot and within 1 km from expressways and highways in New York City Metropolitan area.

Rural Site: Whiteface Mountain, New York, located in a cleared area surrounded by mix of deciduous and evergreen trees, ~2 km away from the closest highway with no major cities within 20 km.

Spectrometer	Inlet Characteristics (Flow Rate [L/Min]; Size Inlet; Dryer Aerodynamic Diameter, µm; Particle Sizing Method)	Volatilization/ Ionization Method[a]	Hit Rates[b]	Mass Spectrometer[c]
AMS	0.1 $PM_{2.5}$ cyclone None 0.02-2.5 Aerosol TOF	T – 700°C/ EI	Quadrupole; Mass weighted size distributions on pre-selected positive ions only.	Data are 10-min averages

Drewnick et al. (2004, 155754)[138]; Drewnick et al. (2004, 155755)[139]; Hogrefe et al. (2004, 099003)[20]

Transport losses were 1.3% on avg.

Inlet losses (at the inlet of AMS) were 1.9%, on avg, ranging from 11% for a 20 nm particle to 9% for a 2.5 µm particle, with a minimum of 0.7% for a 350 nm particle

Overall measurement uncertainty of particle diameter was ~11%.

The AMS was reliable with proper calibration, care, and maintenance. Valid 10 min averages were obtained for all components more than 93% of the time.

The mass to charge ratios (m/z) of fragments from different components may overlap (e.g., NH+, a fragment of NH_4^+ and CH_3^+, a fragment of organic species, have m/z = 15) resulting in an interference (called as isobaric interference) Interfering signals were not used to calculate concentrations. This loss in concentration was adjusted by applying a correction factor determined from laboratory studies.

Typical interferences were from fragments of organic species, water and oxygen.

With adjustments, the SO_4^{2-}, NO_3^- and ammonium concentrations measured by the AMS were consistently lower than that measured by other co-located instruments, probably due to incomplete focusing of the $(NH_4)_2SO_4$ and NH_4NO_3 particles by the aerodynamic lens.

At the urban site, AMS NO_3 was within 10% of the filter NO_3 concentration. At the rural site, it had a slope of 0.51 and R^2 of 0.46.

AMS SO_4 showed good agreement with R&P-8400S at both the rural and urban locations (R^2 = 0.89 to 0.92, slope = 0.99, n = 407 to 695) and was within 70 to 85% of filter SO_4^{2-} concentration.

Comparison of the total non-refractory mass measured by the AMS with the $PM_{2.5}$ TEOM mass (operated at 50°C or with dryer) at the urban location, showed good correlation (R^2 = 0.91) with near zero intercept (0.22 µg/m^3). On avg, the AMS observed 64% of the mass measured by the TEOM.

The unexplained mass (36%) was attributed to transport losses, transmission and optical losses, and refractory components in the aerosol sample (e.g., metals, EC). The mass closure was within the estimated uncertainty of the AMS mass measurements (5-10%).

ATLANTA SUPERSITE, GA: 08/03/99 to 09/01/99
Four km NW of downtown, within 200 m of a bus maintenance yard and several warehouse facilities, representative of a mixed commercial-residential neighborhood.

BALTIMORE SUPERSITE, MD; 04/01/02 to 11/30/02
East of downtown in an urban residential area. Within 91 m of a bus maintenance facility.

Spectrometer	Inlet Characteristics (Flow Rate [L/Min]; Size Inlet; Dryer Aerodynamic Diameter, µm Particle Sizing Method)	Volatilization/ Ionization Method[a]	Hit Rates[b]	Mass Spectrometer[c]
RSMS-III	0.2-18, based on particle size chosen None Nafion 0.045-1.3 Aerodynamic focusing; Need to pre-select sizes to be analyzed	LDI, ArF laser, 193 nm	TOF with dual ion polarity	At each size set point, aerosol was sampled in each cycle for either 10 min or until mass spectra from 30 particles were collected, whichever came first.

Lake et al. (2003, 156669)[140], Lake et al. (2004, 088411)[141]

Utilizing both positive and negative ion detection enables detection of more species. However, detection efficiencies of negative ions decreased for smaller particles.

SO_4^+ concentration (number or mass) was not accurately quantified.

RSMS-III was most efficient in 0.050 to 0.77 µm range.

Particle compositions could be related to specific source categaories.

aEI: Electon Impact; LDI: Laser Desorption / Ionization
bHit rate refers to the number of particles with a mass spectrum as a fraction of the number of particles detected. It does not apply to RSMS and AMS because there is no separate detection
cTOF: Time fo Flight

[1]Chow (1995, 077012); [2]Watson and Chow (2001, 157123); [3] Watson et al. (1983, 045084); [4]Fehsenfeld et al. (2004, 157360); [5]Solomon et al. (2001, 157193); [6]Watson et al. (2005, 157124); [7]Mikel (2001, 156762); [8]Watson et al. (1999, 020949); [9]Solomon and Sioutas (2006, 156995); [10]Graney et al. (2004, 053756); [11]Tanaka et al. (1998, 157041); [12]Pancras et al. (2005, 098120); [13]John et al. (1988, 045903); [14]Hering and Cass (1999, 084958); [15]Fitz et al. (1989, 077387); [16]Hering et al. (1988, 036012); [17]Solomon et al. (2003, 156994); [18]Cabada et al. (2004, 148859); [19]Fine et al. (2003, 155775); [20]Hogrefe et al. (2004, 099003); [21]Drewnick et al. (2003, 099160); [22]Watson et al. (2005, 157125); [23]Ho et al. (2006, 156552); [24]Decesari et al. (2005, 144536); [25] Mayol-Bracero et al. (2002, 045010); [26]Yang et al. (2003, 156167); [27]Turšic et al. (2006, 157063); [28]Mader et al.(2004, 156724); [29]Xiao and Liu (2004, 056801); [30]Kiss et al. (2002, 156646); [31]Cornell and Jickells (1999, 156367); [32] Zheng et al. (2002, 026100); [33]Fraser et al. (2002, 140741); [34] Fraser et al. (2003, 042231) [35]Schauer er al. (2000, 012225); [36]Fine et al. (2004, 141283); [37]Yue et al. (2004, 157169); [38]Rinehart et al. (2006, 115184); [39]Wan and Yu (2006, 157104); [40]Poore (2000, 012839); [41]Fraser et al. (2003, 040266); [42]Engling et al. (2006, 156422); [43]Yu et al. (2005, 157167); [44]Tran et al. (2000, 013025); [45]Yao et al. (2004, 102213); [46]Li and Yu (2005, 156692); [47]Henning et al. (2003, 156539); [48]Zhang and Anastasio (2003, 157182); [49]Emmenegger et al. (2007, 156418); [50] Watson et al. (1989, 046318); [51]Greaves et al. (1985, 156494); [52]Waterman et al. (2000, 157116); [53]Waterman et al. (2001, 157117); [54]Falkovich and Rudich (2001, 156427); [55]Chow et al. (2007, 157209); [56]Miguel et al. (2004, 123260); [57]Crimmins and Baker (2006, 097008); [58]Ho and Yu (2004, 156551); [59]Jeon et al. (2001, 016636); [60]Mazzoleni et al. (2007, 098038); [61]Poore (2002, 051444); [62]Butler et al. (2003, 156313); [63]Chow et al. (2006, 146622); [64]Russell et al. (2004, 082453); [65]Grover et al. (2006, 138080); [66]Grover et al. (2005, 090044); [67]Schwab et al. (2006, 098449); [68]Hauck et al. (2004, 156525); [69]Jaques et al. (2004, 155878); [70]Rupprecht and Patashnick (2003, 157207); [71]Pang et al (2002, 030353); [72]Eatough et al. (2001, 010303); [73]Lee et al. (2005, 128139); [74]Lee et al. (2005, 156680); [75]Babich et al. (2000, 156239); [76]Lee et al. (2005, 155925); [77]Lee et al. (2005, 128139); [78]Anderson and Ogren (1998, 156213); [79]Chung et al. (2001, 156357); [80]Kidwell and Ondov (2004, 155898); [81]Lithgow et al. (2004, 126616); [82]Weber et al. (2003, 157129); [83]Harrison et al. (2004, 136787); [84]Rattigan et al. (2006, 115897); [85]Wittig et al. (2004, 103413); [86]Vaughn et al. (2005, 157089); [87]Chow et al. (2005, 099030); [88]Weber et al (2001, 024640) ; [89]Schwab et al. (2006, 098785); [90]Lim et al. (2003, 037037); [91]Watson and Chow (2002, 037873); [92]Venkatachari et al. (2006, 105918); [93]Bae et al. (2004, 156243); [94]Arhami et al. (2006, 156224); [95]Park et al. (2005, 156843); [96]Bae et al. (2004, 098680); [97]Chow et al. (2006, 156350); [98]Arnott et al. (2005, 156227); [99]Bond et al. (1999, 156281); [100]Virkkula et al. (2005, 157097); [101]Petzold et al. (2002, 156863); [102]Park et al. (2006, 098104); [103]Arnott et al. (1999, 020650); [104]Peters et al. (2001, 016925); [105]Pitchford et al. (1997, 156872); [106]Rees et al. (2004, 097164); [107]Watson et al. (2000, 010354); [108]Lee et al. (2005, 156680); [109]Hering et al. (2004, 155837); [110]Watson et al. (1998, 198805); [111]Chakrabarti et al. (2004, 157426); [112]Mathai et al. (1990, 156741); [113]Kidwell and Ondov (2001, 017092); [114]Stanier et al. (2004, 095955); [115]Khlystov et al. (2005, 156635); [116]Takahama et al. (2004, 157038); [117]Chow et al. (2005, 156348); [118]Zhang et al. (2002, 157181); [119]Subramanian et al. (2004, 081203); [120]Chow et al. (2006, 155207); [121]Birch and Cary (1996, 026004); [122]Birch (1998, 024953); [123]Birch and Cary (1996, 002352); [124]NIOSH (1996, 156810); [125]NIOSH (1999, 156811); [126]Chow et al. (1993, 077459); [127]Chow et al. (2007, 156354); [128]Ellis and Novakov (1982, 156416); [129]Peterson and Richards (2002, 156861); [130]Schauer et al. (2003, 037014); [13]1Middlebrook et al. (2003, 042932); [132]Wenzel et al. (2003, 157139); [133]Jimenez et al. (2003, 156611); [134]Phares et al. (2003, 156866); [135]Qin and Prather (2006, 156895); [136]Zhang et al. (2005, 157185); [137]Bein et al. (2005, 156265); [138]Drewnick et al. (2004, 155754); [139]Drewnick et al. (2004, 155755); [140]Lake et al. (2003, 156669); [141]Lake et al. (2004, 088411)

Source: Chow et al. (2008, 156355)

Table A-17. Summary of key parameters for TD-GC/MS and pyrolysis-GC/MS.

Reference	Sample Type	TD Unit	Analytical Instrument	Total Analysis Time
TD-GC/MS WITH RESISTIVELY HEATED EXTERNAL OVEN				
Greaves et al. (1985, 156494; 1987, 156495); Veltkamp et al. (1996, 081594)	Aerosol sample and NIST SRM 1649	A cylindrical aluminum block containing a heating cartridge connected to a thermocouple	HP 5892A GC/MS in EI mode	ambient sample: 55.5 min NIST standard: 45.5 min
Waterman et al. (2000, 157116)	NIST SRM 1640a	External oven mounted on the top of the GC/MS system	HP 5890 GC/Fisons MD 800 MS, scan range: 40-520 amu	90 min
Waterman et al. (2001, 157117)	NIST SRM 1649a	Same as above	HP 5890 GC/Fisons MD 800 MS, scan range: m/z 40 to 520	90 mins
Sidhu et al. (2001, 155202)	Aerosol collected on glass fiber filters from combustion of alternative diesel fuel.	A stainless steel tube (0.635 cm O.D.) laced in a GC oven	Two GCs and one MS. The first GC is used as the TE unit. The second GC separates the desorbent.	Ua
Hays et al. (2003, 156529; 2004, 156530); Dong et al. (2004, 156409)	Aerosol collected from residential wood combustion, residential oil furnace and fireplace appliance	A glass tube placed in an external oven (TDS2 Gerstel Inc.)	Aglient 6890 GC/5793 MSD, scan range: 50 to 500 amu	99 min
CURIE POINT TD-GC/MS				
Jeon et al. (2001, 016636)	High-volume PM_{10} ambient samples collected along the U.S./Mexico border	Curie point pyrolyzer	HP 5890 GC/5792 MSD	Ua
Neususs et al. (2000, 156804)	Ambient aerosol collected during the 2nd Aerosol Characterization Experiment	Curie point pyrolyzer	Fisons Trio 1000	35 min
IN-INJECTION PORT TED-GC/MS				
Helmig et al. (1990, 156536)	Aerosol samples collected on glass-fiber filters at a forest site	GC injector port, with modified septum cap	Carlo Erba Mega 5160 GC/VG 250/70 SE MS, scan range: 45-400 amu	47 min
Hall et al. (1999, 156512)	NIST SRM 1649	Micro-scale sealed vessel placed inside the injector port	HP 5890 GC/Fisons MD 800 MS, scan range: 40-500 amu	82.5 min
Blanchard and Hopper (1997) (1997, 156277); Blanchard et al. (2002, 047598)	Aerosol samples collected on quartz-and-glass filters in Ontario	A GC injection port was added with three minor components, including a small T-connector, 3-way valve, and needle valve	HP 5892A GC/5972A MS in EI mode	71 min
Falkovich and Rudich (2001, 156427) ; Falkovich et al. (2004, 156428); Graham et al. (2004, 156490)	NIST SRM 1649a; urban aerosols collected with an 8-stage impactor in Tel-Aviv, Israel	Direct Sample Introduction (DSI) device (ChromatoProbe, Varian Co.)	Varian Saturn 3400 GC/MS	64.2 min
Ho and Yu (2004, 156551); Yang et al. (2005, 102388)	Ambient aerosol samples collected on Teflon-impregnated glass-fiber filters in Hong Kong and on quartz filters at Nanjing, China	Conventional GC injection port. No modification of GC injector and liner	HP 5890 GC/5791 MSD, scan range: 50-650 amu	41.5 min
TD-GC X GC-MS				
Welthagen et al. (2003, 104056); Schnelle-Kreis et al. (2005, 112944)	Ambient samples in Augsburg, Germany	Injection port Optic III with autoloader (ATAS-GL, Veldhoven, NL)	Agilent 6890 GC/LECO Pegasus III TOF/MS with a LECO Pegasus 4D GCxGC modulator	175 min
Hamilton et al. (2004, 156516)	$PM_{2.5}$ aerosol collected in London	Conventional GC injection port	The same as above, scan range: 20-350 amu	93.7 min
Hamilton et al. (2005, 088173)	Secondary organic aerosol formed during the photo-oxidation of toluene with OH radicals	The same as above	The same above	102.5 min

Reference	Sample Type	TD Unit	Analytical Instrument	Total Analysis Time
IN SITU SEMI-CONTINUOUS AND CONTINUOUS TD SYSTEMS				
Williams et al. (2006, 156157)	In situ aerosol samples collected in Berkley, CA	Collection-TE cell with conventional GC injection port	Agilent 6890 GC/5793 MSD, scan range: 29-550 amu	59 min
PYROLYSIS TD-GC/MS				
Voorhees et al. (1991, 157101)	$PM_{0.6}$ and $PM_{>0.45}$ collected on quartz fiber in pristine regions of Colorado	A tube furnace directly interfaced to an GC/MS	Extrel Simulscan GC/MS, scan range: 35-450 amu	31.7 min
Subbalakshmi et al. (2000, 157023)	Ambient aerosol collected on glass-fiber filters in Jakarta, Indonesia	A pyroinjector	Agilent 6890 GC/5973 MS, scan range: 50-550 amu	63.5 min
Fabbri et al. (2002, 156426)	PM_{10} collected on glass-fiber filters in an industrial area of Italy	A pyrolyzer directly connected to the GC injector port through an interface heated at 250° C	Varian 3400 GC/Saturn II ion trap MS, scan range: 45-400 amu	57 min
Blazso et al. (2003, 156278)	$PM_{2.6}$ collected on quartz-fiber filters and size-segregated aerosol sampled collected on A1 foils in Brazil	A pyrolyzer	Agilent 6890 GC/5973 MS	30.3 min
Labban et al. (2006, 156665)	PM_{10} of re-suspended soil collected on quartz-fiber filters	Curie point pyrolyzer	HP 5890 GC/5972 MS	25.5. min

[a]Total analysis time could not be determined because of insufficient experimental details

Source: Chow et al. (2007, 157209)

A.1.2. Networks

Table A-18. Relevant Spatial Scales for PM_{10}, $PM_{2.5}$, and $PM_{10-2.5}$ Measurement

Spatial Scales	PM_{10}	$PM_{2.5}$	$PM_{10-2.5}$
Microscale (~5-100 m)	This scale would typify areas such as downtown street canyons, traffic corridors, and fence line stationary source monitoring locations where the general public could be exposed to maximum PM_{10} concentrations. Microscale PM sites should be located near inhabited buildings or locations where the general public can be expected to be exposed to the concentration measured. Emissions from stationary sources such as primary and secondary smelters, power plants, and other large industrial processes may, under certain plume conditions, likewise result in high ground level concentrations at the microscale. In the latter case, the microscale would represent an area impacted by the plume with dimensions extending up to approximately 100 m. Data collected at microscale sites provide information for evaluating and developing hot spot control measures.	This scale would typify areas such as downtown street canyons and traffic corridors where the general public would be exposed to maximum concentrations from mobile sources. In some circumstances, the microscale is appropriate for particulate sites; community-oriented SLAMS sites measured at the microscale level should, however, be limited to urban sites that are representative of long-term human exposure and of many such microenvironments in the area. In general, microscale PM sites should be located near inhabited buildings or locations where the general public can be expected to be exposed to the concentration measured. Emissions from stationary sources such as primary and secondary smelters, power plants, and other large industrial processes may, under certain plume conditions, likewise result in high ground level concentrations at the microscale. In the latter case, the microscale would represent an area impacted by the plume with dimensions extending up to approximately 100 m. Data collected at microscale sites provide information for evaluating and developing hot spot control measures. Unless these sites are indicative of population-oriented monitoring, they may be more appropriately classified as SPM.	This scale would typify relatively small areas immediately adjacent to: industrial sources; locations experiencing ongoing construction, redevelopment, and soil disturbance; and heavily traveled roadways. Data collected at microscale stations would characterize exposure over areas of limited spatial extent and population exposure, and may provide information useful for evaluating and developing source-oriented control measures.
Middle Scale (~100-500 m)	Much of the short-term public exposure to coarse fraction particles (PM_{10}) is on this scale and on the neighborhood scale. People moving through downtown areas or living near major roadways or stationary sources, may encounter particulate pollution that would be adequately characterized by measurements of this spatial scale. Middle scale PM_{10} measurements can be appropriate for the evaluation of possible short-term exposure public health effects. In many situations, monitoring sites that are representative of micro-scale or middle-scale impacts are not unique and are representative of many similar situations. This can occur along traffic corridors or other locations in a residential district. In this case, one location is representative of a neighborhood of small scale sites and is appropriate for evaluation of long-term or chronic effects. This scale also includes the characteristic concentrations for other areas with dimensions of a few hundred meters such as the parking lot and feeder streets associated with shopping centers, stadia, and office buildings. In the case of PM_{10}, unpaved or seldomly swept parking lots associated with these sources could be an important source in addition to the vehicular emissions themselves.	People moving through downtown areas, or living near major roadways, encounter particle concentrations that would be adequately characterized by this spatial scale. Thus, measurements of this type would be appropriate for the evaluation of possible short-term exposure public health effects of PM pollution. In many situations, monitoring sites that are representative of microscale or middle-scale impacts are not unique and are representative of many similar situations. This can occur along traffic corridors or other locations in a residential district. In this case, one location is representative of a number of small scale sites and is appropriate for evaluation of long-term or chronic effects. This scale also includes the characteristic concentrations for other areas with dimensions of a few hundred meters such as the parking lot and feeder streets associated with shopping centers, stadia, and office buildings.	People living or working near major roadways or industrial districts encounter particle concentrations that would be adequately characterized by this spatial scale. Thus, measurements of this type would be appropriate for the evaluation of public health effects of $PM_{10-2.5}$ exposure. Monitors located in populated areas that are nearly adjacent to large industrial point sources of $PM_{10-2.5}$ provide suitable locations for assessing maximum population exposure levels and identifying areas of potentially poor air quality. Similarly, monitors located in populated areas that border dense networks of heavily-traveled traffic are appropriate for assessing the impacts of resuspended road dust. This scale also includes the characteristic concentrations for other areas with dimensions of a few hundred meters such as school grounds and parks that are nearly adjacent to major roadways and industrial point sources, locations exhibiting mixed residential and commercial development, and downtown areas featuring office buildings, shopping centers, and stadiums.

Spatial Scales	PM_{10}	$PM_{2.5}$	$PM_{10-2.5}$
Neighborhood Scale (~500 m-4 km)	Measurements in this category represent conditions throughout some reasonably homogeneous urban sub-region with dimensions of a few kilometers and of generally more regular shape than the middle scale. Homogeneity refers to the PM concentrations, as well as the land use and land surface characteristics. In some cases, a location carefully chosen to provide neighborhood scale data would represent not only the immediate neighborhood but also neighborhoods of the same type in other parts of the city. Neighborhood scale PM_{10} sites provide information about trends and compliance with standards because they often represent conditions in areas where people commonly live and work for extended periods. Neighborhood scale data could provide valuable information for developing, testing, and revising models that describe the larger-scale concentration patterns, especially those models relying on spatially smoothed emission fields for inputs. The neighborhood scale measurements could also be used for neighborhood comparisons within or between cities.	Measurements in this category would represent conditions throughout some reasonably homogeneous urban sub- region with dimensions of a few kilometers and of generally more regular shape than the middle scale. Homogeneity refers to the PM concentrations, as well as the land use and land surface characteristics. Much of the $PM_{2.5}$ exposures are expected to be associated with this scale of measurement. In some cases, a location carefully chosen to provide neighborhood scale data would represent the immediate neighborhood as well as neighborhoods of the same type in other parts of the city. $PM_{2.5}$ sites of this kind provide good information about trends and compliance with standards because they often represent conditions in areas where people commonly live and work for periods comparable to those specified in the NAAQS. In general, most $PM_{2.5}$ monitoring in urban areas should have this scale.	Measurements in this category would represent conditions throughout some reasonably homogeneous urban sub-region with dimensions of a few kilometers and of generally more regular shape than the middle scale. Homogeneity refers to the PM concentrations, as well as the land use and land surface characteristics. This category includes suburban neighborhoods dominated by residences that are somewhat distant from major roadways and industrial districts but still impacted by urban sources, and areas of diverse land use where residences are interspersed with commercial and industrial neighborhoods. In some cases, a location carefully chosen to provide neighborhood scale data would represent the immediate neighborhood as well as neighborhoods of the same type in other parts of the city. The comparison of data from middle scale and neighborhood scale sites would provide valuable information for determining the variation of $PM_{10-2.5}$ levels across urban areas and assessing the spatial extent of elevated concentrations caused by major industrial point sources and heavily traveled roadways. Neighborhood scale sites would provide concentration data that are relevant to informing a large segment of the population of their exposure levels on a given day.
Urban Scale (~4-50 km)		This class of measurement would be used to characterize the PM concentration over an entire metropolitan or rural area ranging in size from 4 to 50 kilometers. Such measurements would be useful for assessing trends in area-wide air quality, and hence, the effectiveness of large scale air pollution control strategies. Community-oriented $PM_{2.5}$ sites may have this scale.	
Regional Scale (~50-100s km)		These measurements would characterize conditions over areas with dimensions of as much as hundreds of kilometers. As noted earlier, using representative conditions for an area implies some degree of homogeneity in that area. For this reason, regional scale measurements would be most applicable to sparsely populated areas. Data characteristics of this scale would provide information about larger scale processes of PM emissions, losses and transport. $PM_{2.5}$ transport contributes to elevated particulate concentrations and may affect multiple urban and State entities with large populations such as in the eastern United States. Development of effective pollution control strategies requires an understanding at regional geographical scales of the emission sources and atmospheric processes that are responsible for elevated $PM_{2.5}$ levels and may also be associated with elevated O_3 and regional haze.	

Table A-19. Major routine operating air monitoring networks[a]

Network	Lead Agency	Number of Sites	Initiated	Measurement Parameters	Location of Information and/or Data
STATE / LOCAL / FEDERAL NETWORKS					
NCore[b] – National Core Monitoring Network	EPA	75	2008	O_3, NO/NO_2/NO_Y, SO_2, CO, $PM_{2.5}$/$_{PM10-2.5}$, $PM_{2.5}$ speciation, NH_3, HNO_3, surface meteorology[c]	http://www.epa.gov/ttN/Amtic/monstratdoc.html
SLAMS1 – State and Local Ambient Monitoring Stations	EPA	~3000	1978	O_3, NO_X/NO_2, SO_2, $PM_{2.5}$/PM_{10}, CO, Pb	http://www.epa.gov/air/oaqps/qa/monprog.html
STN—$PM_{2.5}$ Speciation Trends Network	EPA	300	1999	$PM_{2.5,}$ $PM_{2.5}$ speciation, major Ions, metals	http://www.epa.gov/ttnamti1/specgen.html
PAMS—Photochemical Assessment Monitoring Network	EPA	75	1994	O_3, NO_X/NO_Y, CO, speciated VOCs, carbonyls, surface meteorology & Upper Air	http://www.epa.gov/air/oaqps/pams/
IMPROVE—Interagency Monitoring of Protected Visual Environments	NPS	110 plus 67 protocol sites	1988	$PM_{2.5}$/PM_{10}, major ions, metals, light extinction, scattering coefficient	http://vista.cira.colostate.edu/IMPROVE/
CASTNet – Clean Air Status and Trends Network	EPA	80+	1987	O_3, SO_2, major ions, calculated dry deposition, wet deposition, total deposition for sulfur/nitrogen, surface meteorology	http://www.epa.gov/castnet/
GPMN—Gaseous Pollutant Monitoring Network	NPS	33	1987	O_3, NO_X/NO/NO_2, SO_2, CO, surface meteorology, (plus enhanced monitoring of CO, NO, NO_X, NO_Y, and SO_2 plus canister samples for VOC at 3 sites)	http://www2.nature.nps.gov/air/Monitoring/network.cfm#data
POMS—Portable Ozone Monitoring Stations	NPS	14	2002	O_3, surface meteorology, with CASTNet-protocol filter pack (optional) sulfate, nitrate, ammonium, nitric acid, sulfur dioxide	http://www2.nature.nps.gov/air/studies/portO_3.cfm
Passive Ozone Sampler Monitoring Program	NPS	43	1995	O_3 dose (weekly)	http://www2.nature.nps.gov/air/Studies/Passives.cfm
NADP/NTN—National Atmospheric Deposition Program / National Trends Network	USGS	200+	1978	Major Ions from precipitation chemistry	http://nadp.sws.uiuc.edu/
NADP/MDN—National Atmospheric Deposition Program / Mercury Deposition Network	None	90+	1996	Mercury from precipitation chemistry	http://nadp.sws.uiuc.edu/mdn/

Network	Lead Agency	Number of Sites	Initiated	Measurement Parameters	Location of Information and/or Data
AIRMoN—National Atmospheric Deposition Program / Atmospheric Integrated Research Monitoring Network	NOAA	8	1992	Major Ions from precipitation chemistry Note: some sites began in 1976 as part of the DOE MAP3S program; early data are archived on NADP and ARL servers.	http://nadp.sws.uiuc.edu/AIRMoN/
IADN—Integrated Atmospheric Deposition Network	EPA	20	1990	PAHs, PCBs, and organochlorine compounds are measured in air and precipitation samples	http://www.epa.gov/glnpo/monitoring/air/
NAPS—National Air Pollution Surveillance Network	Canada	152+	1969	SO_2, CO, O_3, NO, NO_2, NO_X, VOCs, SVOCs, PM_{10}, $PM_{2.5}$, TSP, metals	http://www.etc-cte.ec.gc.ca/NAPS/index_e.html
CAPMoN—Canadian Air and Precipitation Monitoring Network	Canada	29	2002	O_3, NO, NO_2, NO_Y, PAN, NH_3, $PM_{2.5}$, PM_{10} and coarse fraction mass, $PM_{2.5}$ speciation, major ions for particles and trace gases, precipitation chemistry for major ions	http://www.msc.ec.gc.ca/capmon/index_e.cfm
Mexican Air Quality Network	Mexico	52-62	Late 1960s	O_3, NO_X, CO, SO_2, PM_{10}, TSP,VOC	http://www.ine.gob.mx/dgicur/calaire/indicadores.html
Mexican City Ambient Air Quality Monitoring Network	Mexico	49	Late 1960s	O_3, NO_X, CO, SO_2, PM_{10}, TSP,VOC	http://www.ine.gob.mx/dgicur/calaire/indicadores.html
AIR TOXICS MONITORING NETWORKS					
NATTS—National Air Toxics Trends Stations	EPA	23	2005	VOCs, Carbonyls, PM_{10} metals[d], Hg	http://www.epa.gov/ttN/Amtic/airtoxpg.html
State/Local Air Toxics Monitoring	EPA	250+	1987	VOCs, Carbonyls, PM_{10} metals[d], Hg	http://www.epa.gov/ttN/Amtic/airtoxpg.html
NDAMN—National Dioxin Air Monitoring Network	EPA	34	1998-2005	CDDs, CDFs, dioxin-like PCBs	http://cfpub.epa.gov/ncea/CFM/recordisplay.cfm?deid=54811
TRIBAL MONITORING NETWORKS					
Tribal Monitoring[f]	EPA	120+	1995	O_3, NO_X/NO_2, SO_2, $PM_{2.5}$/PM_{10}, CO, Pb	http://www.epa.gov/air/tribal/airprogs.html#ambmon
INDUSTRY / RESEARCH NETWORKS					
New Source Permit Monitoring	None	variable	variable	O_3, NO_X/NO_2, SO_2, $PM_{2.5}$/PM_{10}, CO, Pb	Contact specific industrial facilities
HRM Network—Houston Regional Monitoring Network	None	9	1980	O_3, NO_X, $PM_{2.5}$/PM_{10}, CO, SO_2, Pb, VOCs, surface meteorology	http://hrm.radian.com/houston/how/index.htm
ARIES / SEARCH—Aerosol Research Inhalation Epidemiology Study / SouthEastern Aerosol Research and Characterization Study experiment	None	8	1992	O_3, NO/NO_2/NO_Y, SO_2, CO, $PM_{2.5}$/PM_{10}, $PM_{2.5}$ speciation, major Ions, NH_3, HNO_3, scattering coefficient, surface meteorology	http://www.atmospheric-research.com/studies/SEARCH/index.html

Network	Lead Agency	Number of Sites	Initiated	Measurement Parameters	Location of Information and/or Data
SOS – SERON—Southern Oxidant Study - Southeastern Regional Oxidant Networks	EPA	~40	1990	O_3, NO, NO_Y, VOCs, CO, surface meteorology	http://www.ncsu.edu/sos/pubs/sos3/State_of_SOS_3.pdf
NATIONAL/GLOBAL RADIATION NETWORKS					
RadNet—formerly Environmental Radiation Ambient Monitoring System (ERAMS)	EPA	200+	1973	Radionuclides and radiation	http://www.epa.gov/enviro/html/erams/
SASP – Surface Air Sampling Program	DHS	41	1963	89Sr, 90Sr, naturally occurring radionuclides, 7Be, 210Pb	http://www.eml.st.dhs.gov/databases/sasp/
NEWNET–Neighborhood Environmental Watch Network	DOE	26	1993	Ionizing gamma radiation, surface meteorology	http://newnet.lanl.gov/
SOLAR RADIATION NETWORKS					
UV Index – EPA Sunrise Program[g]	EPA	~50 U.S. cities	2002	Calculated UV radiation index	http://www.epa.gov/sunwise/uvindex.html
UV Net – Ultraviolet Monitoring Program	EPA	21	1995/2004	Ultraviolet solar radiation (UV-B and UV-A bands), irradiance, ozone, NO_2	http://www.epa.gov/uvnet/access.html
NEUBrew (NOAA-EPA Brewer Spectrophotometer UV and Ozone Network	NOAA	6	2005	Ultraviolet solar radiation (UV-B and UV-A bands), irradiance, ozone, SO_2	http://www.esrl.noaa.gov/gmd/grad/neubrew/
UV-B Monitoring and Research Program	USDA	35	1992	Ultraviolet-B radiation	http://uvb.nrel.colostate.edu/UVB/index.jsf
SURFRAD – Surface Radiation Budget Network	NOAA	7	1993	Solar and infrared radiation, direct and diffuse solar radiation, photosynthetically active radiation, UVB, spectral solar, and meteorological parameters	http://www.srrb.noaa.gov/surfrad/index.html
AERONET – Aerosol RObotic NETwork	NASA co-located networks	22 + other participants	1998	Aerosol spectral optical depths, aerosol size distributions, and precipitable water	http://aeronet.gsfc.nasa.gov/index.html
MPLNET – Micro-pulse Lidar Network		8	2000	Aerosols and cloud layer heights	http://mplnet.gsfc.nasa.gov/
PRIMENet – Park Research & Intensive Monitoring of Ecosystems NETwork[h]	NPS	14	1997	ozone, wet and dry deposition, visibility, surface meteorology, and ultraviolet radiation	http://www.cfc.umt.edu/primenet/Assets/Announcements/99PReport.pdf

[a]Some networks listed separately may also serve as subcomponents of other larger listed networks; as a result, some double counting of the number of individual monitors is likely.
[b]NCore is a network proposed to replace NAMS, as a component of SLAMS; NAMS are currently designated as national trends sites.
[c]surface meteorology includes wind direction and speed, temperature, precipitation, relative humidity, solar radiation (PAMS only).
[d]PM_{10} metals may include arsenic, beryllium, cadmium, chromium, lead, manganese, nickel, and others.
[e]The number of sites indicated for tribal monitoring is actually the number of monitors, rather than sites. The number of sites with multiple monitors is probably <80.
[f] Sunrise program estimates UV exposure levels through modeling - does not include measurements.
[g]NEUBREW is a subset Original UV brewer network (UV Net); PRIMENET participated in UV Net program.

A.1.3. Monitor Distribution with Respect to Population Density

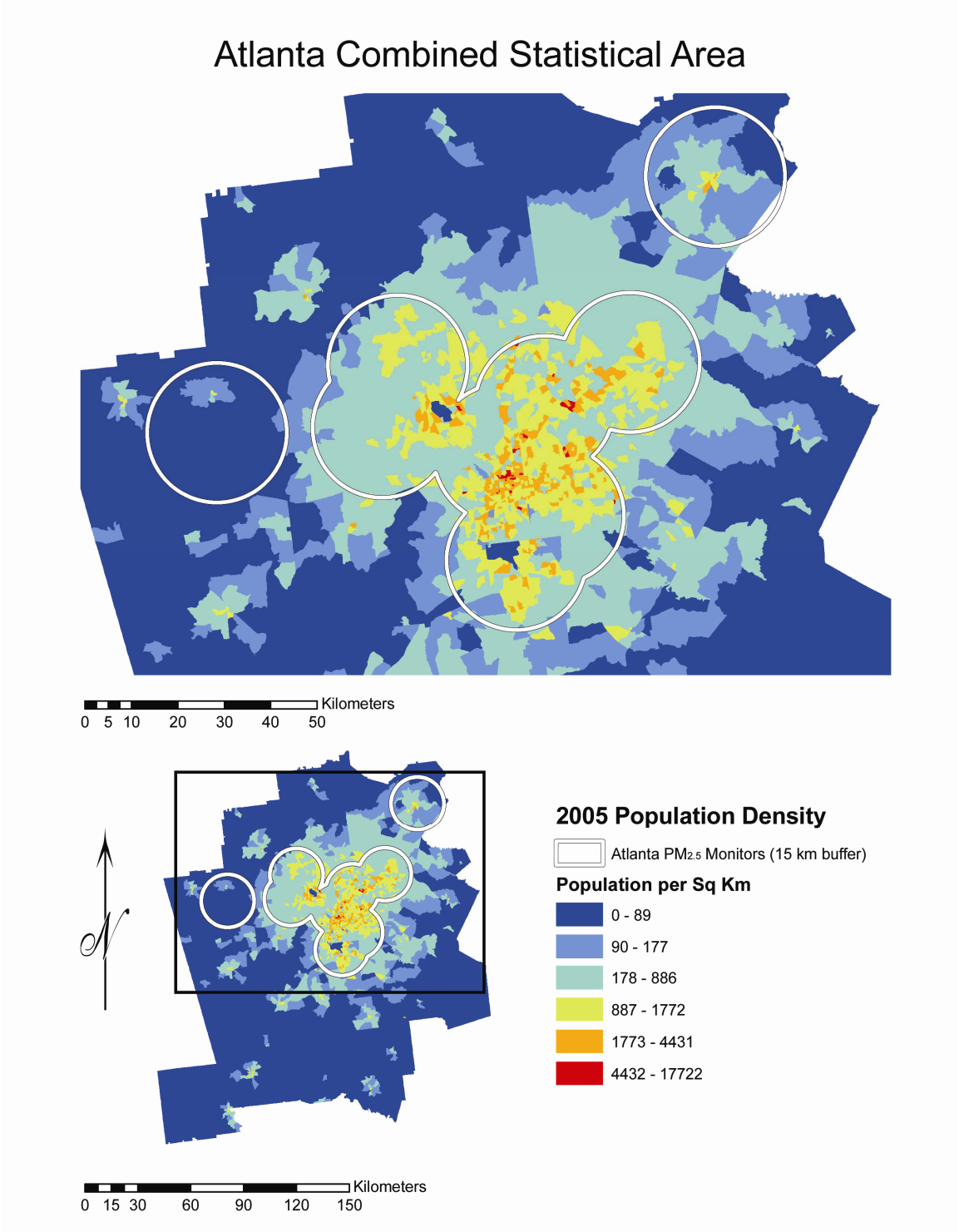


Figure A-1. $PM_{2.5}$ monitor distribution in comparison with population density, Atlanta, GA.

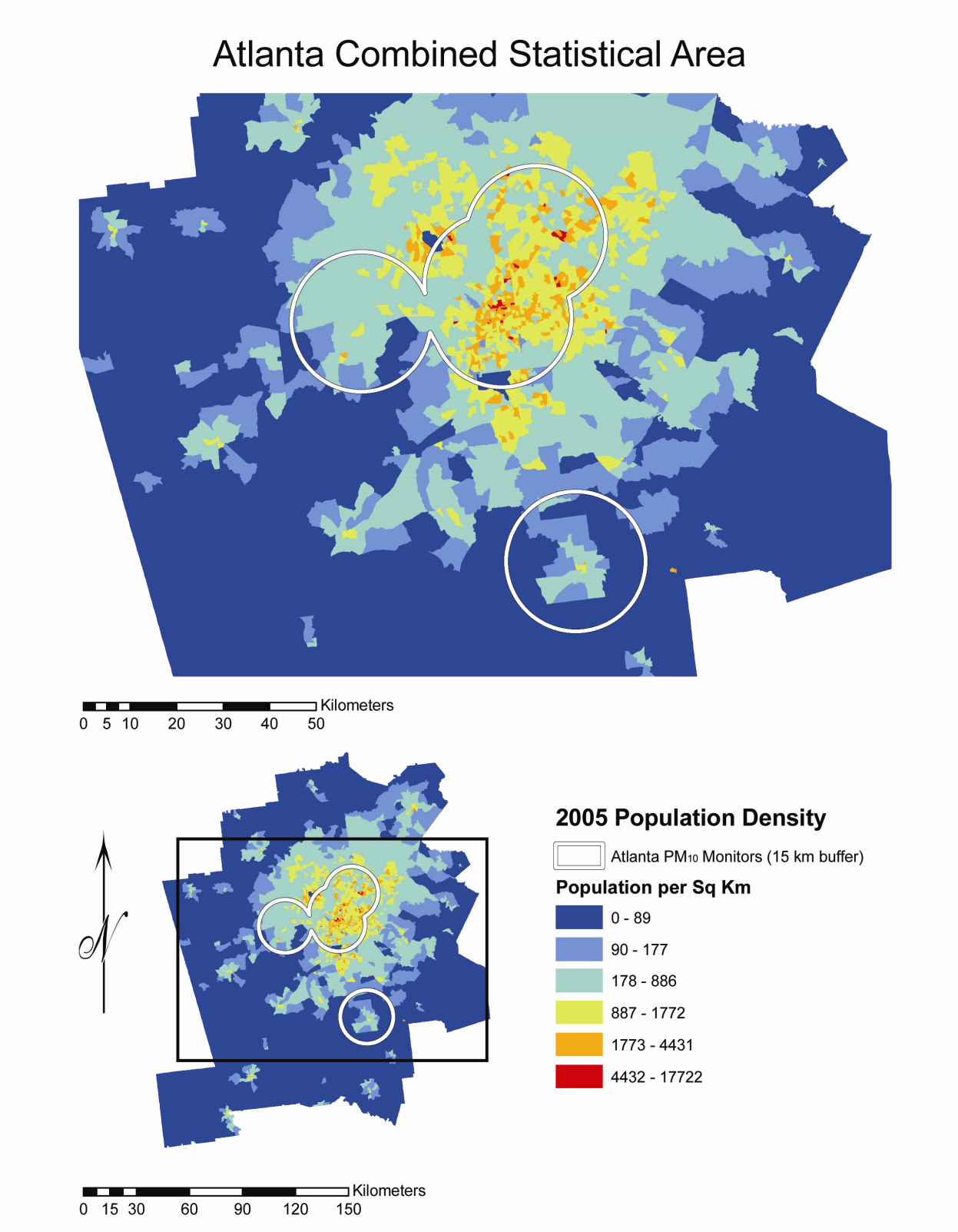


Figure A-2. PM_{10} monitor distribution in comparison with population density, Atlanta, GA.

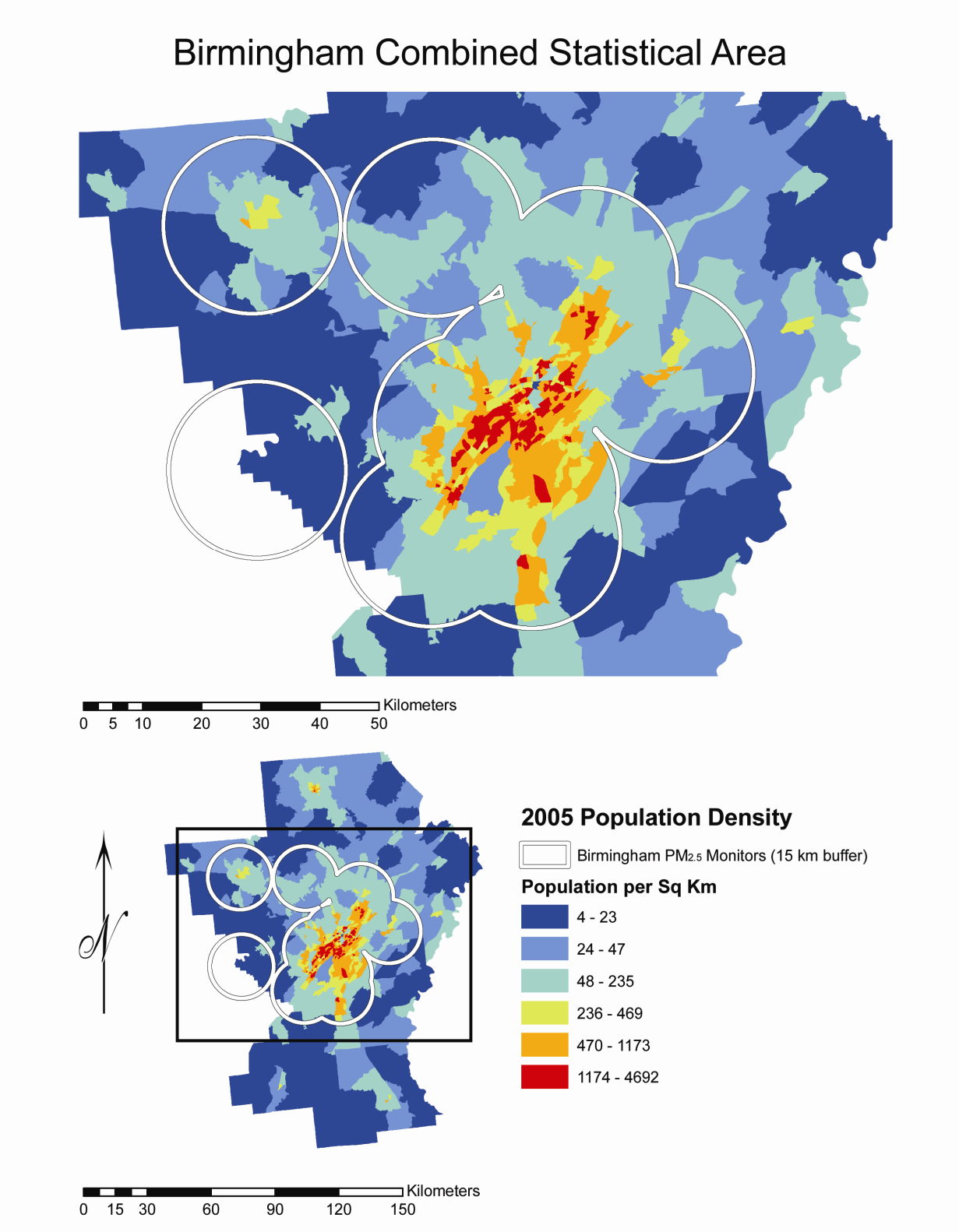


Figure A-3. **$PM_{2.5}$ monitor distribution in comparison with population density, Birmingham, AL.**

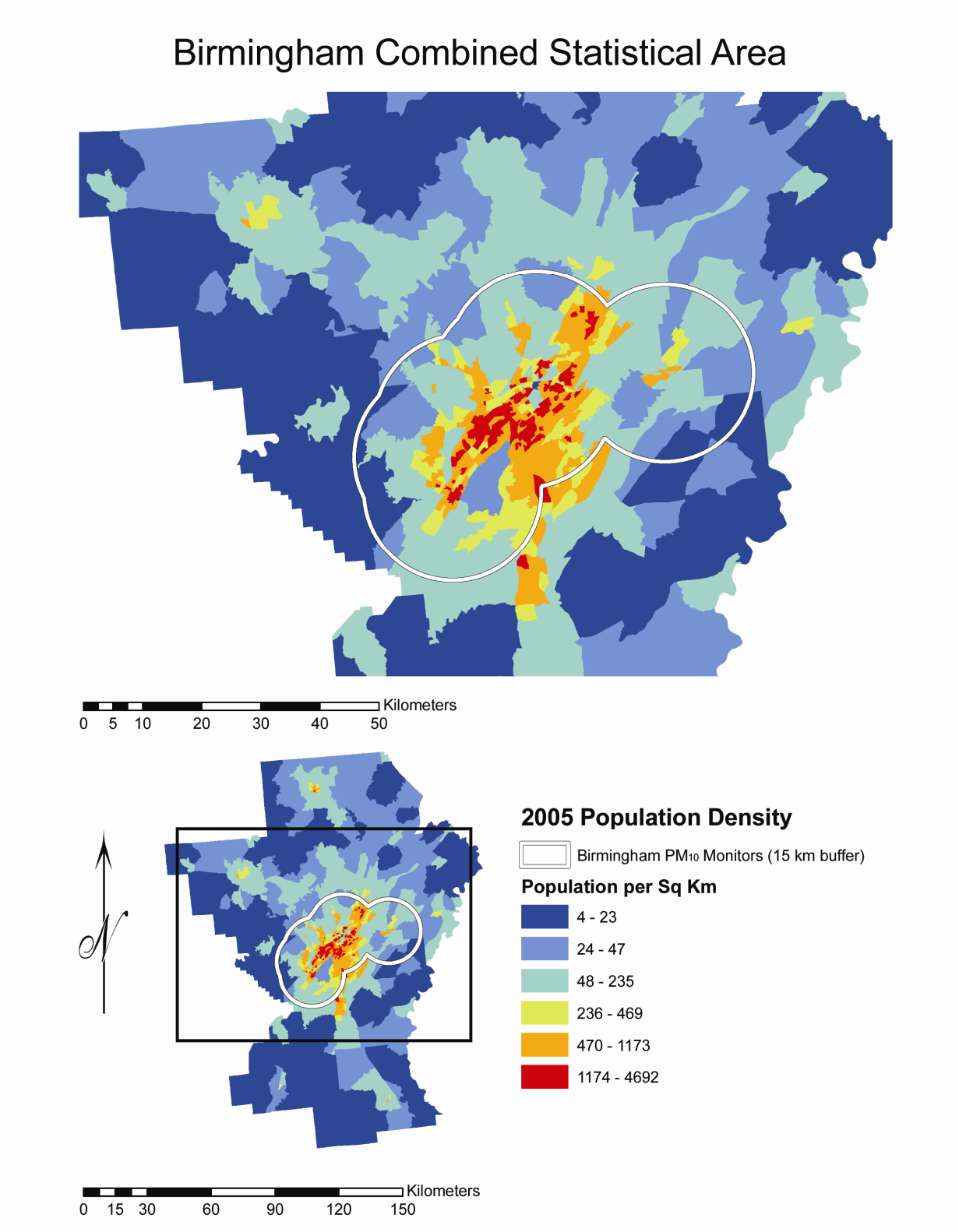


Figure A-4. **PM_{10} monitor distribution in comparison with population density, Birmingham, AL.**

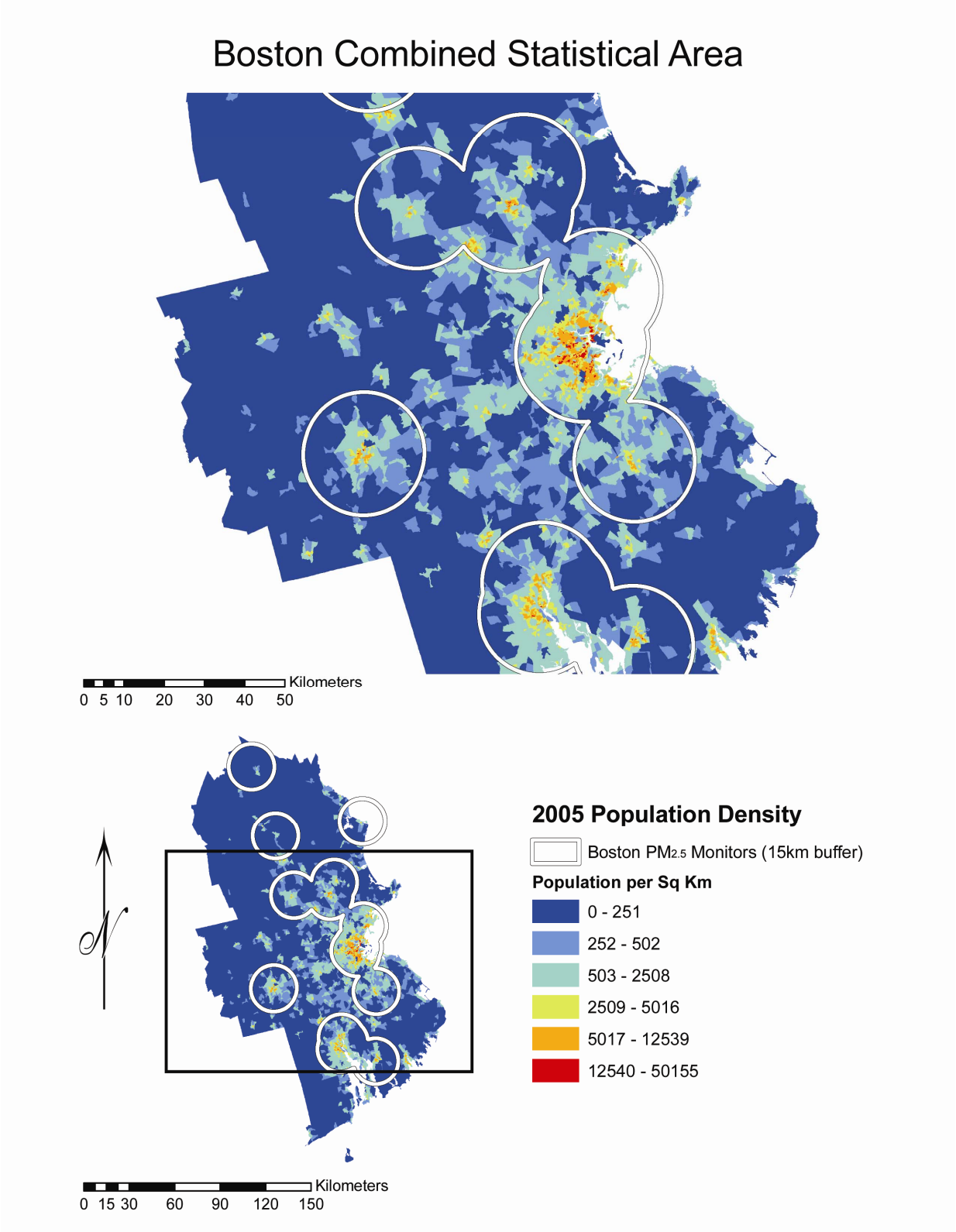


Figure A-5. $PM_{2.5}$ monitor distribution in comparison with population density, Boston, MA.

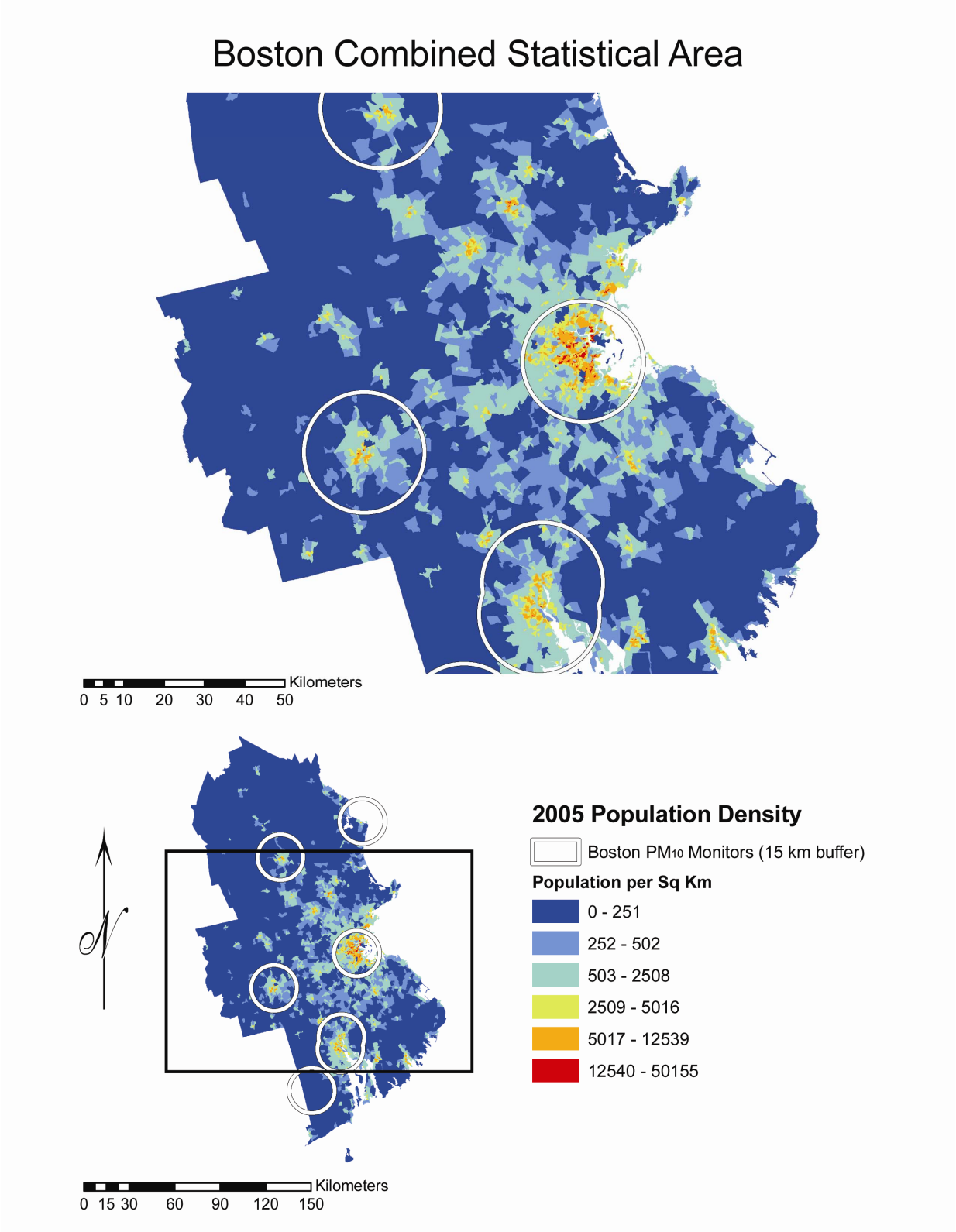


Figure A-6. PM_{10} monitor distribution in comparison with population density, Boston, MA.

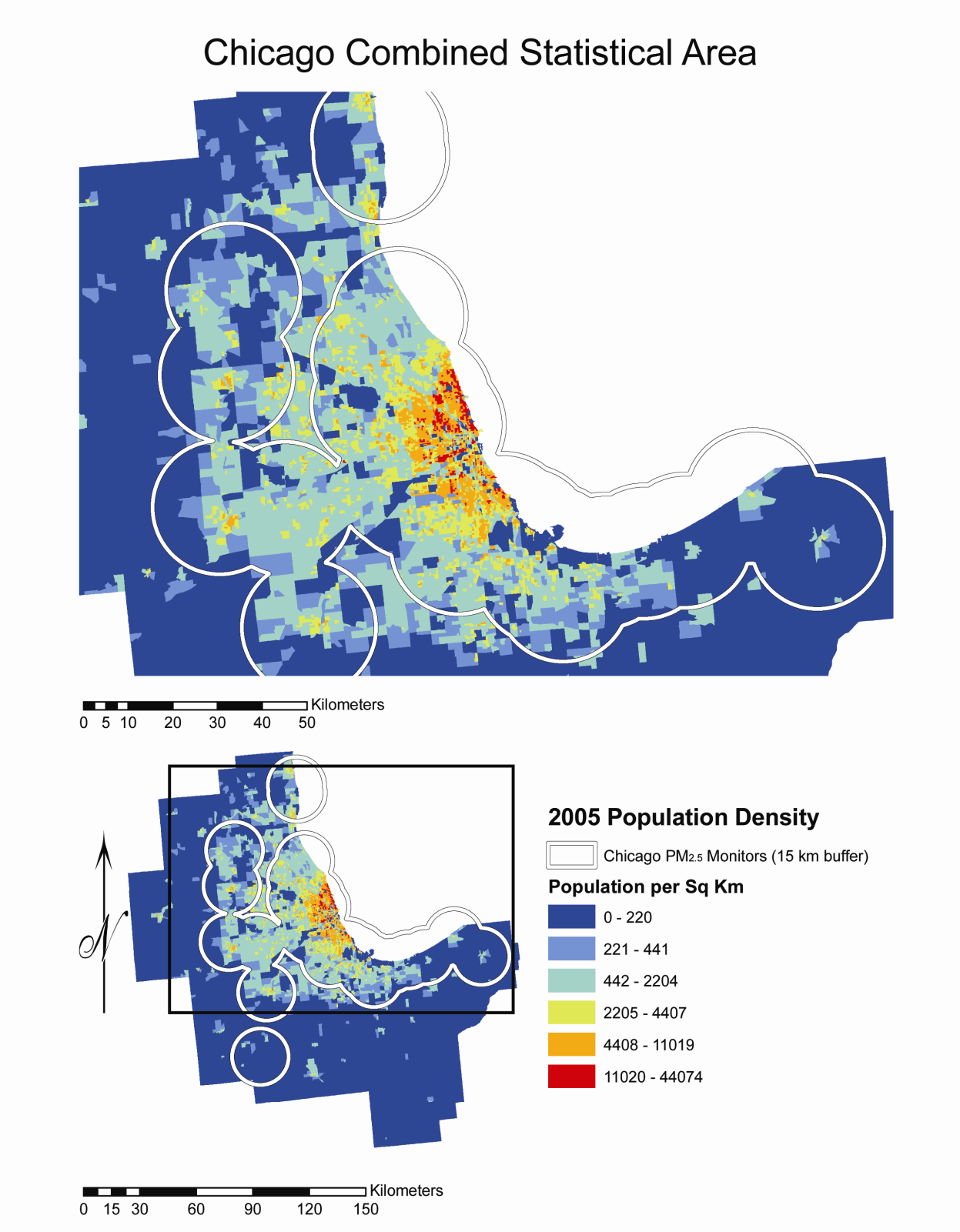


Figure A-7. $PM_{2.5}$ monitor distribution in comparison with population density, Chicago, IL.

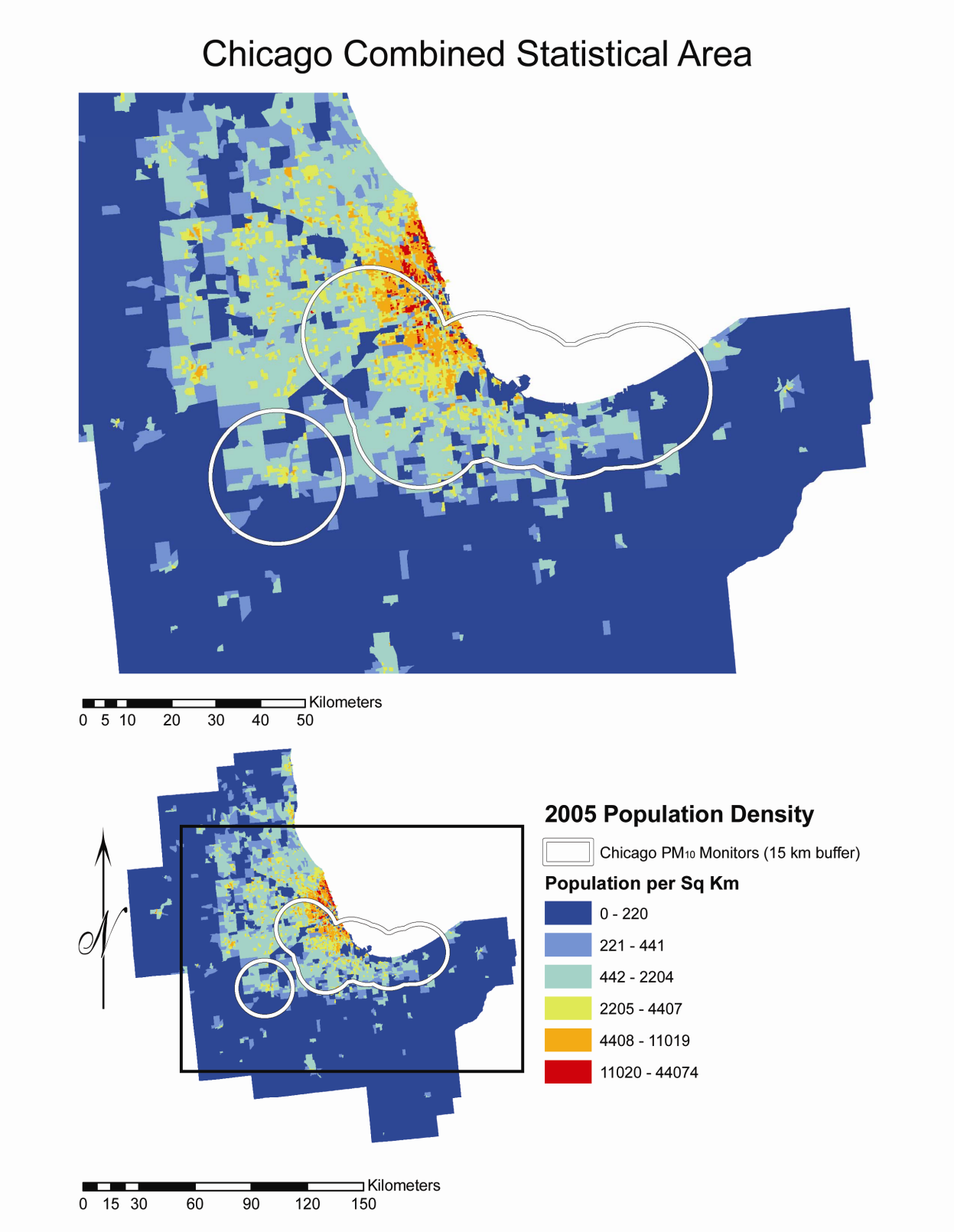


Figure A-8. PM_{10} monitor distribution in comparison with population density, Chicago, IL.

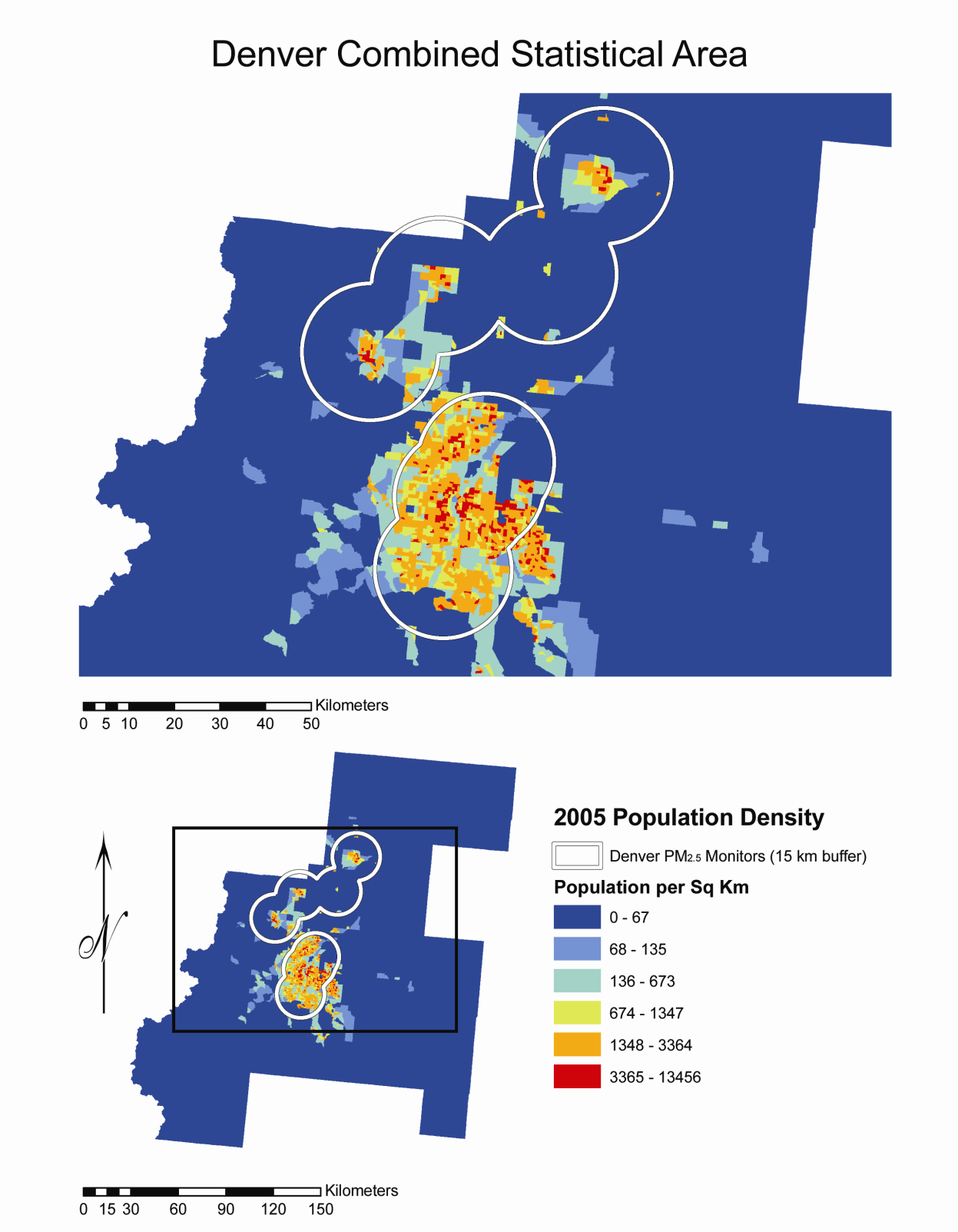


Figure A-9. $PM_{2.5}$ monitor distribution in comparison with population density, Denver, CO.

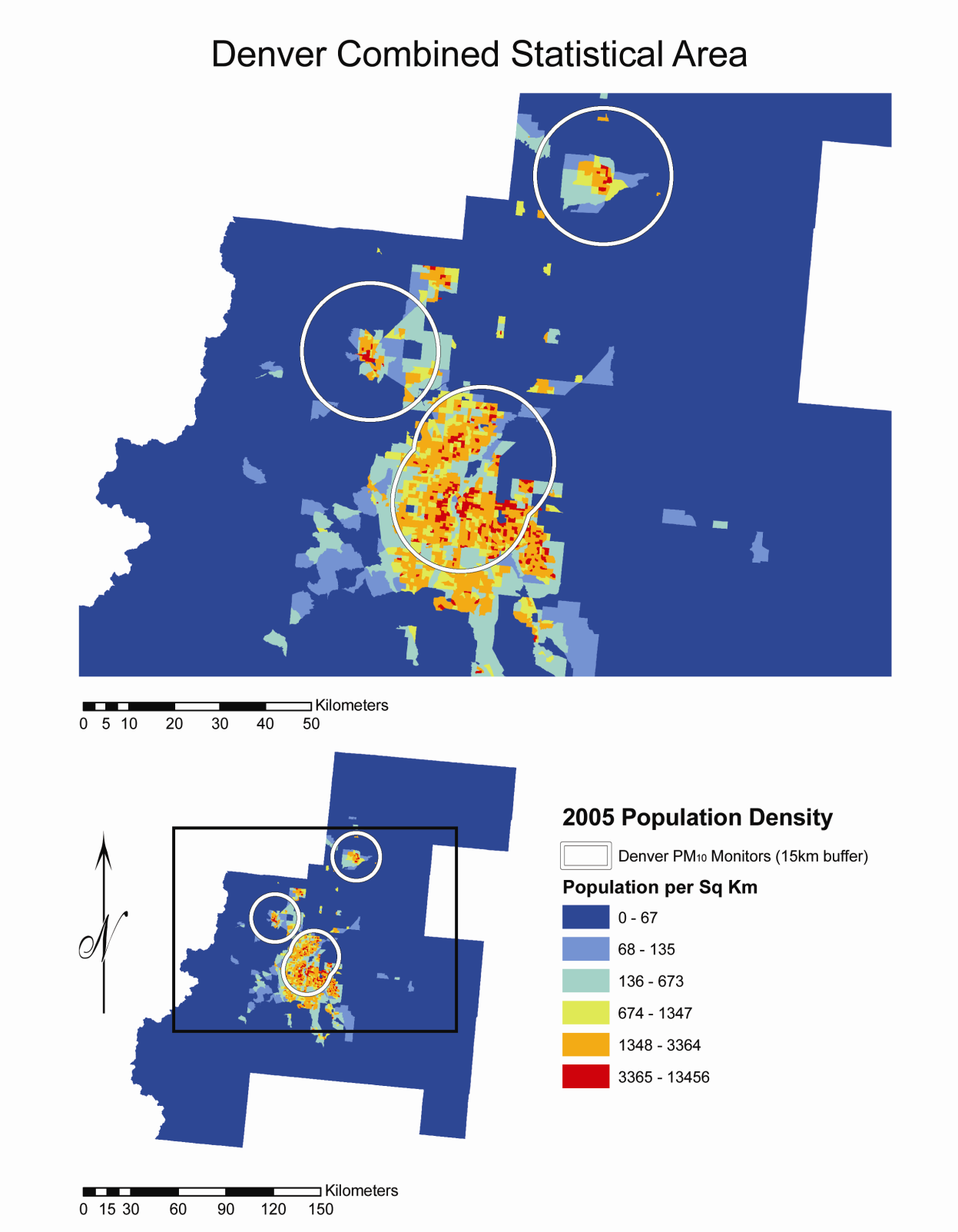


Figure A-10. PM_{10} monitor distribution in comparison with population density, Denver, CO.

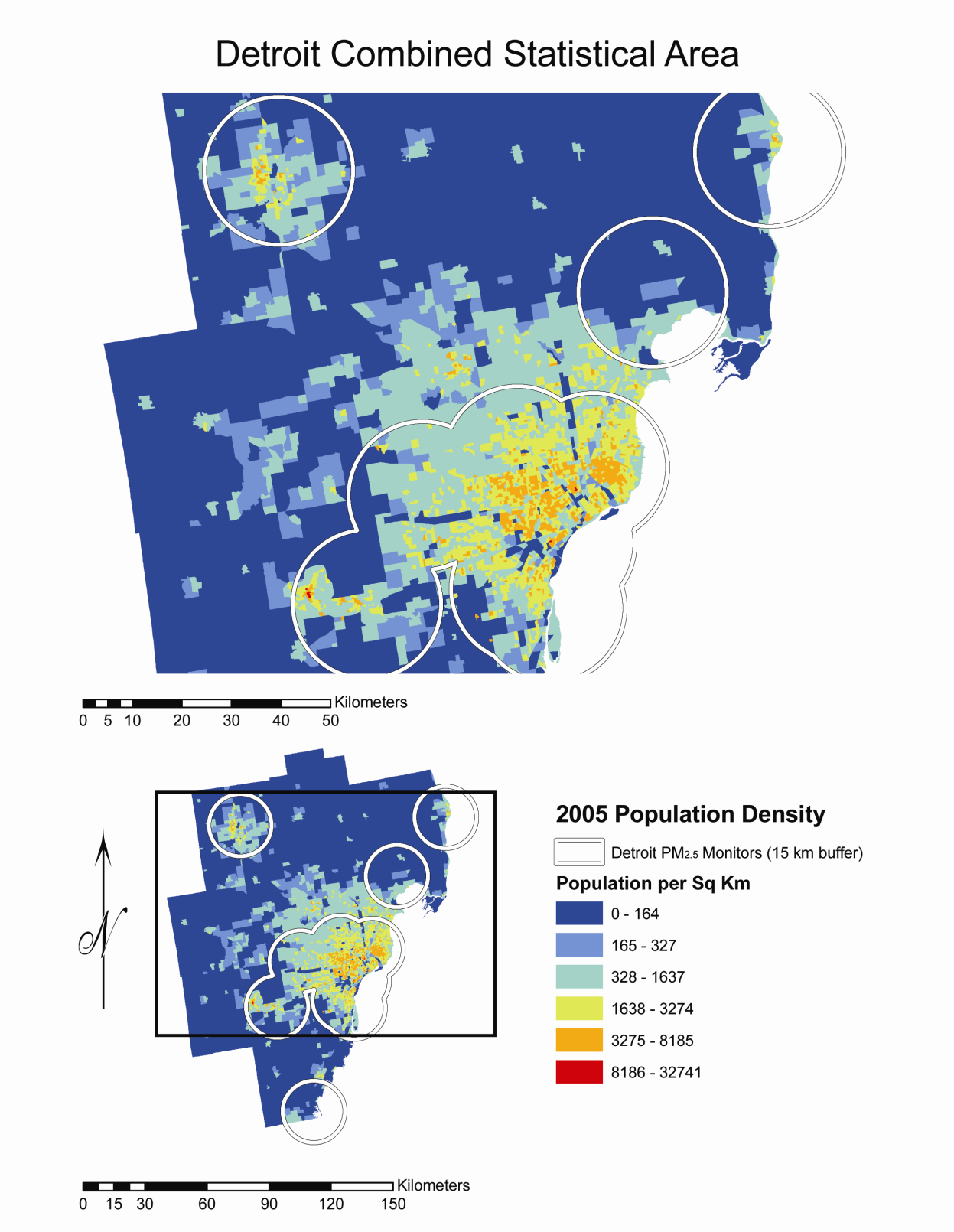


Figure A-11. $PM_{2.5}$ monitor distribution in comparison with population density, Detroit, MI.

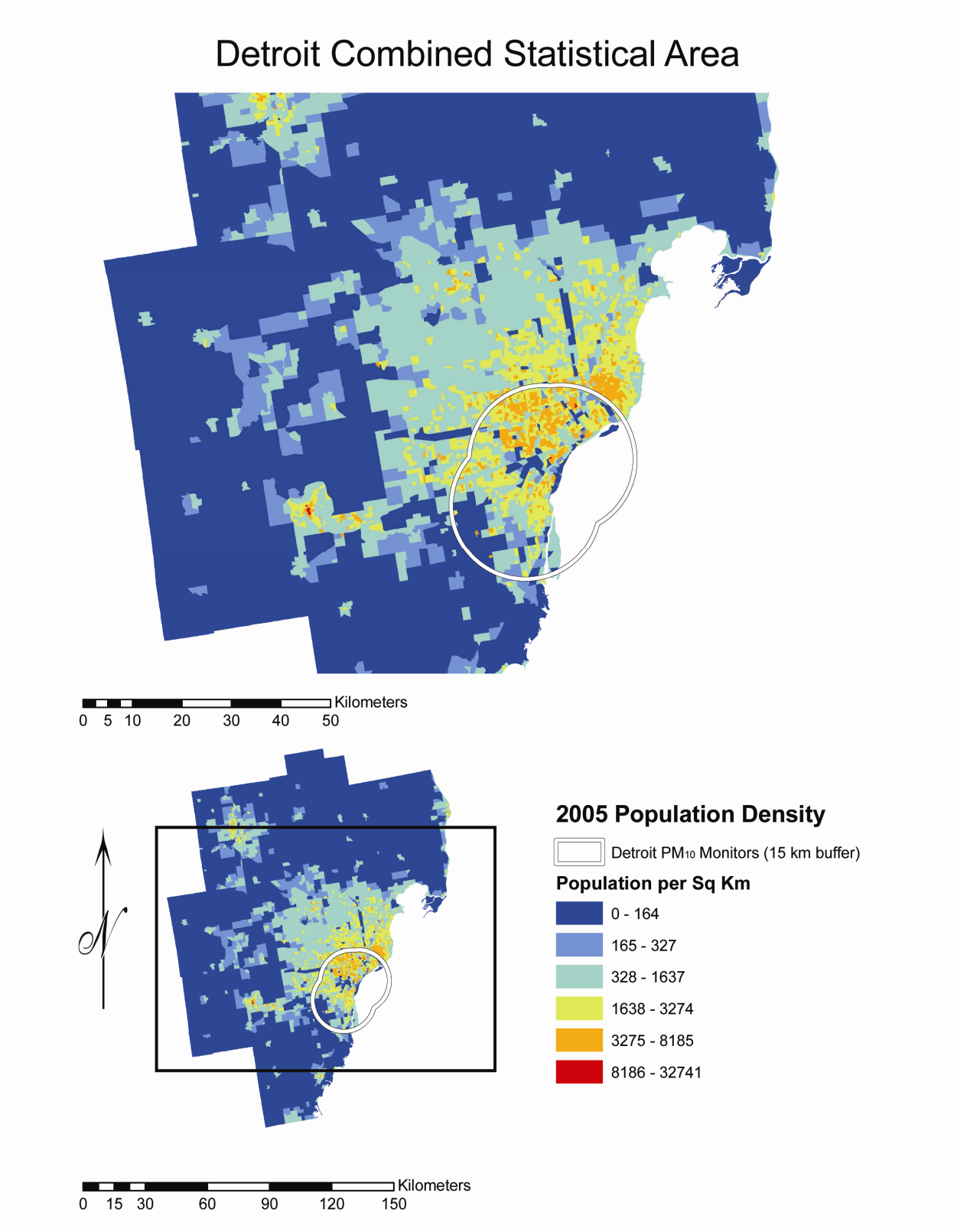


Figure A-12. PM_{10} monitor distribution in comparison with population density, Detroit, MI.

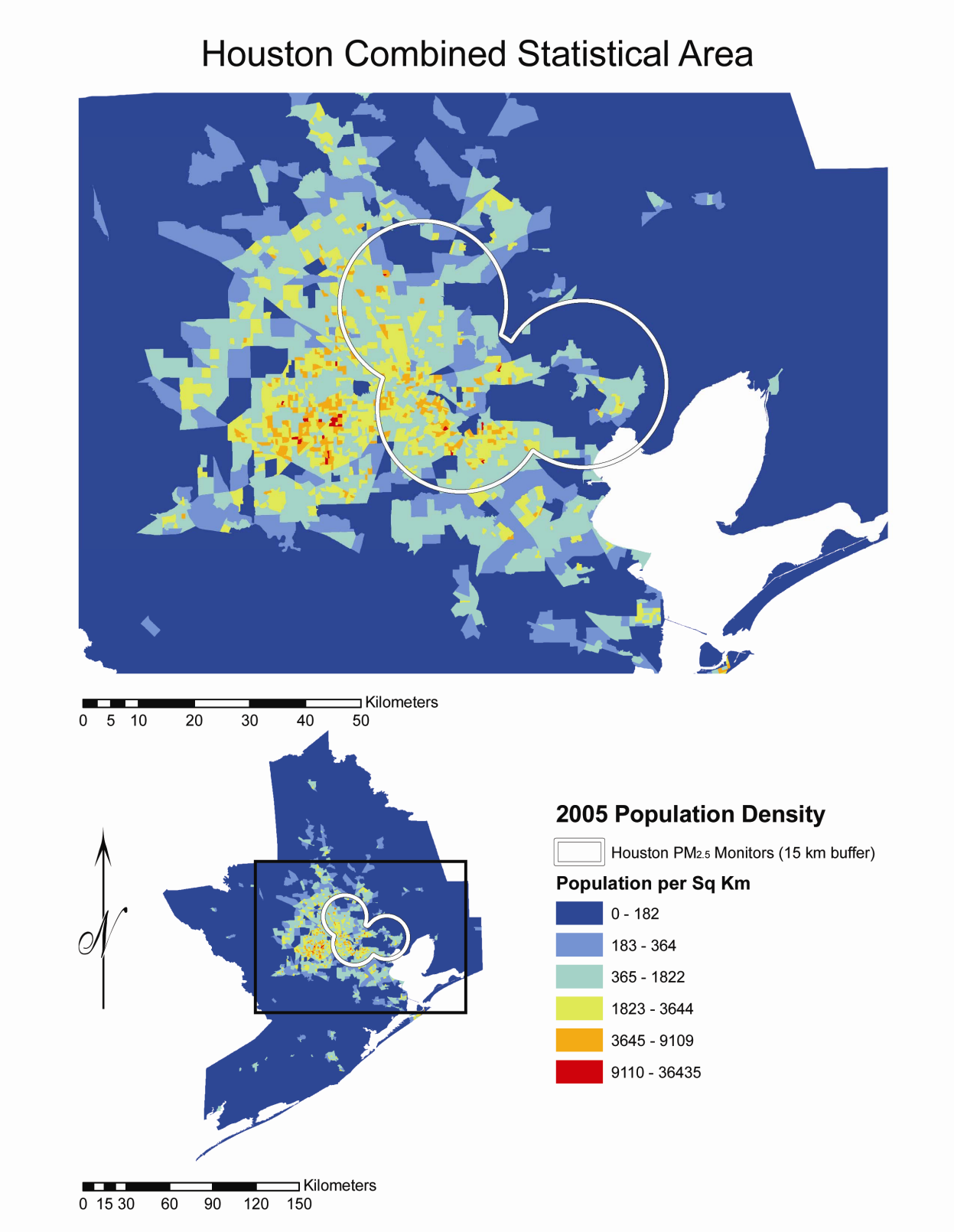


Figure A-13. $PM_{2.5}$ monitor distribution in comparison with population density, Houston, TX.

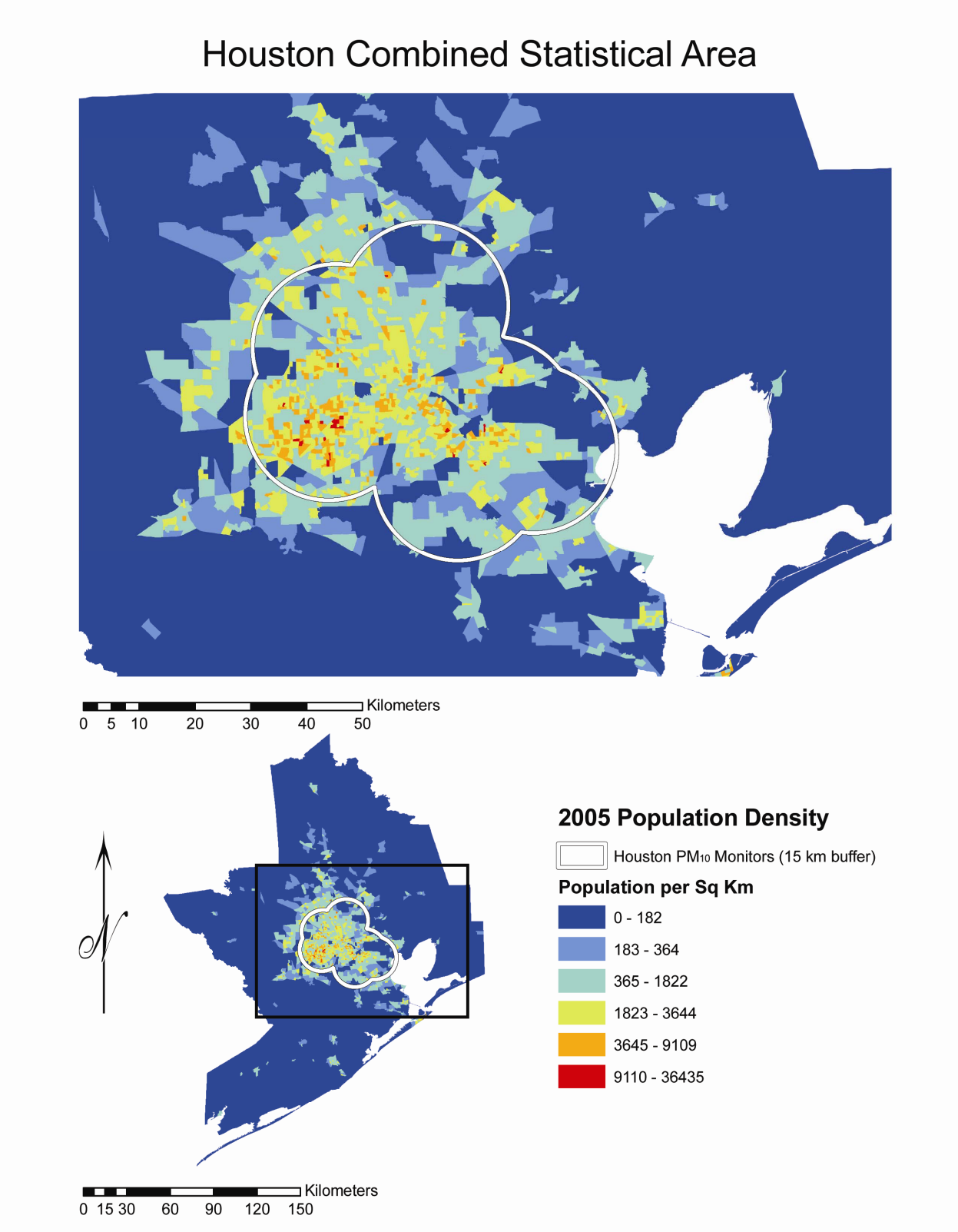


Figure A-14. PM_{10} monitor distribution in comparison with population density, Houston, TX.

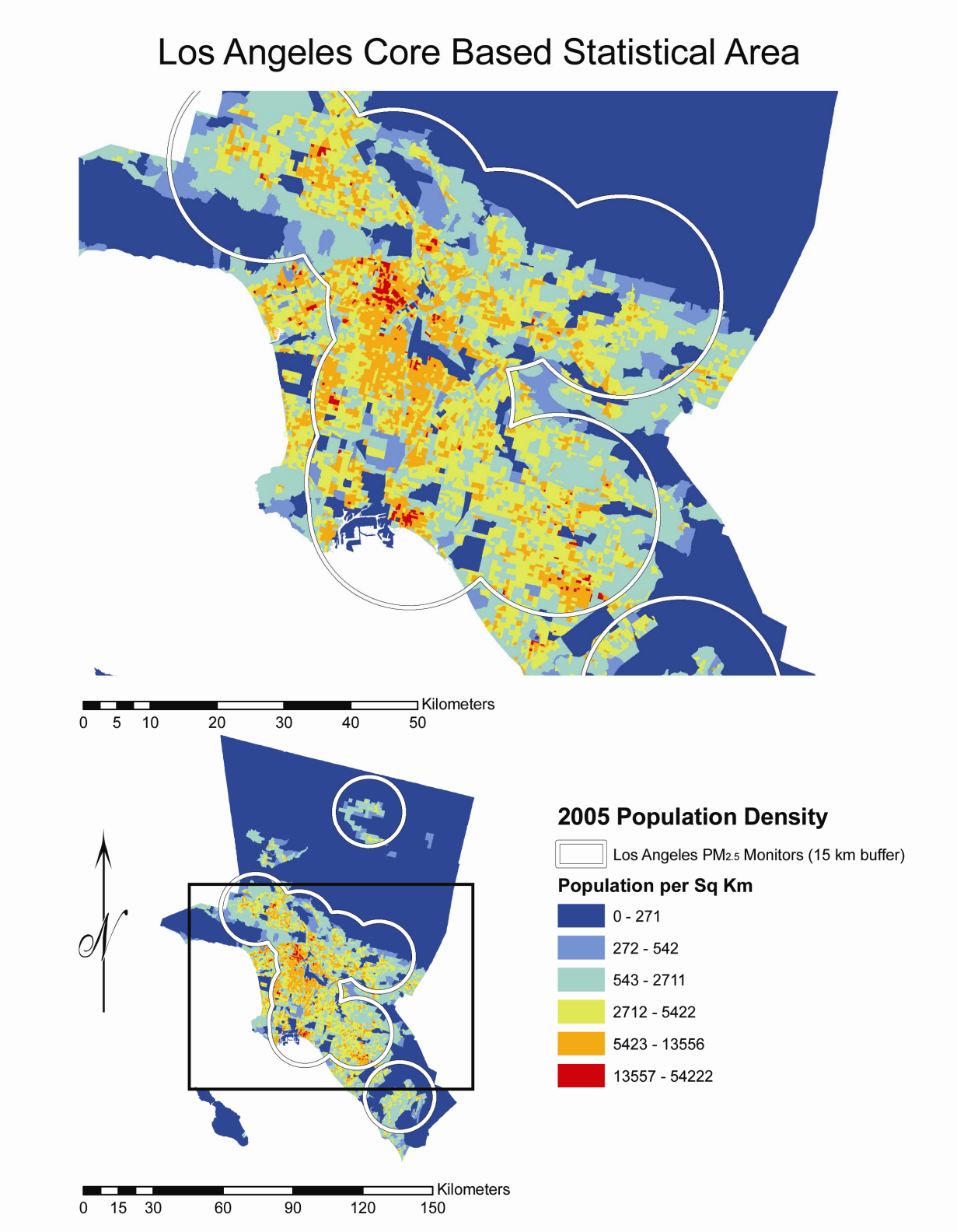


Figure A-15. $PM_{2.5}$ monitor distribution in comparison with population density, Los Angeles, CA.

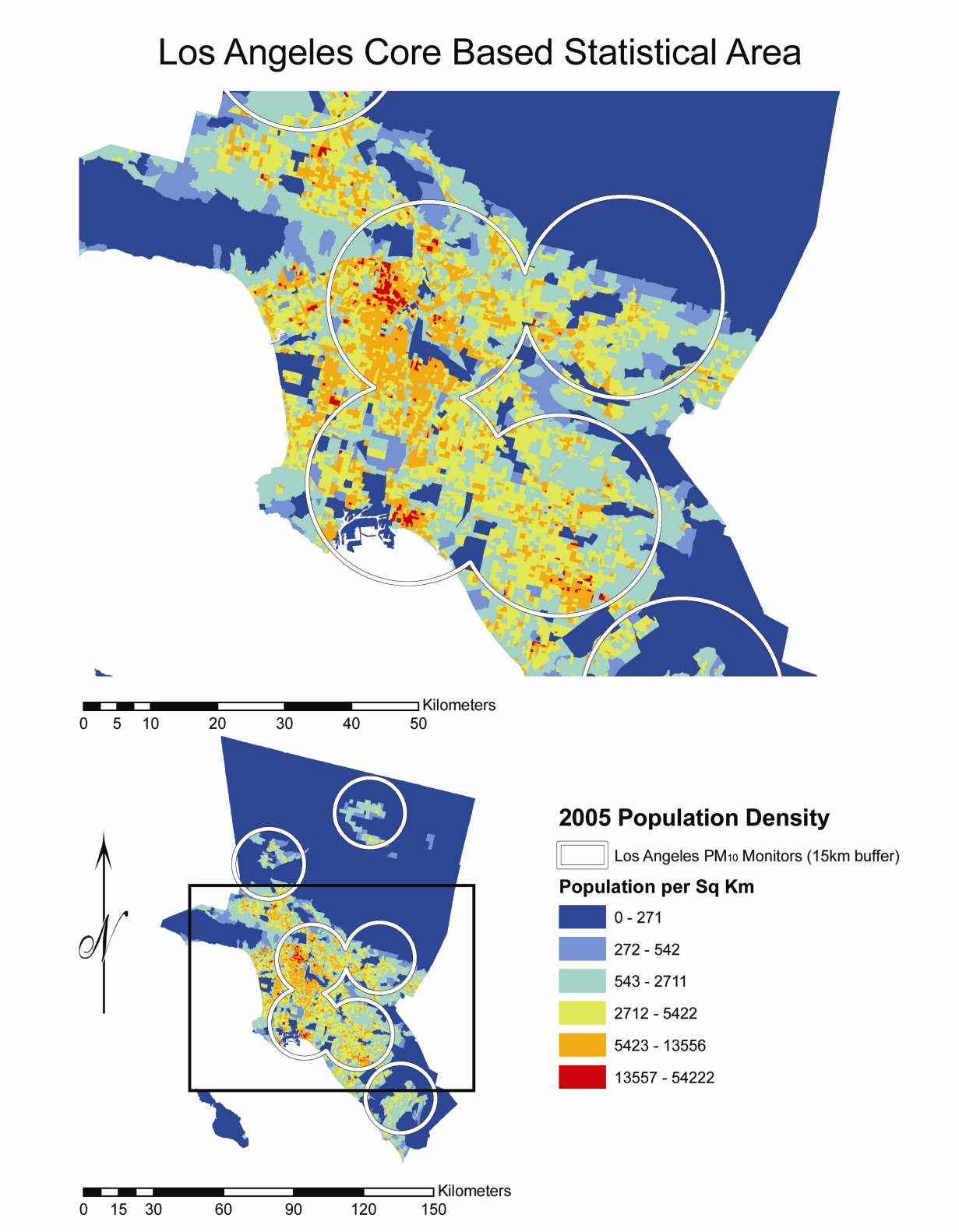


Figure A-16. PM_{10} monitor distribution in comparison with population density, Los Angeles, CA.

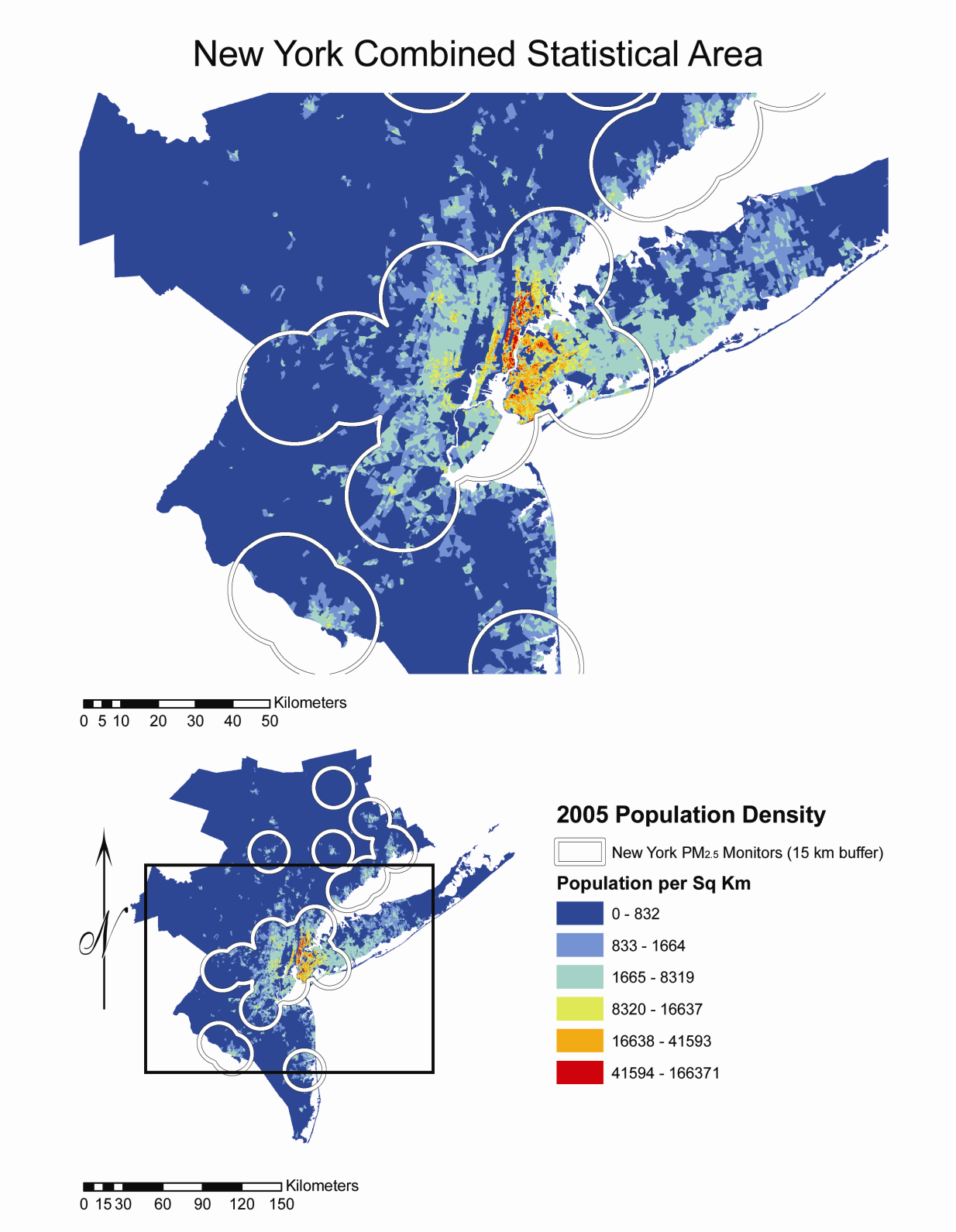


Figure A-17. $PM_{2.5}$ monitor distribution in comparison with population density, New York, NY.

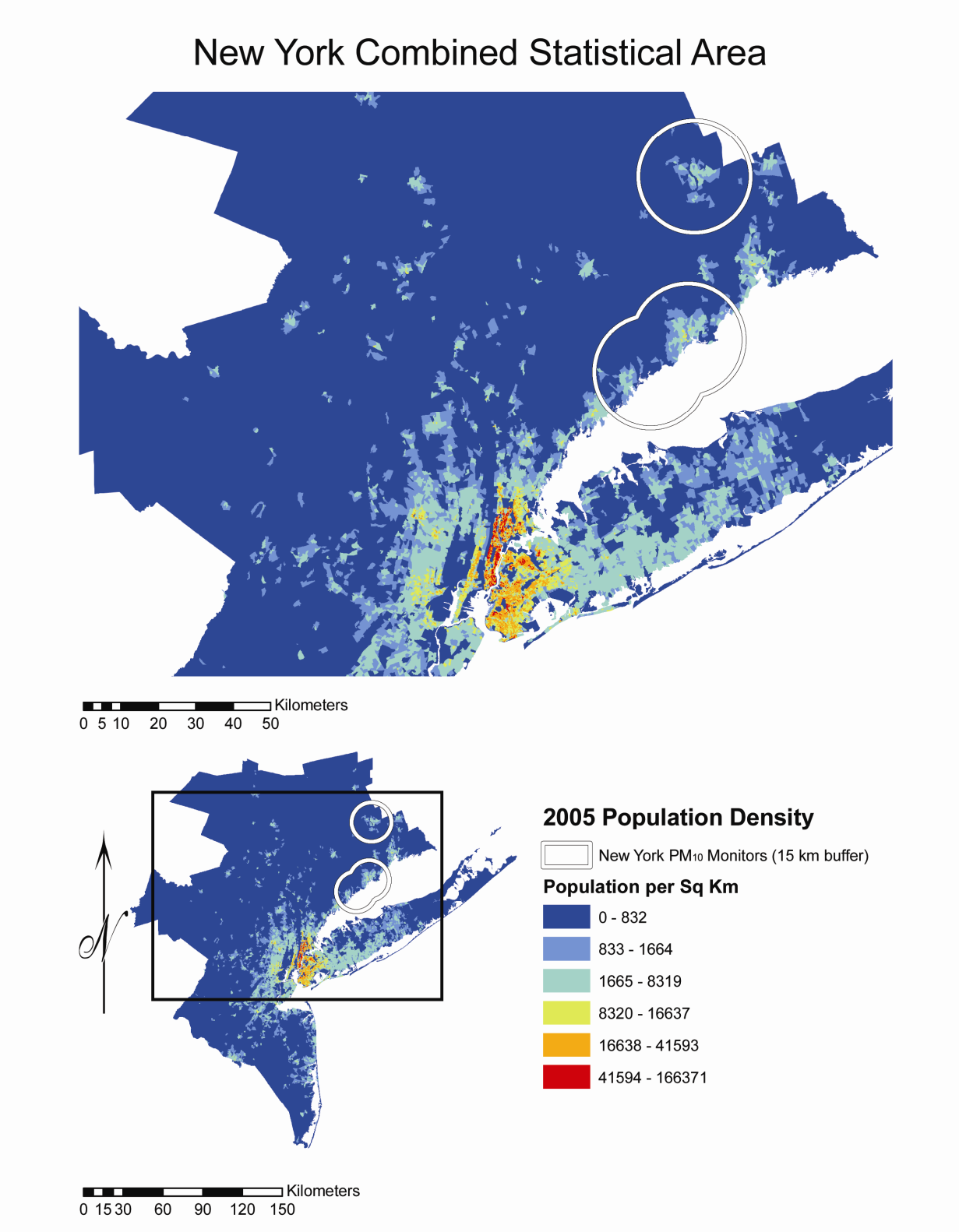


Figure A-18. PM_{10} monitor distribution in comparison with population density, New York, NY.

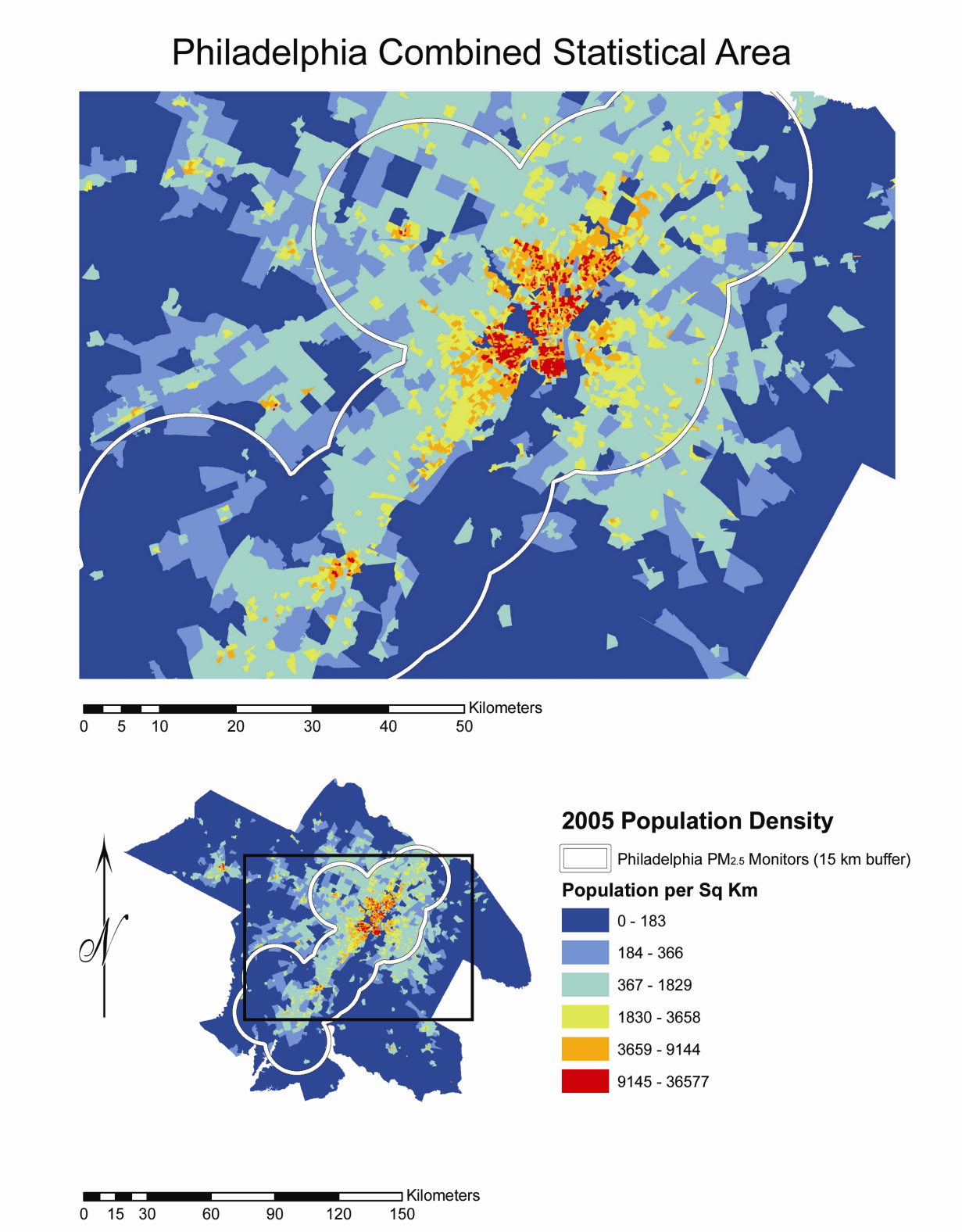


Figure A-19. $PM_{2.5}$ monitor distribution in comparison with population density, Philadelphia, PA.

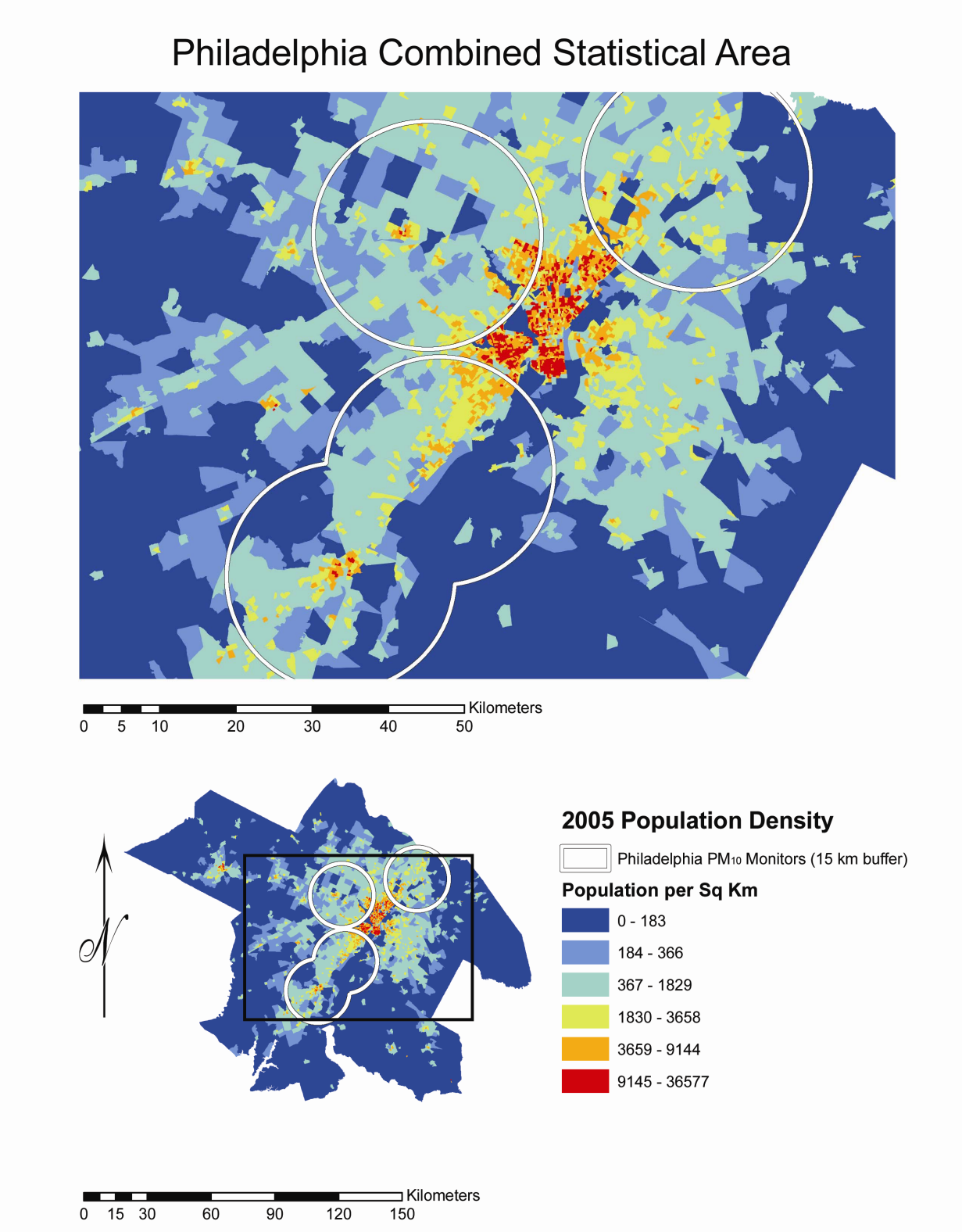


Figure A-20. PM_{10} monitor distribution in comparison with population density, Philadelphia, PA.

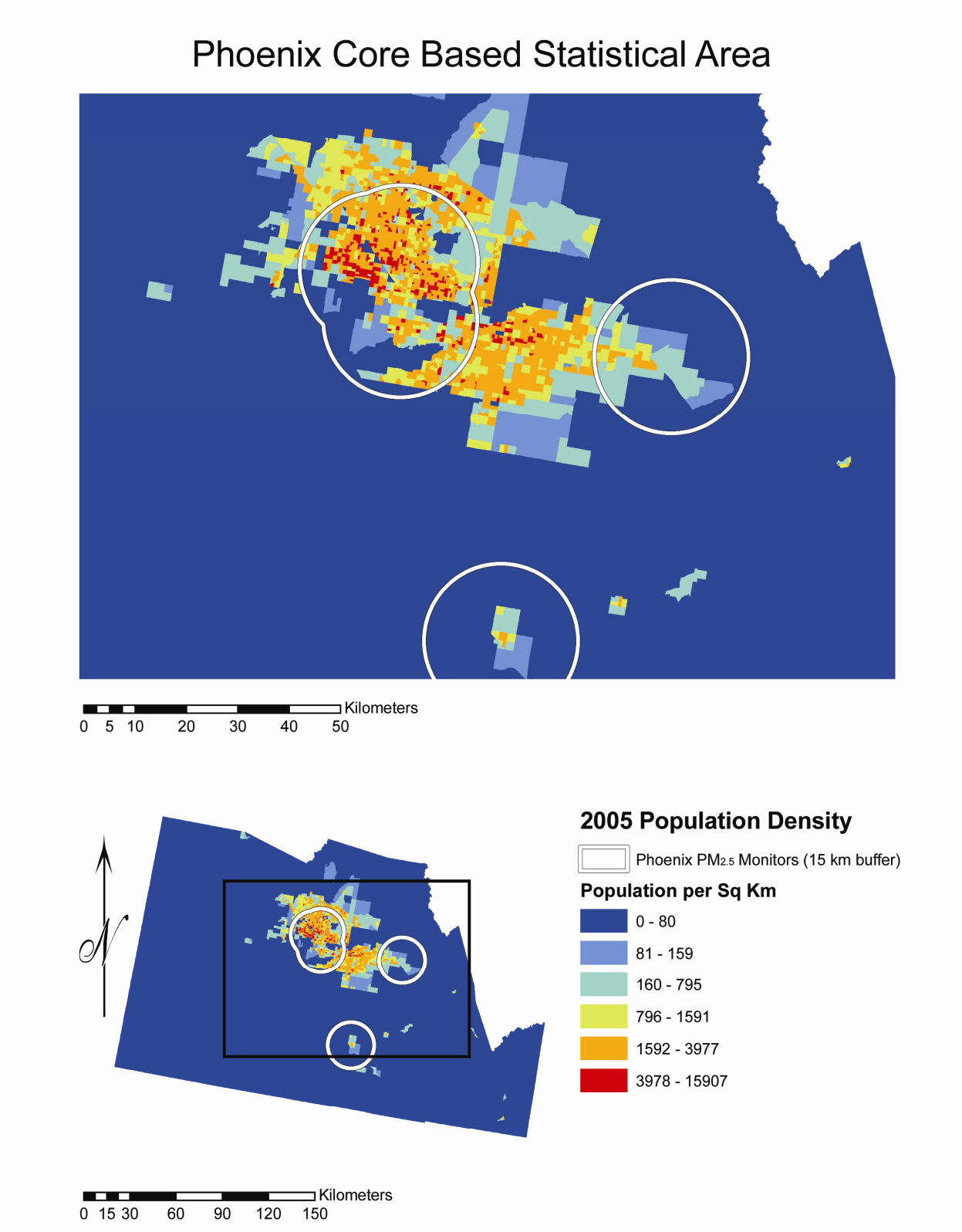


Figure A-21. $PM_{2.5}$ monitor distribution in comparison with population density, Phoenix, AZ.

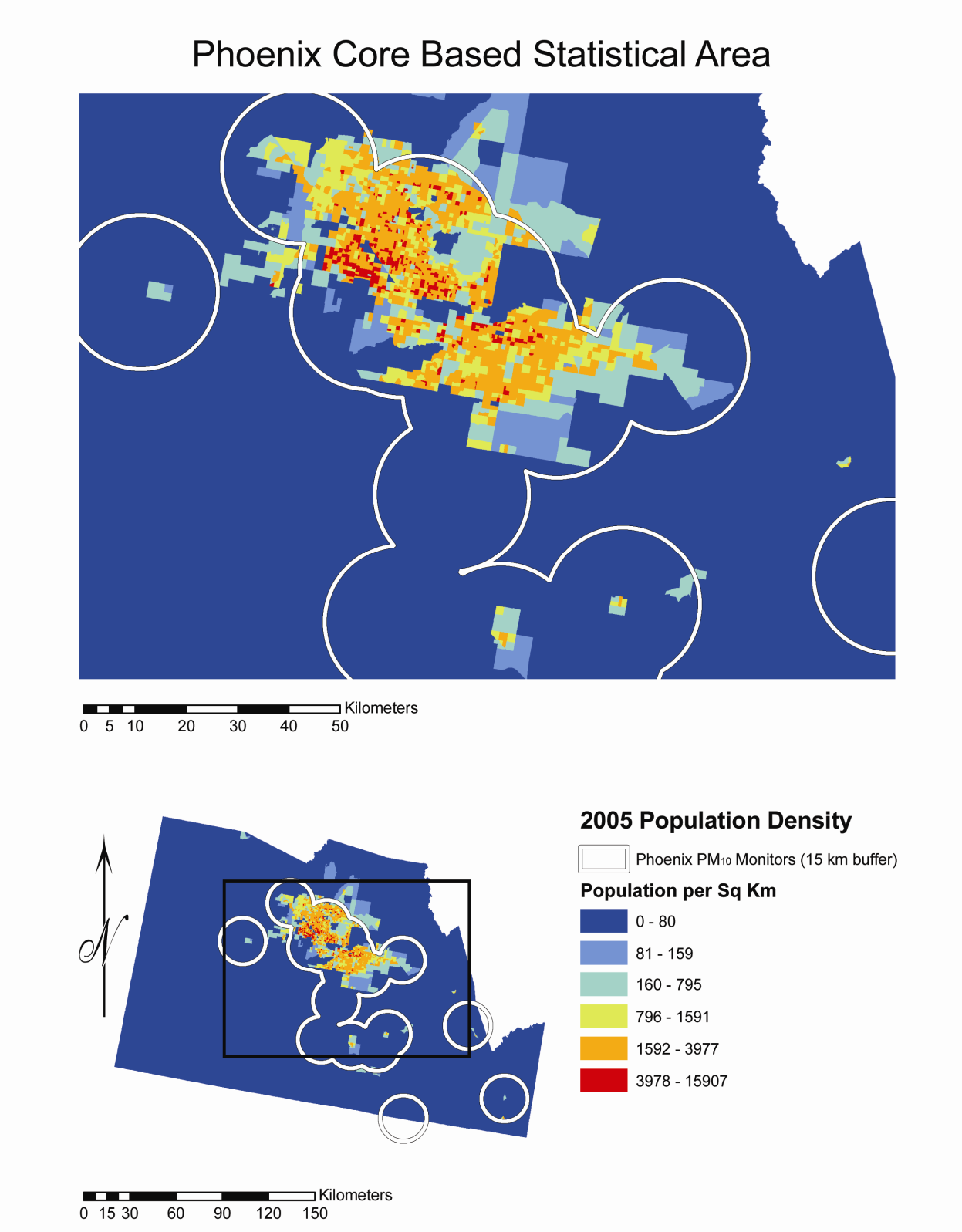


Figure A-22. PM_{10} monitor distribution in comparison with population density, Phoenix, AZ.

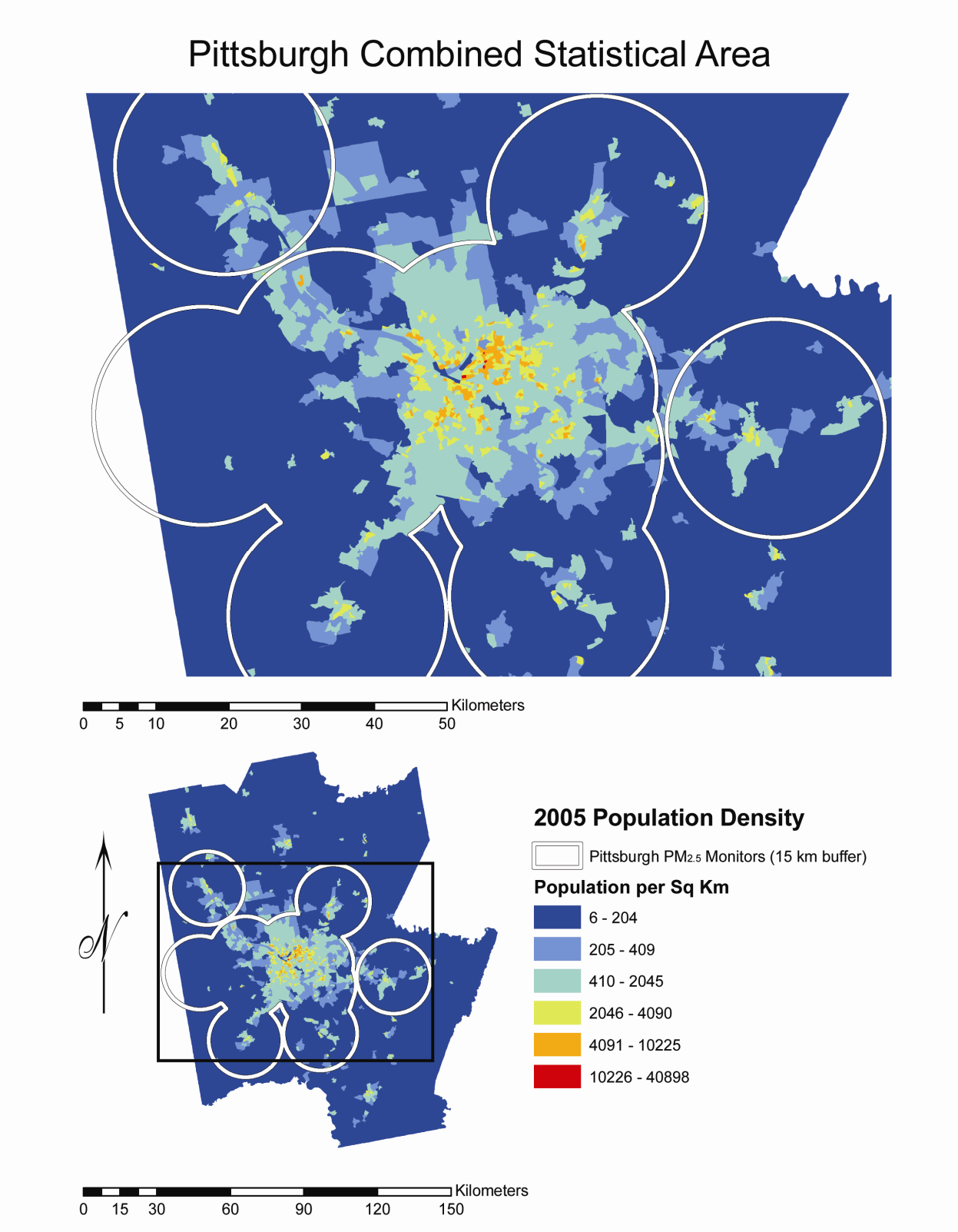


Figure A-23. $PM_{2.5}$ monitor distribution in comparison with population density, Pittsburgh, PA.

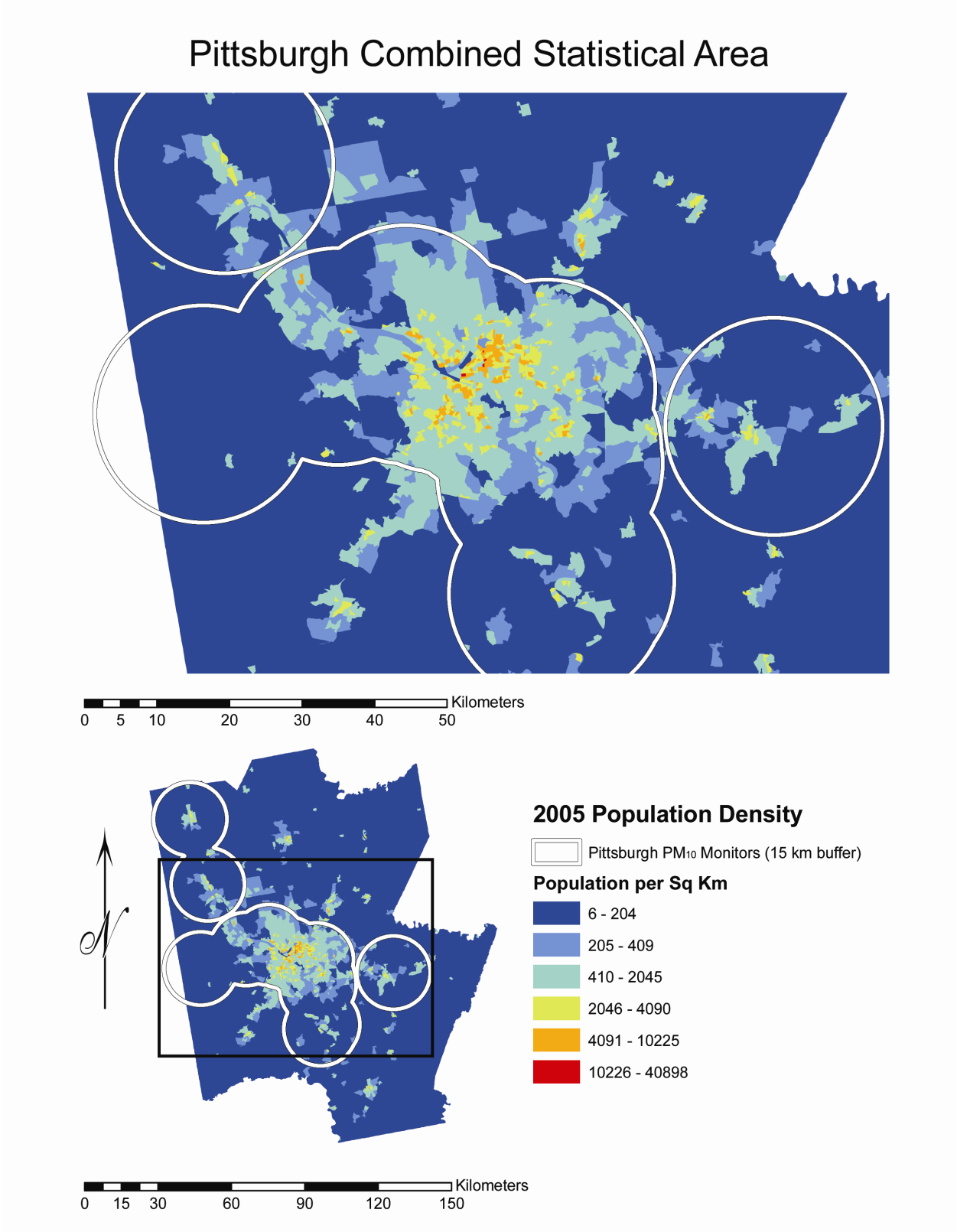


Figure A-24. PM_{10} monitor distribution in comparison with population density, Pittsburgh, PA.

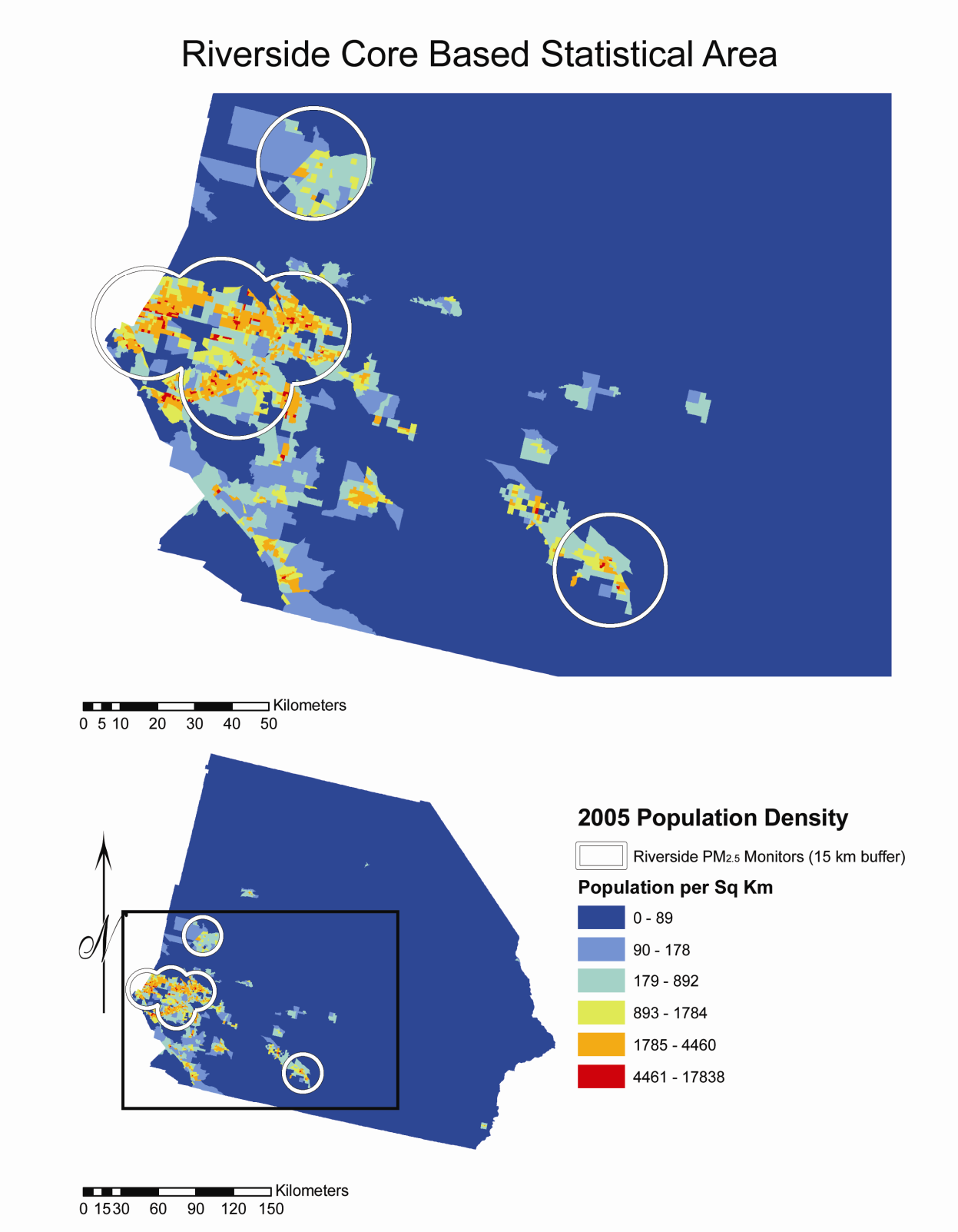


Figure A-25. $PM_{2.5}$ monitor distribution in comparison with population density, Riverside, CA.

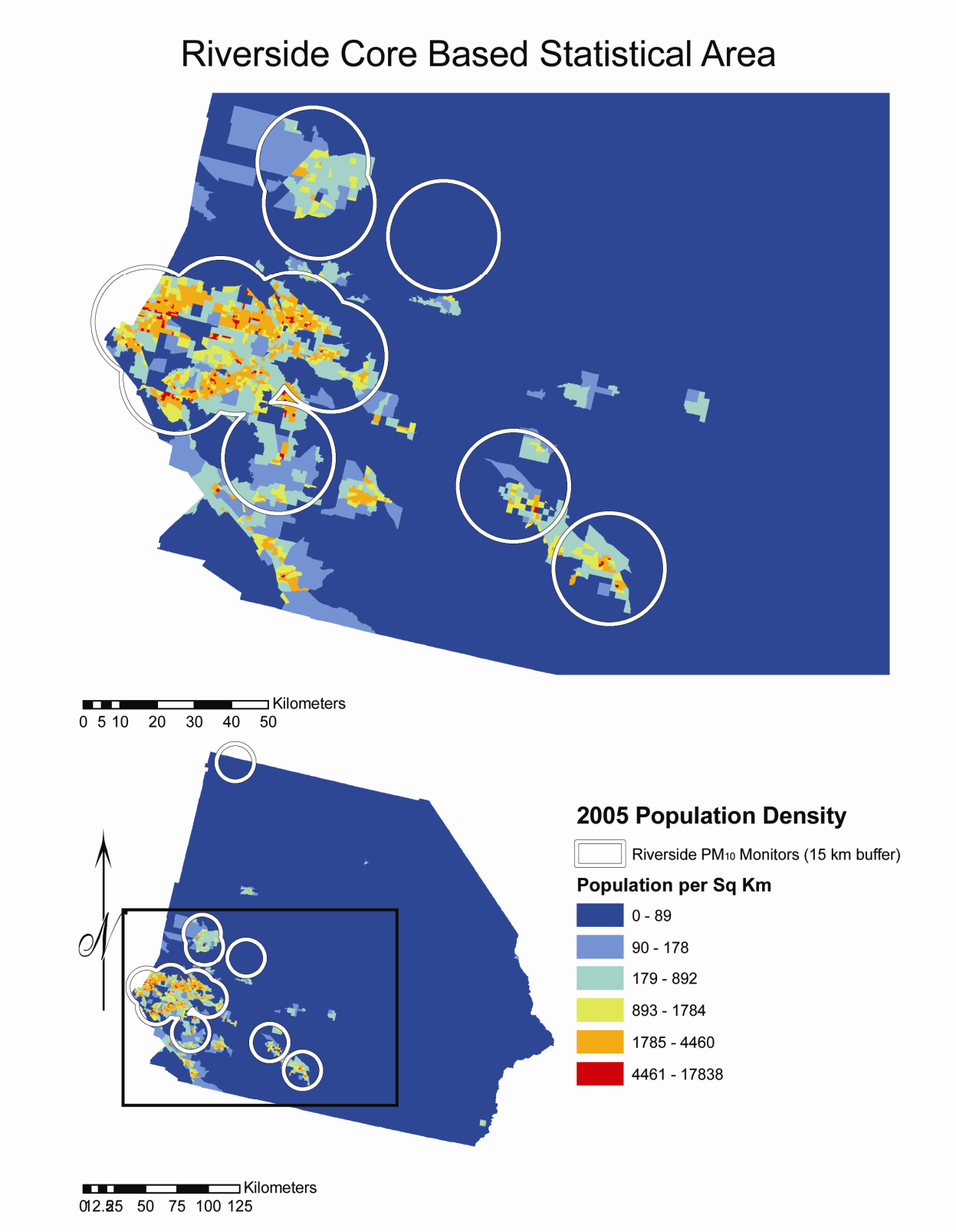


Figure A-26. PM_{10} monitor distribution in comparison with population density, Riverside, CA.

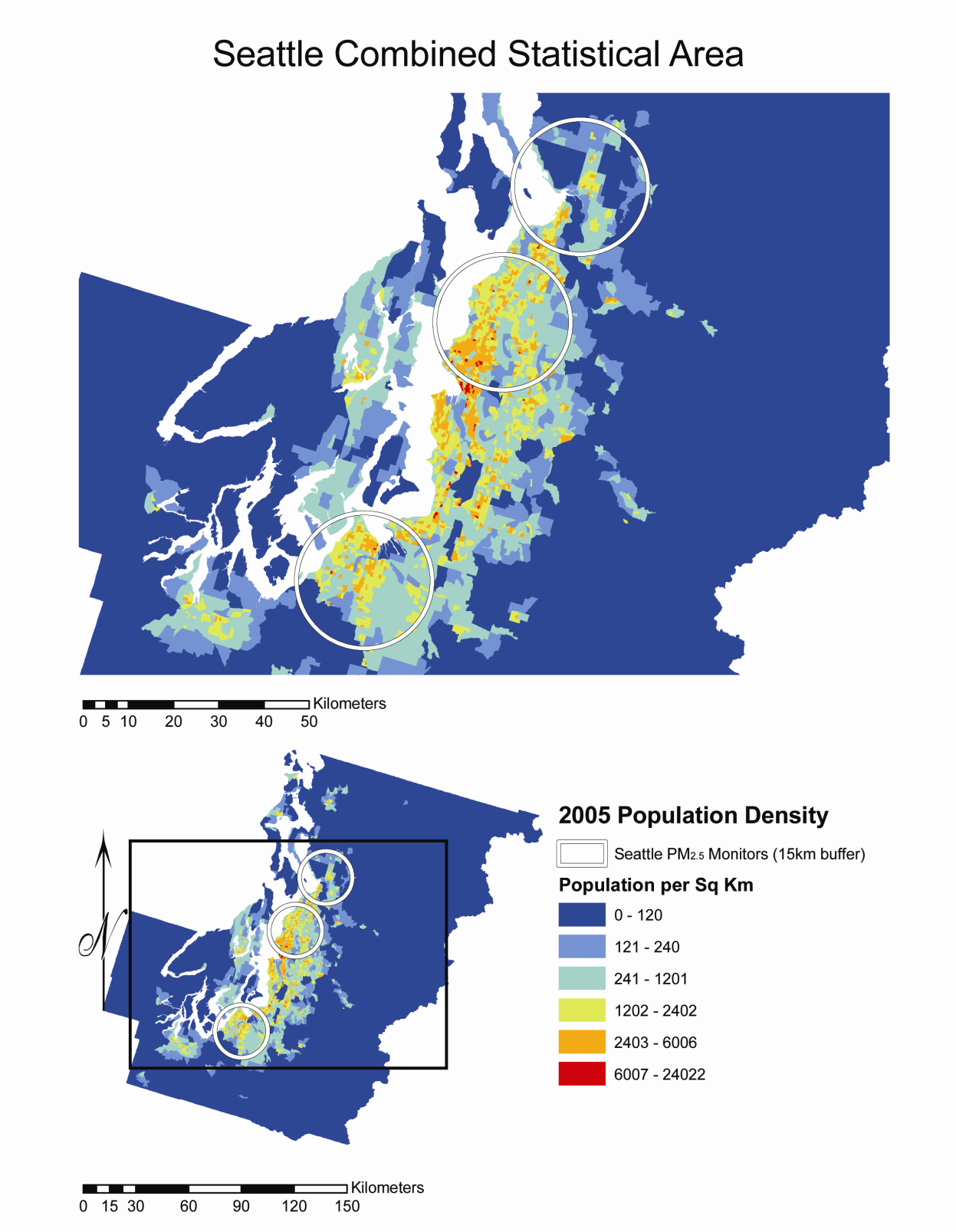


Figure A-27. $PM_{2.5}$ monitor distribution in comparison with population density, Seattle, WA.

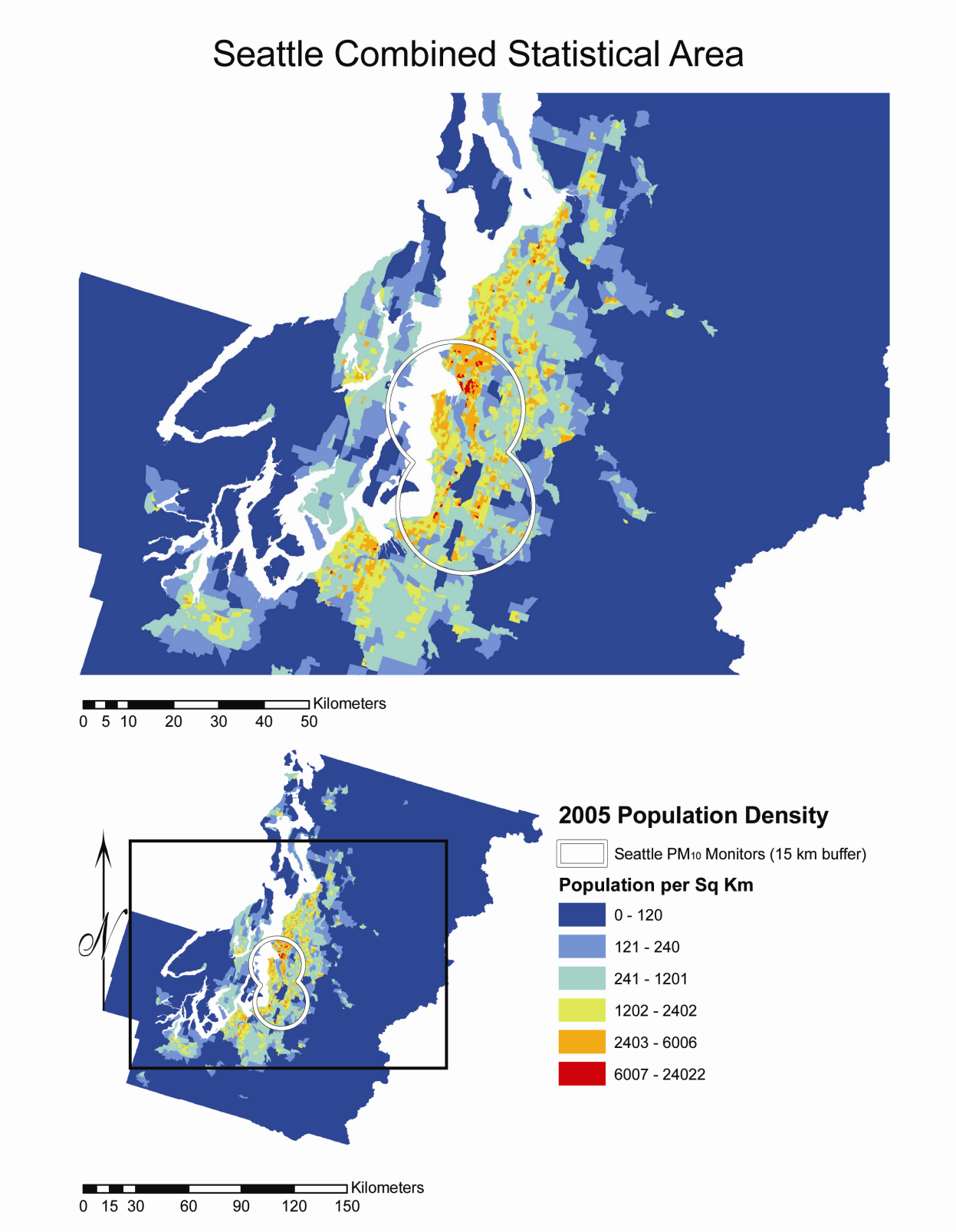


Figure A-28. PM_{10} monitor distribution in comparison with population density, Seattle, WA.

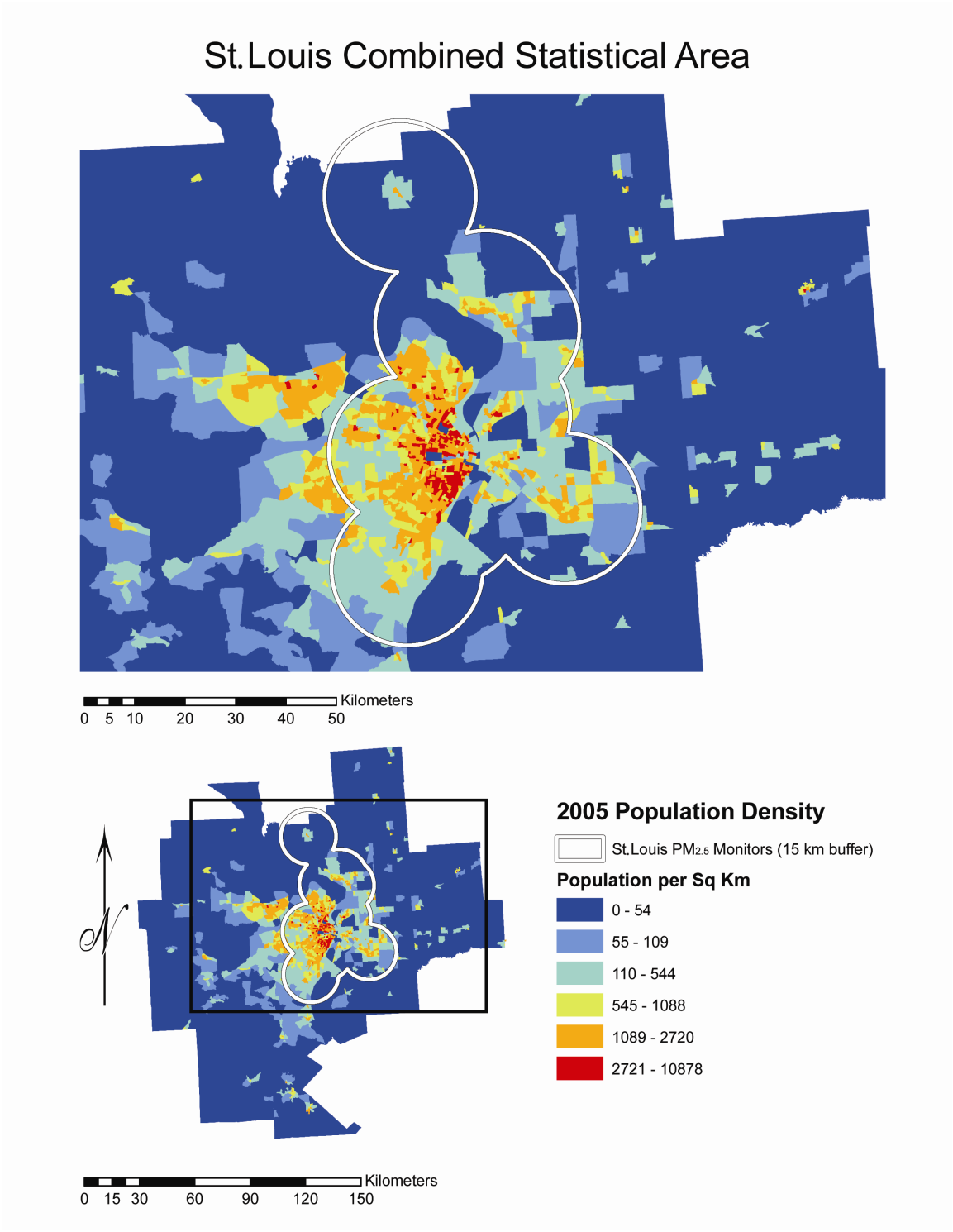


Figure A-29. $PM_{2.5}$ monitor distribution in comparison with population density, St. Louis, MO.

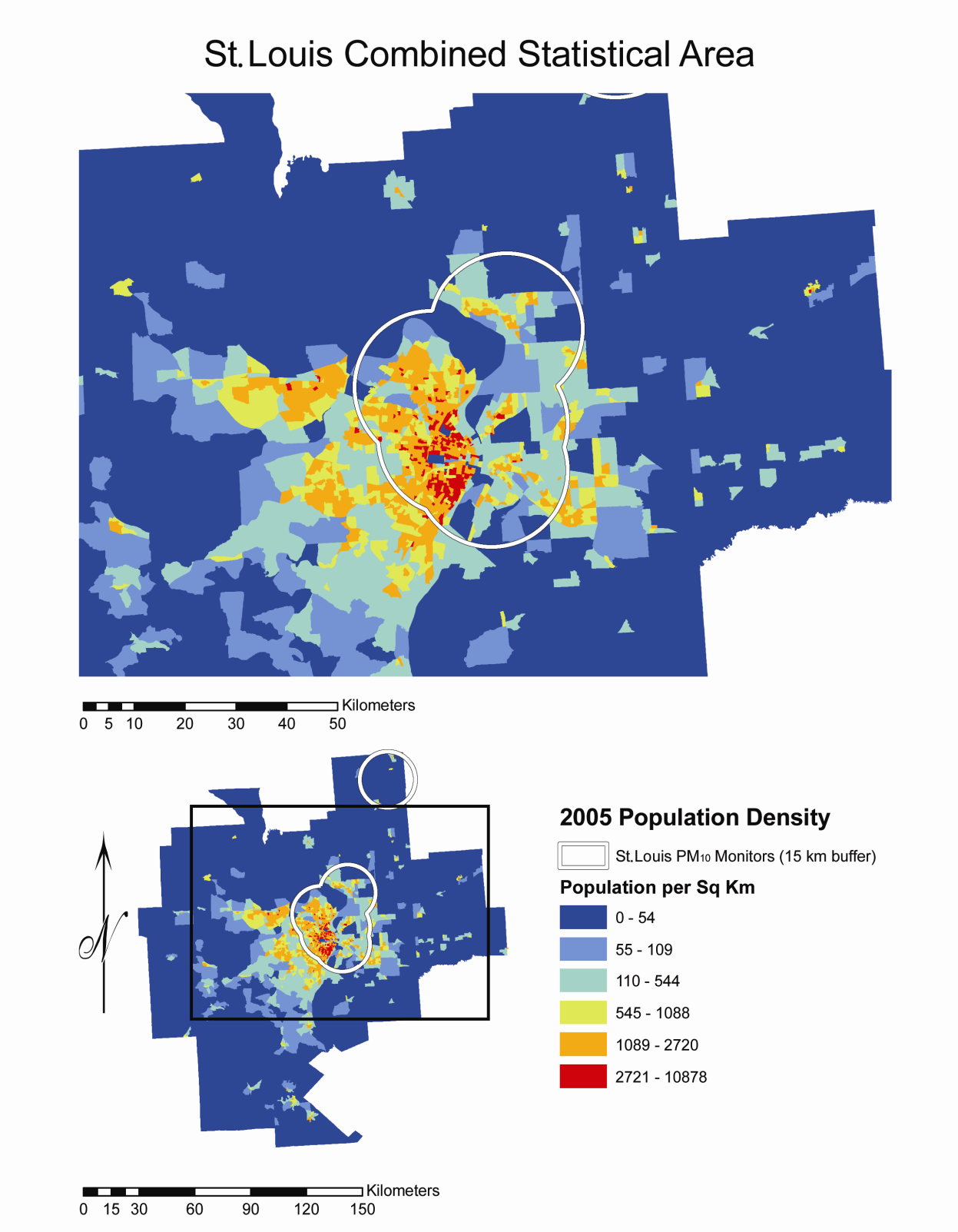


Figure A-30. PM_{10} monitor distribution in comparison with population density, St. Louis, MO.

A.2. Ambient PM Concentration

A.2.1. Speciation Trends Network Site Data

Figure A-31. Three-yr avg of 24-h $PM_{2.5}$ Cu concentrations measured at CSN sites across the U.S., 2005-2007.

Figure A-32. Three-yr avg of 24-h $PM_{2.5}$ Fe concentrations measured at CSN sites across the U.S., 2005-2007

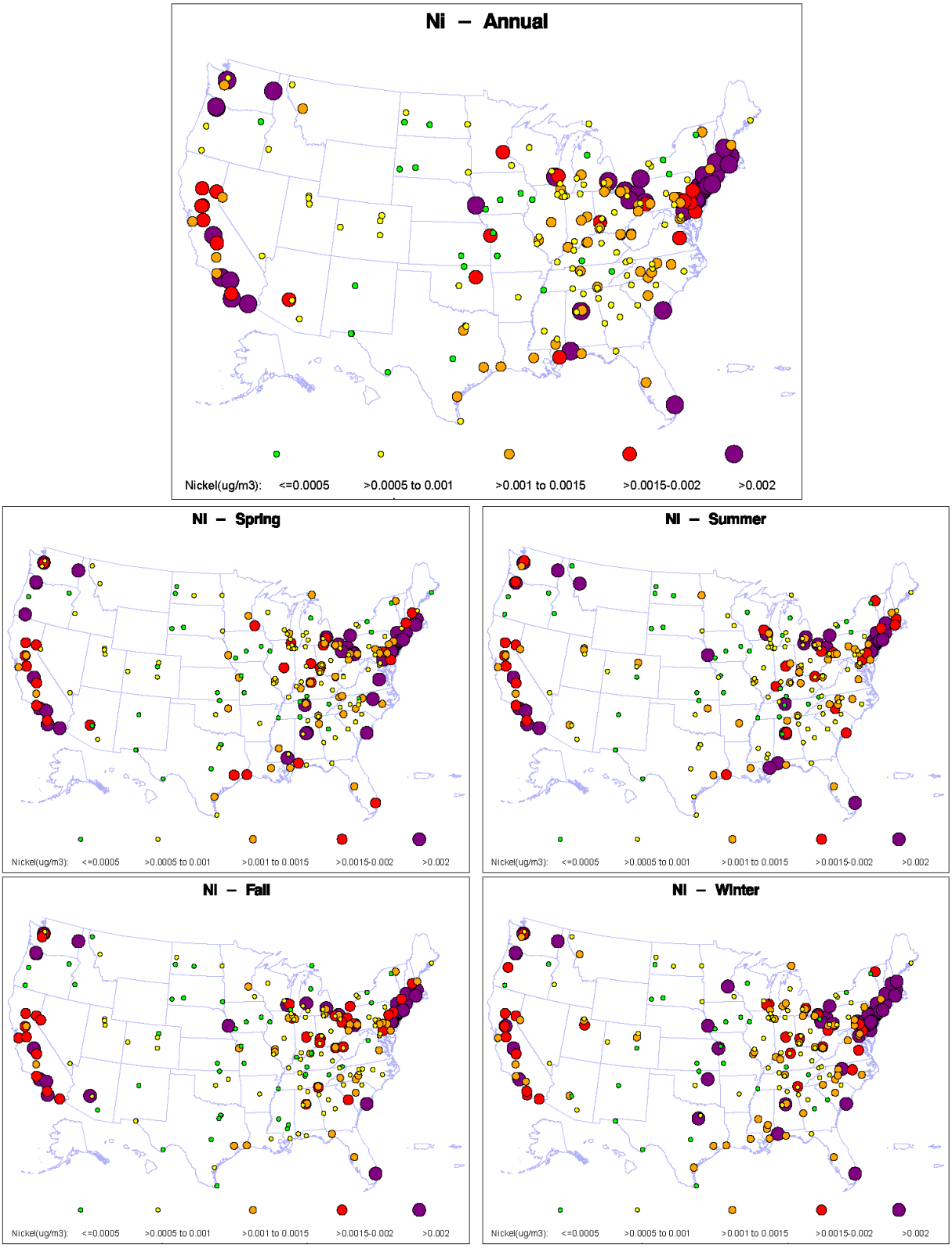


Figure A-33. Three-yr avg of 24-h $PM_{2.5}$ Ni concentrations measured at CSN sites across the U.S., 2005-2007

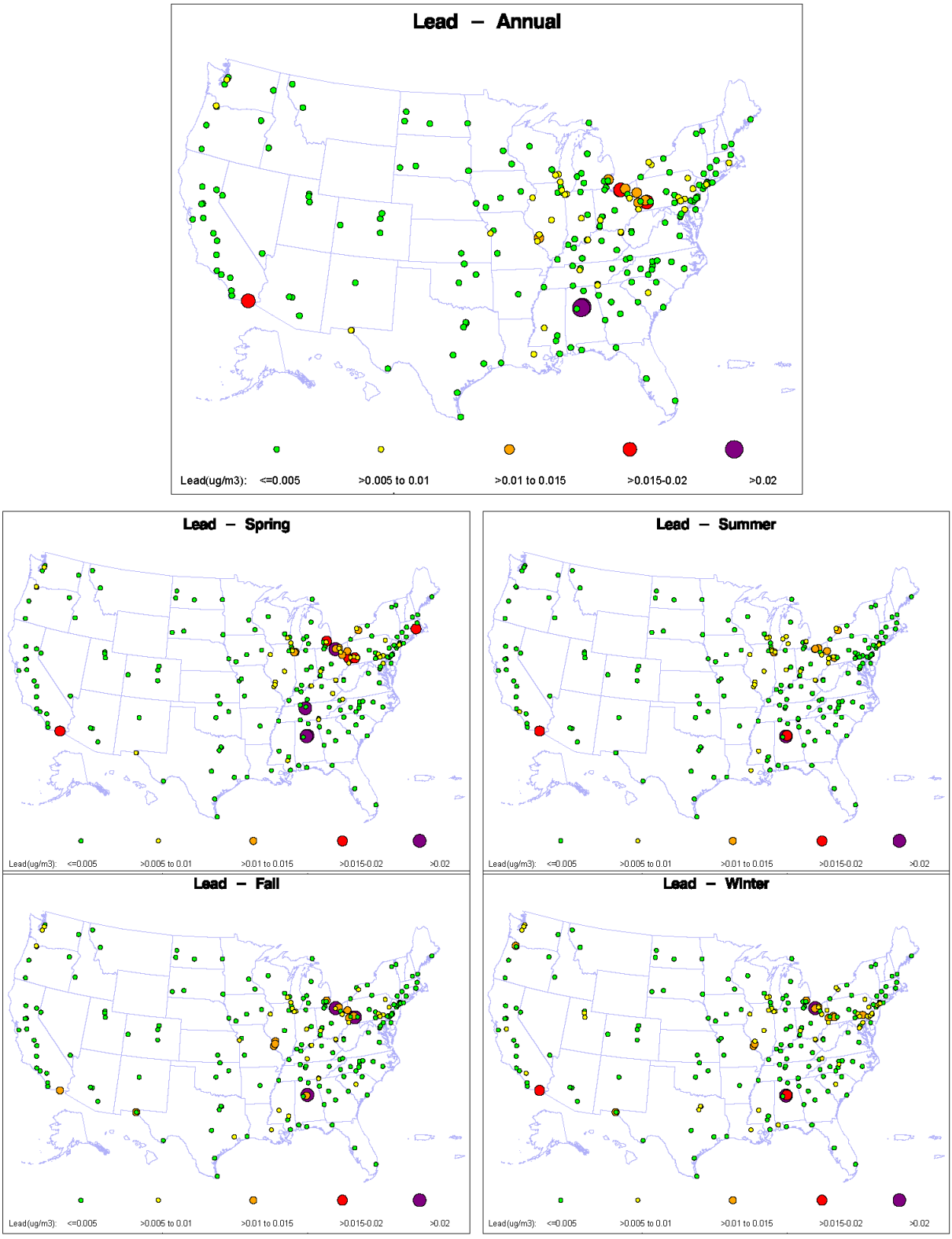


Figure A-34. Three-yr avg of 24-h $PM_{2.5}$ Pb concentrations measured at CSN sites across the U.S., 2005-2007

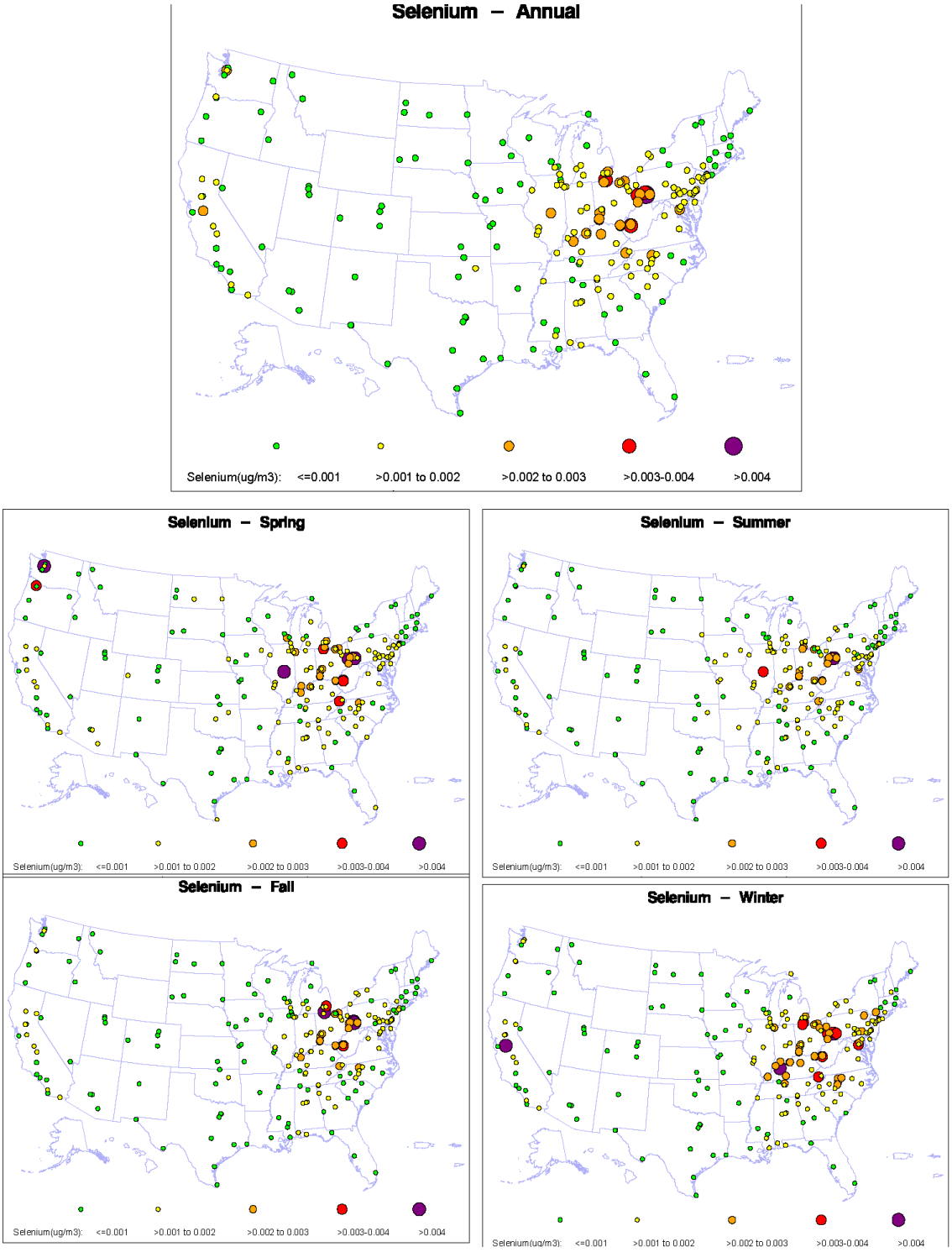


Figure A-35. Three-yr avg of 24-h $PM_{2.5}$ Se concentrations measured at CSN sites across the U.S., 2005-2007

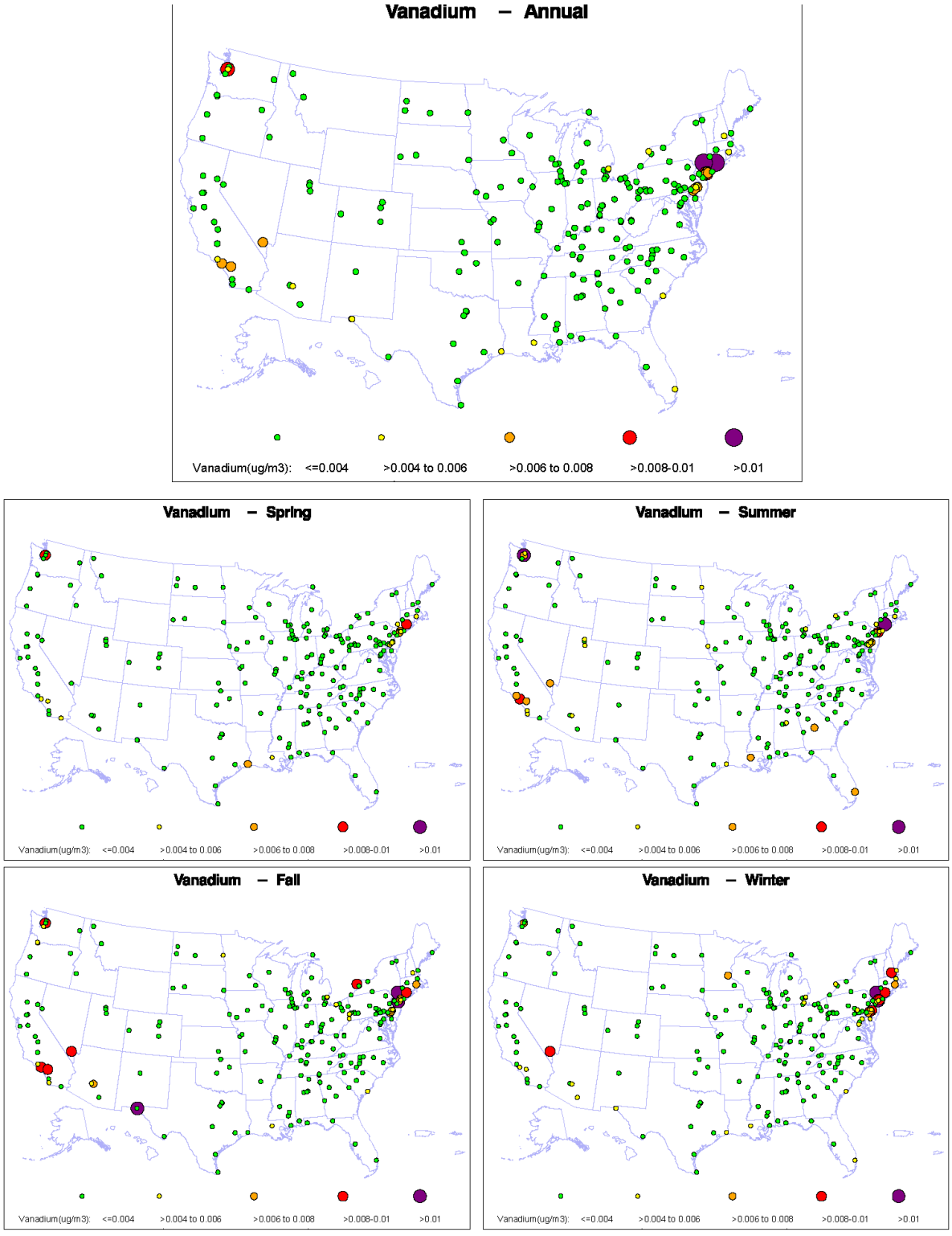


Figure A-36. Three-yr avg of 24-h $PM_{2.5}$ V concentrations measured at CSN sites across the U.S., 2005-2007

A.2.2. Intraurban Variability

The following figures and tables exemplify the intraurban variability among $PM_{2.5}$, $PM_{10-2.5}$ and PM_{10} measurements for select CSAs/CBSAs (2005-2007) including Atlanta, Birmingham, Chicago, Denver, Detroit, Houston, New York City, Philadelphia, Phoenix, Riverside, Seattle and St. Louis. Maps are included to show monitor locations relative to major roadways. Box plots show the median and interquartile range of concentrations with whiskers extending to the 5th and 95th percentiles at each site during (1) winter (December-February); (2) spring (March-May); (3) summer (June-August); and (4) fall (September-November). Tables of inter-sampler comparison statistics and scatter plots of inter-sampler correlation vs. distance illustrate variability present in each area.

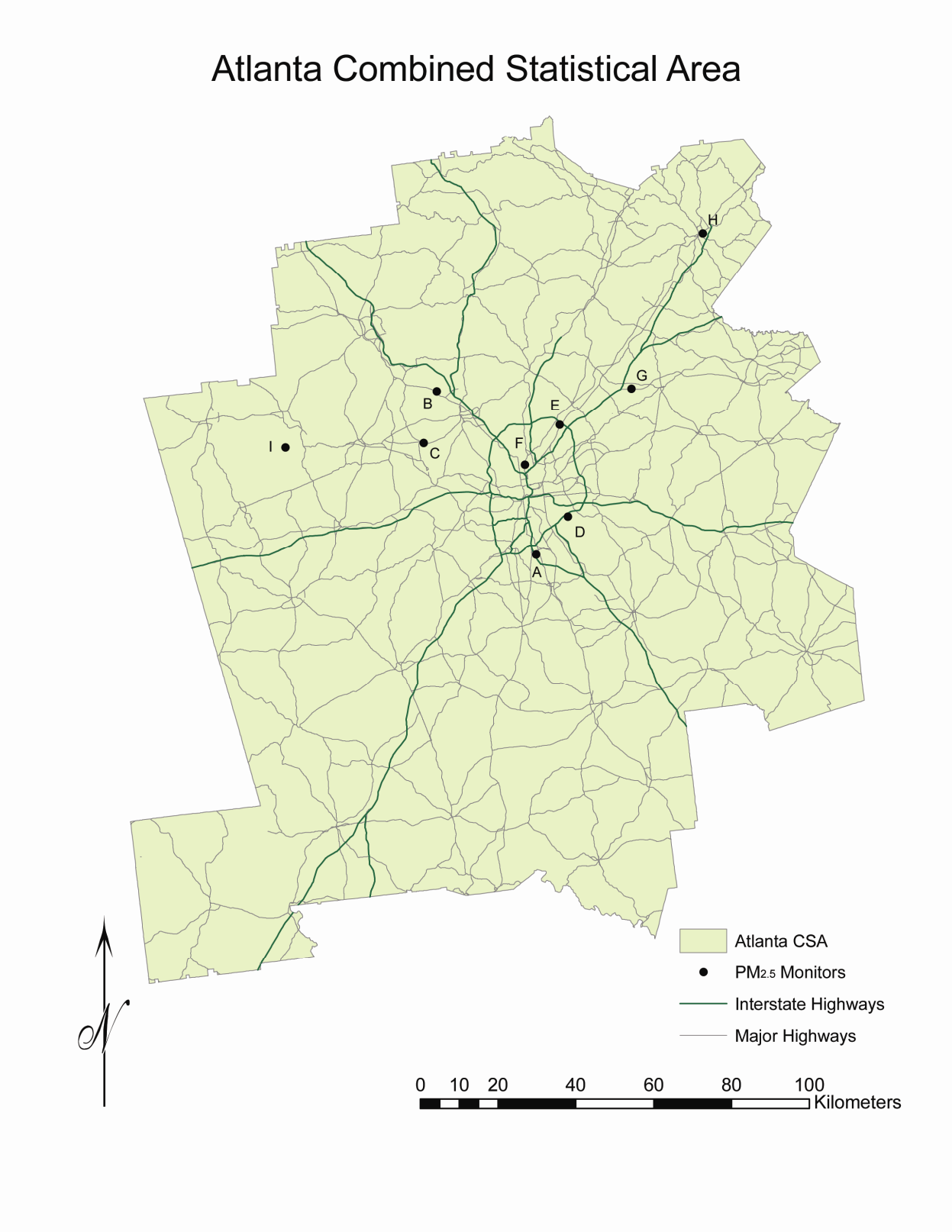


Figure A-37. $PM_{2.5}$ monitor distribution and major highways, Atlanta, GA.

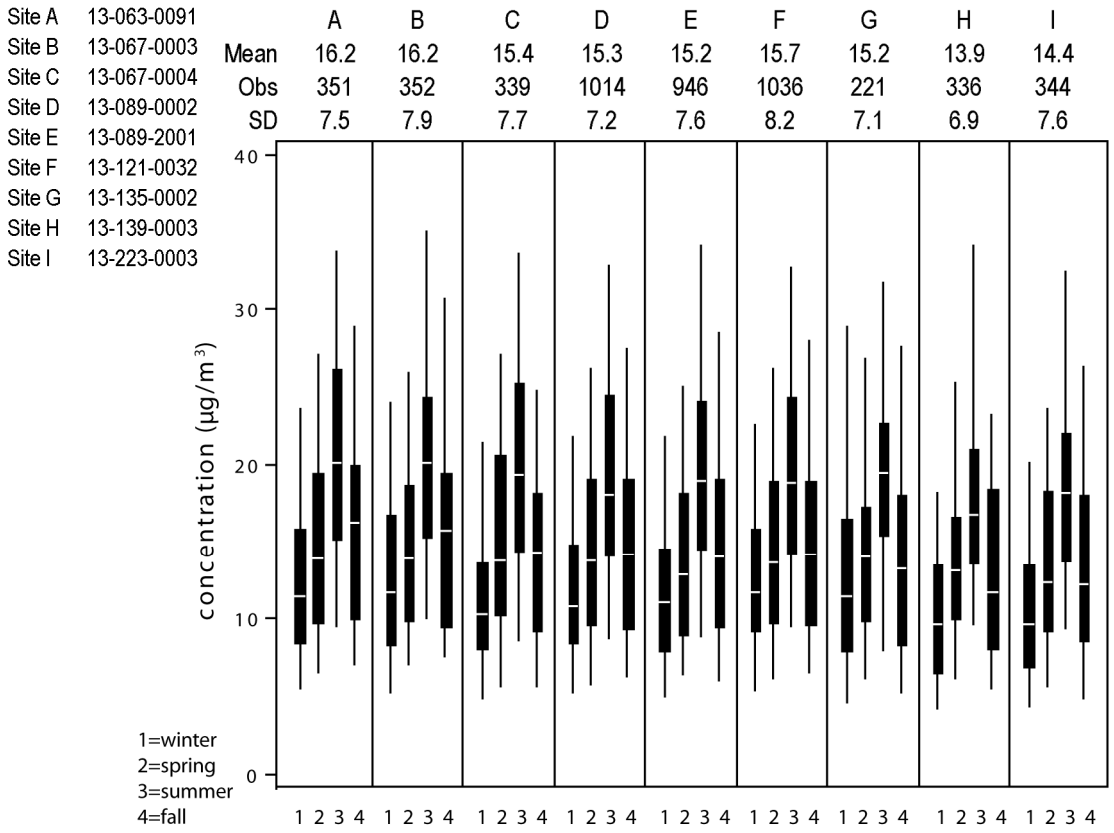


Figure A-38. Box plots illustrating the seasonal distribution of 24-h avg $PM_{2.5}$ concentrations for Atlanta, GA.

Table A-20. Inter-sampler correlation statistics for each pair of $PM_{2.5}$ monitors reporting to AQS for Atlanta, GA.

	A	B	C	D	E	F	G	H	I
A	1.00	0.88	0.87	0.93	0.89	0.91	0.85	0.72	0.85
	(0.0, 0.00)	(5.2, 0.11)	(6.2, 0.12)	(3.9, 0.11)	(5.3, 0.12)	(4.6, 0.11)	(6.9, 0.15)	(8.7, 0.19)	(7.2, 0.15)
	351	330	310	330	315	334	207	319	326
B		1.00	0.96	0.89	0.88	0.91	0.88	0.78	0.88
		(0.0, 0.00)	(4.1, 0.08)	(5.7, 0.12)	(4.6, 0.10)	(3.6, 0.08)	(5.6, 0.13)	(9.0, 0.17)	(6.5, 0.13)
		352	309	327	314	333	205	313	321
C			1.00	0.87	0.86	0.88	0.85	0.79	0.90
			(0.0, 0.00)	(5.2, 0.12)	(5.6, 0.11)	(4.4, 0.10)	(5.8, 0.13)	(7.9, 0.17)	(4.5, 0.11)
			339	315	304	324	193	298	303
D				1.00	0.89	0.80	0.87	0.74	0.82
				(0.0, 0.00)	(4.8, 0.12)	(3.7, 0.11)	(5.8, 0.13)	(8.3, 0.18)	(7.3, 0.15)
				1014	883	978	208	314	322
E					1.00	0.79	0.88	0.74	0.83
					(0.0, 0.00)	(3.8, 0.11)	(5.3, 0.12)	(7.8, 0.17)	(6.4, 0.14)
		LEGEND			946	904	208	305	309
F		**R**				1.00	0.88	0.70	0.84
		(P90, COD)				(0.0, 0.00)	(5.3, 0.12)	(8.5, 0.19)	(6.3, 0.14)
		N				1036	213	321	327
G							1.00	0.73	0.79
							(0.0, 0.00)	(8.8, 0.17)	(7.4, 0.15)
							221	195	198
H								1.00	0.76
								(0.0, 0.00)	(8.7, 0.17)
								336	309
I									1.00
									(0.0, 0.00)
									344

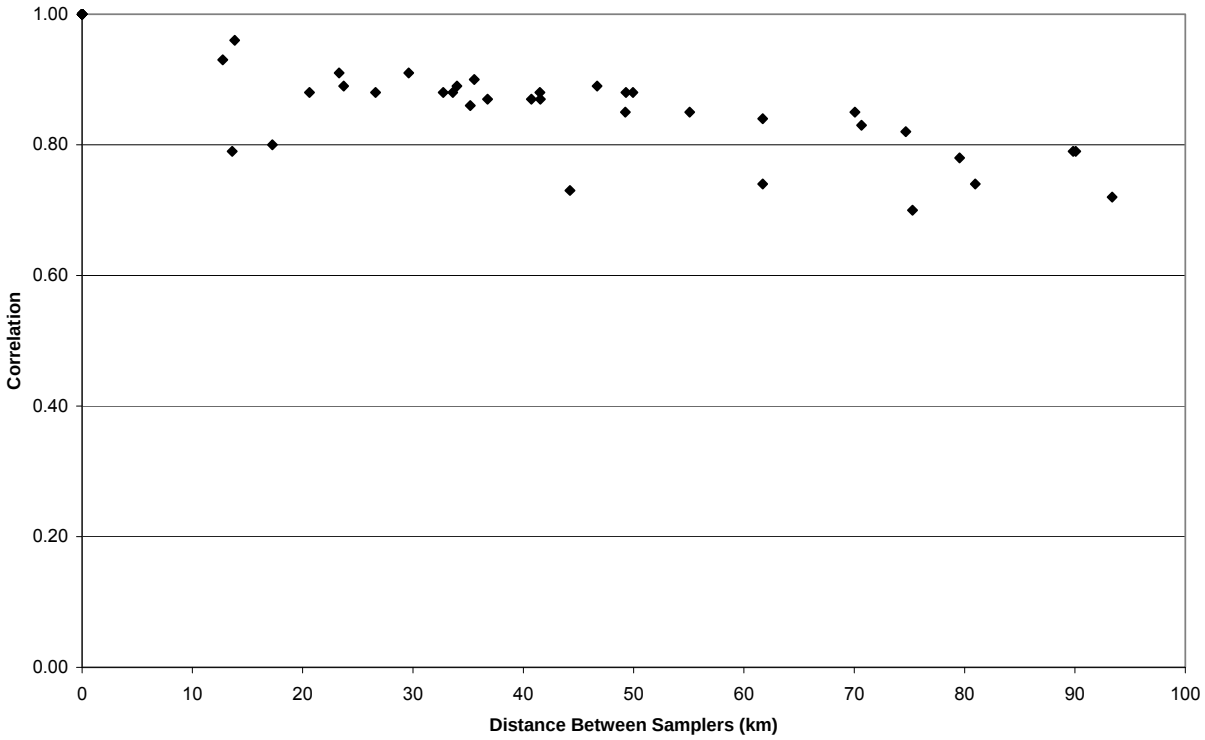


Figure A-39. $PM_{2.5}$ inter-sampler correlations as a function of distance between monitors for Atlanta, GA.

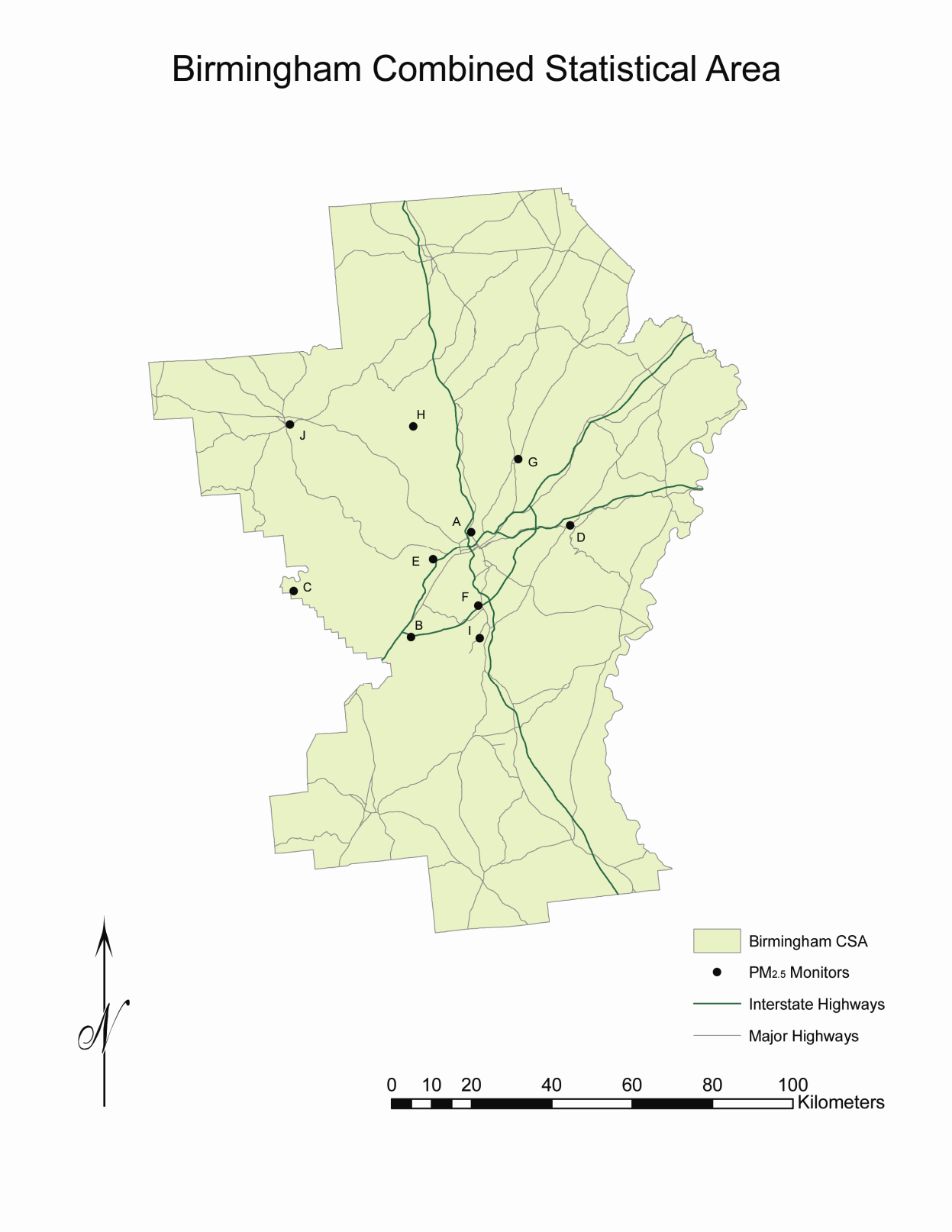


Figure A-40. $PM_{2.5}$ monitor distribution and major highways, Birmingham, AL.

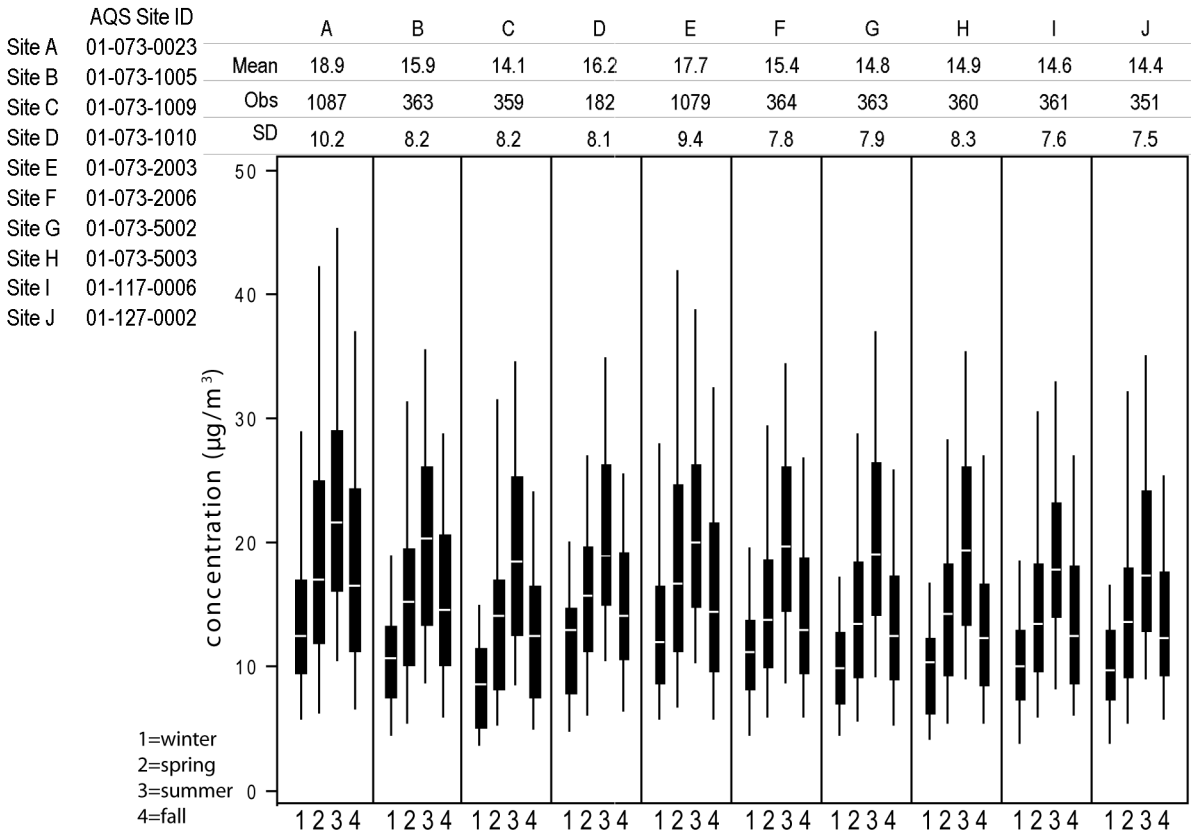


Figure A-41. Box plots illustrating the seasonal distribution of 24-h avg $PM_{2.5}$ concentrations for Birmingham, AL.

Table A-21. Inter-sampler correlation statistics for each pair of $PM_{2.5}$ monitors reporting to AQS for Birmingham, AL.

	A	B	C	D	E	F	G	H	I	J
A	1.00	0.91	0.86	0.91	0.88	0.91	0.87	0.88	0.88	0.84
	(0.0, 0.00)	(10.4, 0.15)	(13.7, 0.21)	(9.7, 0.13)	(8.1, 0.13)	(10.8, 0.15)	(12.6, 0.18)	(11.7, 0.18)	(12.3, 0.18)	(12.5, 0.19)
	1087	360	356	182	1072	361	360	357	358	348
B		1.00	0.93	0.93	0.85	0.96	0.91	0.93	0.93	0.89
		(0.0, 0.00)	(5.3, 0.12)	(4.7, 0.09)	(8.3, 0.15)	(3.6, 0.08)	(5.4, 0.11)	(5.1, 0.11)	(4.9, 0.10)	(6.1, 0.12)
		363	356	181	359	358	360	355	358	348
C			1.00	0.93	0.81	0.93	0.91	0.94	0.90	0.90
			(0.0, 0.00)	(5.9, 0.13)	(10.1, 0.20)	(4.6, 0.12)	(4.3, 0.12)	(4.0, 0.10)	(4.9, 0.12)	(4.9, 0.11)
			359	180	355	354	355	350	353	343
D				1.00	0.88	0.96	0.95	0.95	0.93	0.89
				(0.0, 0.00)	(7.9, 0.12)	(3.6, 0.08)	(3.8, 0.09)	(4.7, 0.10)	(4.7, 0.10)	(6.1, 0.12)
				182	179	179	181	179	180	174
E					1.00	0.87	0.85	0.85	0.86	0.81
					(0.0, 0.00)	(8.1, 0.15)	(8.7, 0.16)	(8.8, 0.17)	(9.2, 0.16)	(10.6, 0.18)
		LEGEND			1079	360	359	356	357	347
F		**R**				1.00	0.95	0.95	0.95	0.90
		(P90, COD)				(0.0, 0.00)	(3.9, 0.09)	(4.1, 0.10)	(3.4, 0.09)	(5.6, 0.11)
		N				364	359	354	357	348
G							1.00	0.96	0.92	0.89
							(0.0, 0.00)	(3.3, 0.08)	(4.5, 0.10)	(4.9, 0.11)
							363	356	359	350
H								1.00	0.91	0.93
								(0.0, 0.00)	(5.0, 0.11)	(4.3, 0.09)
								360	354	344
I									1.00	0.87
									(0.0, 0.00)	(5.8, 0.12)
									361	349
J										1.00
										(0.0, 0.00)
										351

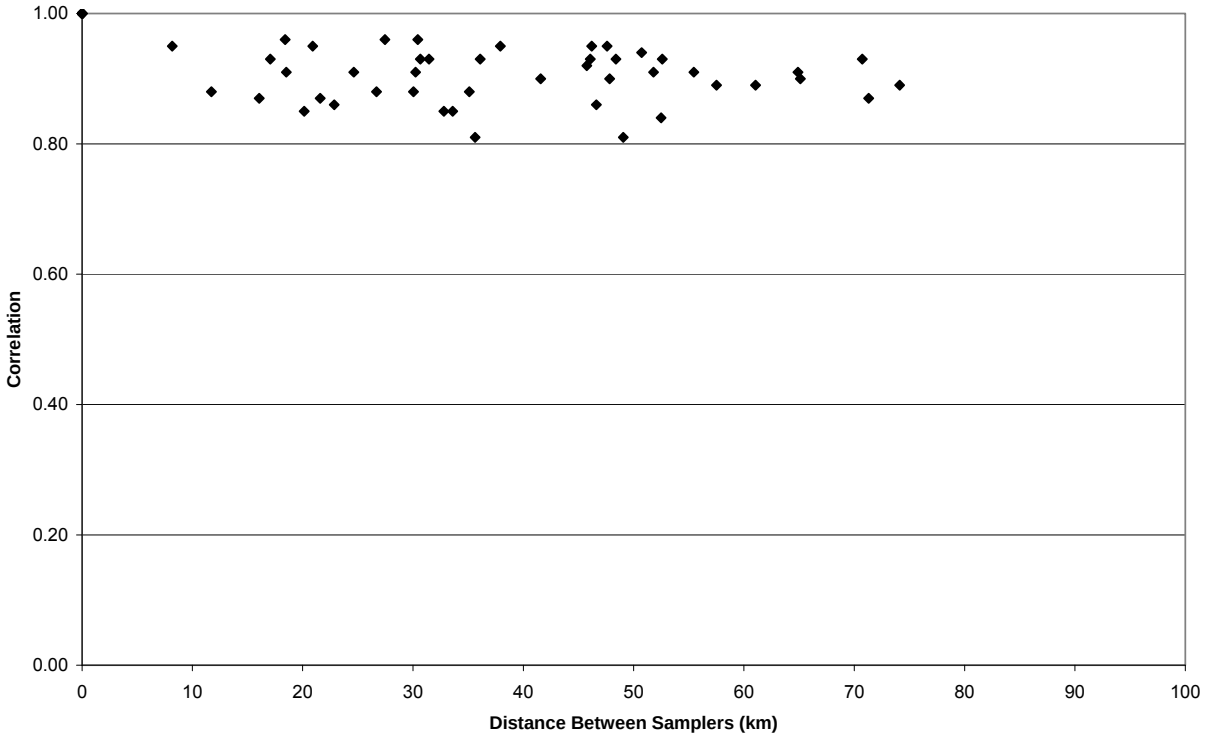


Figure A-42. $PM_{2.5}$ inter-sampler correlations as a function of distance between monitors for Birmingham, AL.

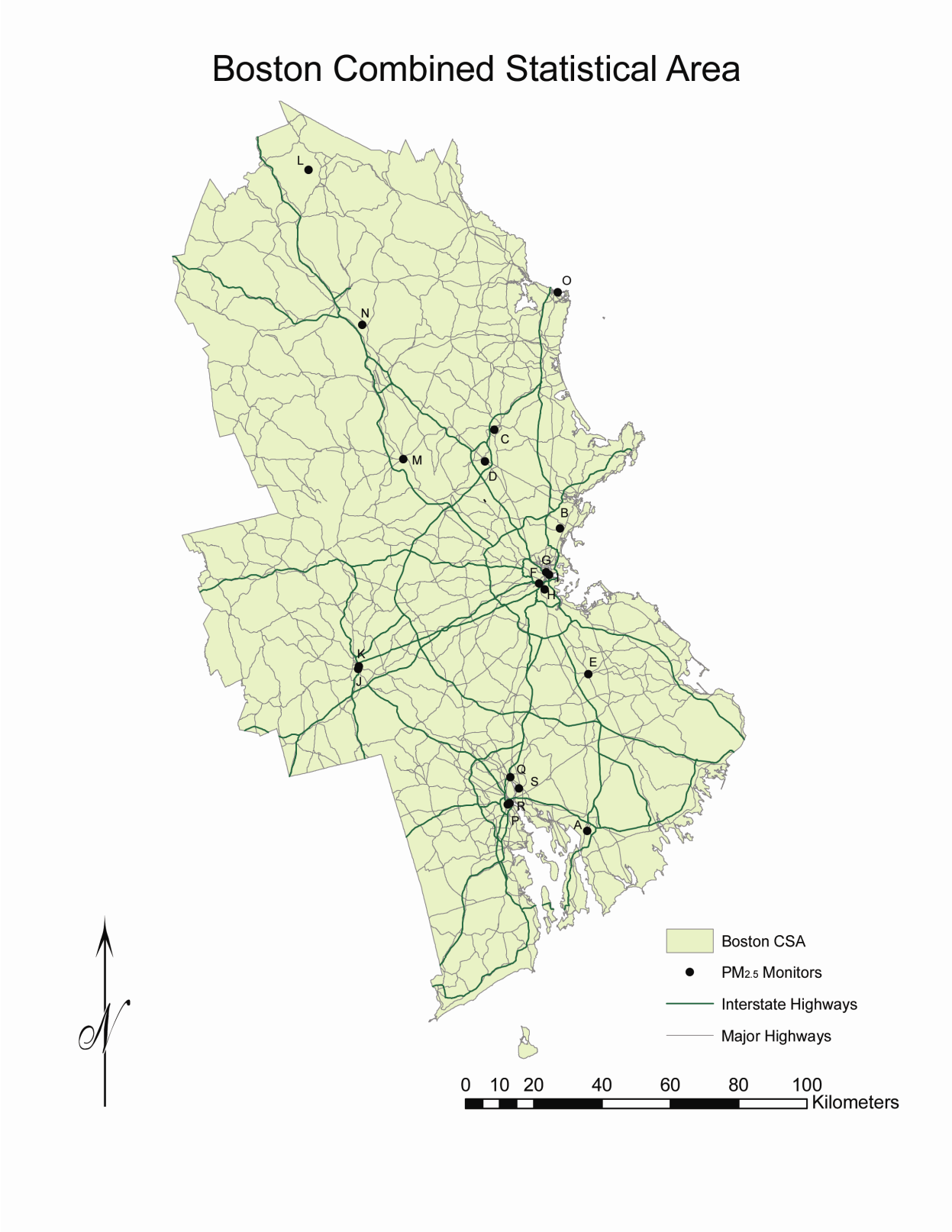


Figure A-43. $PM_{2.5}$ monitor distribution and major highways, Boston, MA.

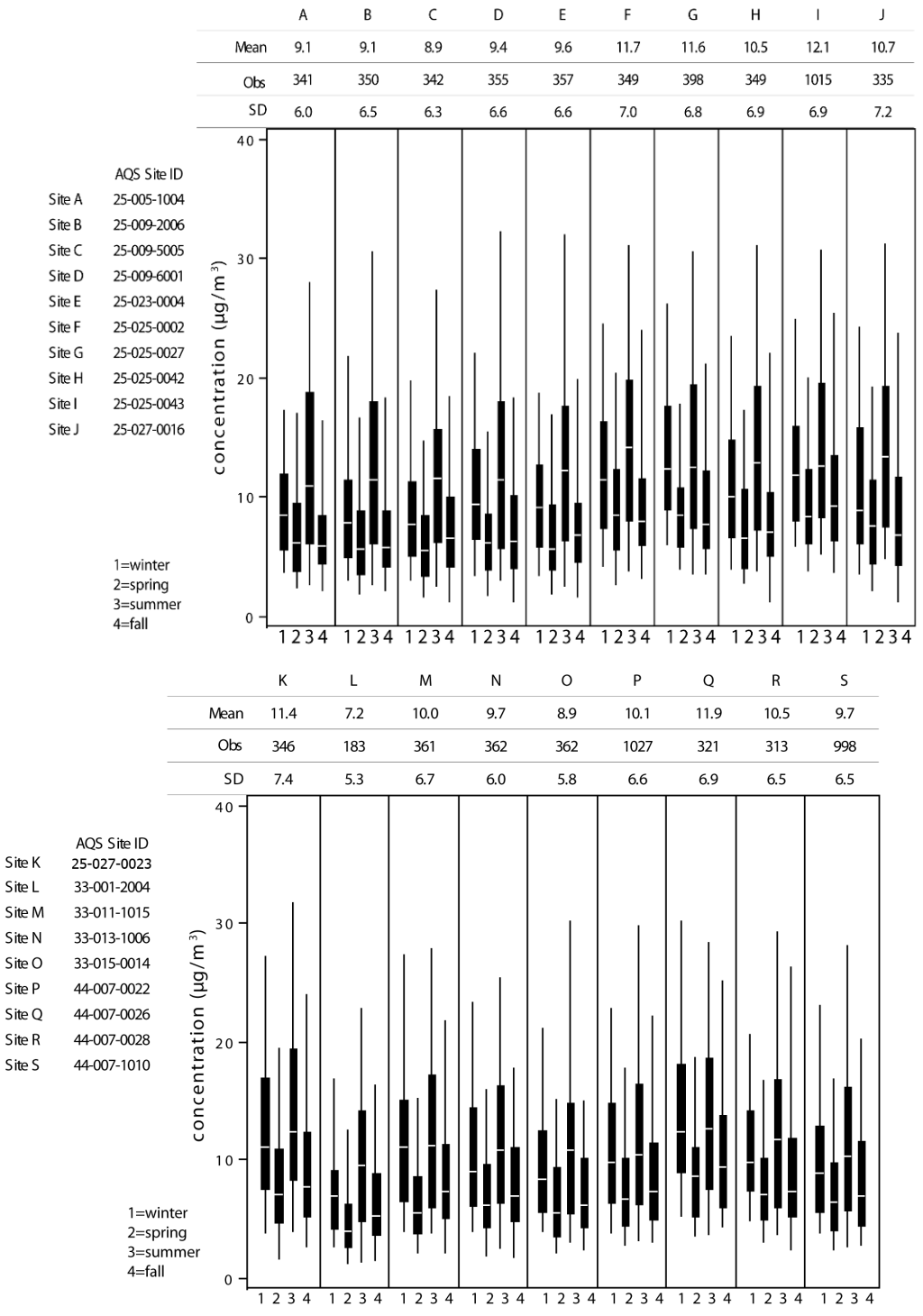


Figure A-44. Box plots illustrating the seasonal distribution of 24-h avg $PM_{2.5}$ concentrations for Boston, MA.

Table A-22. Inter-sampler correlation statistics for each pair of $PM_{2.5}$ monitors reporting to AQS for Boston, MA.

Site	A	B	C	D	E	F	G	H	I	J
A	1.00	0.80	0.77	0.71	0.84	0.79	0.78	0.79	0.79	0.77
	(0.0, 0.00)	(6.6, 0.21)	(6.2, 0.22)	(6.9, 0.23)	(4.8, 0.19)	(8.1, 0.23)	(7.7, 0.24)	(6.8, 0.22)	(7.9, 0.25)	(7.5, 0.24)
	341	326	318	323	329	318	319	325	338	310
B		1.00	0.92	0.87	0.87	0.90	0.90	0.90	0.90	0.85
		(0.0, 0.00)	(4.1, 0.17)	(4.1, 0.18)	(4.7, 0.19)	(6.3, 0.21)	(6.2, 0.23)	(4.9, 0.19)	(7.1, 0.26)	(5.5, 0.21)
		350	328	331	339	326	323	333	343	317
C			1.00	0.90	0.85	0.90	0.89	0.90	0.88	0.86
			(0.0, 0.00)	(3.5, 0.17)	(5.3, 0.21)	(6.3, 0.23)	(6.3, 0.24)	(5.0, 0.20)	(6.8, 0.26)	(6.2, 0.21)
			342	321	331	316	318	326	336	311
D				1.00	0.80	0.88	0.88	0.86	0.86	0.87
				(0.0, 0.00)	(5.6, 0.20)	(5.8, 0.21)	(5.8, 0.22)	(4.6, 0.19)	(7.0, 0.26)	(5.8, 0.19)
				355	336	324	329	332	345	313
E					1.00	0.90	0.90	0.89	0.87	0.87
					(0.0, 0.00)	(5.9, 0.19)	(5.8, 0.21)	(5.0, 0.19)	(6.9, 0.24)	(5.4, 0.20)
					357	330	333	340	350	322
F						1.00	0.94	0.94	0.92	0.92
						(0.0, 0.00)	(3.8, 0.14)	(3.5, 0.15)	(4.5, 0.17)	(5.4, 0.18)
						349	324	324	339	310
G							1.00	0.94	0.94	0.89
							(0.0, 0.00)	(4.0, 0.16)	(4.3, 0.15)	(5.7, 0.20)
							398	325	338	308
H								1.00	0.93	0.89
								(0.0, 0.00)	(4.7, 0.19)	(5.0, 0.17)
								349	342	318
I									1.00	0.86
									(0.0, 0.00)	(6.9, 0.23)
									1015	330
J										1.00
										(0.0, 0.00)
										335

LEGEND
Pearson R
(P90, COD)
n

Site	K	L	M	N	O	P	Q	R	S
A	0.77	0.61	0.71	0.68	0.73	0.87	0.81	0.85	0.86
	(8.1, 0.23)	(8.3, 0.29)	(8.0, 0.23)	(7.9, 0.23)	(7.0, 0.22)	(5.3, 0.18)	(7.2, 0.23)	(5.6, 0.20)	(5.2, 0.18)
	320	173	324	334	331	326	292	285	306
B	0.86	0.80	0.87	0.83	0.88	0.86	0.80	0.85	0.85
	(6.6, 0.21)	(6.2, 0.23)	(5.3, 0.19)	(6.0, 0.21)	(4.7, 0.18)	(5.6, 0.19)	(7.9, 0.26)	(5.7, 0.21)	(6.0, 0.19)
	329	175	331	341	336	335	300	288	314
C	0.86	0.89	0.93	0.90	0.93	0.83	0.79	0.81	0.82
	(6.9, 0.21)	(4.8, 0.23)	(4.4, 0.17)	(4.6, 0.19)	(3.8, 0.18)	(5.9, 0.21)	(7.8, 0.26)	(6.2, 0.23)	(6.0, 0.21)
	321	173	323	335	328	329	290	281	309
D	0.88	0.79	0.91	0.85	0.86	0.80	0.75	0.79	0.80
	(6.4, 0.19)	(5.7, 0.25)	(3.5, 0.16)	(4.7, 0.19)	(4.2, 0.18)	(6.2, 0.20)	(7.8, 0.25)	(6.2, 0.21)	(5.8, 0.20)
	325	174	329	339	334	342	300	287	321
E	0.87	0.72	0.83	0.79	0.84	0.91	0.86	0.88	0.91
	(6.3, 0.20)	(8.3, 0.27)	(5.8, 0.17)	(6.3, 0.20)	(4.8, 0.18)	(4.5, 0.17)	(6.3, 0.22)	(4.9, 0.18)	(3.9, 0.17)
	333	179	338	347	343	343	306	295	324
F	0.91	0.78	0.90	0.85	0.85	0.89	0.86	0.88	0.89
	(4.7, 0.17)	(9.6, 0.33)	(5.3, 0.18)	(6.4, 0.20)	(7.5, 0.22)	(5.2, 0.16)	(6.0, 0.16)	(4.9, 0.16)	(5.5, 0.17)
	323	168	323	334	330	336	295	281	316
G	0.90	0.77	0.90	0.85	0.87	0.88	0.86	0.87	0.88
	(5.0, 0.19)	(9.0, 0.33)	(5.3, 0.19)	(6.3, 0.20)	(7.0, 0.22)	(5.5, 0.17)	(5.3, 0.17)	(5.2, 0.17)	(5.7, 0.19)
	320	172	326	335	329	383	296	282	356
H	0.90	0.75	0.88	0.83	0.84	0.89	0.86	0.87	0.88
	(4.4, 0.17)	(9.4, 0.30)	(4.9, 0.18)	(5.6, 0.21)	(6.8, 0.21)	(4.5, 0.16)	(6.0, 0.19)	(4.5, 0.16)	(5.1, 0.17)
	327	175	332	341	336	335	299	289	314
I	0.87	0.75	0.86	0.82	0.83	0.88	0.84	0.85	0.87
	(6.1, 0.20)	(10.0, 0.36)	(6.7, 0.22)	(7.2, 0.23)	(8.2, 0.25)	(6.1, 0.20)	(6.0, 0.16)	(6.0, 0.18)	(6.3, 0.21)
	341	181	352	356	357	957	314	306	936
J	0.95	0.73	0.87	0.84	0.80	0.90	0.86	0.87	0.88
	(3.0, 0.14)	(9.2, 0.28)	(5.2, 0.18)	(5.9, 0.20)	(7.5, 0.22)	(5.0, 0.17)	(5.9, 0.20)	(5.3, 0.17)	(5.2, 0.18)
	316	167	314	326	323	321	283	272	302
K	1.00	0.71	0.88	0.85	0.81	0.89	0.86	0.87	0.88
	(0.0, 0.00)	(10.3, 0.31)	(6.0, 0.16)	(6.5, 0.19)	(8.2, 0.22)	(5.2, 0.16)	(5.8, 0.18)	(5.5, 0.16)	(5.5, 0.18)
	346	170	326	337	332	331	296	286	313
L		1.00	0.89	0.91	0.90	0.68	0.63	0.72	0.69
		(0.0, 0.00)	(6.7, 0.24)	(5.9, 0.23)	(4.8, 0.21)	(10.0, 0.29)	(12.1, 0.35)	(9.1, 0.30)	(9.8, 0.29)
		183	176	181	177	181	153	149	164
M			1.00	0.94	0.90	0.83	0.81	0.82	0.84
			(0.0, 0.00)	(3.8, 0.13)	(4.6, 0.16)	(5.5, 0.16)	(7.4, 0.20)	(5.8, 0.17)	(5.1, 0.16)
			361	341	336	345	300	288	326
N				1.00	0.90	0.77	0.75	0.78	0.78
				(0.0, 0.00)	(4.4, 0.17)	(6.7, 0.19)	(8.1, 0.22)	(6.4, 0.20)	(6.2, 0.19)
				362	346	347	309	297	327
O					1.00	0.80	0.75	0.79	0.80
					(0.0, 0.00)	(5.8, 0.19)	(8.8, 0.25)	(6.8, 0.21)	(6.0, 0.19)
					362	348	304	292	330
P						1.00	0.95	0.97	0.97
						(0.0, 0.00)	(3.6, 0.14)	(2.0, 0.09)	(2.1, 0.08)

LEGEND
Pearson R
(P90, COD)
n

Site	K	L	M	N	O	P	Q	R	S
						1027	307	299	943
Q							1.00	0.92	0.94
							(0.0, 0.00)	(3.1, 0.13)	(4.0, 0.16)
							321	268	290
R								1.00	0.94
								(0.0, 0.00)	(2.7, 0.12)
								313	280
S									1.00
									(0.0, 0.00)
									998

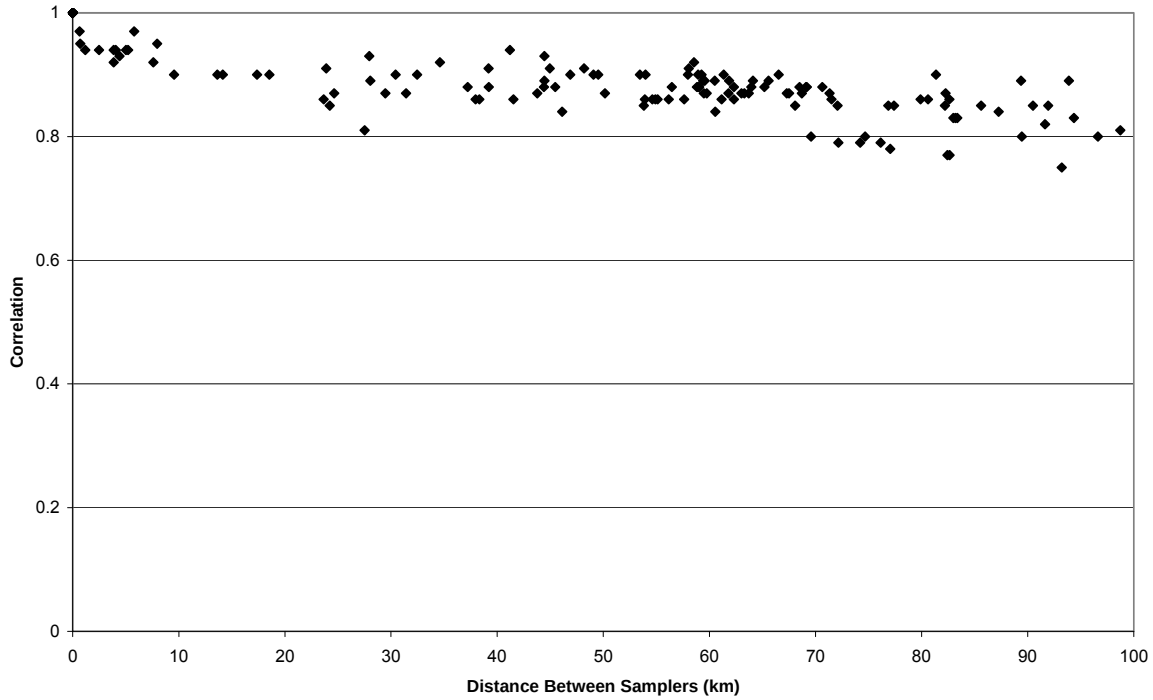


Figure A-45. $PM_{2.5}$ inter-sampler correlations as a function of distance between monitors for Boston, MA.

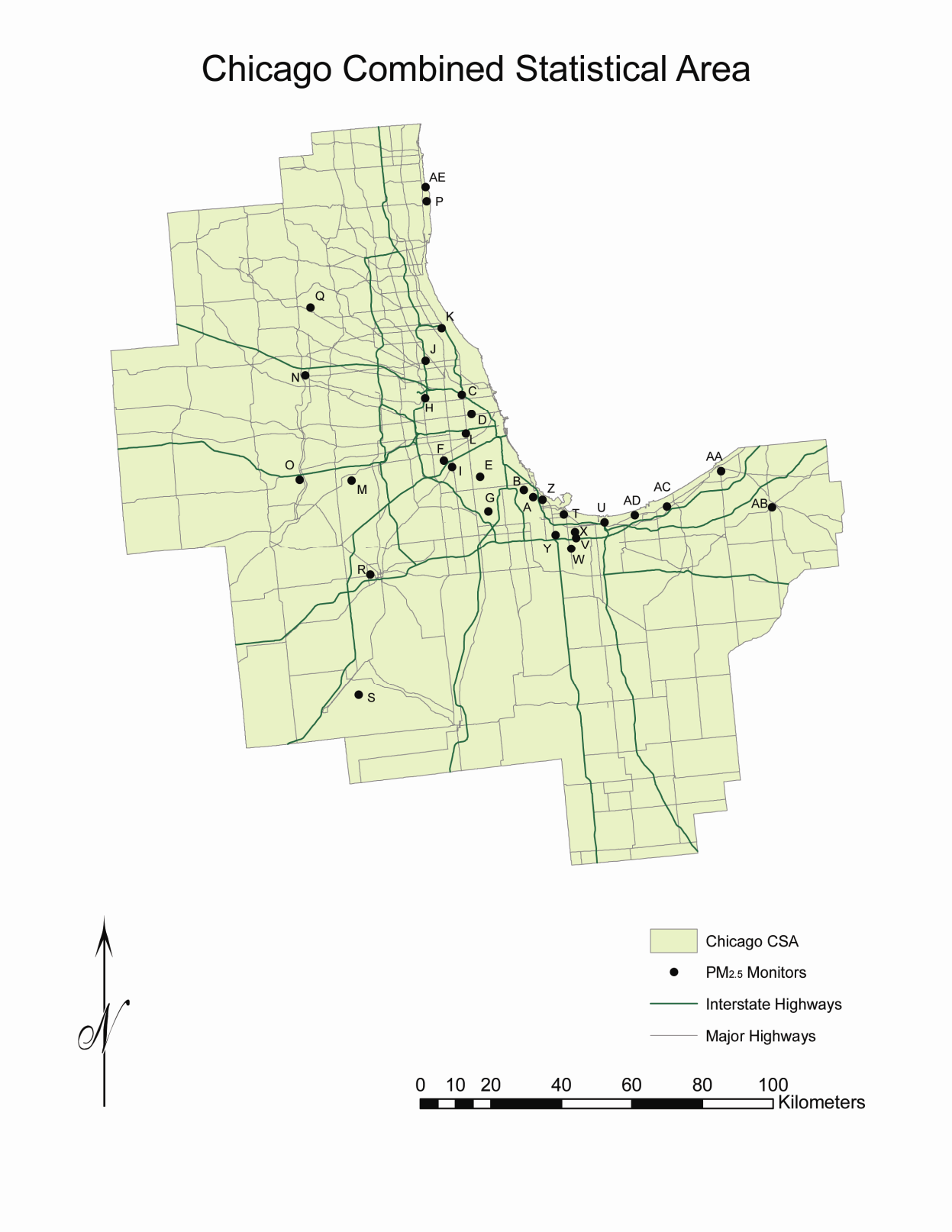
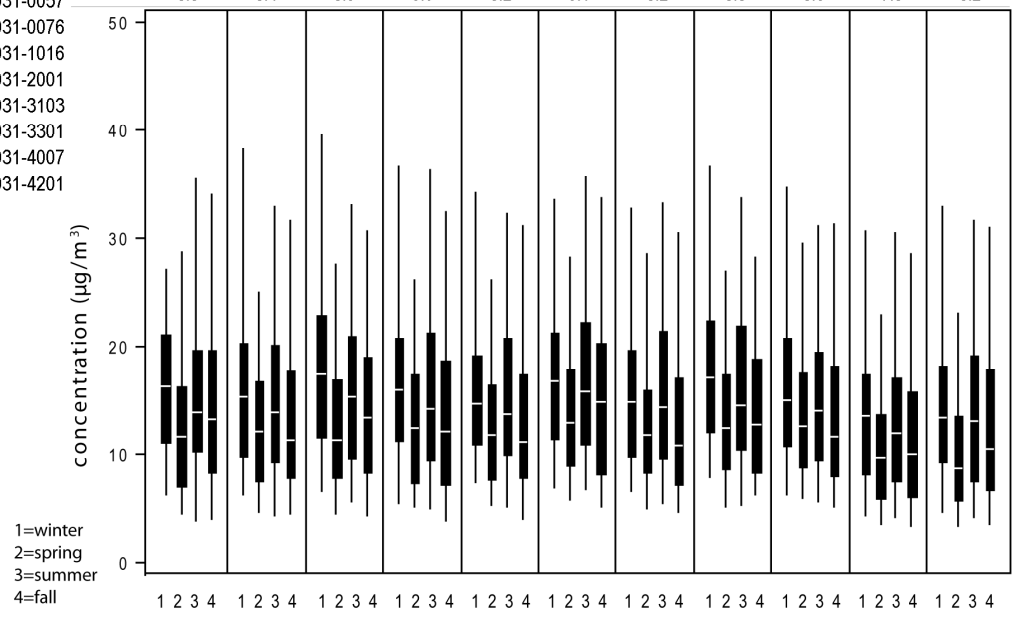
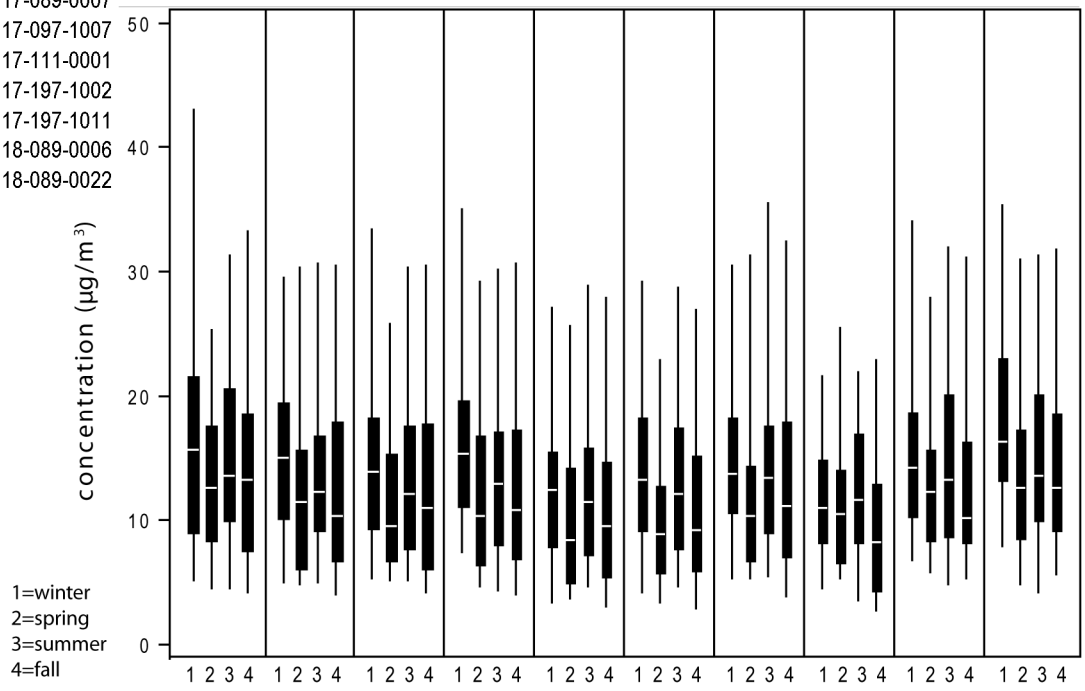


Figure A-46. $PM_{2.5}$ monitor distribution and major highways, Chicago, IL.

	AQS Site ID	A	B	C	D	E	F	G	H	I	J	K
Site A	17-031-0022	Mean	15.3	14.7	15.6	15.1	14.8	16.4	14.6	15.9	15.2	12.6	13.2
Site B	17-031-0050	Obs	178	343	984	333	351	345	350	335	361	356	361
Site C	17-031-0052	SD	8.8	8.4	8.9	9.0	8.2	9.1	8.2	8.5	8.3	7.8	8.2
Site D	17-031-0057												
Site E	17-031-0076												
Site F	17-031-1016												
Site G	17-031-2001												
Site H	17-031-3103												
Site I	17-031-3301												
Site J	17-031-4007												
Site K	17-031-4201												



	AQS Site ID	L	M	N	O	P	Q	R	S	T	U
Site L	17-031-6005	Mean	15.1	14.0	13.5	14.3	12.1	12.3	14.0	11.7	14.4	15.6
Site M	17-043-4002	Obs	331	179	176	174	181	347	175	164	330	351
Site N	17-089-0003	SD	8.7	8.5	8.5	8.9	8.2	7.5	8.5	7.2	7.7	8.2
Site O	17-089-0007											
Site P	17-097-1007											
Site Q	17-111-0001											
Site R	17-197-1002											
Site S	17-197-1011											
Site T	18-089-0006											
Site U	18-089-0022											



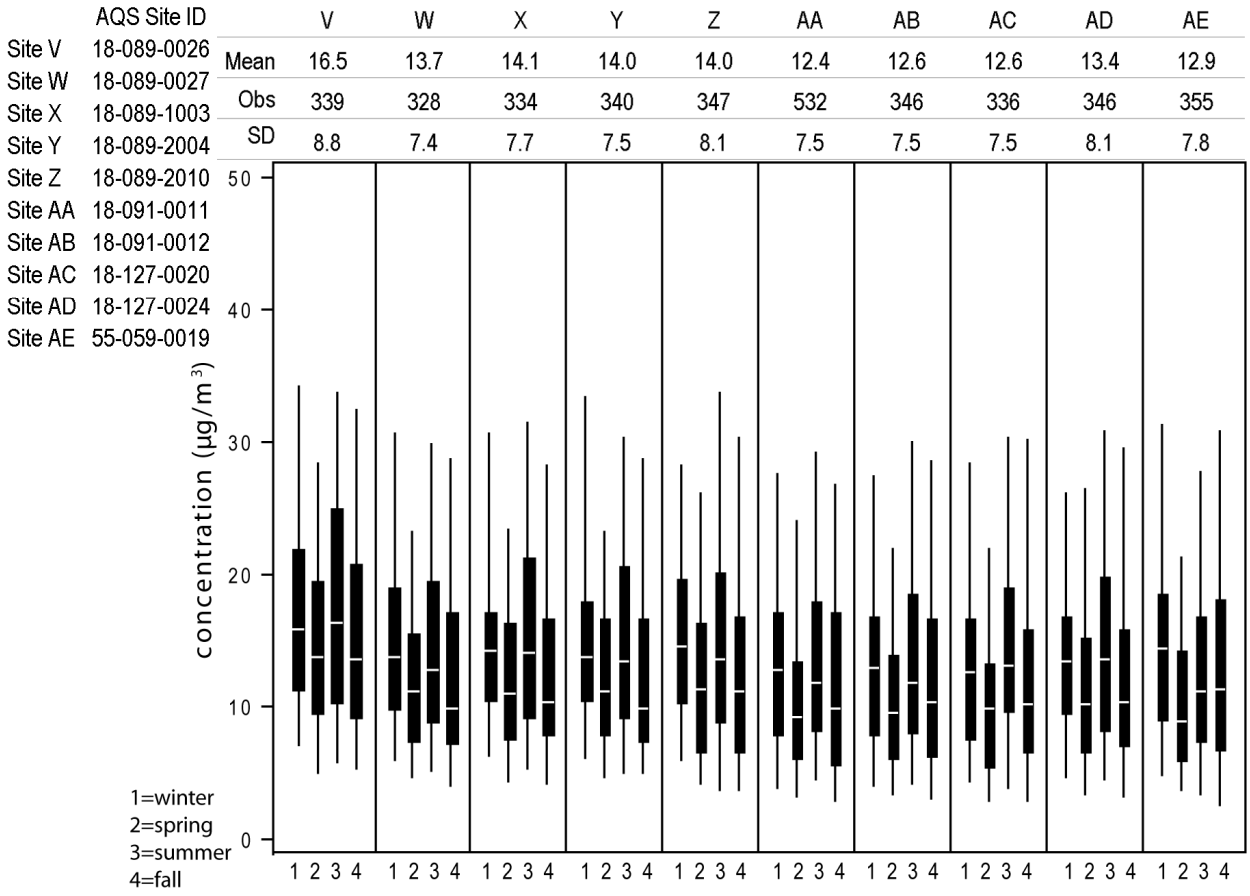


Figure A-47. Box plots illustrating the seasonal distribution of 24-h avg $PM_{2.5}$ concentrations for Chicago, IL.

Table A-23. Inter-sampler correlation statistics for each pair of $PM_{2.5}$ monitors reporting to AQS for Chicago, IL.

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
A	1.00	0.98	0.93	0.94	0.97	0.95	0.97	0.94	0.96	0.91	0.95	0.95	0.91	0.92	0.89
	(0.0, 0.00)	(3.1, 0.08)	(5.5, 0.12)	(4.7, 0.11)	(3.9, 0.09)	(5.7, 0.13)	(3.9, 0.09)	(4.6, 0.12)	(4.2, 0.11)	(6.8, 0.16)	(5.8, 0.14)	(4.6, 0.12)	(5.7, 0.15)	(6.6, 0.15)	(6.0, 0.16)
	178	156	176	149	154	154	151	156	164	163	166	141	165	152	156
B		1.00	0.94	0.95	0.97	0.95	0.97	0.95	0.96	0.93	0.93	0.95	0.92	0.93	0.90
		(0.0, 0.00)	(4.6, 0.11)	(3.6, 0.10)	(3.3, 0.08)	(5.2, 0.13)	(2.7, 0.07)	(4.3, 0.11)	(3.4, 0.09)	(6.3, 0.16)	(6.5, 0.15)	(4.0, 0.10)	(5.1, 0.15)	(5.8, 0.14)	(5.2, 0.15)
		343	320	276	300	296	296	289	312	315	306	288	157	152	150
C			1.00	0.96	0.92	0.91	0.90	0.94	0.92	0.90	0.91	0.92	0.88	0.92	0.86
			(0.0, 0.00)	(4.4, 0.11)	(5.7, 0.11)	(4.8, 0.11)	(6.0, 0.12)	(4.3, 0.11)	(5.5, 0.11)	(8.8, 0.18)	(7.2, 0.17)	(4.5, 0.12)	(7.5, 0.16)	(7.9, 0.16)	(7.5, 0.17)
			984	313	325	318	324	312	336	332	337	311	178	175	173
D				1.00	0.94	0.93	0.94	0.95	0.94	0.93	0.93	0.92	0.89	0.96	0.88
				(0.0, 0.00)	(3.8, 0.10)	(4.2, 0.12)	(3.8, 0.10)	(4.1, 0.13)	(3.3, 0.10)	(6.2, 0.15)	(5.2, 0.14)	(3.6, 0.10)	(5.3, 0.14)	(5.1, 0.13)	(4.5, 0.15)
				333	286	280	283	270	299	296	289	273	151	146	145
E					1.00	0.95	0.98	0.95	0.98	0.92	0.92	0.95	0.95	0.94	0.92
					(0.0, 0.00)	(5.0, 0.11)	(2.4, 0.06)	(4.5, 0.11)	(2.6, 0.07)	(5.8, 0.16)	(5.7, 0.15)	(4.4, 0.10)	(4.8, 0.11)	(5.0, 0.11)	(4.6, 0.13)
					351	306	304	292	320	321	313	286	159	154	152
F						1.00	0.95	0.95	0.96	0.89	0.91	0.94	0.94	0.94	0.94
						(0.0, 0.00)	(5.1, 0.12)	(4.5, 0.12)	(4.5, 0.10)	(8.5, 0.20)	(7.9, 0.19)	(5.7, 0.12)	(7.0, 0.15)	(7.9, 0.17)	(7.9, 0.16)
						345	301	294	322	323	311	285	161	157	154
G							1.00	0.95	0.97	0.90	0.91	0.94	0.95	0.95	0.95
							(0.0, 0.00)	(4.9, 0.12)	(3.0, 0.07)	(6.3, 0.15)	(5.8, 0.14)	(4.7, 0.10)	(4.2, 0.11)	(5.0, 0.12)	(4.4, 0.12)
							350	284	315	318	309	287	154	149	148
H								1.00	0.95	0.91	0.92	0.94	0.93	0.94	0.91
								(0.0, 0.00)	(4.3, 0.11)	(7.4, 0.19)	(6.4, 0.18)	(4.4, 0.13)	(6.4, 0.16)	(7.1, 0.16)	(5.9, 0.17)
								335	311	309	302	275	164	157	156
I									1.00	0.90	0.92	0.96	0.96	0.95	0.93
									(0.0, 0.00)	(6.7, 0.17)	(5.9, 0.16)	(3.9, 0.10)	(4.6, 0.12)	(5.3, 0.13)	(4.6, 0.14)
									361	341	328	304	173	169	166
J										1.00	0.92	0.90	0.91	0.94	0.89
										(0.0, 0.00)	(4.7, 0.13)	(7.0, 0.17)	(5.7, 0.14)	(4.4, 0.12)	(5.4, 0.16)
										356	330	304	171	165	164
K					**LEGEND**						1.00	0.93	0.94	0.96	0.92
					R						(0.0, 0.00)	(5.9, 0.15)	(5.2, 0.13)	(4.0, 0.10)	(4.9, 0.15)
					(P90, COD)						361	292	173	166	167
L					**N**							1.00	0.94	0.95	0.92
												(0.0, 0.00)	(6.4, 0.13)	(5.9, 0.13)	(6.0, 0.14)
												331	147	142	142
M													1.00	0.97	0.95
													(0.0, 0.00)	(3.9, 0.09)	(2.7, 0.11)
													179	160	165
N														1.00	0.95
														(0.0, 0.00)	(3.8, 0.11)
														176	152
O															1.00
															(0.0, 0.00)
															174

	P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD	AE
A	0.90	0.89	0.91	0.83	0.96	0.83	0.93	0.95	0.96	0.95	0.98	0.94	0.93	0.95	0.94	0.88
	(8.0, 0.19)	(7.5, 0.19)	(5.6, 0.16)	(8.0, 0.24)	(4.4, 0.11)	(7.2, 0.16)	(5.9, 0.13)	(4.7, 0.12)	(4.4, 0.10)	(4.5, 0.12)	(3.4, 0.10)	(5.8, 0.17)	(6.8, 0.17)	(6.0, 0.16)	(5.4, 0.15)	(7.1, 0.17)
	166	151	157	145	154	162	159	149	156	160	160	154	159	158	159	162
B	0.90	0.90	0.91	0.83	0.95	0.81	0.94	0.95	0.96	0.96	0.98	0.94	0.92	0.93	0.87	0.87
	(8.0, 0.20)	(6.7, 0.17)	(5.5, 0.16)	(8.0, 0.24)	(3.9, 0.10)	(6.7, 0.15)	(5.2, 0.11)	(5.0, 0.11)	(4.0, 0.10)	(4.2, 0.11)	(2.9, 0.09)	(5.9, 0.17)	(6.8, 0.17)	(6.5, 0.18)	(5.3, 0.16)	(7.2, 0.17)
	159	290	153	143	292	310	300	289	292	300	309	288	308	299	305	311
C	0.89	0.91	0.86	0.78	0.90	0.76	0.89	0.90	0.90	0.90	0.93	0.87	0.88	0.88	0.84	0.79
	(10.2, 0.22)	(8.3, 0.19)	(7.1, 0.17)	(10.4, 0.25)	(6.9, 0.13)	(8.5, 0.18)	(6.4, 0.13)	(7.7, 0.15)	(7.1, 0.14)	(7.9, 0.15)	(6.7, 0.15)	(8.6, 0.20)	(8.9, 0.20)	(9.6, 0.21)	(8.7, 0.18)	(8.5, 0.20)
	180	324	172	164	309	327	315	305	311	317	323	491	323	313	323	333
D	0.90	0.94	0.89	0.80	0.92	0.74	0.91	0.94	0.93	0.93	0.95	0.92	0.90	0.90	0.85	0.87
	(7.6, 0.19)	(6.5, 0.16)	(5.5, 0.14)	(8.6, 0.22)	(5.0, 0.12)	(7.8, 0.19)	(5.9, 0.13)	(5.4, 0.13)	(5.4, 0.13)	(5.8, 0.13)	(4.8, 0.13)	(6.4, 0.17)	(6.9, 0.18)	(7.0, 0.19)	(6.2, 0.17)	(6.9, 0.17)
	153	278	147	135	280	294	283	273	282	284	292	274	291	287	290	297
E	0.91	0.92	0.94	0.87	0.94	0.77	0.94	0.96	0.95	0.96	0.96	0.93	0.91	0.90	0.86	0.87
	(8.3, 0.18)	(5.6, 0.16)	(4.9, 0.12)	(7.1, 0.20)	(4.1, 0.10)	(7.5, 0.17)	(5.6, 0.12)	(4.3, 0.10)	(4.4, 0.11)	(3.9, 0.09)	(3.9, 0.11)	(5.8, 0.17)	(6.9, 0.17)	(6.8, 0.18)	(6.3, 0.16)	(7.3, 0.17)
	160	294	155	142	300	320	310	299	303	310	317	292	314	304	313	318
F	0.91	0.92	0.92	0.87	0.90	0.74	0.93	0.92	0.92	0.92	0.93	0.91	0.90	0.87	0.83	0.84
	(10.5, 0.23)	(8.6, 0.20)	(8.5, 0.17)	(10.0, 0.25)	(6.9, 0.14)	(9.2, 0.19)	(5.4, 0.11)	(8.2, 0.16)	(7.2, 0.15)	(7.6, 0.15)	(6.3, 0.16)	(8.5, 0.22)	(9.4, 0.21)	(9.1, 0.23)	(8.3, 0.20)	(9.3, 0.21)
	163	295	159	144	302	320	308	297	305	311	316	292	317	306	317	322
G	0.91	0.91	0.95	0.88	0.94	0.76	0.95	0.97	0.96	0.97	0.96	0.92	0.92	0.90	0.87	0.85
	(7.9, 0.19)	(5.9, 0.16)	(4.1, 0.12)	(7.1, 0.21)	(3.9, 0.10)	(7.5, 0.17)	(4.7, 0.10)	(3.7, 0.09)	(3.6, 0.09)	(3.5, 0.08)	(3.4, 0.11)	(5.7, 0.17)	(6.8, 0.16)	(6.8, 0.18)	(5.9, 0.15)	(7.5, 0.17)
	156	292	154	140	293	315	303	293	296	303	312	288	311	300	308	314
H	0.91	0.93	0.92	0.82	0.92	0.78	0.92	0.91	0.92	0.92	0.93	0.90	0.89	0.88	0.83	0.88
	(9.3, 0.23)	(7.1, 0.20)	(6.6, 0.17)	(9.6, 0.26)	(5.7, 0.13)	(7.5, 0.17)	(6.1, 0.13)	(6.8, 0.15)	(5.9, 0.15)	(6.7, 0.14)	(5.9, 0.15)	(7.7, 0.22)	(8.1, 0.22)	(8.3, 0.22)	(8.1, 0.20)	(7.6, 0.20)
	165	284	158	145	287	307	297	288	292	299	303	281	301	293	301	307
I	0.91	0.92	0.95	0.87	0.93	0.78	0.94	0.95	0.94	0.95	0.95	0.92	0.91	0.89	0.85	0.86
	(8.2, 0.21)	(6.1, 0.17)	(4.7, 0.12)	(7.7, 0.22)	(4.2, 0.10)	(7.1, 0.17)	(5.0, 0.10)	(4.6, 0.11)	(4.8, 0.11)	(4.7, 0.10)	(4.2, 0.13)	(6.5, 0.18)	(6.8, 0.18)	(7.4, 0.19)	(6.6, 0.17)	(7.0, 0.18)
	175	314	168	154	318	338	327	316	322	328	335	306	334	323	334	339
J	0.92	0.91	0.90	0.85	0.89	0.73	0.89	0.89	0.89	0.89	0.91	0.89	0.88	0.87	0.82	0.87
	(5.6, 0.14)	(5.1, 0.14)	(6.2, 0.16)	(6.7, 0.21)	(6.1, 0.17)	(8.6, 0.22)	(8.7, 0.20)	(6.0, 0.16)	(6.3, 0.16)	(6.2, 0.16)	(5.9, 0.16)	(5.6, 0.16)	(5.8, 0.16)	(6.3, 0.17)	(6.3, 0.17)	(6.4, 0.15)
	173	313	167	153	319	341	329	317	327	329	337	307	335	327	336	340
K	0.94	0.93	0.93	0.86	0.91	0.78	0.89	0.91	0.90	0.91	0.92	0.92	0.91	0.90	0.85	0.91
	(5.2, 0.12)	(4.2, 0.12)	(6.1, 0.16)	(7.2, 0.20)	(5.1, 0.16)	(8.0, 0.21)	(8.4, 0.19)	(5.2, 0.15)	(5.5, 0.15)	(5.2, 0.15)	(5.4, 0.14)	(5.2, 0.15)	(4.9, 0.15)	(5.3, 0.16)	(5.3, 0.16)	(5.1, 0.13)
	176	298	169	155	310	327	319	304	313	319	325	301	325	315	323	328
L	0.90	0.92	0.93	0.86	0.93	0.75	0.92	0.93	0.93	0.92	0.95	0.92	0.92	0.90	0.85	0.89
	(9.3, 0.20)	(6.7, 0.17)	(6.7, 0.14)	(8.9, 0.21)	(5.5, 0.12)	(8.2, 0.19)	(6.2, 0.13)	(5.7, 0.13)	(5.8, 0.13)	(6.2, 0.13)	(5.0, 0.13)	(7.2, 0.17)	(7.6, 0.17)	(7.4, 0.18)	(7.3, 0.16)	(7.1, 0.17)
	151	285	144	132	285	301	290	282	286	293	299	277	299	286	294	301
M	0.92	0.95	0.96	0.88	0.91	0.74	0.90	0.94	0.92	0.93	0.92	0.91	0.91	0.88	0.89	0.89
	(6.2, 0.16)	(4.5, 0.14)	(3.4, 0.09)	(6.3, 0.19)	(5.9, 0.14)	(9.0, 0.22)	(8.0, 0.17)	(4.7, 0.12)	(5.2, 0.14)	(5.0, 0.13)	(5.8, 0.16)	(6.4, 0.17)	(5.5, 0.15)	(6.9, 0.19)	(6.2, 0.17)	(6.9, 0.17)
	175	157	165	152	162	171	166	159	164	168	169	158	168	165	168	171
N	0.92	0.98	0.94	0.89	0.92	0.81	0.91	0.92	0.91	0.93	0.93	0.91	0.91	0.88	0.89	0.90
	(5.4, 0.13)	(2.8, 0.08)	(4.1, 0.12)	(5.8, 0.17)	(6.2, 0.13)	(7.9, 0.20)	(8.3, 0.17)	(4.9, 0.12)	(5.6, 0.14)	(4.6, 0.13)	(4.9, 0.15)	(5.4, 0.15)	(4.9, 0.14)	(6.5, 0.17)	(5.4, 0.16)	(6.0, 0.14)
	162	151	153	140	156	165	160	157	158	162	165	153	162	158	161	165
O	0.88	0.92	0.93	0.86	0.89	0.75	0.89	0.92	0.90	0.91	0.90	0.89	0.90	0.87	0.87	0.87
	(7.5, 0.18)	(4.9, 0.15)	(3.8, 0.13)	(6.5, 0.20)	(5.9, 0.15)	(8.8, 0.22)	(7.6, 0.17)	(5.1, 0.13)	(5.8, 0.15)	(5.5, 0.14)	(5.6, 0.16)	(6.1, 0.17)	(5.7, 0.16)	(7.0, 0.19)	(6.2, 0.17)	(7.0, 0.18)
	166	152	157	145	155	166	161	154	158	161	162	151	161	159	162	166
P	1.00	0.92	0.90	0.84	0.88	0.73	0.87	0.89	0.89	0.89	0.90	0.89	0.90	0.89	0.89	0.92
	(0.0, 0.00)	(5.2, 0.13)	(7.1, 0.17)	(7.2, 0.20)	(8.5, 0.20)	(12.0, 0.26)	(10.9, 0.24)	(6.7, 0.18)	(7.4, 0.18)	(6.9, 0.18)	(7.6, 0.19)	(6.1, 0.16)	(5.7, 0.15)	(6.3, 0.17)	(6.4, 0.17)	(5.7, 0.13)
	181	159	166	152	164	174	168	160	166	169	171	158	170	167	170	173
Q		1.00	0.92	0.85	0.88	0.71	0.89	0.90	0.88	0.90	0.90	0.89	0.88	0.86	0.82	0.91
		(0.0, 0.00)	(5.4, 0.16)	(7.2, 0.19)	(6.1, 0.18)	(9.3, 0.24)	(9.1, 0.21)	(5.5, 0.16)	(6.5, 0.16)	(5.5, 0.16)	(6.3, 0.16)	(5.3, 0.16)	(5.3, 0.16)	(6.3, 0.18)	(5.9, 0.17)	(5.5, 0.14)
		347	154	139	290	309	296	289	294	302	306	292	303	293	303	310
R			1.00	0.91	0.93	0.76	0.90	0.94	0.93	0.94	0.91	0.92	0.92	0.88	0.89	0.89
			(0.0, 0.00)	(5.8, 0.18)	(5.1, 0.13)	(8.6, 0.22)	(7.5, 0.17)	(4.4, 0.11)	(5.0, 0.13)	(4.0, 0.12)	(5.8, 0.17)	(6.2, 0.17)	(5.6, 0.16)	(7.1, 0.19)	(6.4, 0.17)	(7.1, 0.17)
			175	143	157	167	161	153	160	161	164	153	164	160	163	166
S				1.00	0.83	0.66	0.81	0.86	0.83	0.87	0.83	0.84	0.84	0.81	0.82	0.80
				(0.0, 0.00)	(8.5, 0.22)	(11.3, 0.28)	(11.6, 0.26)	(6.7, 0.20)	(8.0, 0.21)	(7.2, 0.19)	(7.3, 0.22)	(6.1, 0.21)	(7.4, 0.20)	(7.8, 0.23)	(7.1, 0.22)	(9.0, 0.22)
				164	144	153	148	143	146	148	151	141	151	149	148	153
T					1.00	0.81	0.93	0.95	0.97	0.96	0.97	0.92	0.91	0.92	0.87	0.85
					(0.0, 0.00)	(5.9, 0.15)	(6.2, 0.12)	(3.4, 0.10)	(3.2, 0.09)	(2.9, 0.08)	(3.2, 0.12)	(5.2, 0.17)	(5.5, 0.16)	(5.4, 0.18)	(4.9, 0.15)	(6.6, 0.18)
					330	318	307	297	302	305	315	284	312	311	313	319
U						1.00	0.77	0.79	0.81	0.81	0.81	0.78	0.76	0.79	0.74	0.69
						(0.0, 0.00)	(7.6, 0.17)	(6.6, 0.17)	(6.0, 0.15)	(6.3, 0.16)	(6.4, 0.17)	(8.1, 0.22)	(8.4, 0.22)	(7.2, 0.21)	(7.0, 0.19)	(10.0, 0.23)
						351	327	319	322	326	336	305	334	324	333	338
V							1.00	0.96	0.97	0.95	0.95	0.93	0.91	0.90	0.88	0.83
							(0.0, 0.00)	(5.9, 0.11)	(4.8, 0.10)	(5.8, 0.12)	(5.7, 0.14)	(7.7, 0.20)	(8.6, 0.20)	(8.3, 0.21)	(6.9, 0.17)	(9.3, 0.22)
							339	306	314	316	325	292	323	314	321	325
W								1.00	0.98	0.98	0.96	0.95	0.93	0.92	0.89	0.85
								(0.0, 0.00)	(2.8, 0.06)	(2.5, 0.07)	(3.6, 0.11)	(4.5, 0.15)	(4.8, 0.15)	(5.4, 0.16)	(3.9, 0.13)	(6.9, 0.17)
								328	299	306	312	281	310	306	311	316
X									1.00	0.98	0.97	0.95	0.93	0.94	0.91	0.85
									(0.0, 0.00)	(2.3, 0.07)	(3.3, 0.10)	(4.6, 0.14)	(4.9, 0.14)	(4.9, 0.15)	(3.6, 0.11)	(6.8, 0.17)
									334	311	318	286	319	305	316	321
Y										1.00	0.97	0.95	0.93	0.92	0.89	0.85
										(0.0, 0.00)	(3.6, 0.11)	(4.7, 0.16)	(5.0, 0.15)	(5.3, 0.17)	(4.4, 0.14)	(6.7, 0.18)
										340	322	296	322	311	321	326
Z											1.00	0.95	0.93	0.94	0.89	0.86
											(0.0, 0.00)	(4.6, 0.15)	(5.3, 0.15)	(4.9, 0.15)	(4.1, 0.14)	(6.8, 0.17)
											347	305	331	321	328	335
AA												1.00	0.98	0.97	0.89	0.88
												(0.0, 0.00)	(2.4, 0.07)	(2.9, 0.08)	(3.2, 0.11)	(5.9, 0.17)
												532	305	287	300	304
AB													1.00	0.96	0.89	0.86
													(0.0, 0.00)	(3.1, 0.09)	(3.7, 0.11)	(6.5, 0.17)
													346	317	328	333
AC														1.00	0.91	0.85
														(0.0, 0.00)	(2.8, 0.10)	(6.7, 0.17)
														336	320	322
AD															1.00	0.79
															(0.0, 0.00)	(7.2, 0.18)
															346	332
AE																1.00

LEGEND
R
(P90, COD)
N

P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD	AE
															(0.0, 0.00)
															355

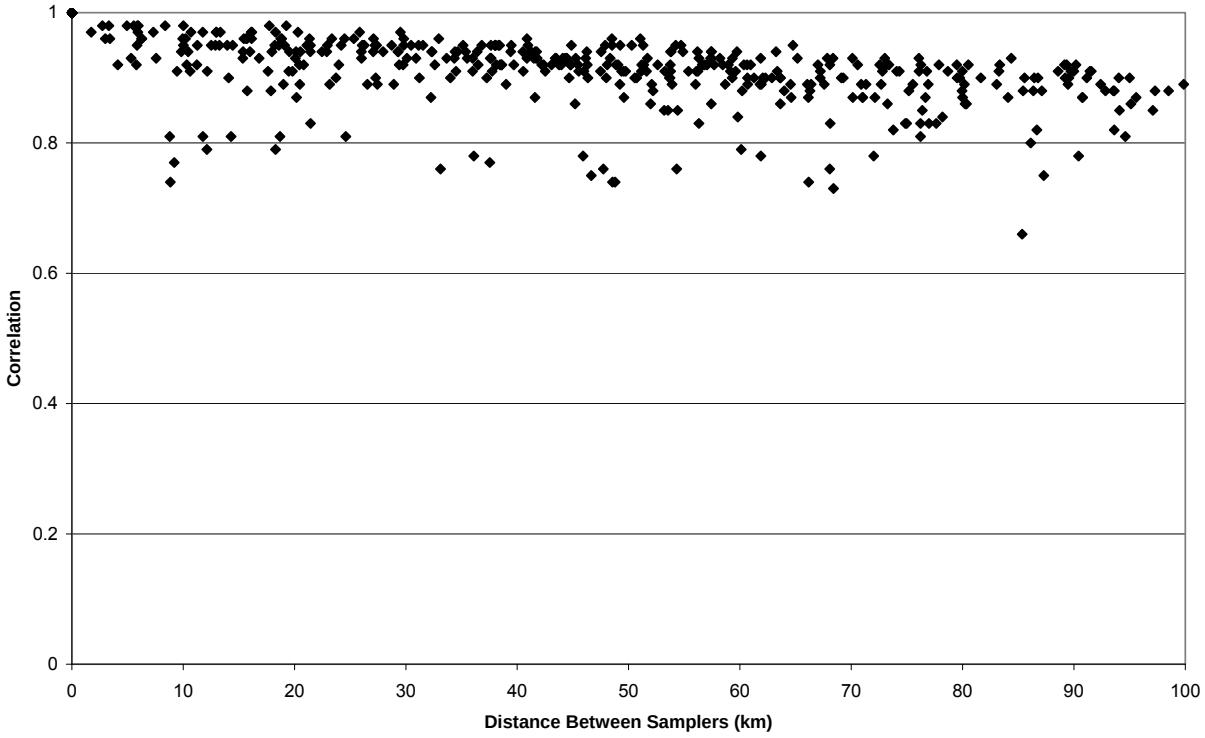


Figure A-48. $PM_{2.5}$ inter-sampler correlations as a function of distance between monitors for Chicago, IL.

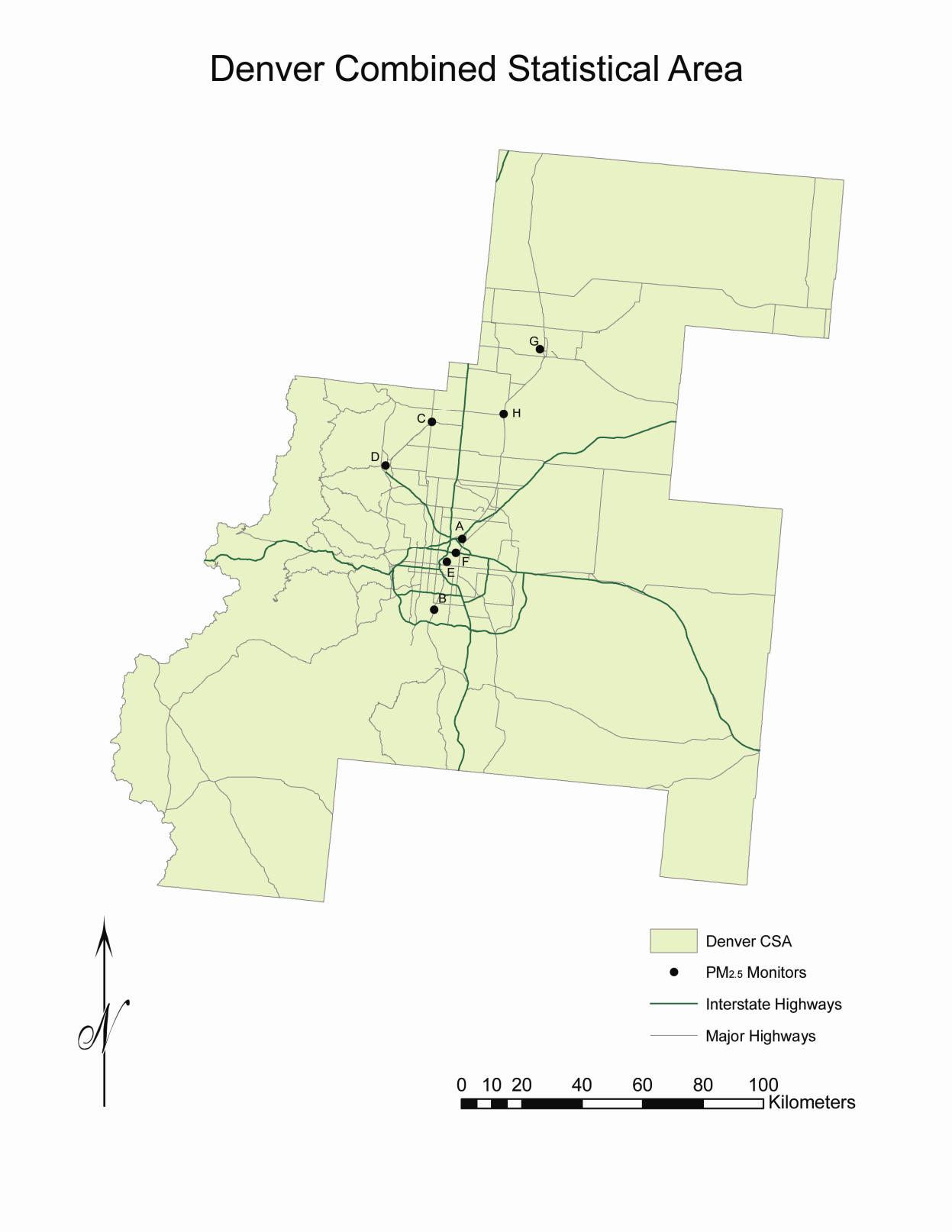


Figure A-49. $PM_{2.5}$ monitor distribution and major highways, Denver, CO.

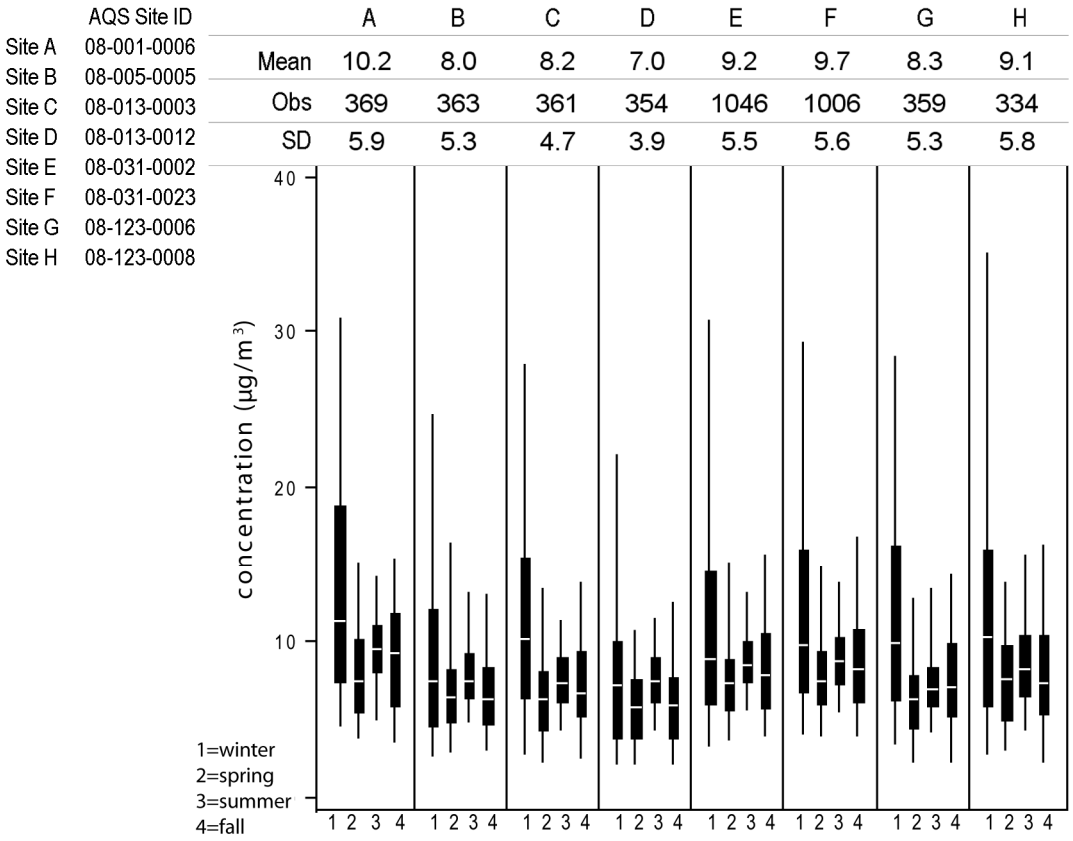


Figure A-50. Box plots illustrating the seasonal distribution of 24-h avg $PM_{2.5}$ concentrations for Denver, CO.

Table A-24. Inter-sampler correlation statistics for each pair of $PM_{2.5}$ monitors reporting to AQS for Denver, CO.

	A	B	C	D	E	F	G	H
A	1.00	0.74	0.84	0.68	0.86	0.91	0.76	0.83
	(0.0, 0.00)	(6.0, 0.21)	(5.4, 0.17)	(7.9, 0.26)	(4.1, 0.14)	(3.0, 0.11)	(5.9, 0.19)	(4.6, 0.14)
	369	353	347	332	362	339	341	325
B		1.00	0.58	0.76	0.92	0.84	0.50	0.49
		(0.0, 0.00)	(5.7, 0.19)	(3.9, 0.17)	(3.2, 0.13)	(4.4, 0.17)	(7.8, 0.23)	(6.6, 0.21)
		363	344	328	356	336	337	323
C			1.00	0.74	0.71	0.75	0.83	0.88
			(0.0, 0.00)	(4.4, 0.19)	(4.5, 0.17)	(5.4, 0.18)	(3.5, 0.14)	(3.7, 0.13)
			361	326	354	336	333	320
D				1.00	0.82	0.77	0.54	0.57
				(0.0, 0.00)	(5.6, 0.21)	(6.0, 0.24)	(7.2, 0.24)	(6.4, 0.24)
				354	347	332	318	305
E					1.00	0.94	0.64	0.60
		LEGEND			(0.0, 0.00)	(2.3, 0.09)	(7.1, 0.21)	(5.6, 0.18)
		R			1046	969	353	330
F		**(P90, COD)**				1.00	0.68	0.69
		N				(0.0, 0.00)	(6.6, 0.21)	(5.9, 0.17)
						1006	333	317
G							1.00	0.88
							(0.0, 0.00)	(3.4, 0.13)
							359	313
H								1.00
								(0.0, 0.00)
								334

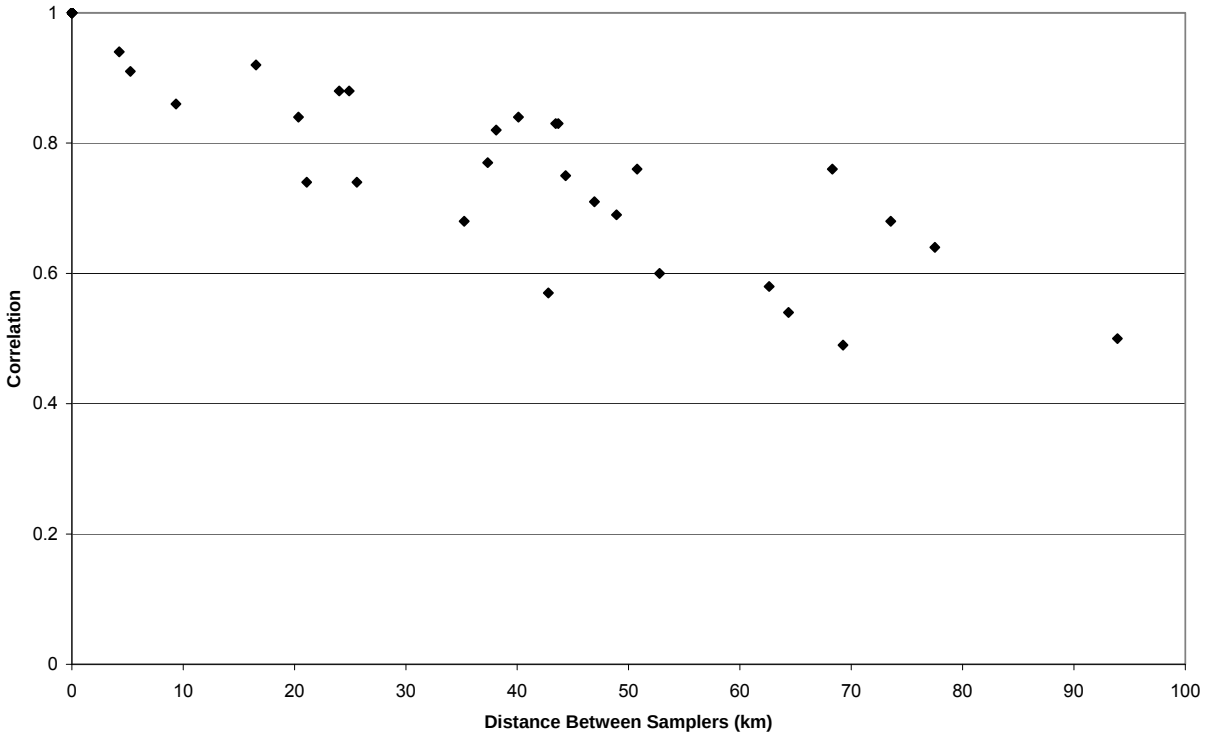


Figure A-51. $PM_{2.5}$ inter-sampler correlations as a function of distance between monitors for Denver, CO.

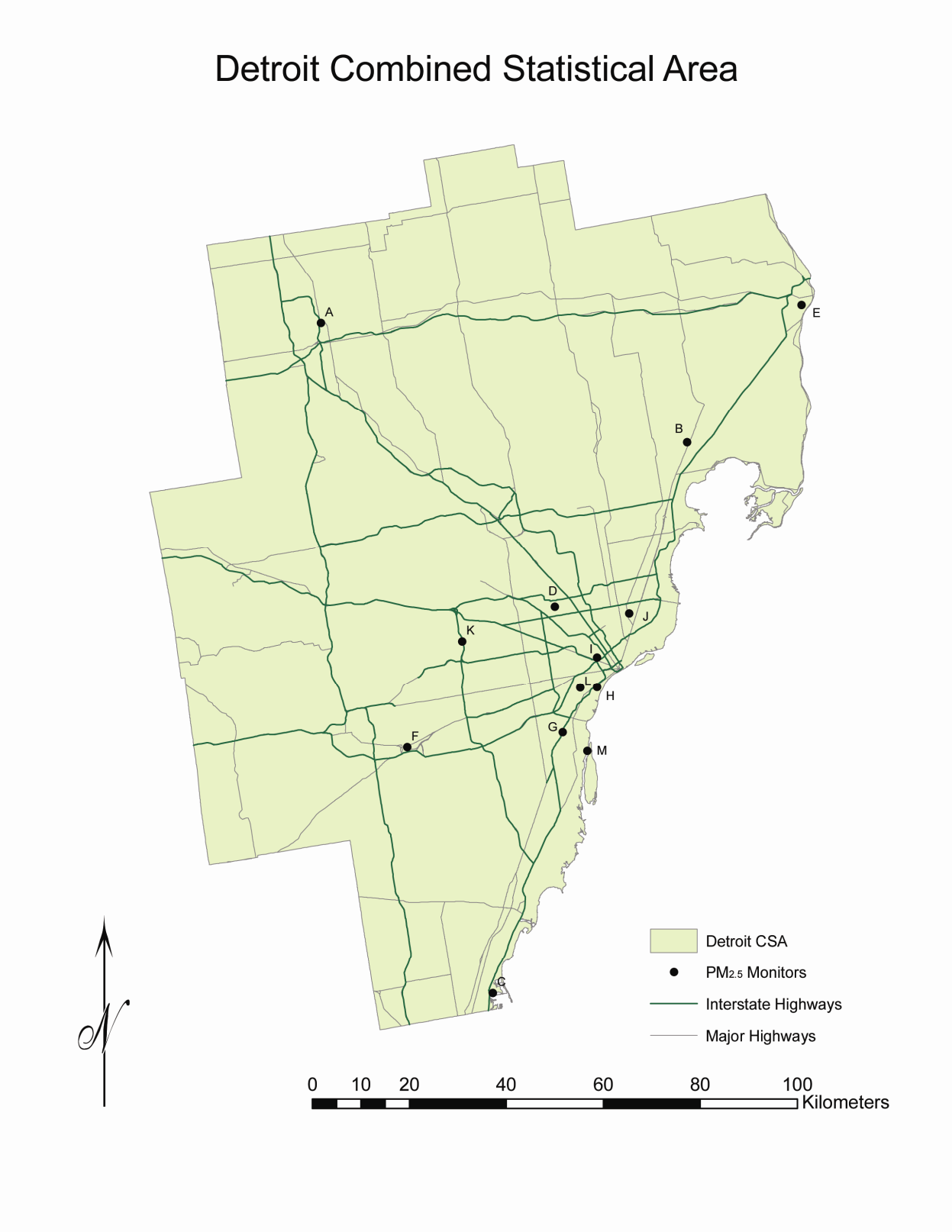


Figure A-52. $PM_{2.5}$ monitor distribution and major highways, Detroit, MI.

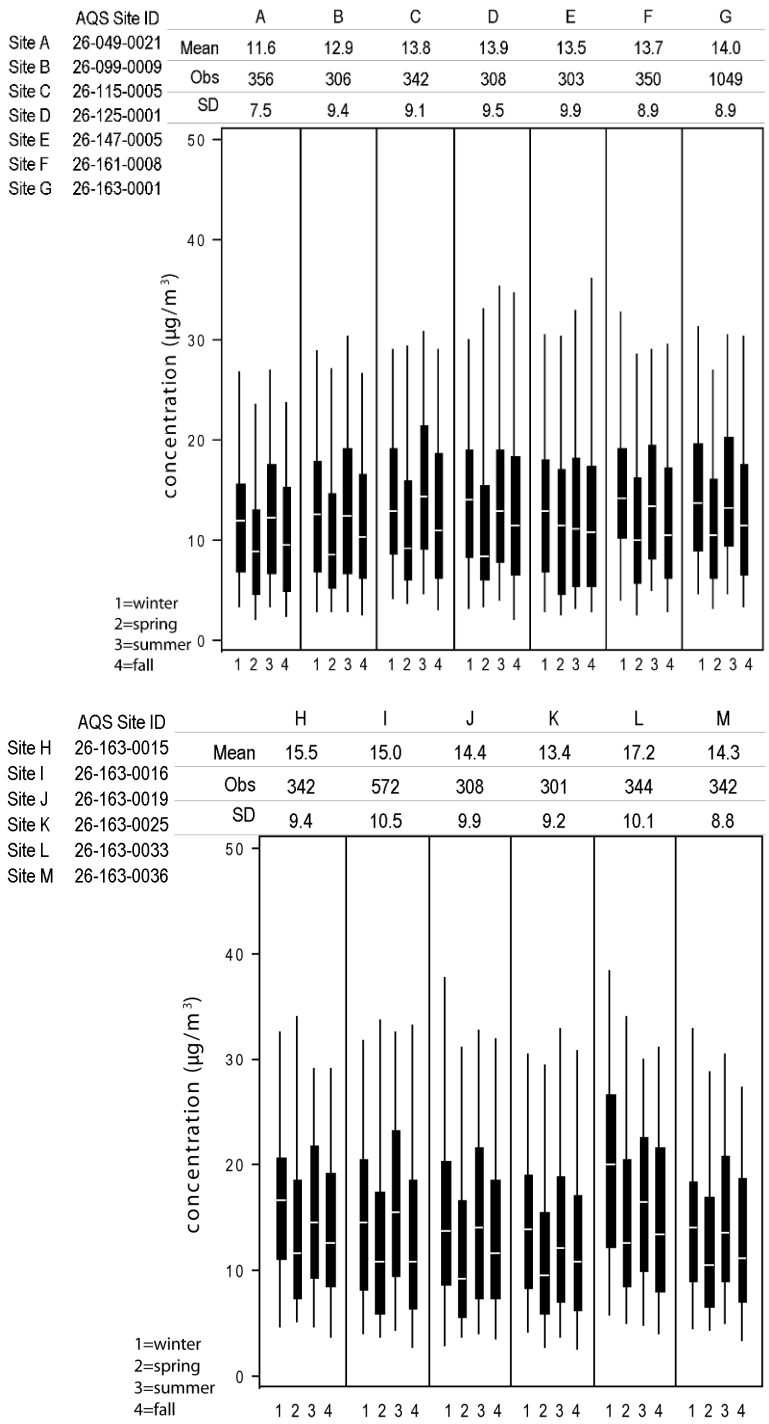


Figure A-53. Box plots illustrating the seasonal distribution of 24-h avg $PM_{2.5}$ concentrations for Detroit, MI.

Table A-25. Inter-sampler correlation statistics for each pair of $PM_{2.5}$ monitors reporting to AQS for Detroit, MI.

	A	B	C	D	E	F	G	H	I	J	K	L	M
A	1.00	0.91	0.86	0.91	0.89	0.90	0.89	0.88	0.89	0.91	0.92	0.87	0.88
	(0.0, 0.00)	(5.9, 0.17)	(7.8, 0.19)	(6.7, 0.17)	(7.6, 0.18)	(5.9, 0.18)	(8.1, 0.20)	(8.3, 0.22)	(8.0, 0.19)	(7.3, 0.17)	(5.5, 0.16)	(11.0, 0.26)	(7.8, 0.21)
	356	299	333	301	296	341	349	334	284	301	293	336	333
B		1.00	0.90	0.94	0.92	0.92	0.93	0.90	0.92	0.91	0.92	0.89	0.91
		(0.0, 0.00)	(6.8, 0.17)	(5.3, 0.14)	(5.9, 0.16)	(5.8, 0.17)	(6.2, 0.18)	(7.5, 0.21)	(5.8, 0.18)	(4.9, 0.16)	(5.4, 0.17)	(10.2, 0.24)	(6.1, 0.19)
		306	286	296	290	294	300	288	277	297	286	292	288
C			1.00	0.90	0.87	0.91	0.93	0.90	0.91	0.90	0.89	0.87	0.93
			(0.0, 0.00)	(7.0, 0.16)	(8.8, 0.20)	(5.5, 0.15)	(5.9, 0.14)	(7.2, 0.17)	(6.3, 0.16)	(6.2, 0.14)	(6.2, 0.16)	(10.4, 0.20)	(4.9, 0.13)
			342	289	284	326	335	320	273	286	279	321	319
D				1.00	0.93	0.94	0.96	0.92	0.94	0.94	0.94	0.91	0.92
				(0.0, 0.00)	(6.3, 0.15)	(4.5, 0.14)	(4.3, 0.13)	(5.8, 0.16)	(4.5, 0.12)	(3.8, 0.11)	(3.6, 0.13)	(8.2, 0.18)	(6.2, 0.15)
				308	292	296	303	291	281	297	291	290	290
E					1.00	0.90	0.90	0.89	0.90	0.90	0.90	0.87	0.87
					(0.0, 0.00)	(7.5, 0.18)	(7.3, 0.20)	(8.2, 0.22)	(7.0, 0.19)	(6.4, 0.18)	(6.9, 0.18)	(10.7, 0.25)	(7.7, 0.21)
					303	291	297	286	276	292	284	288	288
F						1.00	0.95	0.90	0.92	0.92	0.95	0.89	0.93
						(0.0, 0.00)	(4.5, 0.13)	(6.2, 0.17)	(5.7, 0.15)	(5.2, 0.14)	(3.9, 0.12)	(9.8, 0.21)	(5.7, 0.15)
						350	343	326	280	297	288	329	326
G							1.00	0.94	0.95	0.92	0.93	0.90	0.95
							(0.0, 0.00)	(5.1, 0.14)	(4.9, 0.12)	(4.5, 0.14)	(5.6, 0.16)	(8.2, 0.18)	(4.7, 0.12)
							1049	336	549	302	295	337	335
H								1.00	0.93	0.91	0.89	0.91	0.91
								(0.0, 0.00)	(4.8, 0.15)	(5.4, 0.15)	(6.9, 0.18)	(7.6, 0.16)	(6.1, 0.15)
								342	273	290	288	321	319
I			**LEGEND**						1.00	0.92	0.90	0.92	0.93
			R						(0.0, 0.00)	(4.4, 0.13)	(6.1, 0.14)	(7.9, 0.18)	(5.8, 0.14)
			(P90, COD)						572	279	271	274	274
J			**N**							1.00	0.91	0.90	0.91
										(0.0, 0.00)	(5.3, 0.15)	(8.1, 0.17)	(5.6, 0.13)
										308	288	291	291
K											1.00	0.88	0.91
											(0.0, 0.00)	(9.5, 0.21)	(6.3, 0.16)
											301	281	283
L												1.00	0.91
												(0.0, 0.00)	(8.5, 0.17)
												344	322
M													1.00
													(0.0, 0.00)
													342

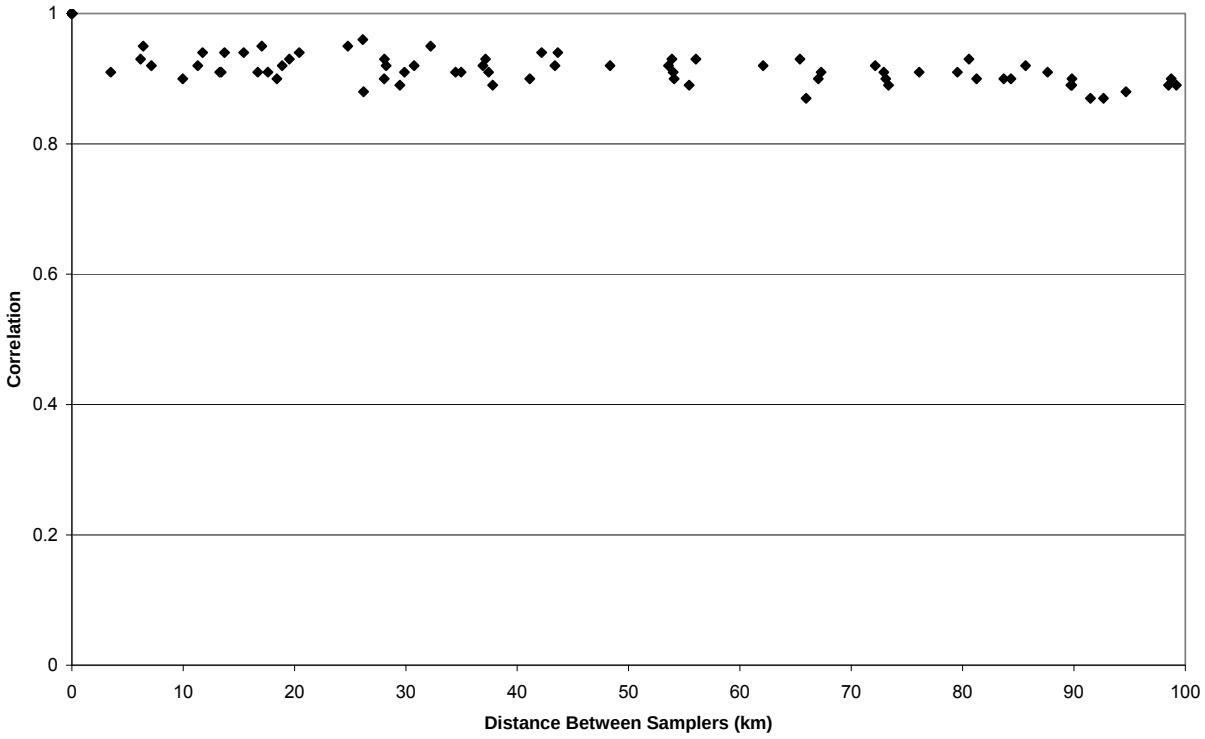


Figure A-54. $PM_{2.5}$ inter-sampler correlations as a function of distance between monitors for Detroit, MI.

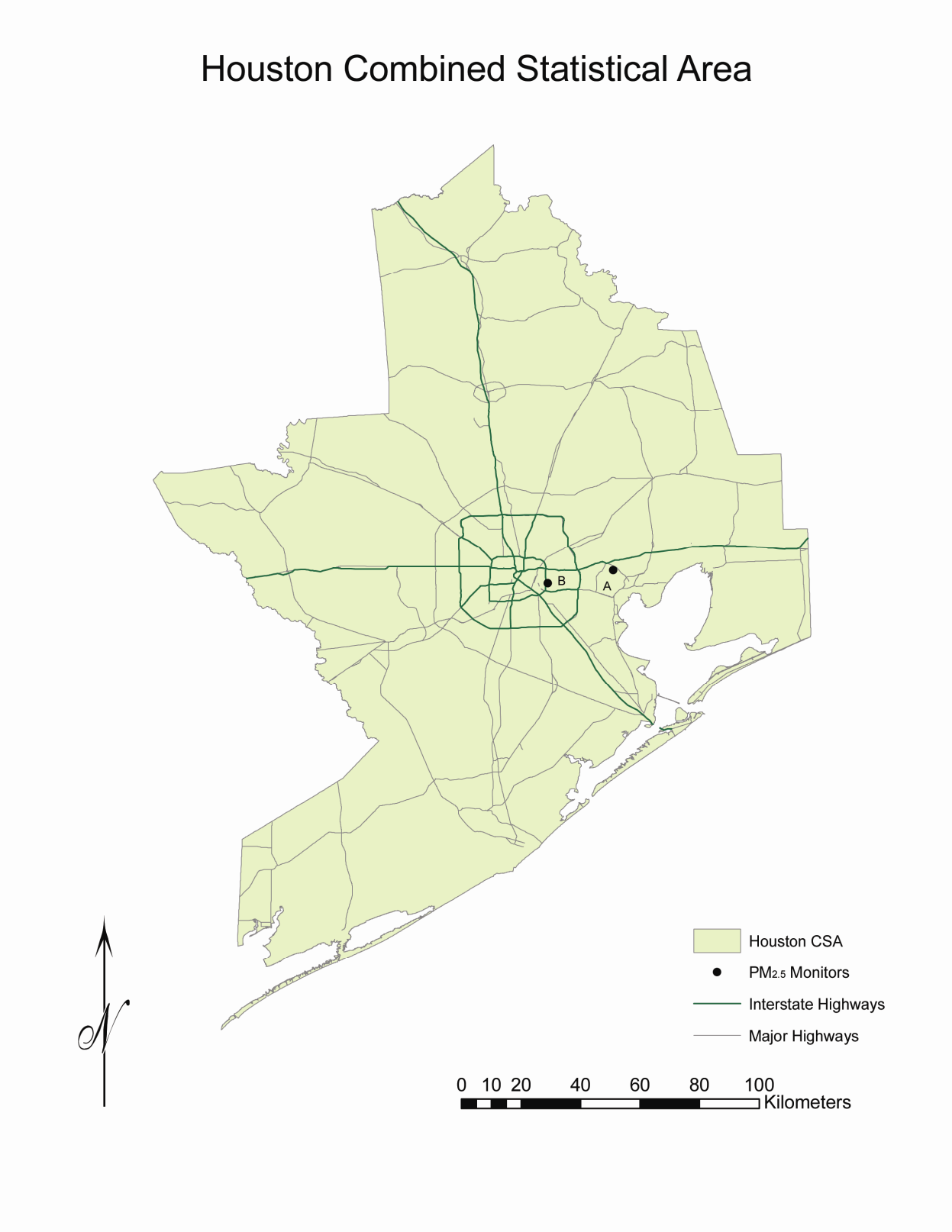


Figure A-55. $PM_{2.5}$ monitor distribution and major highways, Houston, TX.

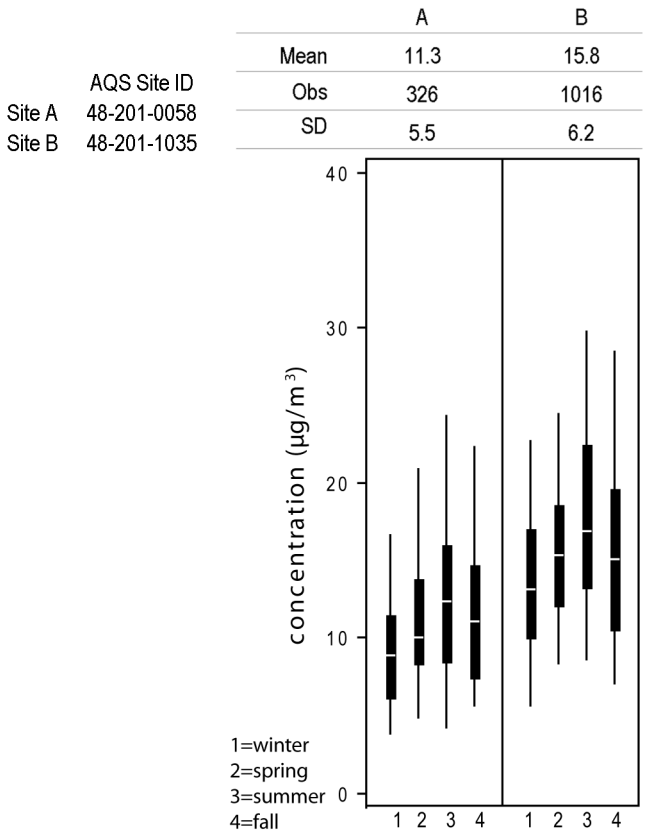


Figure A-56. Box plots illustrating the seasonal distribution of 24-h avg $PM_{2.5}$ concentrations for Houston, TX.

Table A-26. Inter-sampler correlation statistics for each pair of $PM_{2.5}$ monitors reporting to AQS for Houston, TX.

	A	B
A	1.00	0.66
	(0.0, 0.00)	(10.0, 0.24)
	326	310
B		1.00
		(0.0, 0.00)
		1016
LEGEND		
R		
(P90, COD)		
N		

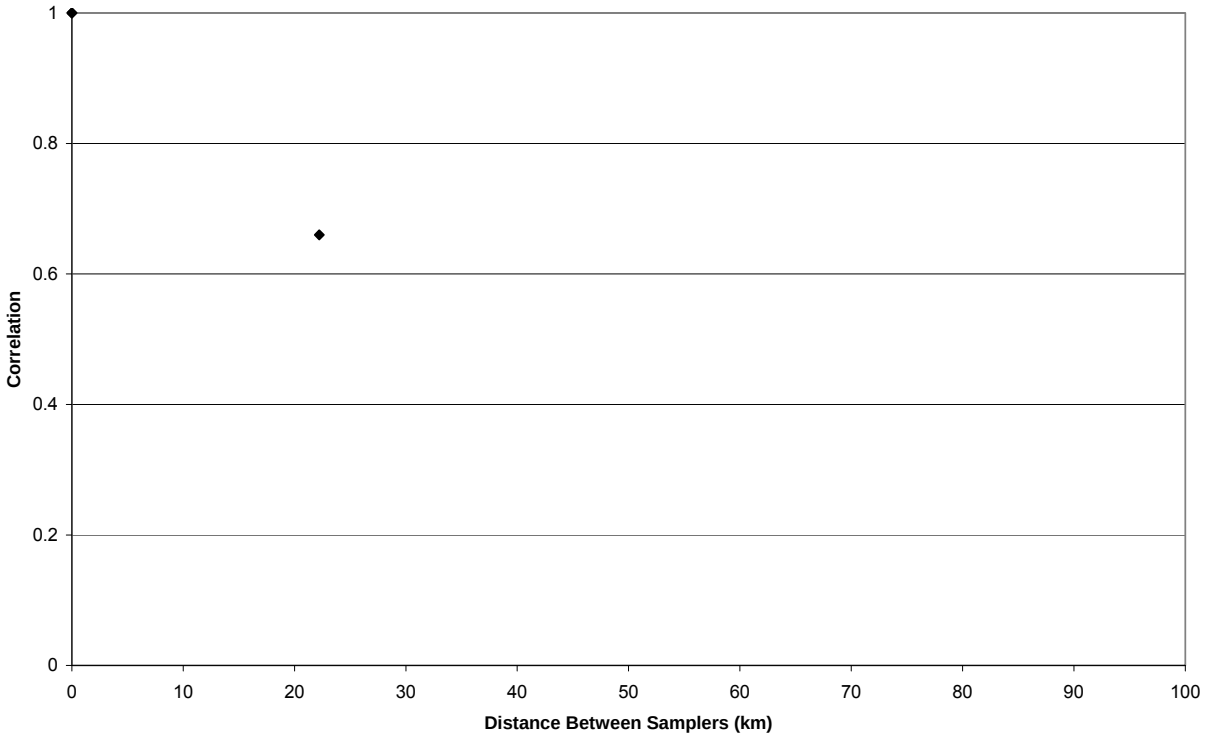


Figure A-57. $PM_{2.5}$ inter-sampler correlations as a function of distance between monitors for Houston, TX.

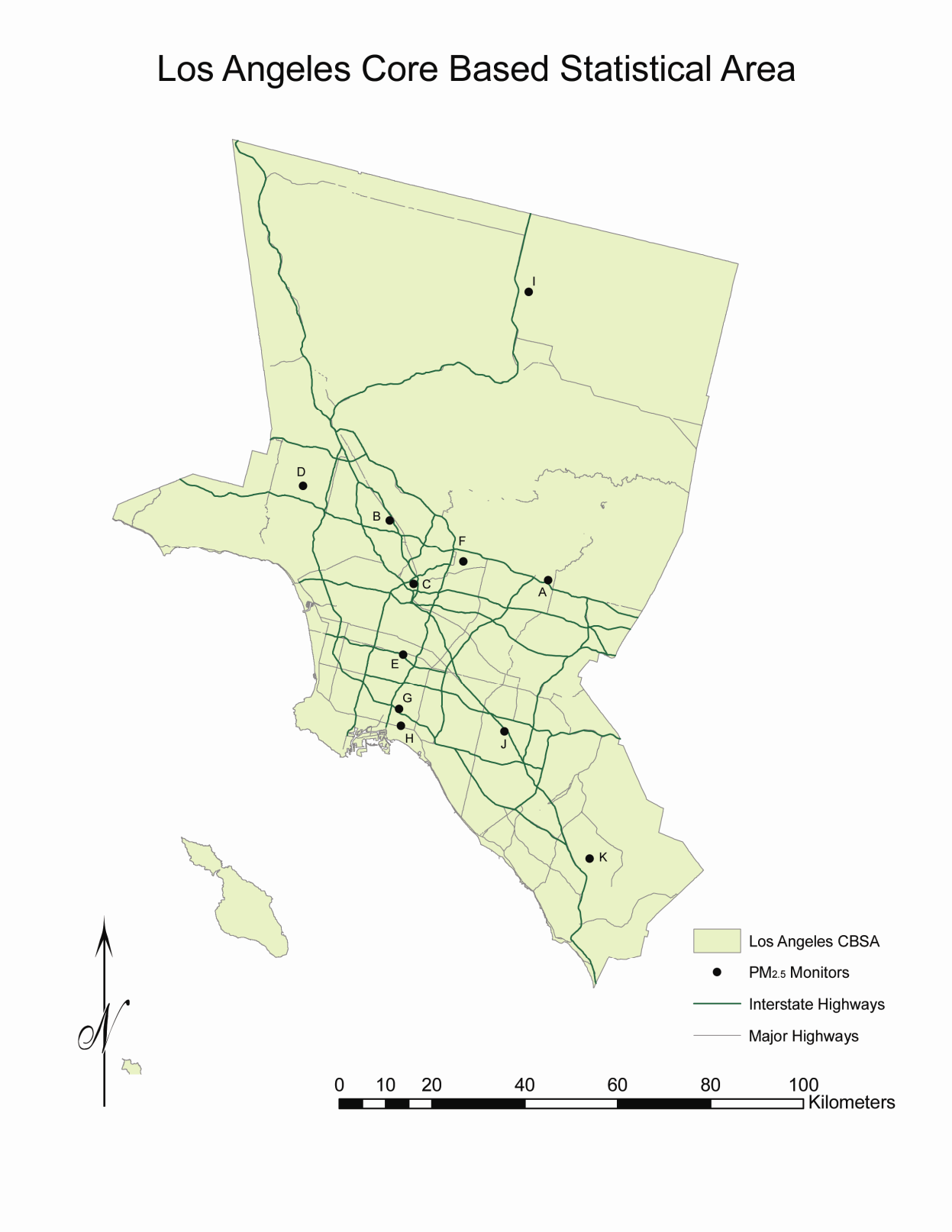


Figure A-58. $PM_{2.5}$ monitor distribution and major highways, Los Angeles, CA.

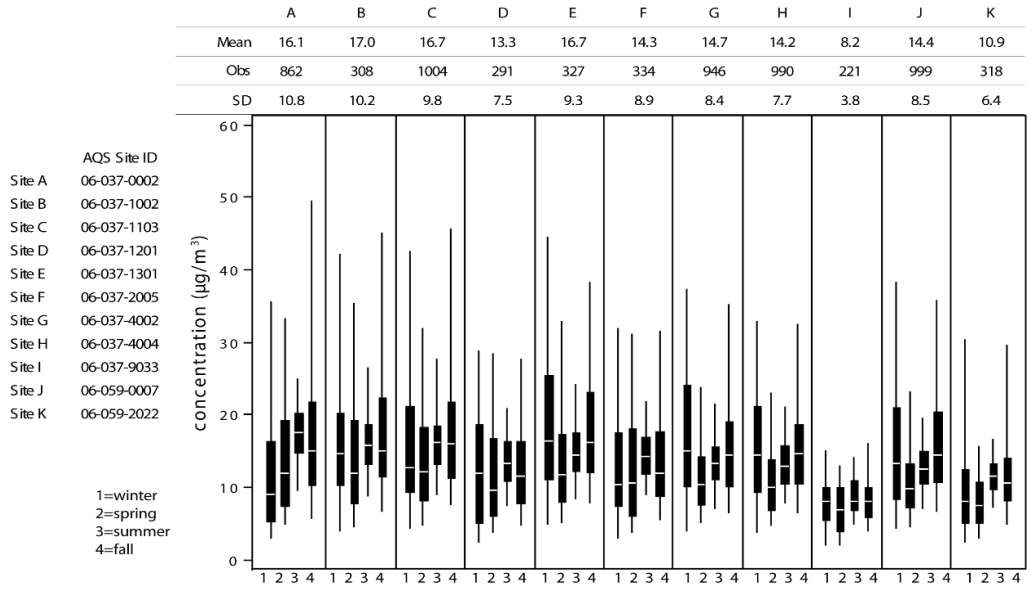


Figure A-59. Box plots illustrating the seasonal distribution of 24-h avg $PM_{2.5}$ concentrations for Los Angeles, CA.

Table A-27. Inter-sampler correlation statistics for each pair of $PM_{2.5}$ monitors reporting to AQS for Los Angeles, CA.

	A	B	C	D	E	F	G	H	I	J	K
A	1.00	0.86	0.87	0.81	0.80	0.88	0.68	0.64	0.30	0.70	0.82
	(0.0, 0.00)	(9.0, 0.18)	(7.7, 0.16)	(9.0, 0.19)	(9.7, 0.21)	(5.8, 0.14)	(11.5, 0.22)	(12.4, 0.23)	(18.0, 0.36)	(10.5, 0.21)	(11.4, 0.23)
	862	252	803	238	262	269	761	793	179	804	259
B		1.00	0.92	0.87	0.83	0.88	0.77	0.73	0.31	0.74	0.71
		(0.0, 0.00)	(5.5, 0.11)	(9.1, 0.19)	(9.0, 0.15)	(7.6, 0.15)	(9.8, 0.17)	(11.6, 0.18)	(24.1, 0.38)	(11.9, 0.19)	(15.0, 0.27)
		308	293	250	278	279	268	282	177	292	277
C			1.00	0.80	0.89	0.92	0.84	0.79	0.29	0.82	0.78
			(0.0, 0.00)	(9.6, 0.20)	(5.8, 0.11)	(6.4, 0.13)	(9.0, 0.15)	(10.0, 0.17)	(18.6, 0.38)	(9.4, 0.16)	(13.2, 0.25)
			1004	274	315	319	880	913	213	920	305
D				1.00	0.69	0.77	0.63	0.60	0.41	0.64	0.60
				(0.0, 0.00)	(10.9, 0.23)	(7.4, 0.18)	(11.3, 0.22)	(11.1, 0.22)	(14.8, 0.31)	(9.6, 0.21)	(11.6, 0.23)
				291	263	263	256	268	164	274	261
E					1.00	0.79	0.95	0.92	0.34	0.88	0.76
					(0.0, 0.00)	(9.1, 0.19)	(5.9, 0.11)	(7.6, 0.13)	(19.7, 0.39)	(8.2, 0.15)	(13.7, 0.27)
					327	301	289	301	192	307	291
F						1.00	0.70	0.70	0.33	0.69	0.72
						(0.0, 0.00)	(10.5, 0.18)	(9.2, 0.19)	(14.8, 0.34)	(9.8, 0.19)	(9.9, 0.21)
						334	290	302	184	311	293
G							1.00	0.96	0.23	0.92	0.78
							(0.0, 0.00)	(4.0, 0.09)	(17.0, 0.35)	(5.4, 0.12)	(11.0, 0.21)
							946	859	194	882	277
H								1.00	0.26	0.91	0.78
								(0.0, 0.00)	(15.3, 0.34)	(5.9, 0.12)	(9.5, 0.21)
								990	208	914	294
I									1.00	0.21	0.31
									(0.0, 0.00)	(18.3, 0.35)	(9.7, 0.28)
									221	205	180
J										1.00	0.84
										(0.0, 0.00)	(9.8, 0.19)
										999	298
K											1.00
											(0.0, 0.00)
											318

LEGEND
Pearson R
(P90, COD)
n

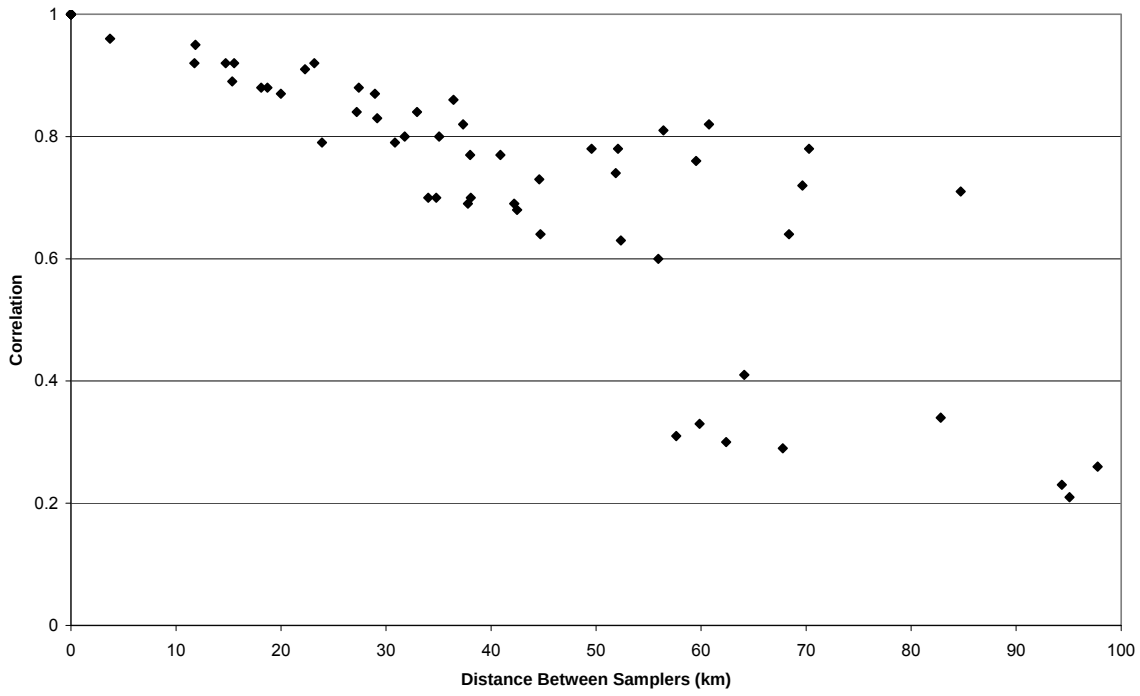


Figure A-60. $PM_{2.5}$ inter-sampler correlations as a function of distance between monitors for Los Angeles, CA.

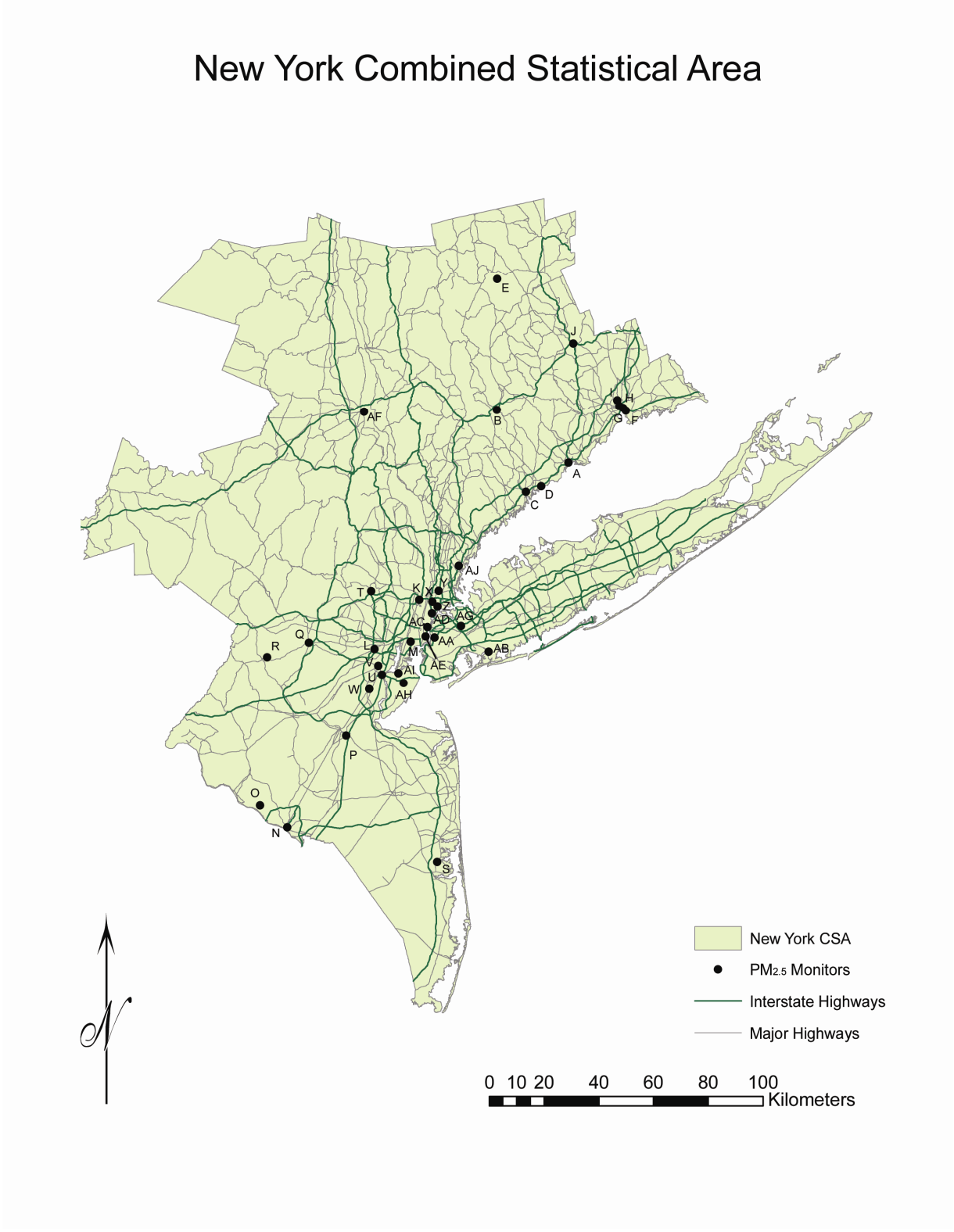
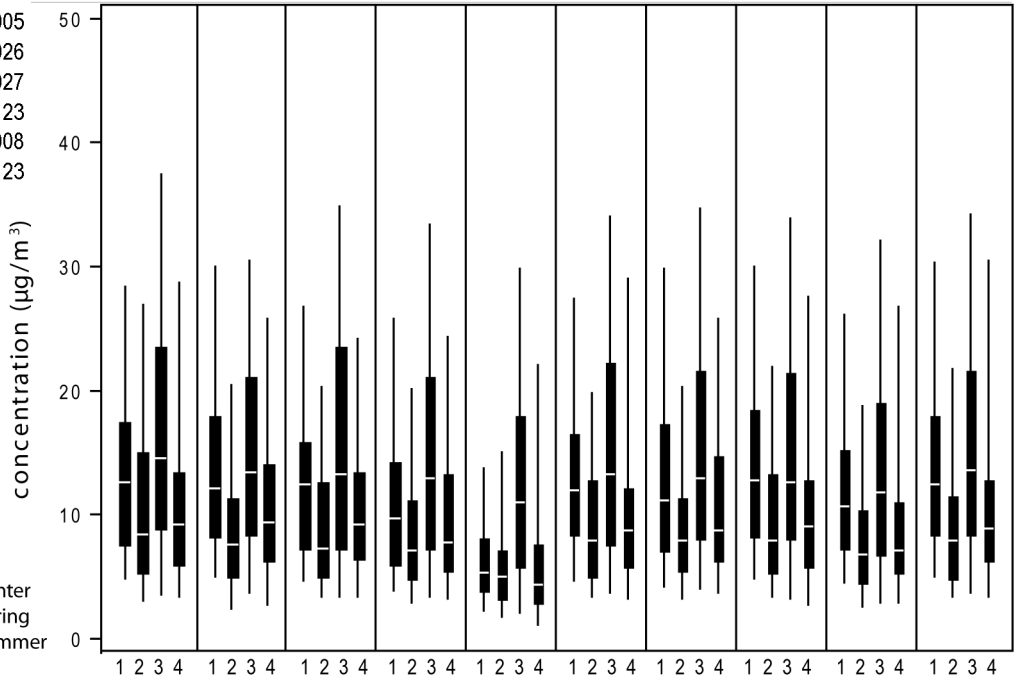


Figure A-61. $PM_{2.5}$ monitor distribution and major highways, New York City, NY.

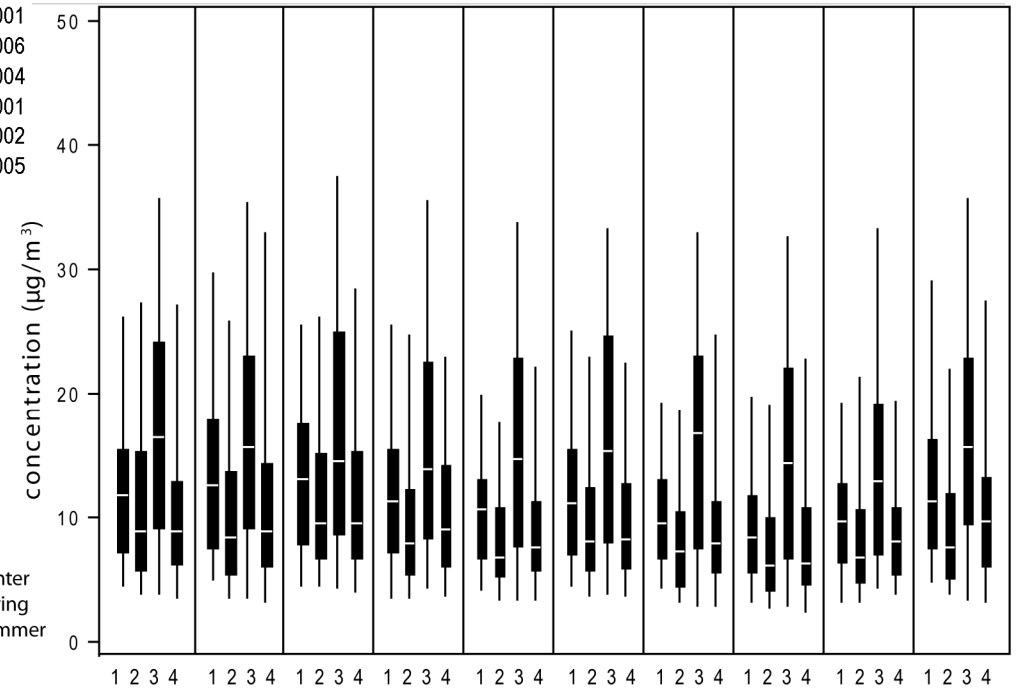
	AQS Site ID
Site A	09-001-0010
Site B	09-001-1123
Site C	09-001-3005
Site D	09-001-9003
Site E	09-005-0005
Site F	09-009-0026
Site G	09-009-0027
Site H	09-009-1123
Site I	09-009-2008
Site J	09-009-2123

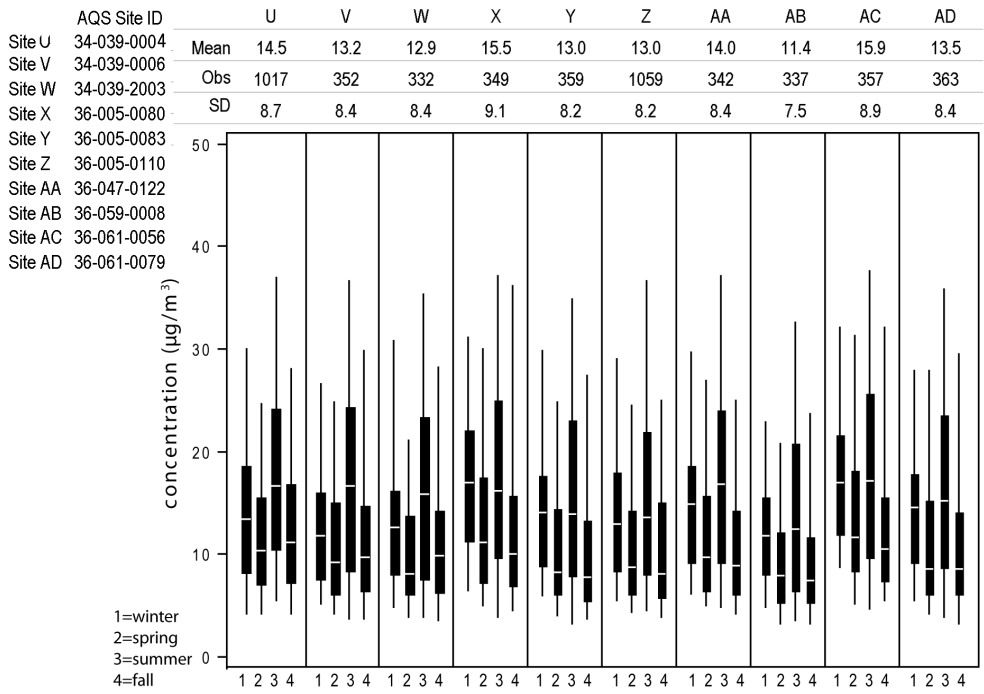
	A	B	C	D	E	F	G	H	I	J
Mean	13.2	12.5	12.3	11.2	8.0	12.1	12.4	12.8	11.1	12.6
Obs	349	339	332	565	341	341	992	338	344	352
SD	8.7	8.3	8.1	7.6	6.8	8.0	8.1	8.6	7.5	8.2



	AQS Site ID
Site K	34-003-0003
Site L	34-013-0015
Site M	34-017-1003
Site N	34-021-0008
Site O	34-021-8001
Site P	34-023-0006
Site Q	34-027-0004
Site R	34-027-3001
Site S	34-029-2002
Site T	34-031-0005

	K	L	M	N	O	P	Q	R	S	T
Mean	13.2	13.3	13.7	12.3	10.8	12.1	11.3	10.0	10.6	12.9
Obs	345	334	559	545	313	336	336	357	550	330
SD	8.9	8.8	8.5	7.7	7.0	7.7	7.7	7.4	6.8	8.7





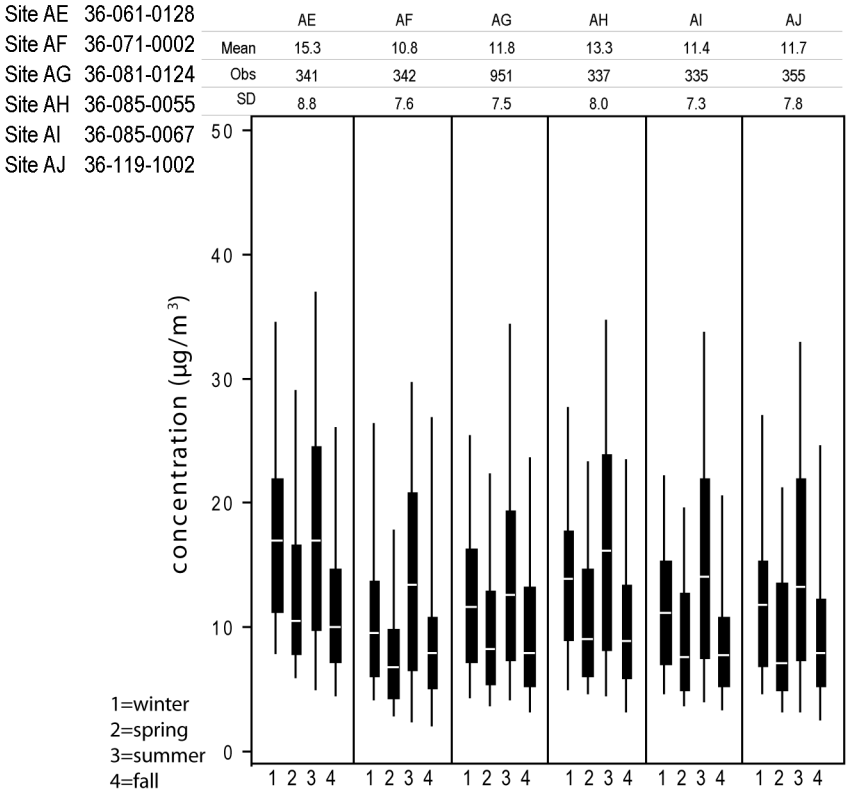


Figure A-62. Box plots illustrating the seasonal distribution of 24-h avg $PM_{2.5}$ concentrations for New York, NY.

Table A-28. Inter-sampler correlation statistics for each pair of $PM_{2.5}$ monitors reporting to AQS for New York, NY.

Site	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R
A	1.00	0.89	0.97	0.97	0.82	0.96	0.96	0.96	0.96	0.93	0.91	0.91	0.92	0.88	0.84	0.87	0.89	0.84
	(0.0, 0.00)	(5.3, 0.15)	(3.6, 0.09)	(4.8, 0.11)	(11.8, 0.33)	(3.8, 0.11)	(4.0, 0.11)	(3.4, 0.10)	(4.6, 0.12)	(5.1, 0.12)	(5.8, 0.12)	(5.7, 0.12)	(5.5, 0.13)	(6.6, 0.16)	(9.1, 0.19)	(8.3, 0.16)	(7.6, 0.16)	(9.3, 0.21)
	349	322	316	322	325	328	321	324	326	335	329	316	331	301	296	321	318	316
B		1.00	0.93	0.91	0.78	0.91	0.92	0.91	0.91	0.92	0.83	0.84	0.85	0.82	0.79	0.82	0.82	0.78
		(0.0, 0.00)	(4.5, 0.13)	(5.3, 0.14)	(10.4, 0.32)	(4.7, 0.13)	(4.6, 0.13)	(4.6, 0.14)	(5.0, 0.14)	(4.5, 0.13)	(7.3, 0.17)	(7.1, 0.17)	(7.8, 0.19)	(7.2, 0.19)	(7.7, 0.20)	(7.6, 0.18)	(6.6, 0.18)	(8.4, 0.22)
		339	312	315	319	316	313	313	315	330	319	305	321	291	292	310	307	305
C			1.00	0.98	0.82	0.96	0.95	0.96	0.97	0.94	0.91	0.91	0.91	0.89	0.84	0.88	0.89	0.84
			(0.0, 0.00)	(3.4, 0.08)	(10.8, 0.32)	(3.9, 0.10)	(4.1, 0.11)	(3.6, 0.10)	(4.0, 0.11)	(4.8, 0.11)	(5.7, 0.13)	(5.8, 0.14)	(6.5, 0.15)	(5.4, 0.15)	(6.9, 0.17)	(6.3, 0.14)	(6.2, 0.15)	(8.2, 0.20)
			332	314	309	310	308	307	310	319	314	299	316	287	289	307	305	297
D				1.00	0.85	0.96	0.96	0.94	0.96	0.92	0.90	0.89	0.91	0.88	0.87	0.89	0.90	0.86
				(0.0, 0.00)	(8.4, 0.29)	(3.4, 0.11)	(3.8, 0.11)	(5.0, 0.13)	(3.0, 0.10)	(5.5, 0.13)	(7.1, 0.15)	(6.9, 0.15)	(6.7, 0.18)	(6.3, 0.17)	(6.5, 0.16)	(6.0, 0.15)	(5.5, 0.14)	(6.6, 0.18)
				565	314	316	532	315	313	325	319	308	517	506	288	311	309	330
E					1.00	0.82	0.82	0.79	0.83	0.81	0.80	0.77	0.76	0.76	0.79	0.78	0.87	0.87
					(0.0, 0.00)	(10.0, 0.31)	(10.7, 0.33)	(11.4, 0.33)	(8.8, 0.28)	(10.3, 0.32)	(12.5, 0.34)	(13.0, 0.34)	(13.8, 0.39)	(11.6, 0.35)	(9.1, 0.30)	(10.4, 0.32)	(7.9, 0.28)	(7.3, 0.24)
					341	321	313	317	319	330	322	305	323	294	291	316	311	305
F						1.00	0.99	0.98	0.98	0.94	0.88	0.89	0.89	0.86	0.85	0.88	0.87	0.83
						(0.0, 0.00)	(2.1, 0.07)	(2.9, 0.09)	(2.8, 0.09)	(4.7, 0.11)	(6.7, 0.14)	(6.8, 0.15)	(6.8, 0.16)	(6.4, 0.17)	(6.8, 0.18)	(6.1, 0.15)	(7.3, 0.16)	(7.5, 0.21)
						341	314	319	321	328	321	308	323	293	295	312	310	308
G							1.00	0.96	0.98	0.93	0.88	0.89	0.89	0.84	0.84	0.86	0.87	0.82
							(0.0, 0.00)	(2.9, 0.10)	(3.6, 0.11)	(5.2, 0.12)	(7.1, 0.15)	(6.7, 0.15)	(6.9, 0.16)	(6.9, 0.18)	(8.0, 0.19)	(7.6, 0.16)	(8.1, 0.17)	(8.4, 0.23)
							992	315	319	326	319	309	526	513	286	310	306	327
H								1.00	0.98	0.94	0.88	0.89	0.89	0.84	0.82	0.85	0.85	0.79
								(0.0, 0.00)	(3.7, 0.10)	(3.7, 0.10)	(7.1, 0.14)	(7.1, 0.14)	(6.6, 0.16)	(6.7, 0.18)	(8.1, 0.20)	(7.8, 0.17)	(7.5, 0.17)	(9.2, 0.23)
								338	320	324	318	303	321	292	285	310	307	304
I									1.00	0.95	0.89	0.90	0.89	0.87	0.85	0.87	0.88	0.83
									(0.0, 0.00)	(4.1, 0.11)	(7.0, 0.16)	(7.0, 0.16)	(7.7, 0.20)	(6.4, 0.18)	(6.6, 0.17)	(6.5, 0.16)	(6.5, 0.15)	(7.6, 0.19)
									344	327	324	307	323	296	291	313	313	310
J										1.00	0.87	0.87	0.87	0.84	0.79	0.82	0.84	0.79
										(0.0, 0.00)	(7.0, 0.16)	(7.2, 0.16)	(8.5, 0.17)	(6.9, 0.18)	(7.9, 0.20)	(8.1, 0.18)	(7.5, 0.17)	(9.0, 0.22)
										352	332	316	334	303	299	321	322	316
K											1.00	0.95	0.93	0.88	0.86	0.90	0.92	0.86
											(0.0, 0.00)	(3.4, 0.09)	(4.5, 0.12)	(6.4, 0.15)	(7.5, 0.17)	(5.7, 0.13)	(5.8, 0.14)	(8.7, 0.20)
											345	314	330	301	296	317	319	312
L												1.00	0.97	0.91	0.86	0.94	0.93	0.87
												(0.0, 0.00)	(4.1, 0.10)	(6.4, 0.14)	(8.0, 0.18)	(5.2, 0.12)	(5.9, 0.13)	(8.3, 0.20)
												334	321	289	288	309	303	301
M													1.00	0.91	0.86	0.93	0.92	0.85
													(0.0, 0.00)	(5.5, 0.14)	(8.4, 0.21)	(6.7, 0.15)	(7.5, 0.18)	(9.7, 0.25)
													559	499	300	326	318	337
N														1.00	0.93	0.95	0.91	0.88
														(0.0, 0.00)	(4.7, 0.14)	(4.1, 0.11)	(5.8, 0.15)	(7.2, 0.20)
														545	270	293	292	316
O															1.00	0.93	0.91	0.94
															(0.0, 0.00)	(4.3, 0.12)	(4.9, 0.14)	(4.3, 0.14)
															313	294	287	279
P																1.00	0.94	0.91
																(0.0, 0.00)	(4.9, 0.12)	(5.5, 0.16)
																336	308	303
Q																	1.00	0.95
																	(0.0, 0.00)	(3.8, 0.13)
																	336	307
R																		1.00
																		(0.0, 0.00)
																		357

LEGEND
R
(P90, COD)
N

	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD	AE	AF	AG	AH	AI	AJ
A	0.75	0.89	0.90	0.90	0.88	0.92	0.94	0.93	0.93	0.88	0.89	0.94	0.88	0.89	0.93	0.90	0.89	0.96
	(10.4, 0.21)	(6.1, 0.13)	(7.1, 0.15)	(6.0, 0.13)	(7.2, 0.15)	(7.2, 0.16)	(4.0, 0.11)	(4.7, 0.12)	(5.5, 0.13)	(7.6, 0.18)	(7.3, 0.18)	(4.4, 0.11)	(7.2, 0.19)	(6.7, 0.16)	(5.1, 0.12)	(6.2, 0.15)	(7.5, 0.16)	(4.4, 0.12)
	323	315	337	299	316	332	342	348	325	320	340	346	326	323	299	317	318	338
B	0.68	0.84	0.83	0.83	0.84	0.84	0.88	0.85	0.84	0.81	0.81	0.86	0.81	0.92	0.84	0.87	0.86	0.88
	(10.8, 0.23)	(5.9, 0.16)	(8.6, 0.20)	(6.5, 0.18)	(6.8, 0.18)	(9.0, 0.21)	(5.9, 0.16)	(6.8, 0.17)	(7.3, 0.18)	(7.9, 0.20)	(8.4, 0.22)	(7.0, 0.17)	(8.8, 0.23)	(5.8, 0.16)	(6.6, 0.17)	(6.8, 0.18)	(7.1, 0.18)	(5.5, 0.15)
	314	307	328	290	305	325	334	338	317	313	331	336	315	316	292	311	309	329
C	0.76	0.89	0.88	0.89	0.89	0.92	0.95	0.93	0.92	0.89	0.88	0.93	0.88	0.89	0.93	0.91	0.89	0.96
	(8.5, 0.20)	(6.1, 0.14)	(7.8, 0.18)	(6.4, 0.15)	(6.0, 0.15)	(7.8, 0.18)	(4.4, 0.11)	(5.4, 0.13)	(5.6, 0.15)	(6.1, 0.16)	(7.5, 0.20)	(5.3, 0.12)	(7.4, 0.20)	(6.7, 0.15)	(4.7, 0.11)	(5.7, 0.14)	(6.0, 0.15)	(3.5, 0.10)
	307	304	321	283	297	317	326	331	311	306	325	330	308	312	282	305	302	322
D	0.80	0.88	0.88	0.87	0.88	0.89	0.94	0.92	0.91	0.89	0.87	0.92	0.85	0.90	0.92	0.90	0.91	0.96
	(7.7, 0.19)	(7.3, 0.16)	(8.1, 0.20)	(7.1, 0.17)	(6.9, 0.17)	(9.7, 0.21)	(5.6, 0.14)	(6.2, 0.15)	(7.0, 0.17)	(5.9, 0.16)	(9.6, 0.23)	(6.6, 0.15)	(9.2, 0.23)	(5.4, 0.14)	(4.8, 0.12)	(6.5, 0.16)	(5.3, 0.14)	(3.7, 0.10)
	509	306	537	326	304	324	332	548	315	313	330	336	315	313	496	308	310	328
E	0.67	0.79	0.74	0.76	0.75	0.75	0.80	0.78	0.76	0.73	0.74	0.79	0.70	0.88	0.77	0.75	0.80	0.84
	(9.8, 0.32)	(11.3, 0.34)	(14.9, 0.40)	(11.7, 0.36)	(12.1, 0.36)	(15.2, 0.41)	(11.5, 0.34)	(13.1, 0.36)	(13.9, 0.38)	(10.1, 0.33)	(15.7, 0.43)	(13.1, 0.35)	(15.0, 0.42)	(7.6, 0.26)	(11.3, 0.32)	(12.5, 0.36)	(9.4, 0.31)	(9.8, 0.29)
	315	306	329	290	307	324	334	340	319	314	332	338	316	316	294	310	309	331
F	0.79	0.87	0.86	0.86	0.87	0.89	0.93	0.91	0.90	0.90	0.87	0.91	0.86	0.89	0.93	0.89	0.89	0.94
	(7.9, 0.19)	(6.7, 0.15)	(8.5, 0.19)	(6.8, 0.16)	(6.6, 0.16)	(8.2, 0.19)	(5.0, 0.12)	(6.4, 0.14)	(6.7, 0.15)	(5.6, 0.16)	(8.4, 0.20)	(6.3, 0.14)	(8.0, 0.21)	(6.4, 0.16)	(4.6, 0.12)	(5.7, 0.15)	(5.3, 0.15)	(4.1, 0.12)
	316	306	329	293	309	325	335	340	320	317	334	339	319	317	290	312	310	332
G	0.77	0.87	0.87	0.86	0.88	0.89	0.92	0.90	0.90	0.88	0.86	0.91	0.85	0.88	0.90	0.89	0.88	0.93
	(8.7, 0.21)	(6.3, 0.15)	(7.8, 0.18)	(7.0, 0.16)	(6.3, 0.15)	(8.3, 0.17)	(5.4, 0.13)	(5.7, 0.14)	(7.1, 0.15)	(7.5, 0.17)	(8.1, 0.19)	(6.4, 0.14)	(8.2, 0.20)	(6.7, 0.17)	(5.2, 0.13)	(6.1, 0.15)	(6.1, 0.16)	(5.0, 0.14)
	513	304	928	327	303	319	329	958	315	308	327	333	314	311	856	312	309	325
H	0.74	0.86	0.86	0.87	0.87	0.90	0.92	0.89	0.90	0.88	0.87	0.91	0.86	0.88	0.90	0.88	0.86	0.93
	(9.6, 0.22)	(6.6, 0.15)	(8.4, 0.18)	(7.1, 0.16)	(6.9, 0.16)	(7.5, 0.17)	(5.2, 0.13)	(5.6, 0.14)	(6.4, 0.15)	(7.3, 0.19)	(7.9, 0.19)	(5.7, 0.13)	(7.3, 0.20)	(6.9, 0.17)	(5.6, 0.14)	(6.8, 0.16)	(6.4, 0.17)	(5.0, 0.13)
	314	304	326	289	306	322	331	337	315	310	329	335	313	313	290	308	308	327
I	0.76	0.88	0.87	0.88	0.88	0.90	0.93	0.92	0.91	0.87	0.87	0.92	0.86	0.90	0.93	0.89	0.89	0.94
	(8.1, 0.20)	(7.1, 0.17)	(8.7, 0.21)	(7.4, 0.17)	(6.9, 0.17)	(9.4, 0.22)	(5.7, 0.15)	(6.5, 0.16)	(7.2, 0.18)	(6.2, 0.17)	(9.6, 0.24)	(6.3, 0.16)	(9.2, 0.24)	(5.5, 0.13)	(5.1, 0.14)	(6.7, 0.18)	(5.8, 0.16)	(4.1, 0.12)
	315	308	332	293	309	326	334	343	323	313	332	338	318	319	296	310	311	330
J	0.67	0.84	0.85	0.86	0.86	0.88	0.90	0.88	0.86	0.81	0.85	0.89	0.84	0.90	0.88	0.87	0.84	0.91
	(11.1, 0.22)	(6.6, 0.16)	(9.0, 0.19)	(6.7, 0.16)	(6.8, 0.17)	(8.8, 0.19)	(6.1, 0.14)	(7.1, 0.16)	(7.3, 0.17)	(8.2, 0.19)	(9.0, 0.21)	(6.9, 0.15)	(8.9, 0.22)	(6.4, 0.16)	(6.4, 0.15)	(7.5, 0.16)	(7.7, 0.18)	(5.6, 0.14)
	327	316	343	301	318	337	345	351	330	324	343	349	327	329	301	321	320	341
K	0.74	0.94	0.92	0.95	0.92	0.92	0.93	0.92	0.93	0.84	0.90	0.93	0.88	0.89	0.90	0.91	0.89	0.92
	(10.9, 0.21)	(3.9, 0.11)	(5.7, 0.14)	(3.4, 0.10)	(4.3, 0.12)	(6.0, 0.15)	(3.8, 0.12)	(4.2, 0.12)	(4.3, 0.12)	(8.5, 0.19)	(6.2, 0.17)	(3.8, 0.11)	(6.2, 0.18)	(7.4, 0.17)	(5.9, 0.13)	(5.0, 0.13)	(6.5, 0.15)	(4.8, 0.13)
	320	317	336	302	317	330	339	344	324	318	338	343	321	321	294	318	314	335
L	0.78	0.94	0.97	0.98	0.95	0.94	0.93	0.94	0.95	0.86	0.91	0.95	0.91	0.89	0.92	0.96	0.92	0.92
	(9.8, 0.20)	(3.9, 0.11)	(4.5, 0.12)	(2.9, 0.08)	(4.0, 0.10)	(6.3, 0.15)	(4.5, 0.12)	(4.2, 0.11)	(4.1, 0.11)	(8.1, 0.18)	(6.3, 0.17)	(4.2, 0.10)	(5.9, 0.17)	(6.8, 0.17)	(5.4, 0.12)	(4.0, 0.11)	(6.4, 0.14)	(5.4, 0.13)
	313	303	325	292	303	314	323	333	306	305	322	327	309	306	283	305	299	319
M	0.80	0.93	0.97	0.97	0.96	0.95	0.95	0.96	0.97	0.88	0.94	0.96	0.93	0.88	0.95	0.96	0.93	0.93
	(9.9, 0.22)	(5.4, 0.13)	(3.8, 0.09)	(3.5, 0.09)	(4.7, 0.11)	(4.9, 0.11)	(4.7, 0.12)	(3.5, 0.10)	(3.4, 0.09)	(8.3, 0.20)	(4.5, 0.12)	(3.5, 0.10)	(4.5, 0.13)	(8.5, 0.21)	(5.0, 0.14)	(4.3, 0.10)	(6.8, 0.16)	(5.7, 0.17)
	504	318	534	341	319	331	342	545	326	320	339	345	326	323	484	319	318	338
N	0.88	0.86	0.90	0.91	0.91	0.86	0.90	0.89	0.91	0.89	0.85	0.90	0.85	0.85	0.91	0.92	0.92	0.90
	(6.4, 0.17)	(6.5, 0.16)	(6.5, 0.15)	(5.7, 0.13)	(4.5, 0.13)	(8.2, 0.18)	(5.9, 0.14)	(5.4, 0.15)	(5.3, 0.14)	(5.6, 0.17)	(8.1, 0.18)	(5.3, 0.14)	(7.7, 0.18)	(7.5, 0.20)	(4.9, 0.14)	(4.6, 0.13)	(5.3, 0.14)	(5.4, 0.16)
	492	287	519	313	290	301	309	529	297	289	308	313	294	292	477	292	293	306
O	0.87	0.82	0.86	0.87	0.88	0.84	0.87	0.86	0.88	0.89	0.82	0.88	0.81	0.84	0.88	0.89	0.92	0.88
	(5.6, 0.16)	(7.2, 0.18)	(9.9, 0.22)	(7.3, 0.18)	(6.4, 0.16)	(11.1, 0.24)	(6.7, 0.18)	(8.6, 0.19)	(8.2, 0.20)	(5.2, 0.15)	(10.3, 0.25)	(8.4, 0.18)	(10.6, 0.25)	(7.0, 0.18)	(6.1, 0.16)	(6.1, 0.18)	(4.7, 0.14)	(5.4, 0.16)
	295	289	302	280	284	299	308	312	292	295	307	311	290	290	269	290	283	304
P	0.86	0.89	0.92	0.94	0.95	0.88	0.90	0.89	0.92	0.89	0.87	0.91	0.87	0.87	0.91	0.94	0.95	0.91
	(6.2, 0.15)	(6.2, 0.14)	(7.4, 0.17)	(5.0, 0.12)	(4.0, 0.11)	(8.9, 0.19)	(5.9, 0.14)	(6.8, 0.15)	(6.4, 0.14)	(5.3, 0.14)	(8.9, 0.21)	(6.4, 0.14)	(8.3, 0.20)	(6.7, 0.16)	(5.5, 0.13)	(4.7, 0.12)	(3.5, 0.10)	(5.0, 0.14)
	312	307	325	296	305	319	329	335	312	309	327	333	313	311	285	307	306	326
Q	0.79	0.92	0.91	0.93	0.92	0.89	0.90	0.90	0.90	0.83	0.90	0.91	0.87	0.91	0.89	0.90	0.91	0.92
	(8.1, 0.19)	(5.0, 0.14)	(8.2, 0.20)	(6.2, 0.14)	(5.4, 0.15)	(9.7, 0.22)	(6.3, 0.16)	(7.3, 0.17)	(7.3, 0.18)	(6.9, 0.19)	(9.9, 0.24)	(6.9, 0.16)	(9.5, 0.24)	(4.8, 0.14)	(6.0, 0.15)	(6.3, 0.17)	(5.3, 0.14)	(5.5, 0.13)
	313	303	327	287	304	321	328	335	314	306	329	332	311	312	287	303	302	324
R	0.82	0.86	0.84	0.85	0.87	0.82	0.87	0.84	0.86	0.83	0.81	0.86	0.78	0.88	0.86	0.87	0.90	0.88
	(6.5, 0.20)	(7.6, 0.21)	(10.9, 0.26)	(8.2, 0.21)	(7.0, 0.20)	(11.6, 0.28)	(8.6, 0.21)	(10.0, 0.23)	(9.1, 0.24)	(7.0, 0.21)	(11.2, 0.30)	(9.5, 0.22)	(11.0, 0.30)	(6.2, 0.17)	(7.6, 0.20)	(7.8, 0.22)	(5.7, 0.17)	(6.3, 0.17)
	330	296	347	291	304	314	323	355	309	301	324	327	309	308	304	298	302	320
S	1.00	0.69	0.77	0.75	0.78	0.72	0.78	0.79	0.82	0.88	0.74	0.78	0.73	0.69	0.85	0.82	0.88	0.79
	(0.0, 0.00)	(10.4, 0.22)	(10.5, 0.24)	(10.5, 0.21)	(9.2, 0.19)	(12.5, 0.25)	(8.6, 0.19)	(9.3, 0.21)	(9.4, 0.20)	(5.0, 0.16)	(11.6, 0.26)	(9.9, 0.20)	(11.5, 0.25)	(10.3, 0.22)	(7.2, 0.17)	(8.5, 0.18)	(5.5, 0.14)	(8.1, 0.19)
	550	306	525	324	306	325	336	536	319	314	333	339	322	316	478	310	312	331
T		1.00	0.92	0.93	0.93	0.92	0.91	0.91	0.90	0.80	0.87	0.93	0.85	0.89	0.88	0.90	0.86	0.91
		(0.0, 0.00)	(6.0, 0.15)	(4.5, 0.12)	(4.8, 0.13)	(6.7, 0.16)	(5.2, 0.14)	(4.9, 0.13)	(5.6, 0.14)	(8.4, 0.20)	(6.9, 0.18)	(4.9, 0.12)	(7.2, 0.20)	(6.3, 0.17)	(6.2, 0.14)	(5.8, 0.14)	(7.3, 0.17)	(5.9, 0.14)
		330	319	293	301	313	323	329	308	303	321	327	306	308	281	306	298	319
U			1.00	0.98	0.97	0.92	0.91	0.93	0.94	0.84	0.91	0.94	0.90	0.86	0.90	0.96	0.91	0.90
			(0.0, 0.00)	(3.9, 0.10)	(5.0, 0.12)	(5.4, 0.12)	(6.9, 0.15)	(5.2, 0.13)	(4.9, 0.12)	(9.9, 0.22)	(5.0, 0.12)	(5.2, 0.12)	(5.9, 0.14)	(9.6, 0.23)	(6.9, 0.17)	(5.8, 0.12)	(8.4, 0.18)	(7.5, 0.19)
			1017	341	325	337	347	987	332	326	346	351	330	330	878	325	323	343
V				1.00	0.97	0.93	0.92	0.92	0.94	0.83	0.90	0.94	0.91	0.88	0.89	0.96	0.91	0.91
				(0.0, 0.00)	(2.8, 0.09)	(6.1, 0.14)	(5.0, 0.13)	(4.4, 0.12)	(4.2, 0.12)	(8.2, 0.19)	(6.6, 0.16)	(4.3, 0.11)	(6.1, 0.16)	(7.0, 0.18)	(5.8, 0.15)	(4.0, 0.10)	(6.4, 0.15)	(5.3, 0.15)
				352	288	300	307	351	294	290	305	311	294	290	301	291	287	304
W					1.00	0.90	0.91	0.91	0.92	0.85	0.89	0.93	0.88	0.87	0.89	0.96	0.92	0.90
					(0.0, 0.00)	(7.0, 0.16)	(5.5, 0.13)	(5.3, 0.13)	(4.8, 0.13)	(7.0, 0.18)	(6.8, 0.17)	(5.0, 0.12)	(6.9, 0.18)	(6.8, 0.18)	(5.1, 0.14)	(3.7, 0.10)	(4.9, 0.13)	(5.0, 0.15)
					332	316	325	331	310	309	323	328	308	310	281	304	303	320
X						1.00	0.96	0.97	0.95	0.86	0.94	0.97	0.93	0.88	0.93	0.92	0.88	0.93
						(0.0, 0.00)	(5.8, 0.13)	(4.4, 0.11)	(5.0, 0.11)	(10.0, 0.23)	(3.3, 0.09)	(4.5, 0.11)	(4.1, 0.11)	(9.8, 0.24)	(6.9, 0.17)	(6.5, 0.14)	(9.2, 0.20)	(8.2, 0.19)
						349	344	349	328	324	342	348	326	326	301	319	319	340
Y							1.00	0.97	0.96	0.90	0.93	0.98	0.93	0.89	0.97	0.93	0.92	0.97
							(0.0, 0.00)	(3.2, 0.08)	(3.9, 0.09)	(6.5, 0.16)	(5.4, 0.15)	(2.8, 0.08)	(5.4, 0.15)	(6.5, 0.18)	(3.3, 0.09)	(4.9, 0.12)	(5.3, 0.13)	(3.5, 0.11)
							359	359	338	333	352	358	337	335	308	328	329	350
Z								1.00	0.97	0.90	0.94	0.98	0.92	0.88	0.95	0.93	0.91	0.95
								(0.0, 0.00)	(2.9, 0.09)	(7.2, 0.17)	(4.4, 0.13)	(1.8, 0.07)	(4.6, 0.14)	(7.8, 0.19)	(4.0, 0.10)	(4.7, 0.11)	(6.1, 0.14)	(4.9, 0.14)
								1059	342	337	357	363	341	342	919	337	335	355
AA									1.00	0.92	0.94	0.98	0.93	0.87	0.97	0.95	0.94	0.95
									(0.0, 0.00)	(7.1, 0.18)	(3.8, 0.11)	(2.9, 0.07)	(4.1, 0.11)	(8.1, 0.20)	(4.0, 0.11)	(4.3, 0.10)	(6.6, 0.15)	(5.1, 0.15)
									342	317	336	341	319	319	292	313	312	335
AB										1.00	0.85	0.89	0.86	0.79	0.95	0.90	0.93	0.90
										(0.0, 0.00)	(9.2, 0.24)	(7.2, 0.17)	(9.0, 0.23)	(8.1, 0.20)	(4.1, 0.13)	(6.1, 0.16)	(3.8, 0.12)	(5.5, 0.16)
										337	330	337	316	313	291	310	310	329
AC											1.00	0.95	0.98	0.84	0.96	0.91	0.89	0.91
											(0.0, 0.00)	(4.4, 0.13)	(3.0, 0.08)	(10.4, 0.26)	(6.6, 0.18)	(6.6, 0.15)	(9.3, 0.21)	(7.4, 0.22)
											357	356	334	336	304	326	326	348
AD												1.00	0.93	0.89	0.97	0.95	0.93	0.96
												(0.0, 0.00)	(4.6, 0.14)	(7.1, 0.18)	(4.0, 0.10)	(4.4, 0.10)	(6.0, 0.13)	(4.6, 0.13)
												363	341	339	311	333	333	354
AE													1.00	0.82	0.94	0.92	0.89	0.89

LEGEND
R
(P90, COD)
N

	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD	AE	AF	AG	AH	AI	AJ
													(0.0, 0.00)	(10.0, 0.26)	(6.2, 0.18)	(5.6, 0.15)	(8.4, 0.20)	(8.0, 0.22)
													341	319	290	313	314	332
AF														1.00	0.86	0.87	0.87	0.91
														(0.0, 0.00)	(7.0, 0.16)	(7.1, 0.18)	(6.4, 0.16)	(5.5, 0.14)
														342	289	310	313	331
AG															1.00	0.93	0.94	0.96
															(0.0, 0.00)	(4.8, 0.12)	(4.5, 0.11)	(3.7, 0.11)
															951	289	283	304
AH																1.00	0.97	0.92
																(0.0, 0.00)	(4.1, 0.10)	(4.9, 0.15)
																337	307	327
AI																	1.00	0.92
																	(0.0, 0.00)	(4.8, 0.14)
																	335	324
AJ																		1.00
																		(0.0, 0.00)
																		355

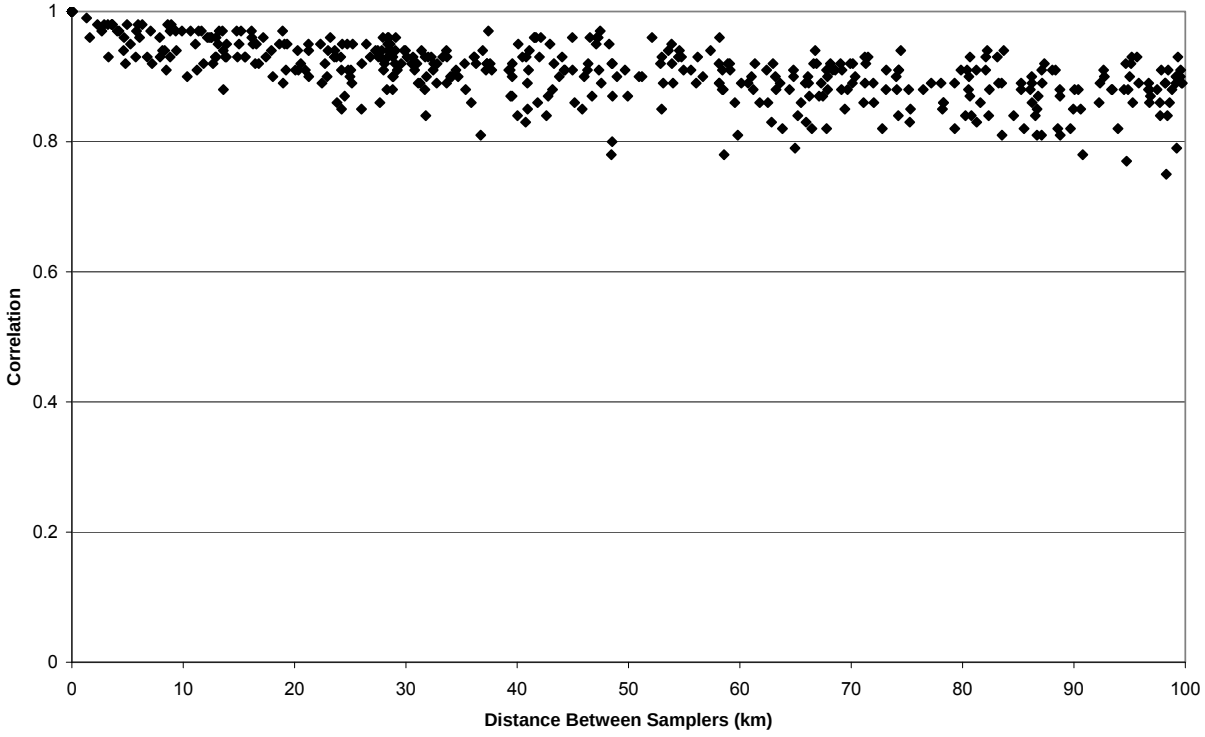


Figure A-63 $PM_{2.5}$ inter-sampler correlations as a function of distance between monitors for New York, NY.

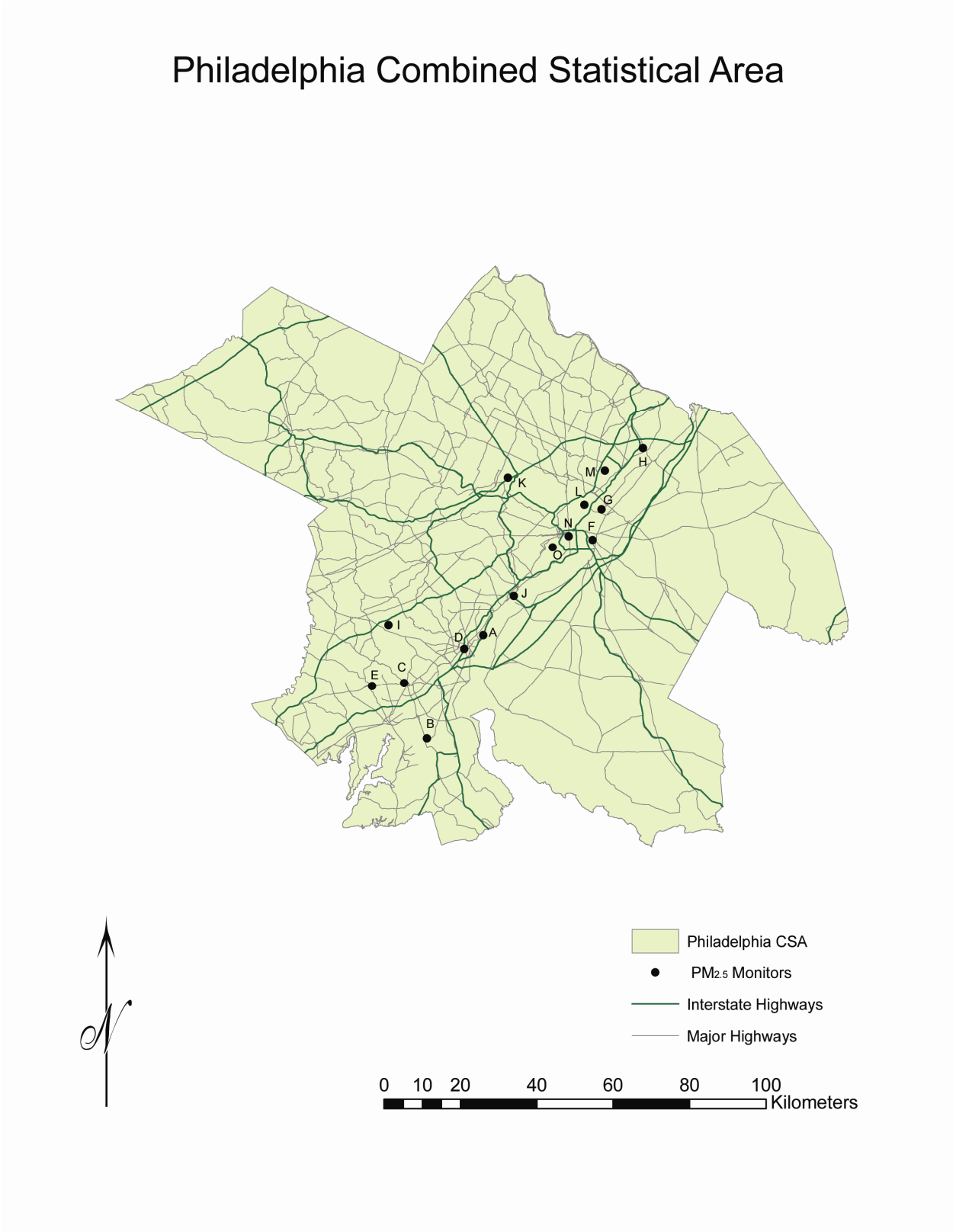


Figure A-64. $PM_{2.5}$ monitor distribution and major highways, Philadelphia, PA.

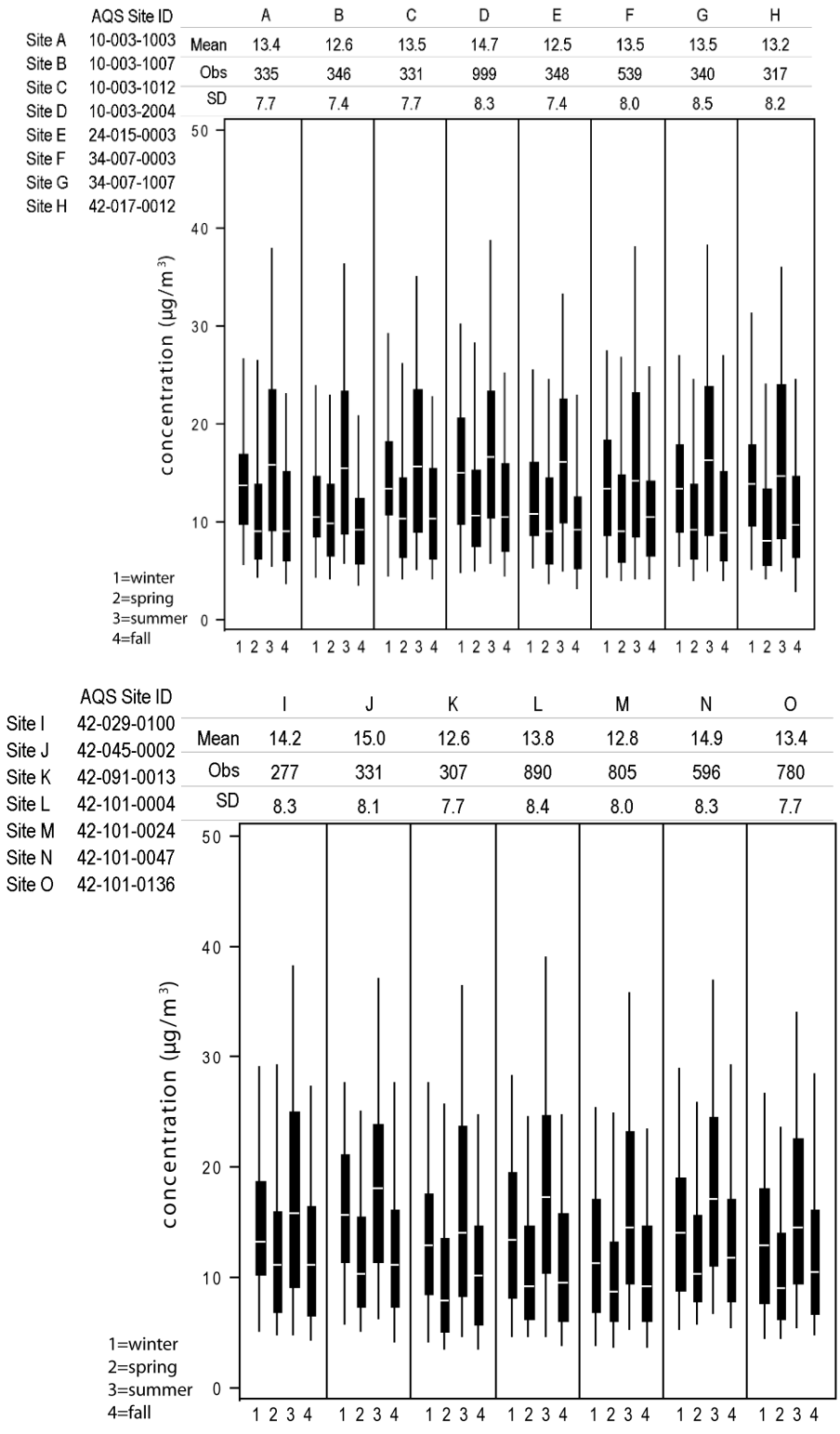


Figure A-65. Box plots illustrating the seasonal distribution of 24-h avg $PM_{2.5}$ concentrations for Philadelphia, PA.

Table A-29. Inter-sampler correlation statistics for each pair of $PM_{2.5}$ monitors reporting to AQS for Philadelphia, PA.

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
A	1.00	0.94	0.96	0.98	0.92	0.96	0.93	0.89	0.95	0.92	0.86	0.96	0.96	0.95	0.97
	(0.0, 0.00)	(4.7, 0.12)	(3.1, 0.08)	(3.2, 0.08)	(4.8, 0.12)	(3.5, 0.10)	(4.2, 0.11)	(5.3, 0.13)	(4.2, 0.12)	(4.6, 0.14)	(4.7, 0.15)	(3.5, 0.08)	(3.7, 0.10)	(4.5, 0.12)	(3.2, 0.08)
	335	305	282	318	311	312	308	289	247	298	277	283	243	236	236
B		1.00	0.95	0.93	0.94	0.92	0.88	0.83	0.90	0.87	0.81	0.91	0.92	0.88	0.89
		(0.0, 0.00)	(4.3, 0.12)	(6.4, 0.15)	(3.4, 0.11)	(5.2, 0.14)	(6.0, 0.15)	(6.8, 0.17)	(6.7, 0.17)	(6.5, 0.18)	(5.9, 0.18)	(6.5, 0.14)	(5.0, 0.14)	(7.3, 0.17)	(5.9, 0.13)
		346	288	329	318	313	315	293	253	302	285	293	253	238	246
C			1.00	0.96	0.95	0.94	0.88	0.88	0.93	0.88	0.84	0.93	0.93	0.91	0.93
			(0.0, 0.00)	(4.3, 0.09)	(3.5, 0.11)	(4.7, 0.12)	(5.3, 0.14)	(6.0, 0.14)	(3.5, 0.12)	(6.6, 0.16)	(5.5, 0.17)	(5.0, 0.12)	(4.8, 0.13)	(6.0, 0.14)	(4.6, 0.11)
			331	312	289	292	286	270	242	278	261	281	245	225	237
D				1.00	0.91	0.94	0.92	0.88	0.94	0.90	0.85	0.95	0.93	0.93	0.95
				(0.0, 0.00)	(6.5, 0.15)	(4.9, 0.12)	(5.0, 0.14)	(6.3, 0.15)	(4.1, 0.12)	(5.3, 0.14)	(5.8, 0.18)	(4.3, 0.11)	(5.6, 0.14)	(4.2, 0.10)	(4.5, 0.11)
				999	325	490	317	297	257	312	287	801	732	540	704
E					1.00	0.91	0.87	0.83	0.90	0.86	0.86	0.88	0.90	0.87	0.89
					(0.0, 0.00)	(5.6, 0.14)	(6.1, 0.15)	(6.7, 0.16)	(6.6, 0.16)	(7.1, 0.19)	(5.7, 0.15)	(6.8, 0.15)	(5.3, 0.13)	(7.0, 0.18)	(5.7, 0.13)
					348	320	321	301	255	310	287	296	255	242	254
F						1.00	0.95	0.90	0.92	0.89	0.87	0.96	0.96	0.95	0.96
						(0.0, 0.00)	(3.4, 0.09)	(5.3, 0.13)	(5.4, 0.14)	(5.9, 0.16)	(4.4, 0.15)	(3.7, 0.10)	(3.6, 0.10)	(4.5, 0.13)	(3.4, 0.09)
						539	317	296	261	309	284	466	437	414	396
G							1.00	0.90	0.90	0.87	0.85	0.93	0.97	0.92	0.96
							(0.0, 0.00)	(4.8, 0.14)	(5.9, 0.16)	(6.2, 0.17)	(4.7, 0.16)	(3.7, 0.09)	(3.1, 0.09)	(5.7, 0.13)	(3.5, 0.08)
							340	295	258	305	289	288	251	235	240
H								1.00	0.84	0.83	0.89	0.90	0.94	0.87	0.89
								(0.0, 0.00)	(5.7, 0.16)	(8.0, 0.19)	(4.4, 0.13)	(5.0, 0.13)	(4.0, 0.12)	(5.9, 0.17)	(4.8, 0.13)
								317	240	288	275	273	234	215	227
I									1.00	0.87	0.81	0.91	0.92	0.90	0.92
									(0.0, 0.00)	(5.5, 0.17)	(5.7, 0.17)	(4.9, 0.14)	(5.4, 0.15)	(5.2, 0.16)	(5.1, 0.14)
			LEGEND						277	248	228	235	215	196	195
			R												
J			**(P90, COD)**							1.00	0.79	0.89	0.89	0.89	0.91
			N							(0.0, 0.00)	(7.4, 0.21)	(5.8, 0.15)	(6.4, 0.17)	(5.7, 0.13)	(5.0, 0.14)
										331	278	282	246	237	231
K											1.00	0.87	0.95	0.84	0.86
											(0.0, 0.00)	(4.7, 0.15)	(3.7, 0.13)	(6.8, 0.20)	(4.3, 0.13)
											307	268	230	211	212
L												1.00	0.98	0.95	0.97
												(0.0, 0.00)	(3.1, 0.09)	(3.7, 0.11)	(3.4, 0.07)
												890	672	512	630
M													1.00	0.95	0.96
													(0.0, 0.00)	(4.7, 0.14)	(3.2, 0.09)
													805	495	563
N														1.00	0.97
														(0.0, 0.00)	(3.5, 0.10)
														596	447
O															1.00
															(0.0, 0.00)
															780

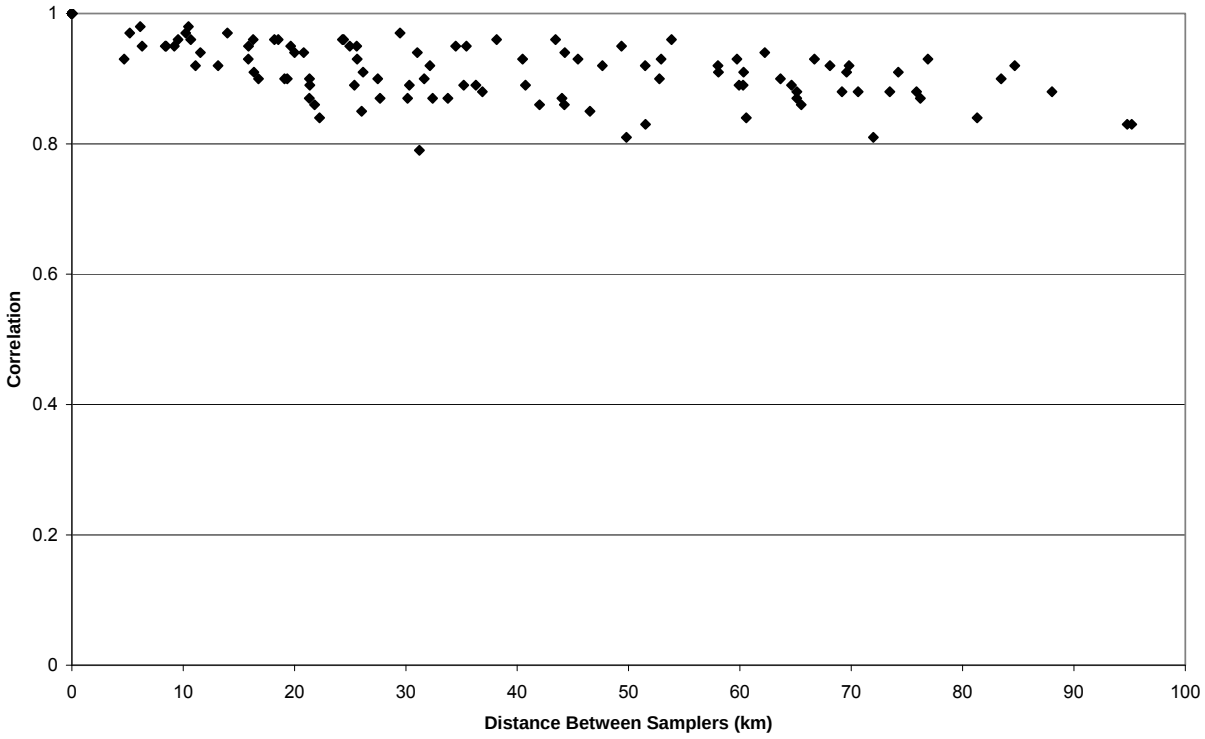


Figure A-66. $PM_{2.5}$ inter-sampler correlations as a function of distance between monitors for Philadelphia, PA.

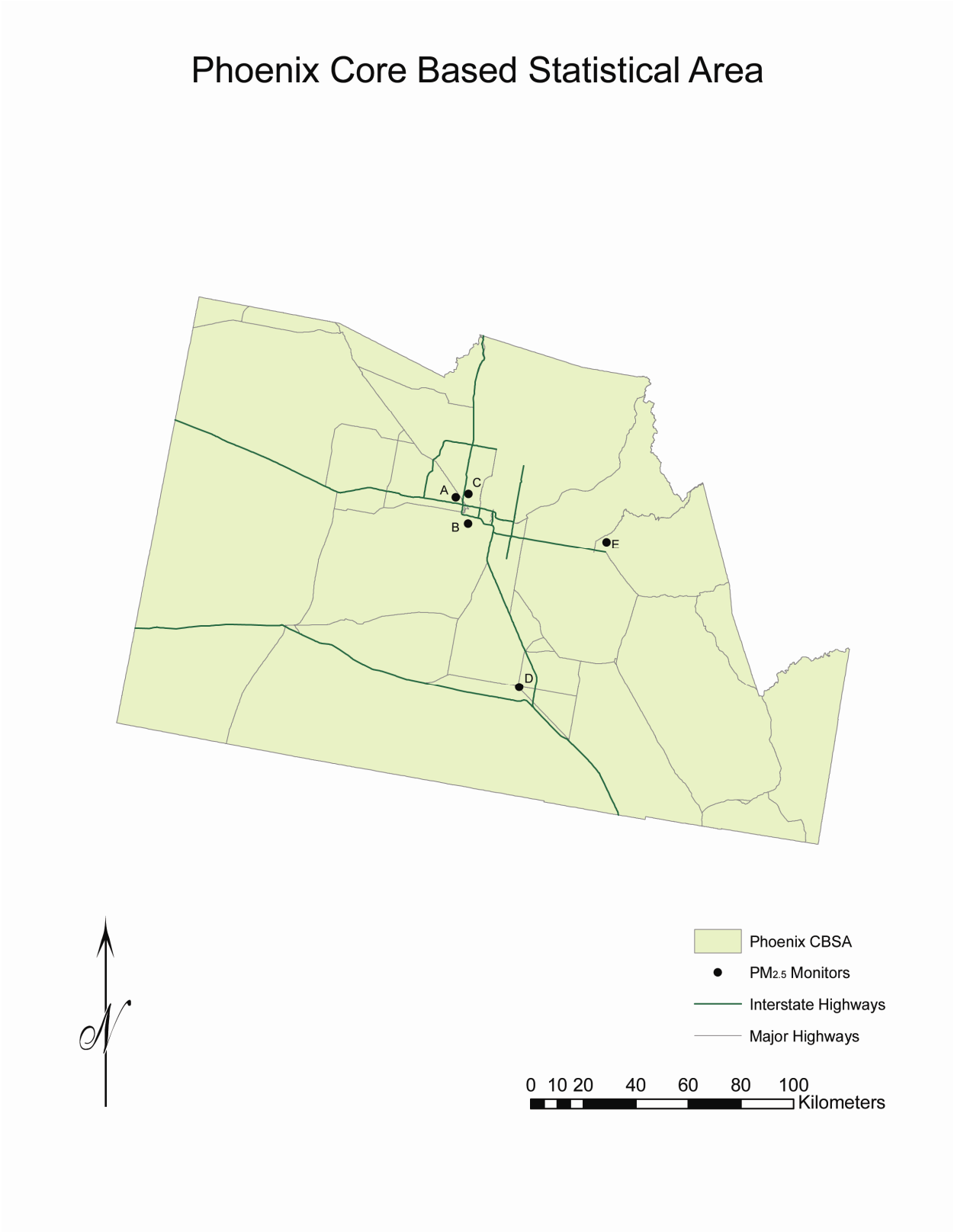


Figure A-67. $PM_{2.5}$ monitor distribution and major highways, Phoenix, AZ.

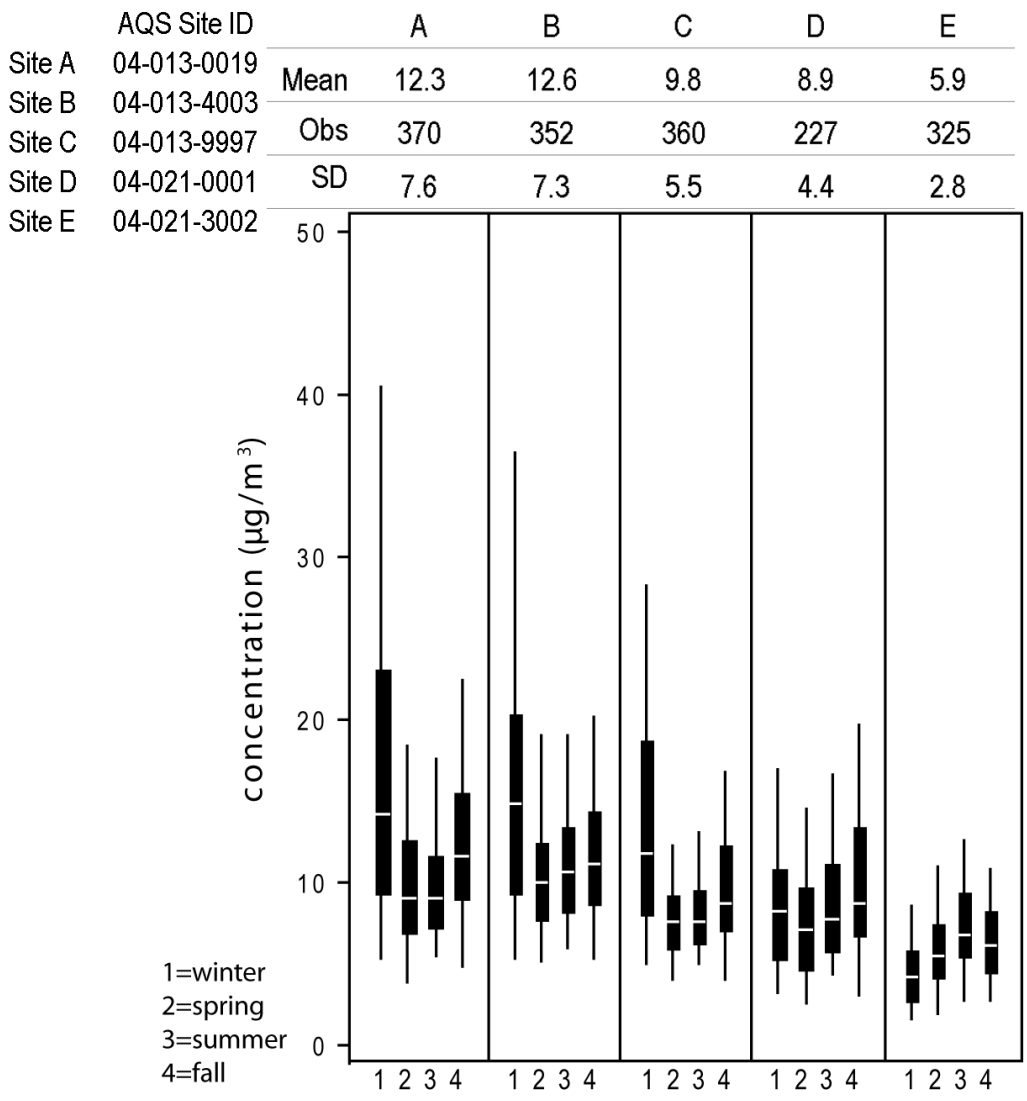


Figure A-68. Box plots illustrating the seasonal distribution of 24-h avg $PM_{2.5}$ concentrations for Phoenix, AZ.

Table A-30. Inter-sampler correlation statistics for each pair of $PM_{2.5}$ monitors reporting to AQS for Phoenix, AZ.

	A	B	C	D	E
A	1.00	0.87	0.92	0.50	0.12
	(0.0, 0.00)	(6.4, 0.15)	(6.5, 0.16)	(10.4, 0.25)	(14.4, 0.40)
	370	345	355	222	321
B		1.00	0.89	0.54	0.23
		(0.0, 0.00)	(6.8, 0.17)	(9.6, 0.25)	(13.2, 0.40)
		352	338	212	307
C			1.00	0.54	0.18
			(0.0, 0.00)	(7.2, 0.20)	(9.3, 0.33)
			360	216	315
D	**LEGEND**			1.00	0.51
	R			(0.0, 0.00)	(7.8, 0.27)
	(P90, COD)			227	200
E	**N**				1.00
					(0.0, 0.00)
					325

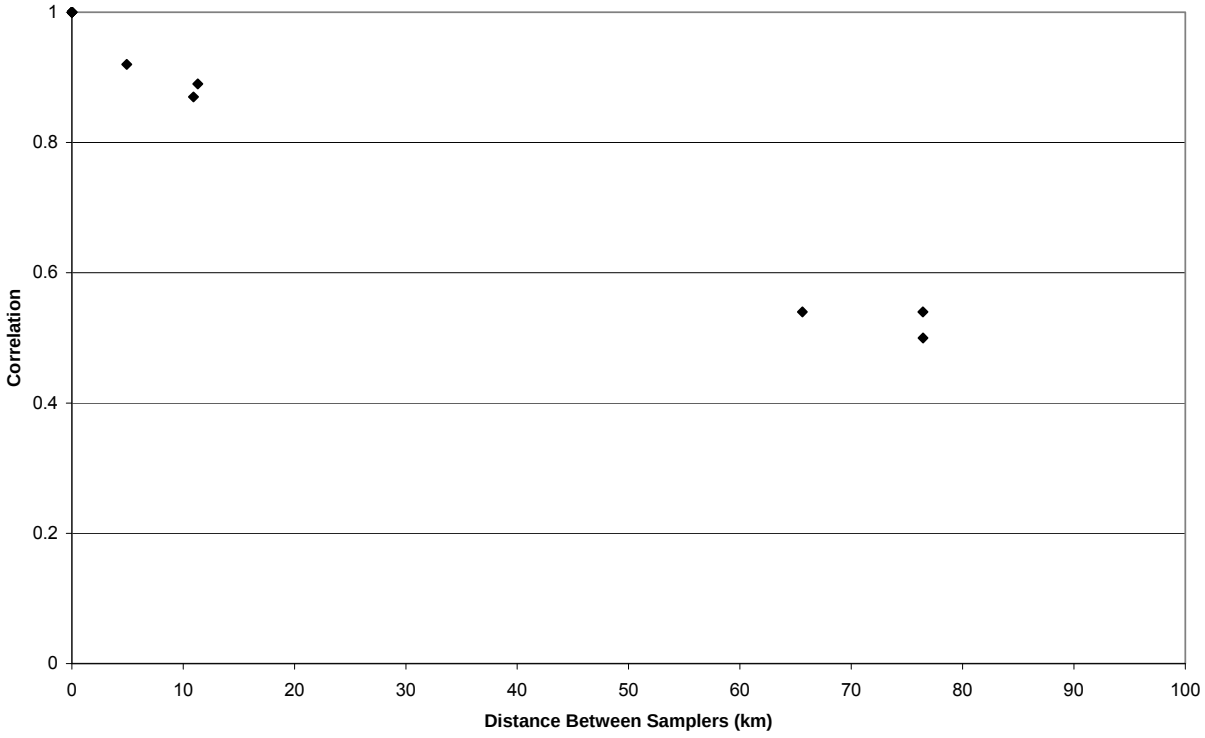


Figure A-69. $PM_{2.5}$ inter-sampler correlations as a function of distance between monitors for Phoenix, AZ.

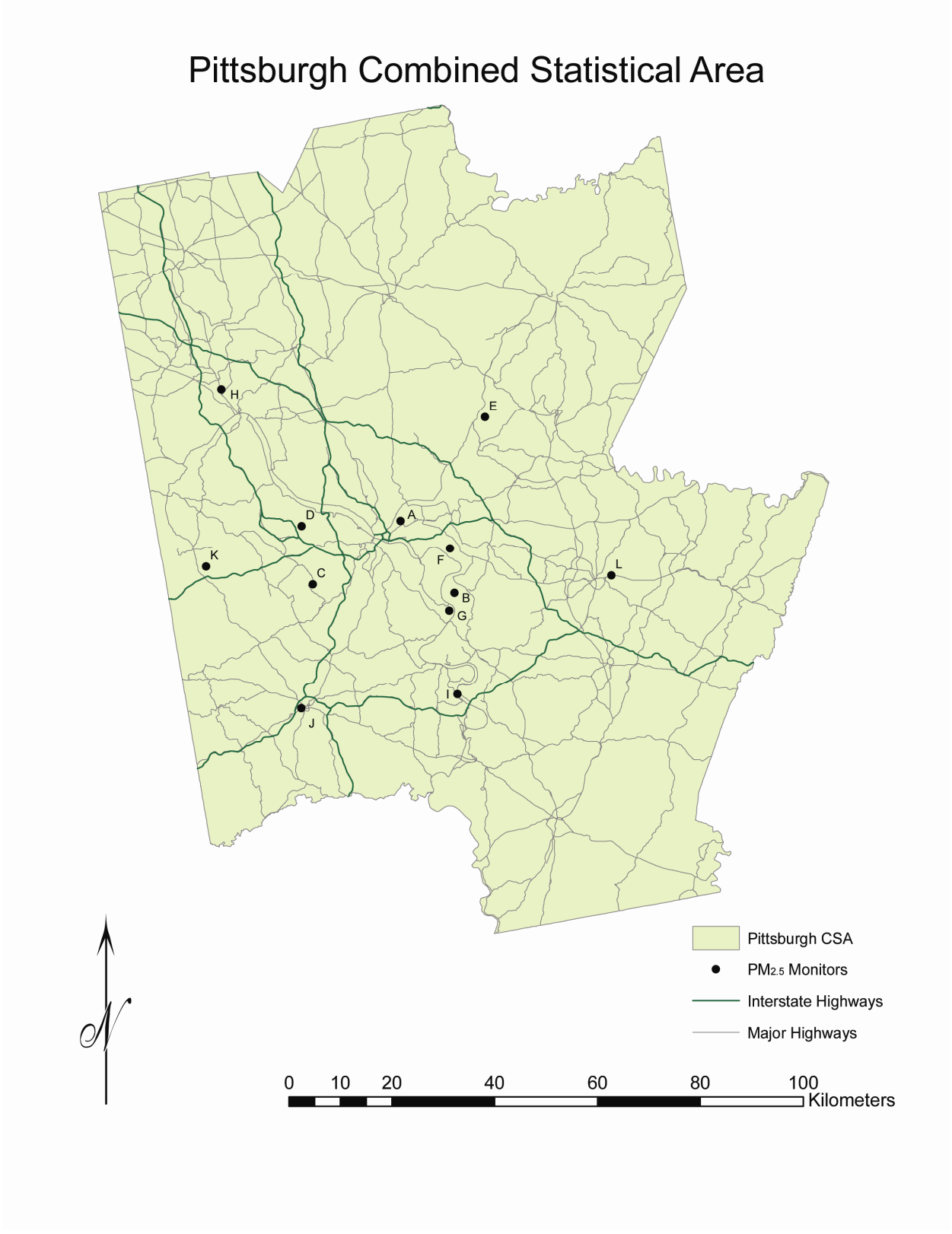


Figure A-70. $PM_{2.5}$ monitor distribution and major highways, Pittsburgh, PA.

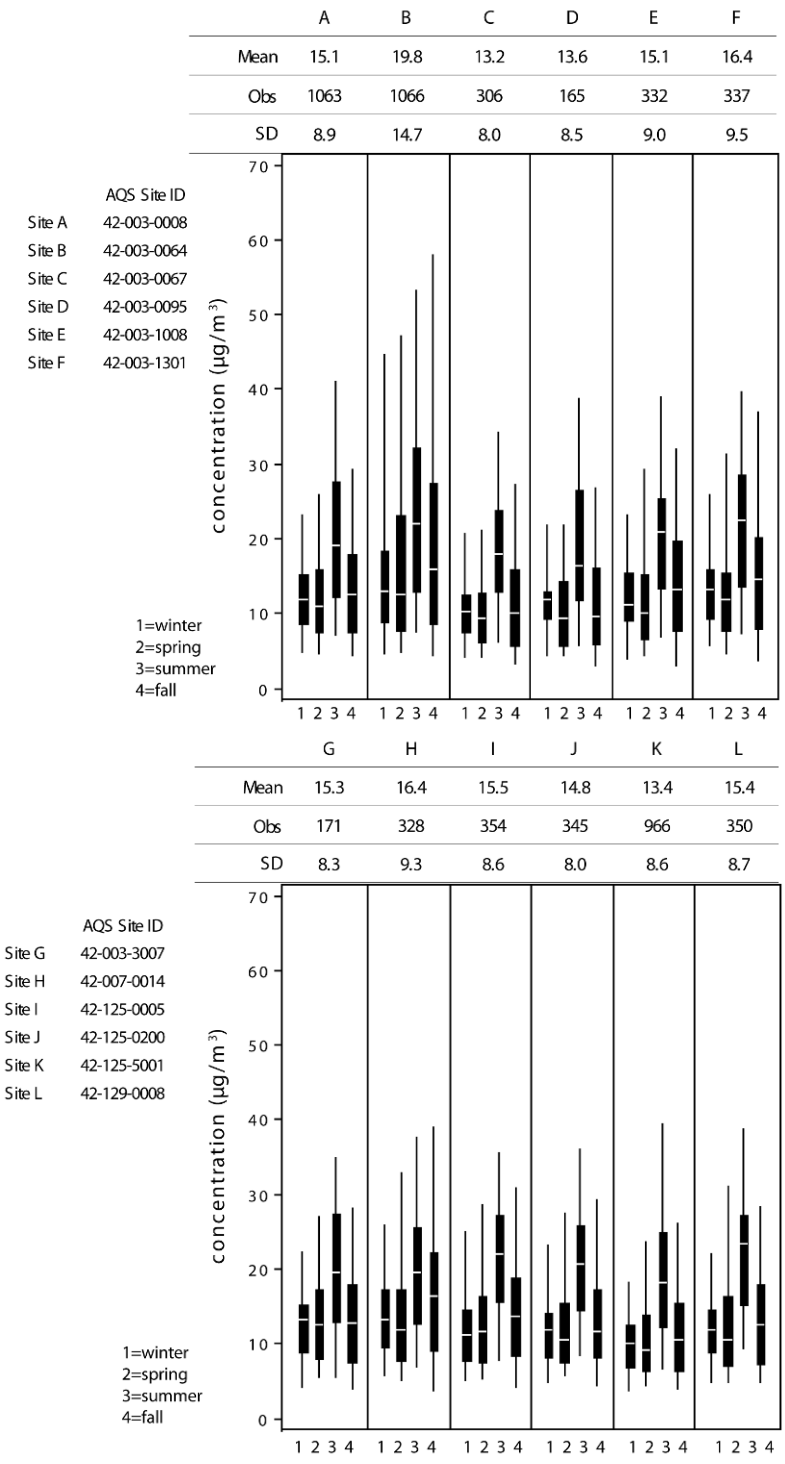


Figure A-71. Box plots illustrating the seasonal distribution of 24-h avg $PM_{2.5}$ concentrations for Pitsburgh, PA.

Table A-31. Inter-sampler correlation statistics for each pair of $PM_{2.5}$ monitors reporting to AQS for Pittsburgh, PA.

	A	B	C	D	E	F	G	H	I	J	K	L
A	1.00	0.79	0.95	0.92	0.93	0.95	0.95	0.85	0.90	0.93	0.91	0.88
	(0.0, 0.00)	(15.9, 0.19)	(5.6, 0.13)	(4.7, 0.11)	(4.7, 0.11)	(4.9, 0.10)	(3.8, 0.10)	(6.4, 0.13)	(6.4, 0.13)	(5.0, 0.12)	(6.0, 0.13)	(5.6, 0.12)
	1063	1035	298	164	323	329	170	319	344	337	934	340
B		1.00	0.71	0.65	0.80	0.85	0.76	0.69	0.71	0.68	0.68	0.67
		(0.0, 0.00)	(16.9, 0.24)	(17.4, 0.25)	(14.4, 0.19)	(12.5, 0.14)	(15.7, 0.20)	(17.0, 0.19)	(15.7, 0.21)	(17.8, 0.23)	(19.3, 0.25)	(15.9, 0.21)
		1066	303	165	329	335	171	324	350	341	938	346
C			1.00	0.93	0.90	0.91	0.94	0.80	0.93	0.96	0.95	0.91
			(0.0, 0.00)	(2.8, 0.09)	(6.6, 0.16)	(8.7, 0.17)	(6.0, 0.14)	(9.4, 0.19)	(6.7, 0.15)	(4.6, 0.12)	(4.5, 0.10)	(6.5, 0.15)
			306	144	282	282	148	268	290	286	270	286
D				1.00	0.84	0.87	0.91	0.79	0.89	0.91	0.97	0.85
				(0.0, 0.00)	(6.4, 0.15)	(8.5, 0.16)	(5.8, 0.13)	(9.2, 0.17)	(5.9, 0.13)	(4.6, 0.11)	(3.1, 0.08)	(6.5, 0.15)
				165	153	161	158	156	158	155	146	157
E					1.00	0.90	0.90	0.84	0.85	0.86	0.88	0.83
					(0.0, 0.00)	(6.4, 0.13)	(6.5, 0.13)	(6.8, 0.14)	(8.3, 0.16)	(7.7, 0.16)	(7.6, 0.15)	(7.3, 0.15)
					332	313	157	295	320	315	290	318
F						1.00	0.91	0.82	0.88	0.88	0.89	0.86
						(0.0, 0.00)	(6.7, 0.13)	(7.4, 0.14)	(7.1, 0.15)	(7.9, 0.15)	(8.8, 0.17)	(7.0, 0.14)
						337	167	302	327	319	296	322
G							1.00	0.78	0.94	0.93	0.90	0.91
							(0.0, 0.00)	(7.3, 0.16)	(4.0, 0.10)	(5.0, 0.11)	(6.6, 0.15)	(5.0, 0.13)
							171	159	163	159	149	161
H								1.00	0.80	0.78	0.82	0.70
								(0.0, 0.00)	(8.4, 0.15)	(8.2, 0.17)	(9.0, 0.18)	(9.2, 0.18)
								328	317	309	288	314
I									1.00	0.93	0.89	0.88
									(0.0, 0.00)	(5.0, 0.11)	(7.2, 0.16)	(6.0, 0.13)
									354	334	310	339
J										1.00	0.93	0.88
										(0.0, 0.00)	(5.5, 0.12)	(5.9, 0.13)
										345	302	331
K											1.00	0.86
											(0.0, 0.00)	(6.9, 0.15)
											966	306
L												1.00
												(0.0, 0.00)
												350

LEGEND
Pearson R
(P90, COD)
n

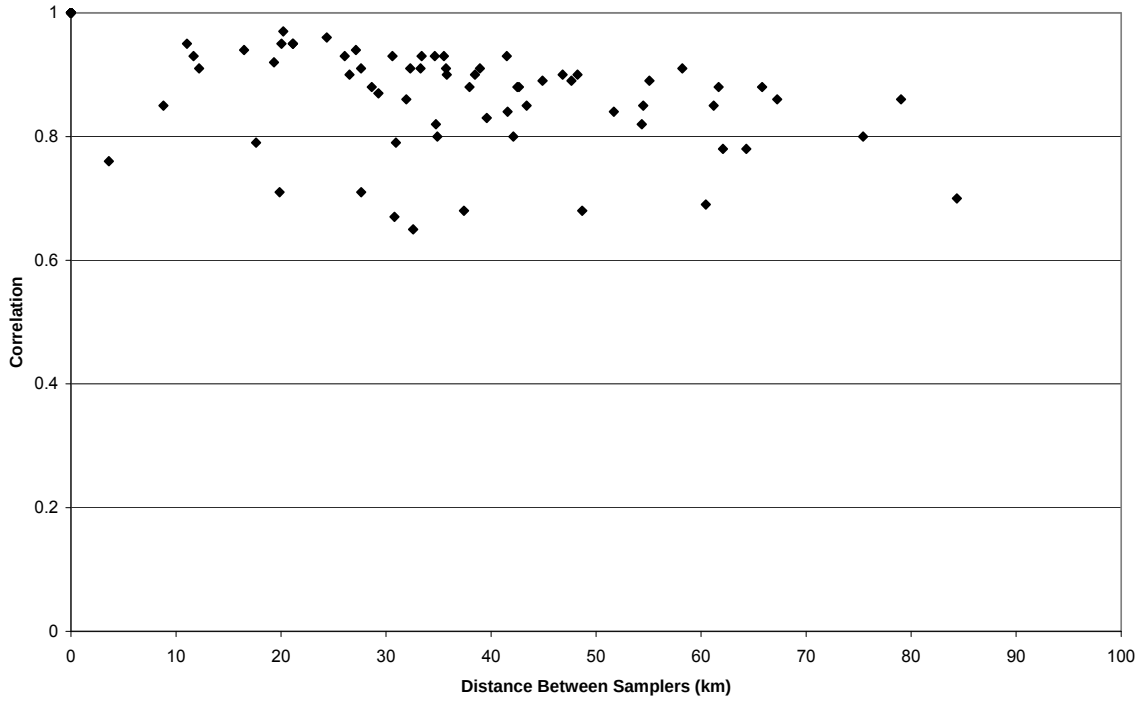


Figure A-72. $PM_{2.5}$ inter-sampler correlations as a function of distance between monitors for Pittsburgh, PA.

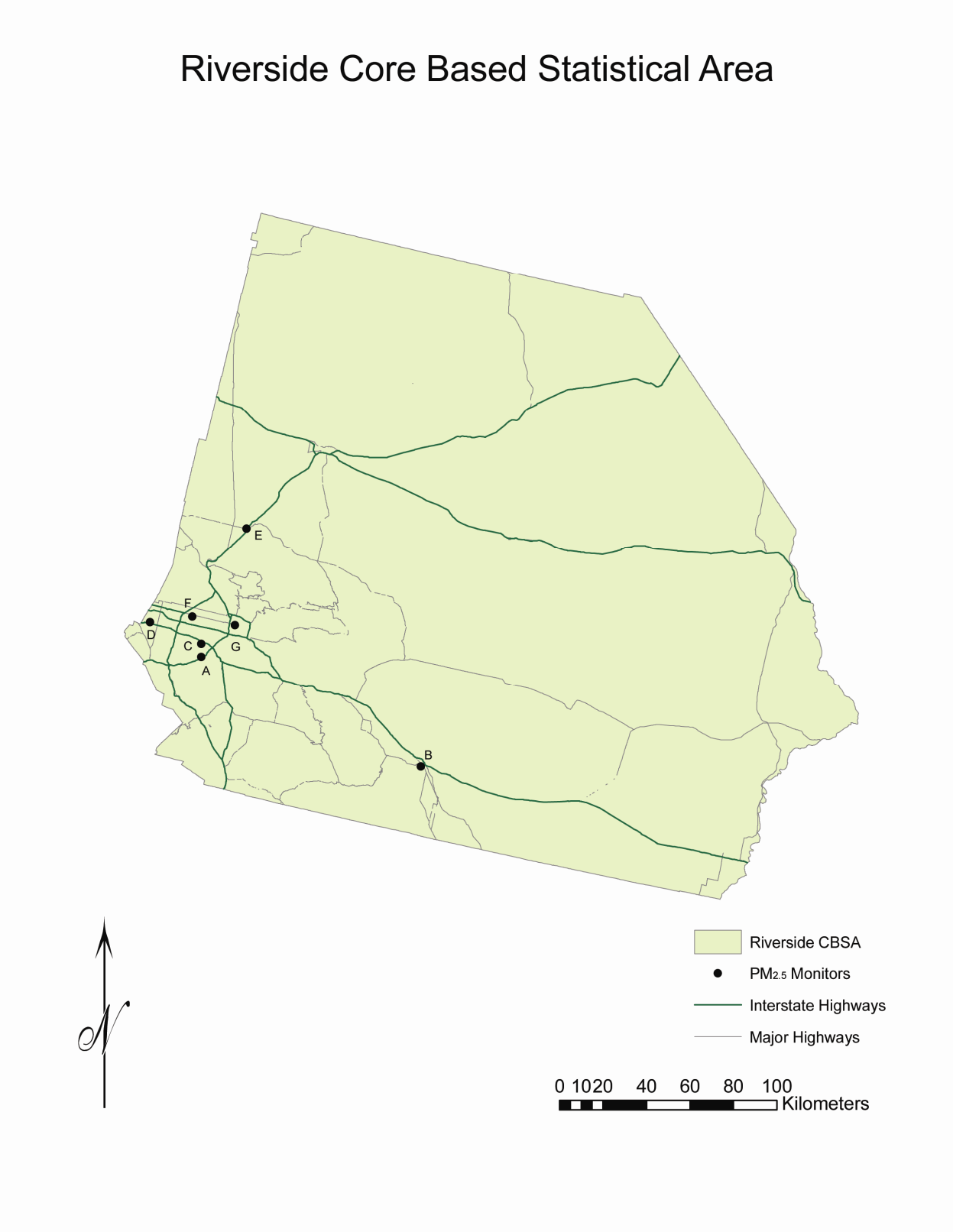


Figure A-73. $PM_{2.5}$ monitor distribution and major highways, Riverside, CA.

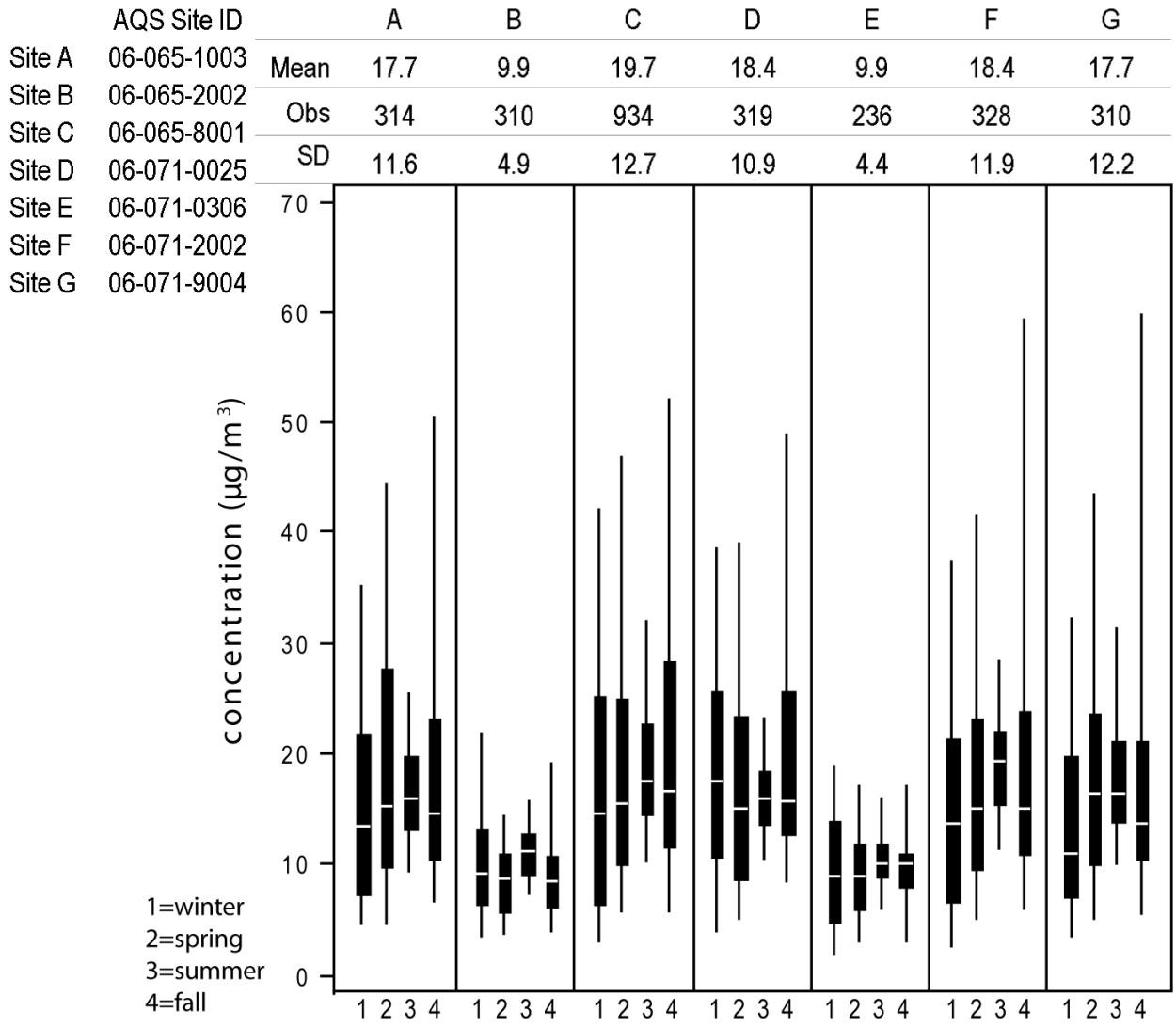


Figure A-74. Box plots illustrating the seasonal distribution of 24-h avg $PM_{2.5}$ concentrations for Riverside, CA.

Table A-32. Inter-sampler correlation statistics for each pair of $PM_{2.5}$ monitors reporting to AQS for Riverside, CA.

	A	B	C	D	E	F	G
A	1.00	0.45	0.96	0.92	0.36	0.94	0.90
	(0.0, 0.00)	(20.6, 0.32)	(5.0, 0.10)	(7.2, 0.13)	(22.1, 0.35)	(6.0, 0.12)	(5.7, 0.13)
	314	269	297	282	191	281	273
B		1.00	0.49	0.49	0.42	0.49	0.50
		(0.0, 0.00)	(22.7, 0.35)	(20.9, 0.34)	(8.2, 0.25)	(19.7, 0.33)	(18.8, 0.31)
		310	289	270	203	285	266
C			1.00	0.91	0.37	0.92	0.91
			(0.0, 0.00)	(8.2, 0.14)	(26.6, 0.37)	(6.9, 0.12)	(7.6, 0.12)
			934	300	227	302	287
D				1.00	0.36	0.93	0.82
				(0.0, 0.00)	(20.1, 0.35)	(6.7, 0.14)	(9.6, 0.17)
		LEGEND		319	195	289	274
E		**R**			1.00	0.40	0.41
		(P90, COD)			(0.0, 0.00)	(21.1, 0.36)	(21.6, 0.34)
		N			236	201	190
F						1.00	0.90
						(0.0, 0.00)	(6.7, 0.12)
						328	276
G							1.00
							(0.0, 0.00)
							310

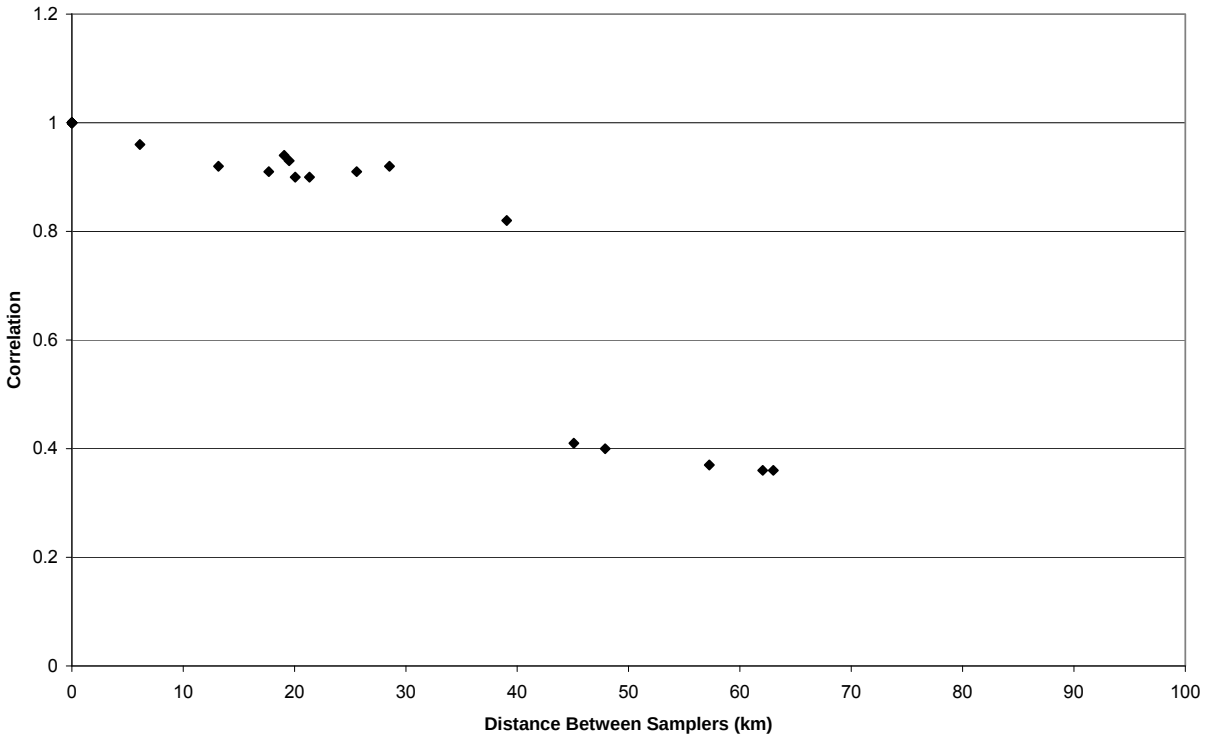


Figure A-75. $PM_{2.5}$ inter-sampler correlations as a function of distance between monitors for Riverside CA.

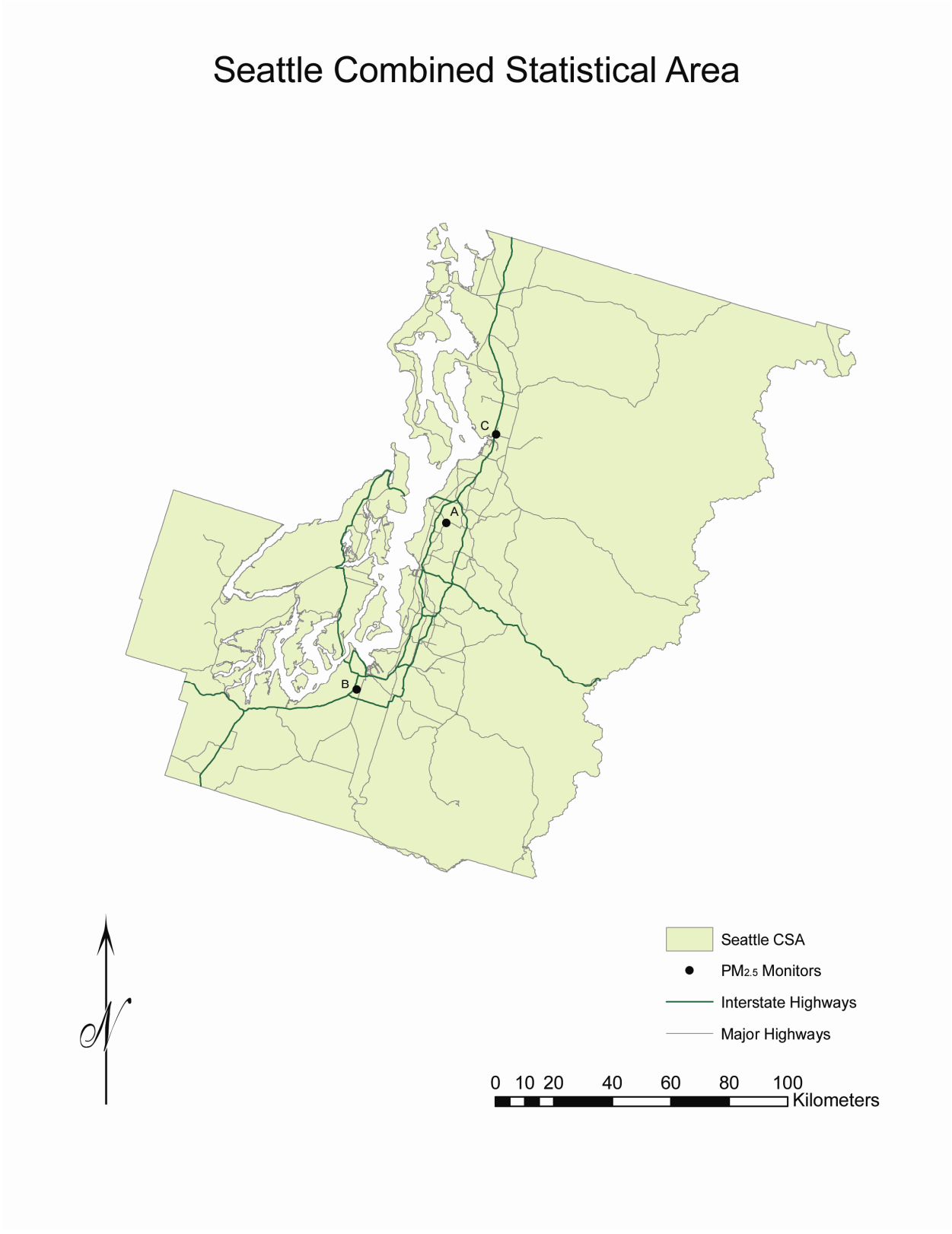


Figure A-76. $PM_{2.5}$ monitor distribution and major highways, Seattle, WA.

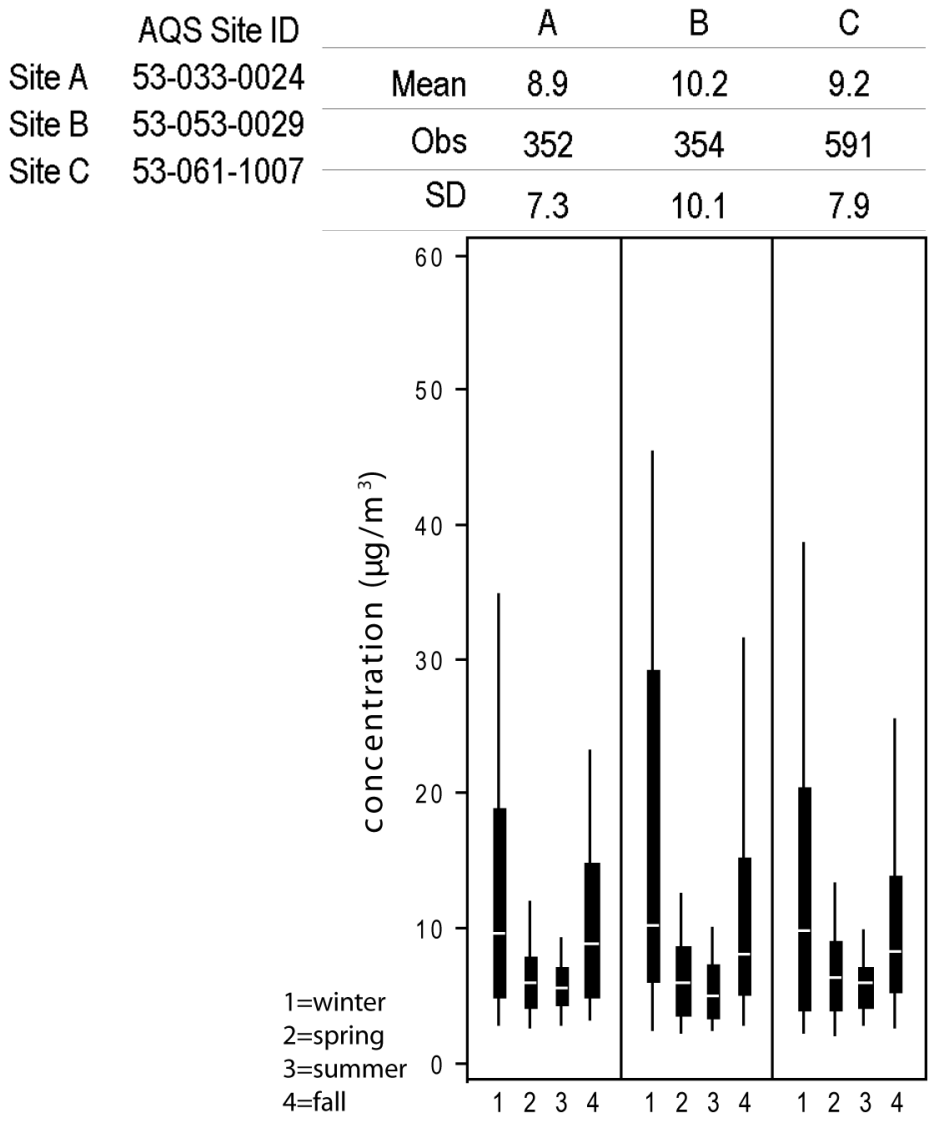


Figure A-77. Box plots illustrating the seasonal distribution of 24-h avg $PM_{2.5}$ concentrations for Seattle, WA.

Table A-33. Inter-sampler correlation statistics for each pair of $PM_{2.5}$ monitors reporting to AQS for Seattle, WA.

		A	B	C
A		1.00	0.89	0.86
		(0.0, 0.00)	(6.3, 0.16)	(4.5, 0.14)
		352	337	331
B	**LEGEND**		1.00	0.80
	R		(0.0, 0.00)	(7.8, 0.20)
	(P90, COD)		354	335
C	**N**			1.00
				(0.0, 0.00)
				591

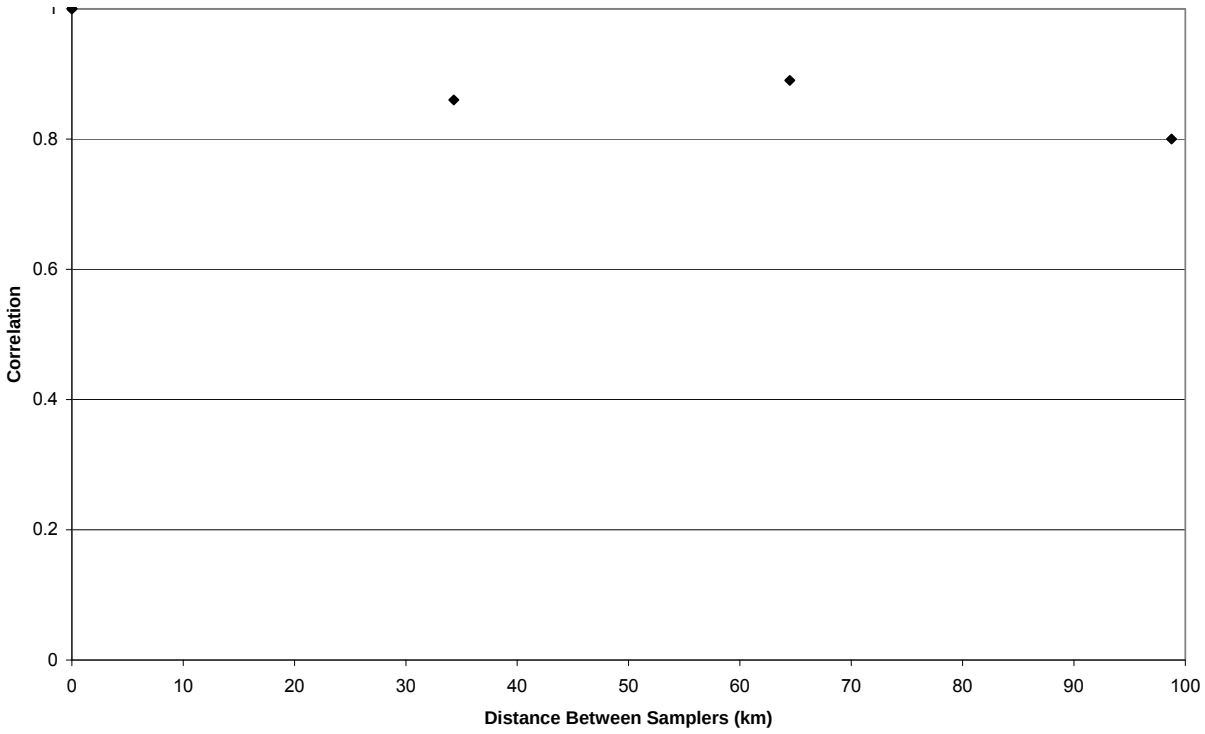


Figure A-78. $PM_{2.5}$ inter-sampler correlations as a function of distance between monitors for Seattle, WA.

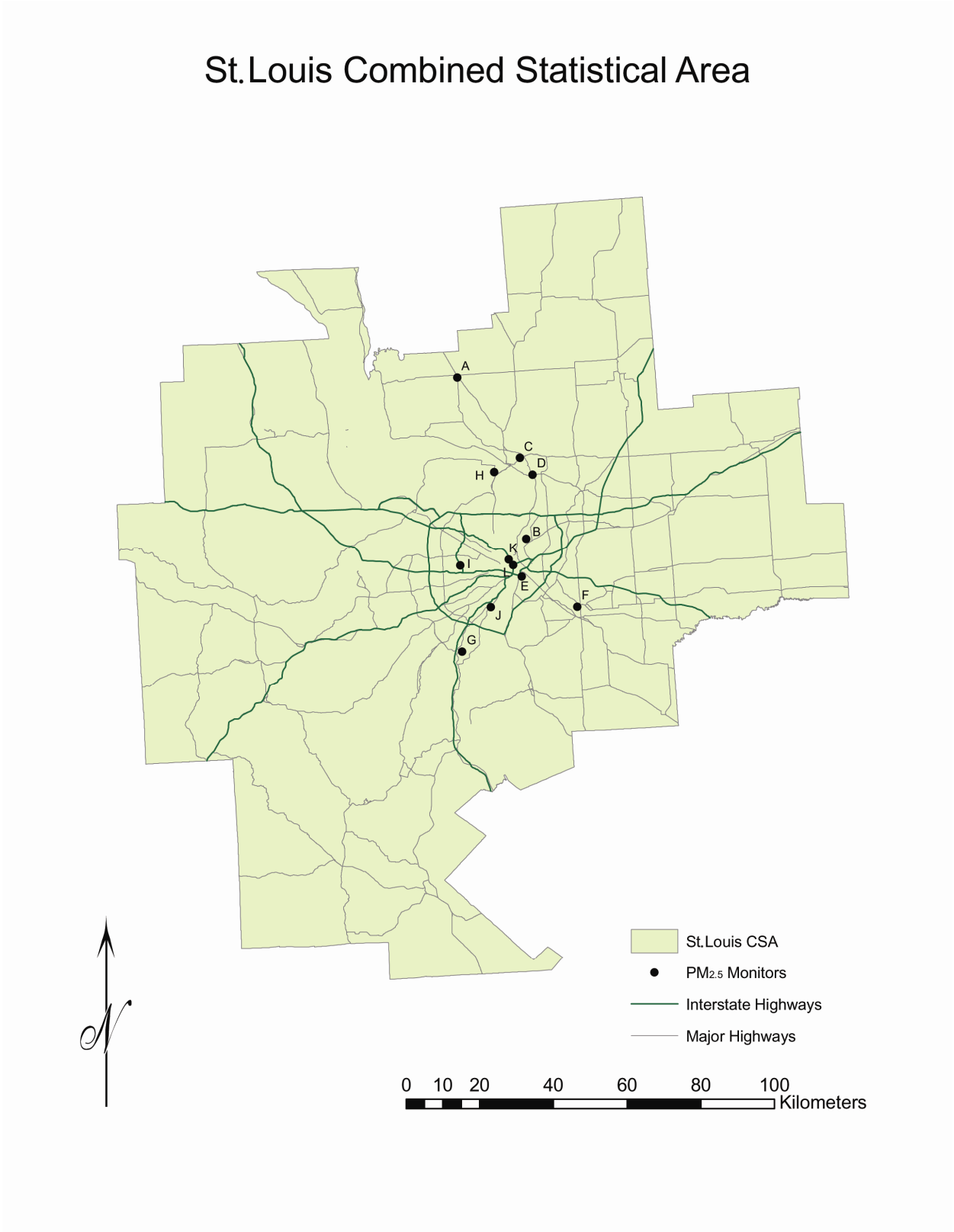


Figure A-79. $PM_{2.5}$ monitor distribution and major highways, St. Louis, MO.

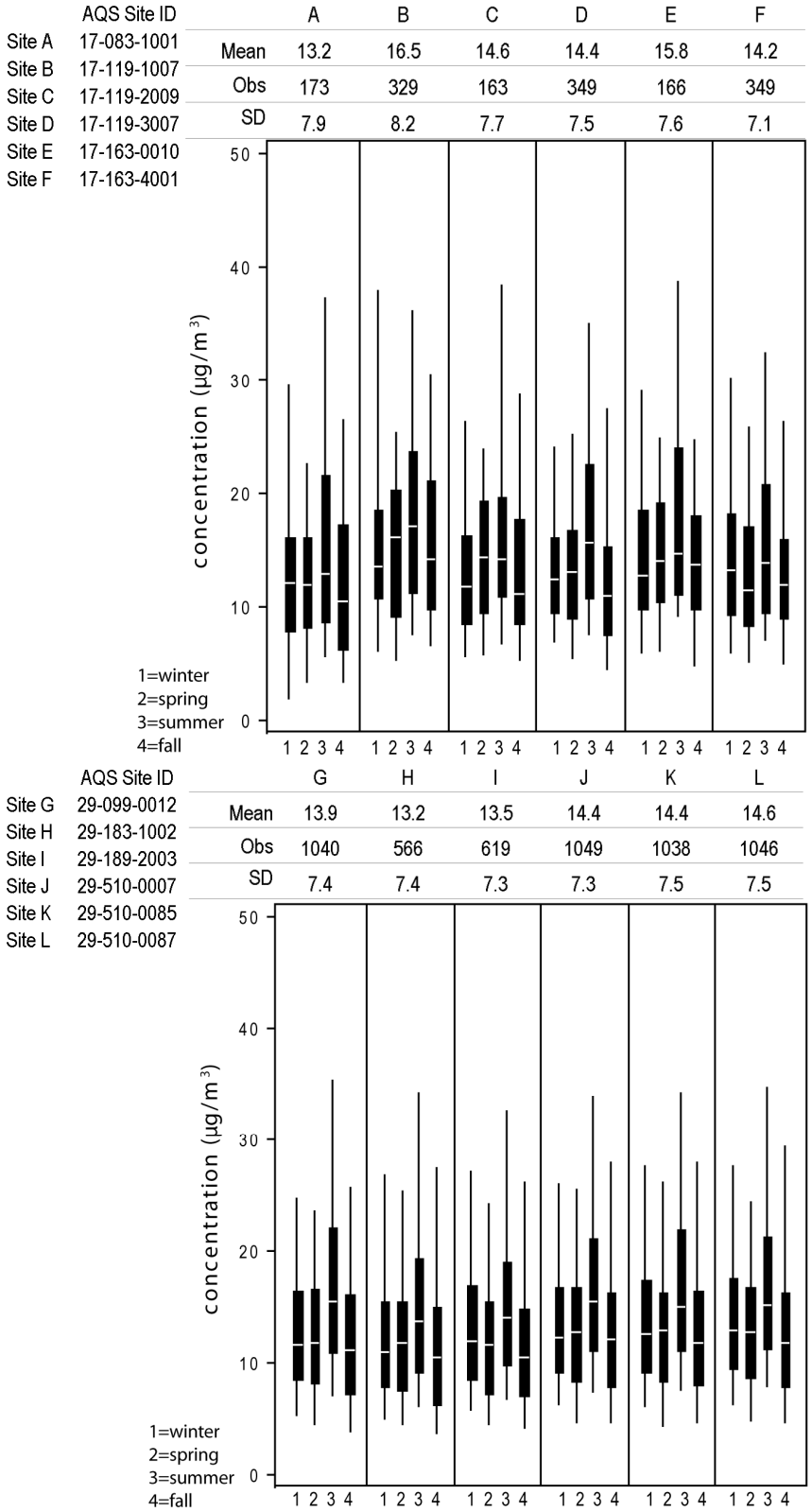


Figure A-80. Box plots illustrating the seasonal distribution of 24-h avg $PM_{2.5}$ concentrations for St. Louis, MO.

Table A-34. Inter-sampler correlation statistics for each pair of $PM_{2.5}$ monitors reporting to AQS for St. Louis, MO.

Site	A	B	C	D	E	F	G	H	I	J	K	L
A	1.00	0.85	0.93	0.89	0.88	0.86	0.85	0.93	0.86	0.84	0.84	0.88
	(0.0, 0.00)	(10.5, 0.23)	(4.7, 0.17)	(5.0, 0.17)	(7.3, 0.20)	(6.2, 0.18)	(4.8, 0.17)	(4.1, 0.13)	(4.4, 0.16)	(6.0, 0.18)	(5.7, 0.19)	(5.3, 0.17)
	173	156	129	162	146	156	167	158	162	168	169	166
B		1.00	0.89	0.86	0.85	0.82	0.88	0.89	0.88	0.86	0.87	0.89
		(0.0, 0.00)	(8.6, 0.16)	(7.4, 0.16)	(7.7, 0.16)	(8.6, 0.17)	(7.8, 0.17)	(8.2, 0.18)	(7.9, 0.17)	(7.7, 0.17)	(7.5, 0.16)	(6.8, 0.14)
		329	135	301	156	306	312	305	318	316	316	315
C			1.00	0.94	0.91	0.88	0.90	0.96	0.94	0.90	0.89	0.94
			(0.0, 0.00)	(4.0, 0.11)	(6.4, 0.13)	(5.7, 0.13)	(5.5, 0.13)	(3.9, 0.11)	(5.3, 0.11)	(5.7, 0.13)	(5.6, 0.14)	(4.4, 0.11)
			163	139	124	133	158	141	144	158	160	156
D				1.00	0.89	0.84	0.89	0.94	0.92	0.89	0.88	0.92
				(0.0, 0.00)	(5.7, 0.13)	(6.0, 0.15)	(4.9, 0.12)	(4.3, 0.12)	(4.5, 0.11)	(4.7, 0.13)	(4.6, 0.12)	(3.9, 0.11)
				349	156	314	331	315	326	335	332	336
E					1.00	0.90	0.91	0.90	0.91	0.93	0.91	0.95
					(0.0, 0.00)	(5.5, 0.12)	(6.2, 0.13)	(5.8, 0.16)	(5.3, 0.14)	(5.1, 0.13)	(4.9, 0.13)	(3.7, 0.10)
					166	152	159	153	157	160	163	160
F						1.00	0.89	0.86	0.88	0.88	0.85	0.88
						(0.0, 0.00)	(5.4, 0.12)	(6.1, 0.16)	(5.4, 0.13)	(5.3, 0.14)	(5.6, 0.14)	(5.4, 0.13)
		LEGEND				349	333	317	332	337	332	334
G		**R**					1.00	0.93	0.94	0.96	0.93	0.94
		(P90, COD)					(0.0, 0.00)	(4.3, 0.10)	(3.3, 0.08)	(2.9, 0.08)	(3.9, 0.10)	(3.8, 0.10)
		N					1040	533	586	994	987	992
H								1.00	0.96	0.95	0.95	0.96
								(0.0, 0.00)	(3.0, 0.08)	(4.1, 0.12)	(3.8, 0.12)	(4.0, 0.11)
								566	550	552	546	544
I									1.00	0.96	0.95	0.96
									(0.0, 0.00)	(3.1, 0.09)	(3.1, 0.10)	(3.4, 0.09)
									619	605	599	598
J										1.00	0.96	0.97
										(0.0, 0.00)	(2.5, 0.09)	(2.5, 0.08)
										1049	1001	1007
K											1.00	0.97
											(0.0, 0.00)	(1.9, 0.07)
											1038	991
L												1.00
												(0.0, 0.00)
												1046

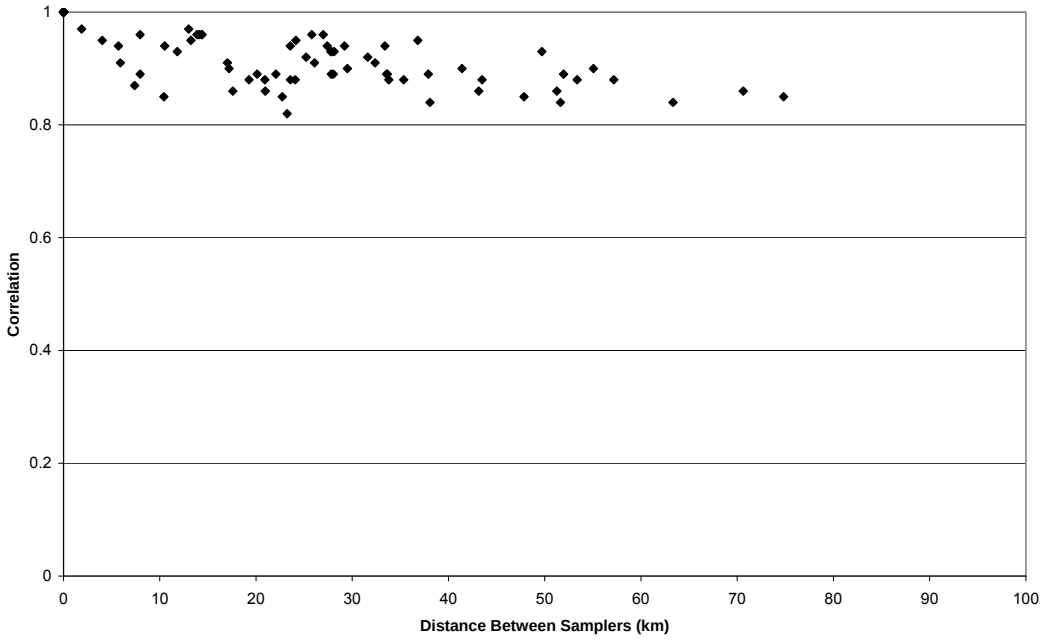


Figure A-81 $PM_{2.5}$ inter-sampler correlations as a function of distance between monitors for St. Louis, MO.

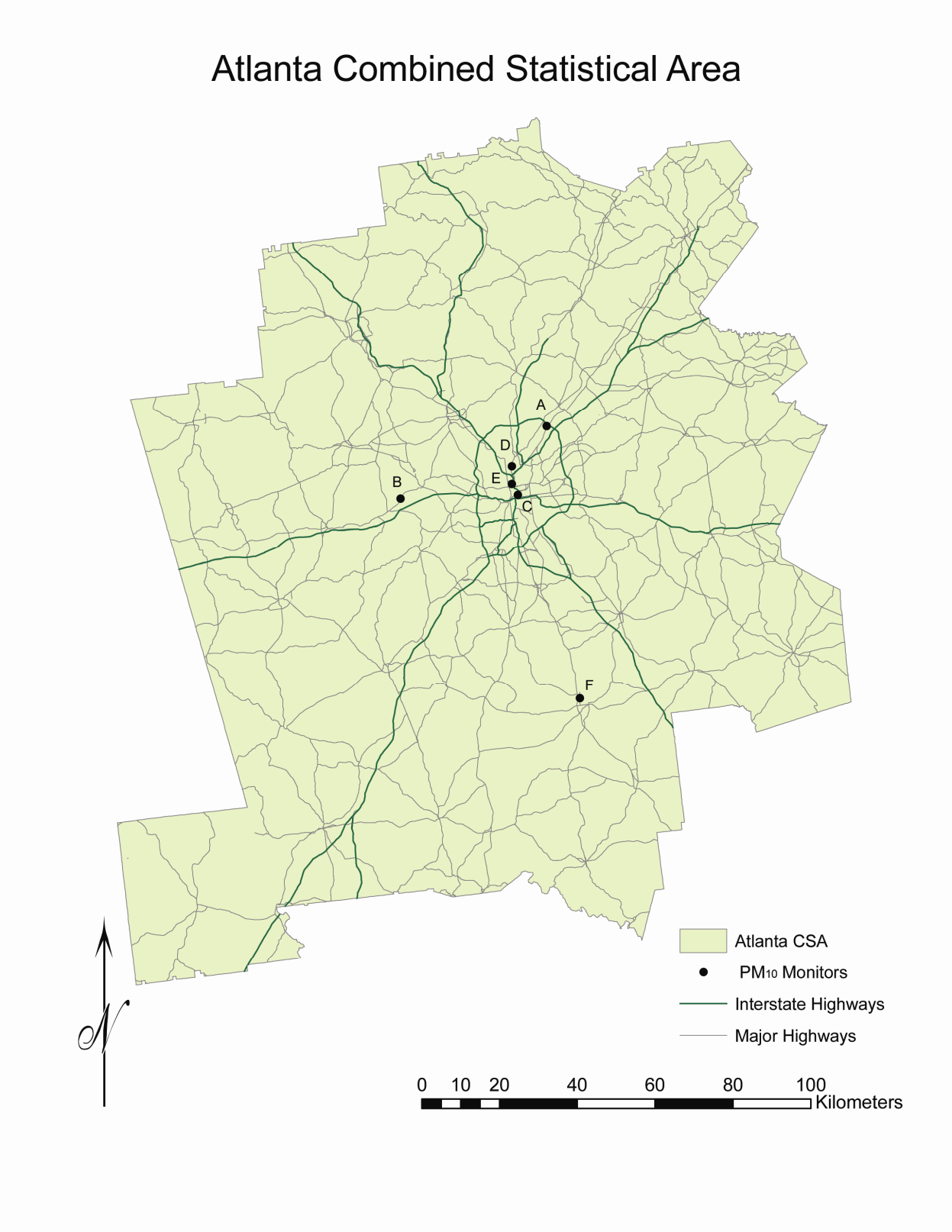


Figure A-82. PM_{10} monitor distribution and major highways, Atlanta, GA.

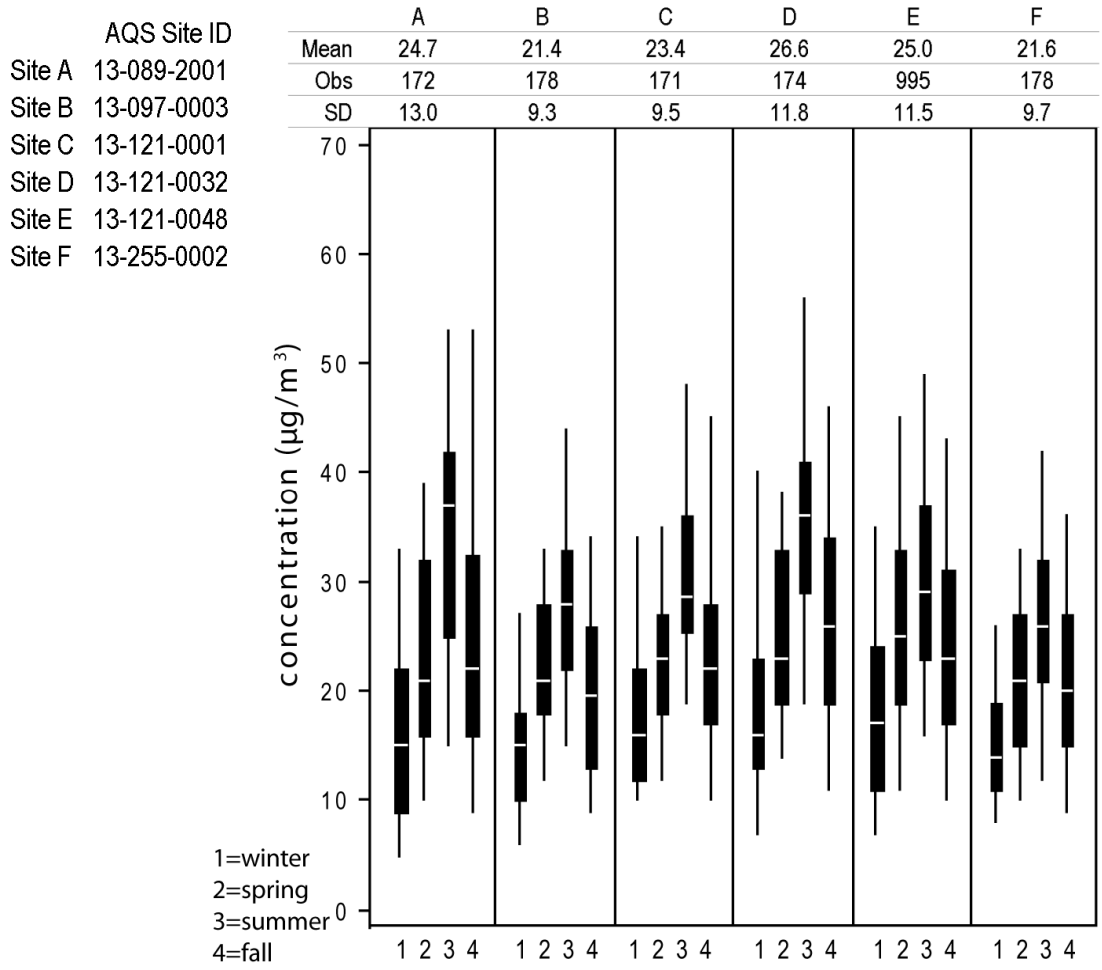


Figure A-83. Box plots illustrating the seasonal distribution of 24-h avg PM_{10} concentrations for Atlanta, GA.

Table A-35. Inter-sampler correlation statistics for each pair of PM_{10} monitors reporting to AQS for Atlanta, GA.

Site	A	B	C	D	E	F
A	1.00	0.69	0.74	0.78	0.70	0.59
	(0.0, 0.00)	(18.0, 0.22)	(15.0, 0.20)	(13.0, 0.20)	(16.0, 0.22)	(20.0, 0.24)
	172	169	162	165	158	164
B		1.00	0.88	0.79	0.71	0.82
		(0.0, 0.00)	(6.0, 0.12)	(14.5, 0.17)	(16.0, 0.18)	(10.0, 0.14)
		178	167	170	162	169
C			1.00	0.88	0.84	0.82
			(0.0, 0.00)	(9.0, 0.13)	(10.0, 0.13)	(9.0, 0.15)
			171	162	155	161
D	**LEGEND**			1.00	0.75	0.74
	R			(0.0, 0.00)	(12.0, 0.15)	(15.0, 0.20)
	(P90, COD)			174	158	166
E	**N**				1.00	0.67
					(0.0, 0.00)	(17.0, 0.19)
					995	163
F						1.00
						(0.0, 0.00)
						178

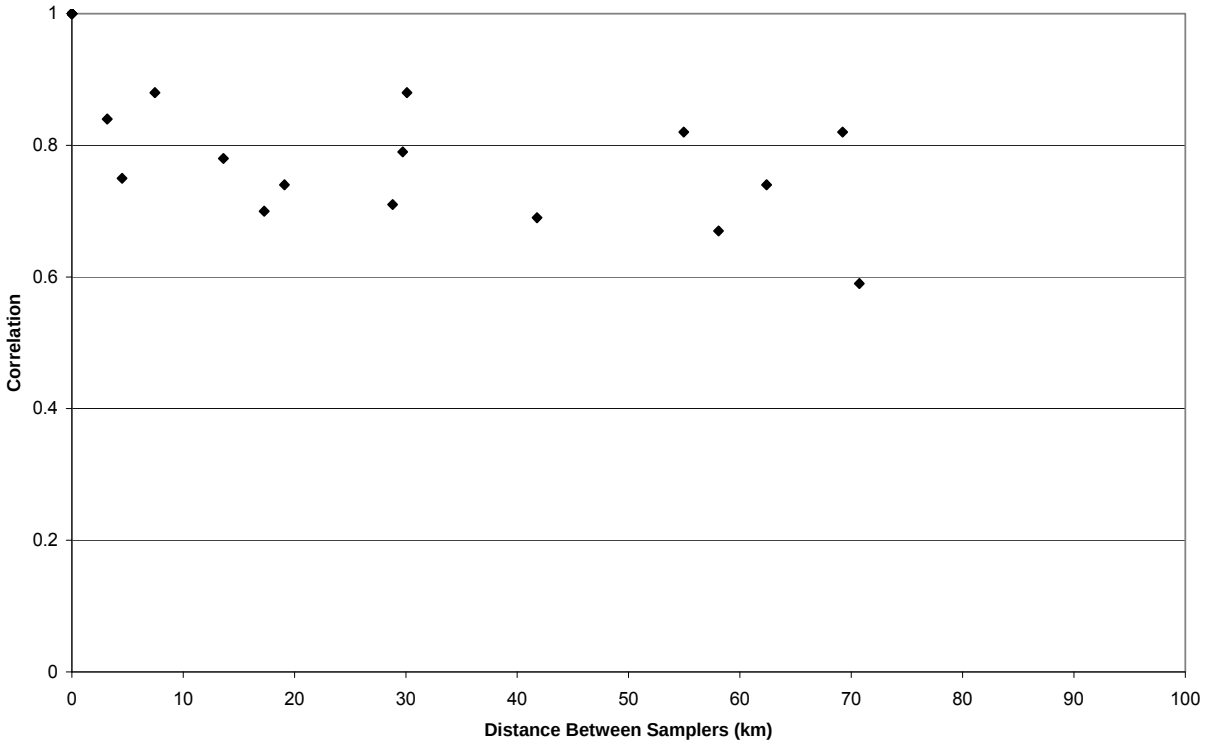


Figure A-84. PM_{10} inter-sampler correlations as a function of distance between monitors for Atlanta, GA.

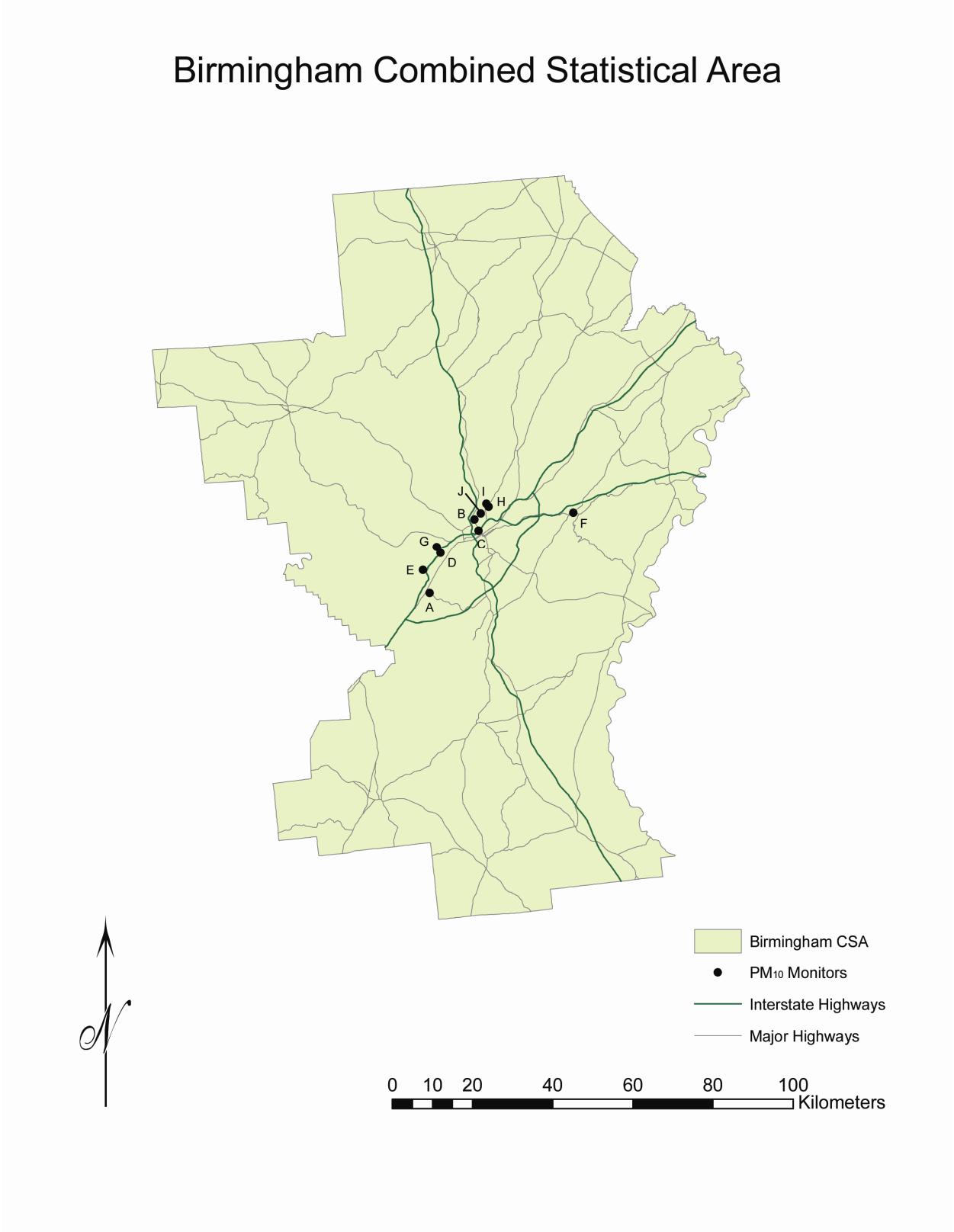


Figure A-85. PM_{10} monitor distribution and major highways, Birmingham, AL.

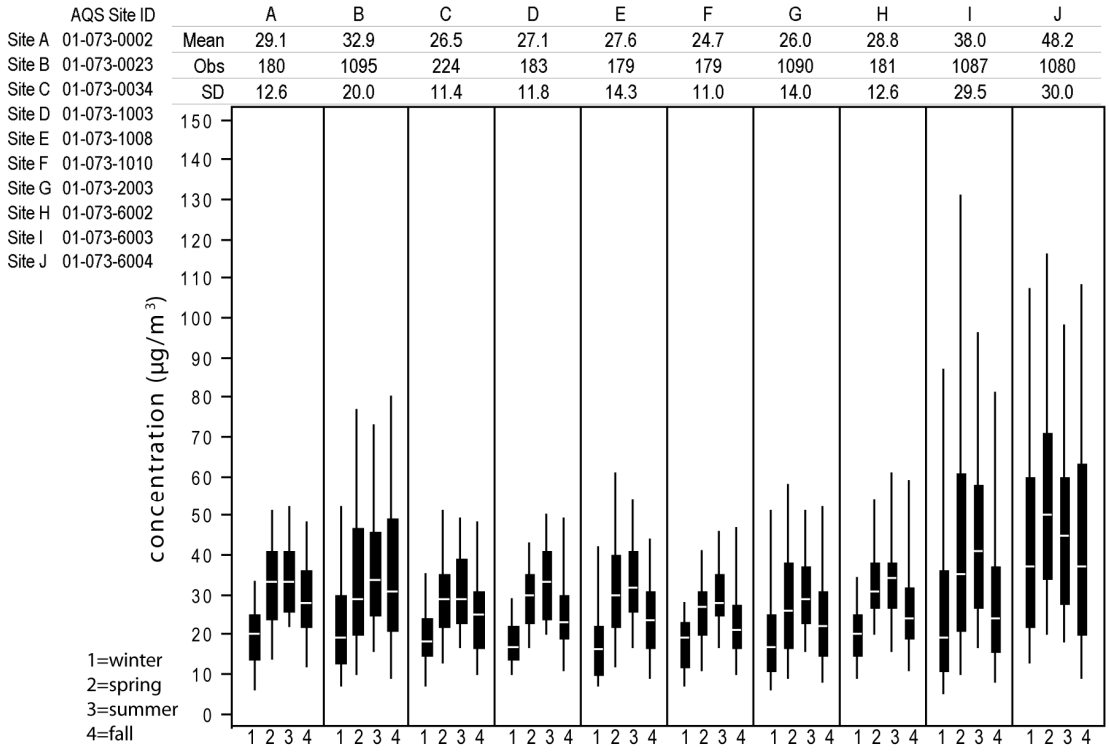


Figure A-86. Box plots illustrating the seasonal distribution of 24-h avg PM_{10} concentrations for Birmingham, AL.

Table A-36. Inter-sampler correlation statistics for each pair of PM_{10} monitors reporting to AQS for Birmingham, AL.

	A	B	C	D	E	F	G	H	I	J
A	1.00	0.80	0.88	0.86	0.78	0.84	0.77	0.78	0.41	0.29
	(0.0, 0.00)	(23.0, 0.16)	(11.0, 0.11)	(12.0, 0.13)	(12.0, 0.14)	(13.0, 0.13)	(15.0, 0.18)	(14.0, 0.15)	(41.0, 0.30)	(68.0, 0.34)
	180	180	174	180	176	171	180	178	179	177
B		1.00	0.82	0.74	0.61	0.73	0.75	0.71	0.26	0.23
		(0.0, 0.00)	(23.0, 0.17)	(25.0, 0.21)	(26.0, 0.20)	(26.0, 0.19)	(25.0, 0.20)	(25.0, 0.22)	(51.0, 0.33)	(57.0, 0.36)
		1095	224	183	179	179	1090	181	1087	1080
C			1.00	0.84	0.66	0.78	0.74	0.80	0.33	0.41
			(0.0, 0.00)	(10.0, 0.12)	(15.0, 0.16)	(12.0, 0.14)	(14.0, 0.17)	(13.0, 0.15)	(43.0, 0.32)	(62.0, 0.34)
			224	175	171	168	224	173	222	221
D				1.00	0.67	0.79	0.76	0.84	0.45	0.41
				(0.0, 0.00)	(15.0, 0.17)	(12.0, 0.15)	(14.0, 0.17)	(11.0, 0.12)	(42.0, 0.30)	(65.5, 0.34)
				183	178	173	183	180	182	180
E					1.00	0.67	0.64	0.56	0.33	0.12
					(0.0, 0.00)	(16.0, 0.15)	(18.0, 0.18)	(19.0, 0.20)	(45.0, 0.32)	(71.0, 0.39)
					179	169	179	176	178	176
F						1.00	0.75	0.74	0.36	0.21
		LEGEND				(0.0, 0.00)	(14.0, 0.16)	(15.0, 0.17)	(43.0, 0.32)	(71.0, 0.38)
		R				179	179	171	178	177
G		**(P90, COD)**					1.00	0.76	0.59	0.15
		N					(0.0, 0.00)	(15.0, 0.19)	(43.0, 0.27)	(63.0, 0.39)
							1090	181	1083	1075
H								1.00	0.58	0.50
								(0.0, 0.00)	(38.0, 0.27)	(59.0, 0.31)
								181	180	178
I									1.00	0.05
									(0.0, 0.00)	(72.0, 0.40)
									1087	1072
J										1.00
										(0.0, 0.00)
										1080

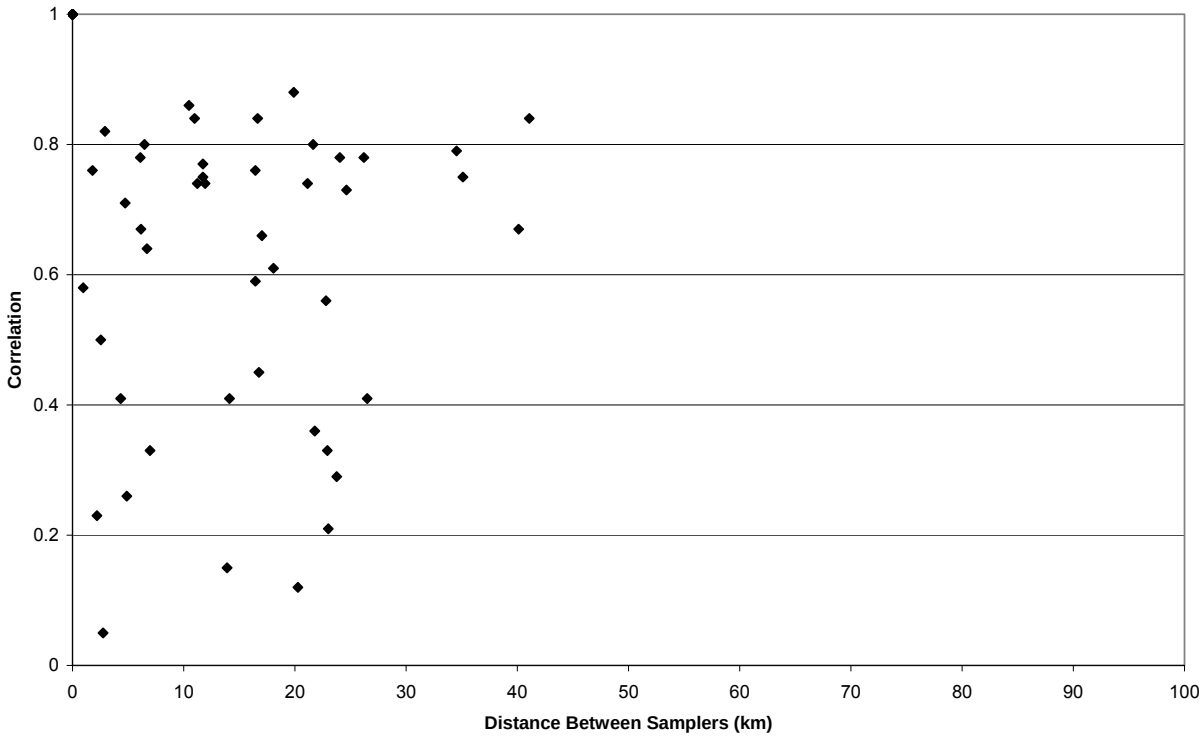


Figure A-87 PM_{10} inter-sampler correlations as a function of distance between monitors for Birmingham, AL.

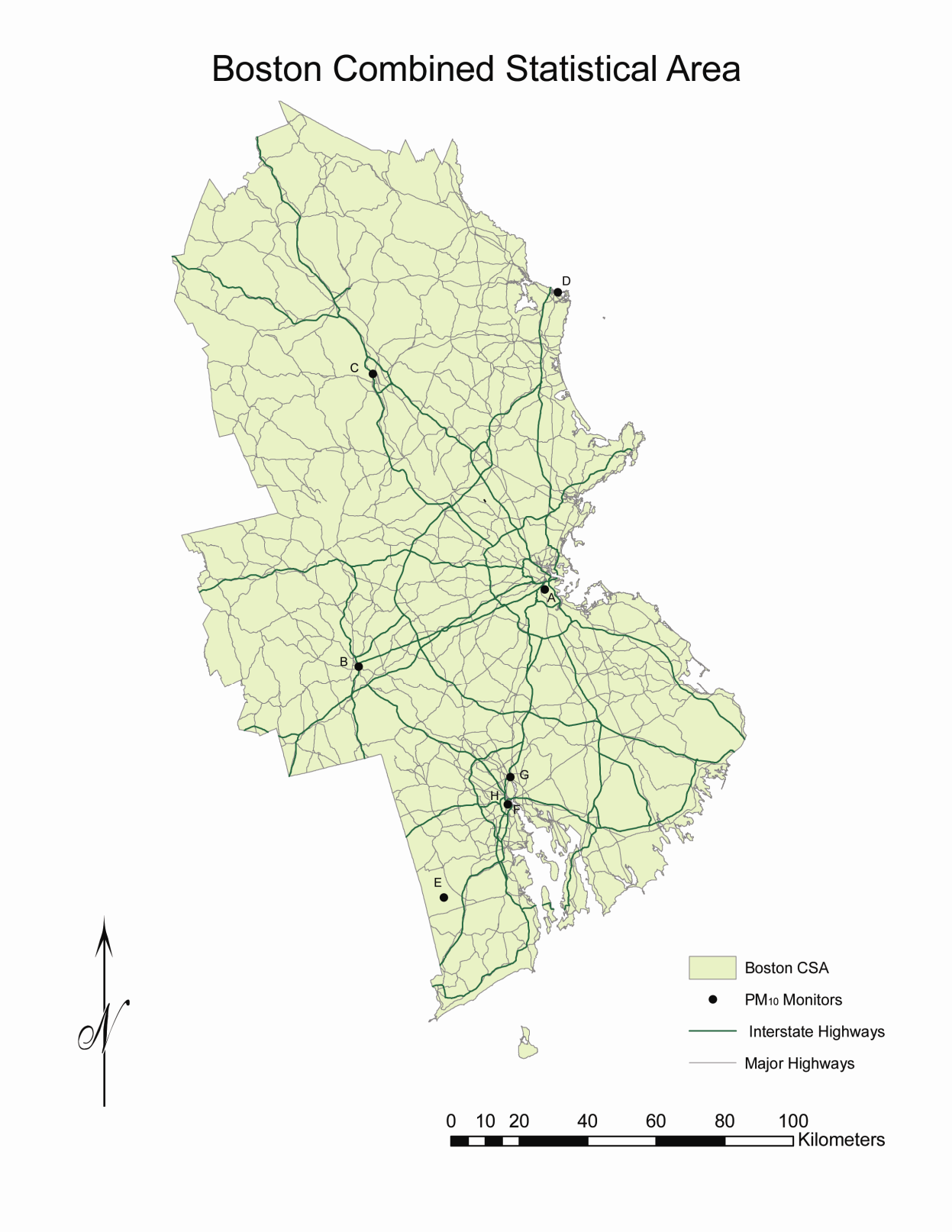


Figure A-88. PM_{10} monitor distribution and major highways, Boston, MA.

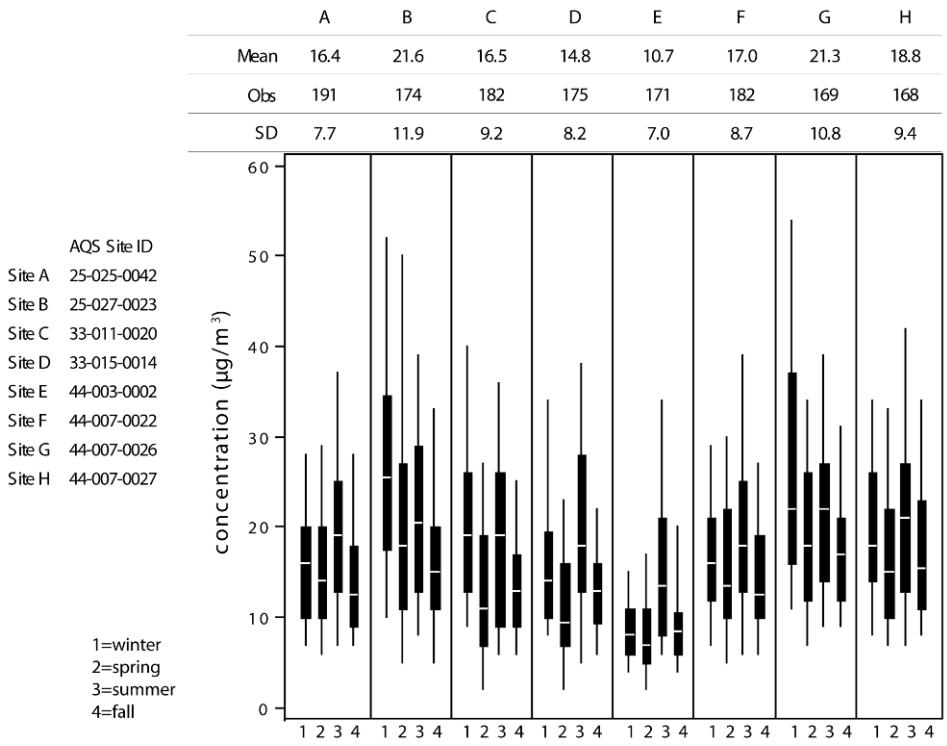


Figure A-89. Box plots illustrating the seasonal distribution of 24-h avg PM_{10} concentrations for Boston, MA.

Table A-37. Inter-sampler correlation statistics for each pair of PM_{10} monitors reporting to AQS for Boston, MA.

Site	A	B	C	D	E	F	G	H
A	1.00	0.69	0.69	0.73	0.71	0.84	0.70	0.79
	(0.0, 0.00)	(15.0, 0.22)	(12.0, 0.20)	(10.0, 0.22)	(13.0, 0.30)	(8.0, 0.14)	(15.0, 0.20)	(10.0, 0.17)
	191	169	179	173	171	182	169	167
B		1.00	0.66	0.56	0.45	0.69	0.77	0.65
		(0.0, 0.00)	(17.0, 0.24)	(19.0, 0.28)	(24.0, 0.39)	(15.0, 0.21)	(12.0, 0.17)	(16.0, 0.20)
		174	167	161	158	169	156	154
C			1.00	0.72	0.47	0.62	0.64	0.59
			(0.0, 0.00)	(10.0, 0.22)	(17.0, 0.33)	(12.0, 0.21)	(16.0, 0.26)	(16.0, 0.24)
			182	170	168	179	166	164
D				1.00	0.63	0.68	0.59	0.69
				(0.0, 0.00)	(11.0, 0.29)	(10.0, 0.23)	(19.0, 0.30)	(13.0, 0.26)
				175	163	173	161	158
E					1.00	0.84	0.58	0.80
					(0.0, 0.00)	(13.0, 0.29)	(22.0, 0.38)	(15.0, 0.33)
					171	171	161	157
F						1.00	0.81	0.95
						(0.0, 0.00)	(11.0, 0.16)	(5.0, 0.11)
						182	169	167
G							1.00	0.79
							(0.0, 0.00)	(10.0, 0.13)
							169	154
H								1.00
								(0.0, 0.00)
								168

LEGEND
Pearson R
(P90, COD)
n

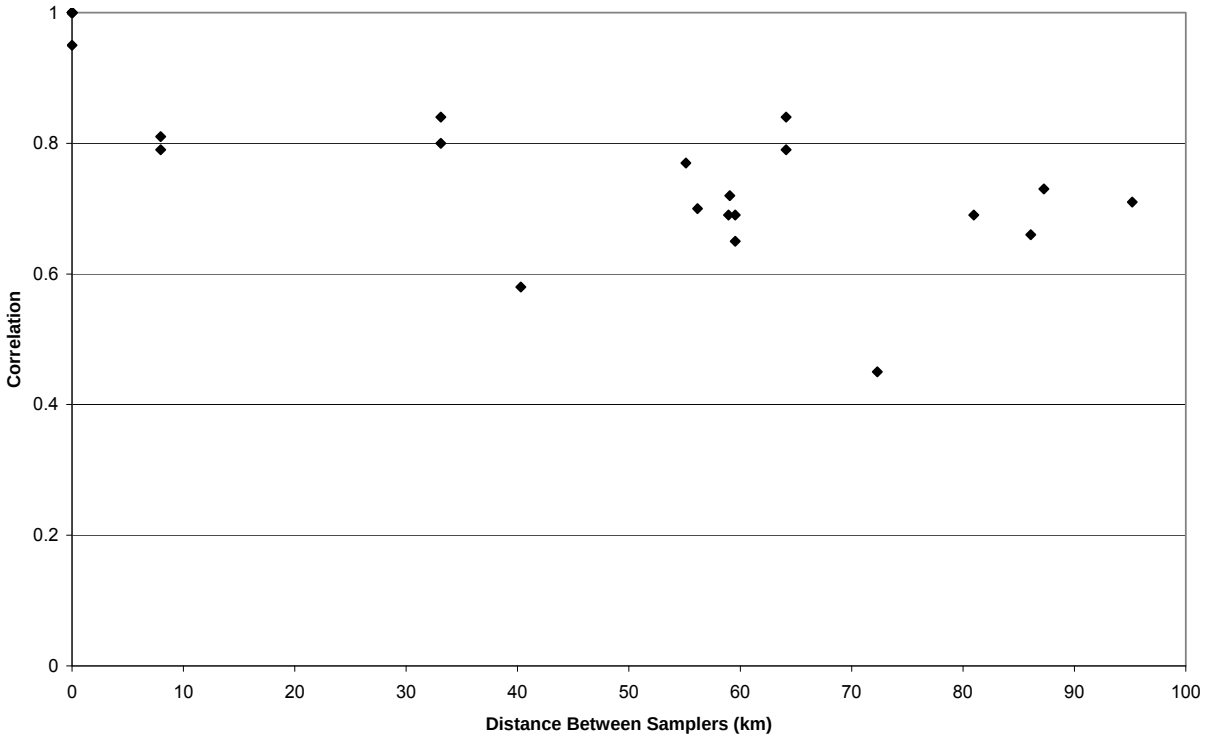


Figure A-90 PM_{10} inter-sampler correlations as a function of distance between monitors for Boston, MA.

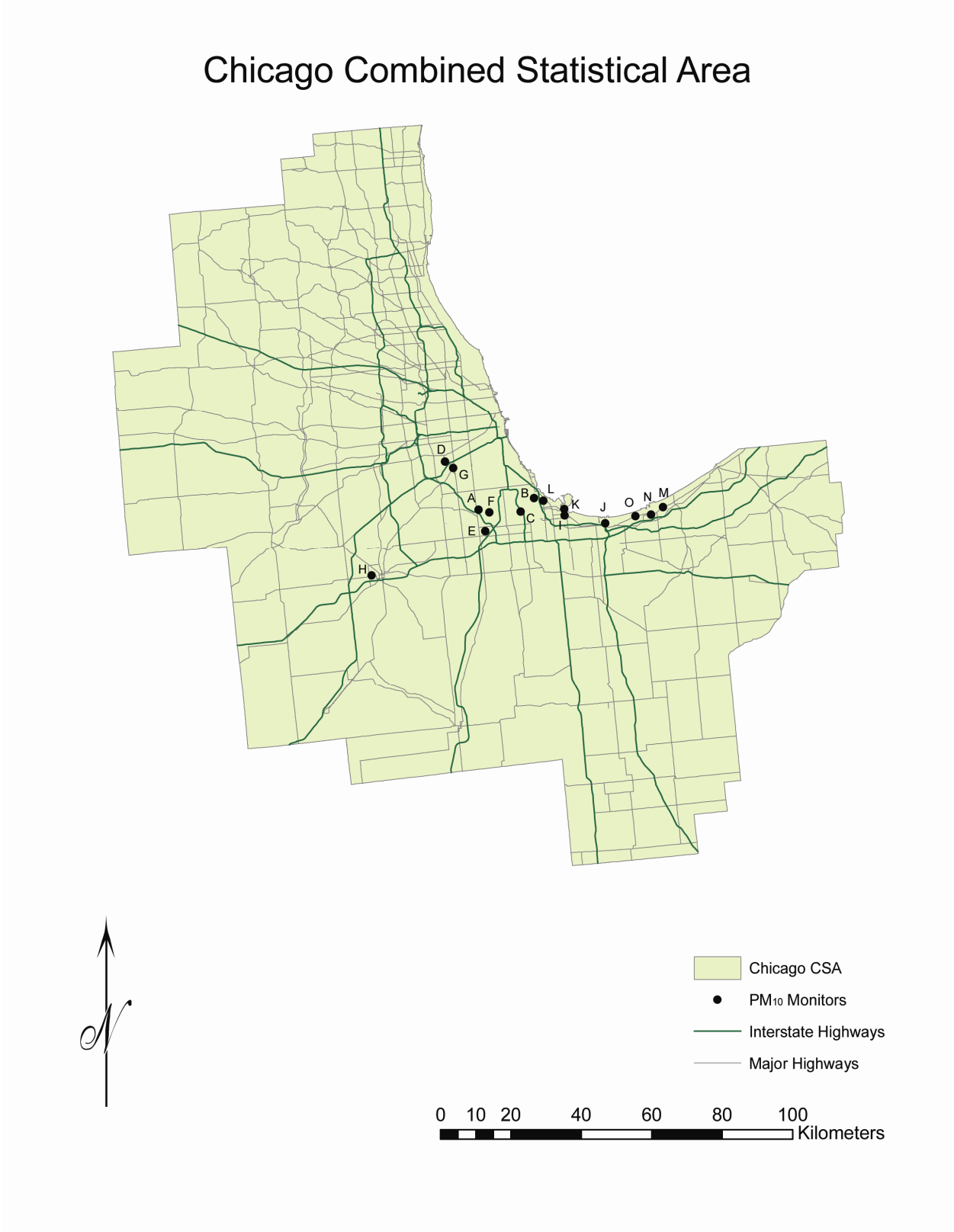


Figure A-91. PM_{10} monitor distribution and major highways, Chicago, IL.

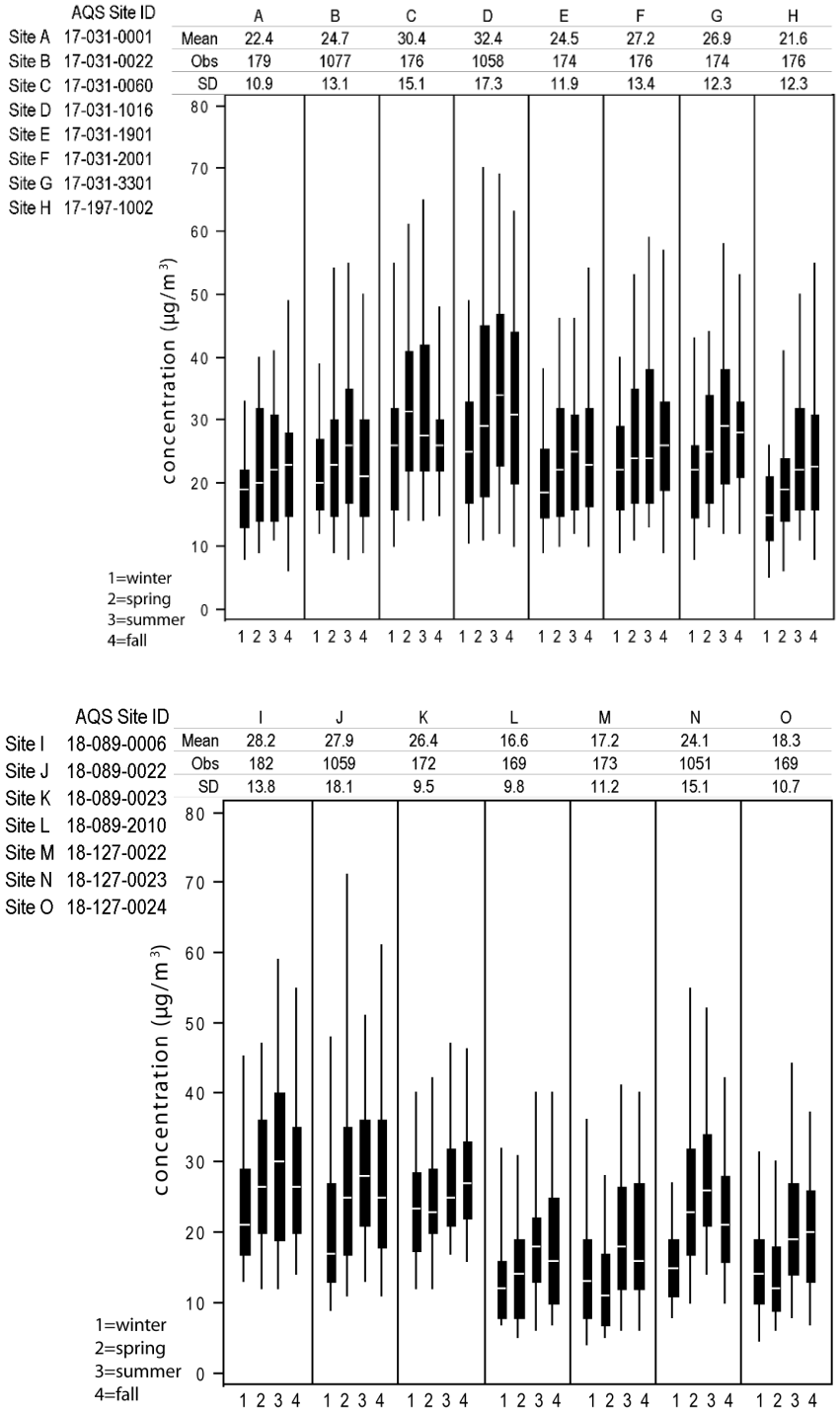


Figure A-92. Box plots illustrating the seasonal distribution of 24-h avg PM_{10} concentrations for Chicago, IL.

Table A-38. Inter-sampler correlation statistics for each pair of PM_{10} monitors reporting to AQS for Chicago, IL.

Site	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
A	1.00	0.78	0.68	0.83	0.93	0.92	0.86	0.79	0.75	0.14	0.69	0.89	0.55	0.27	0.75
	(0.0, 0.00)	(15.0, 0.18)	(23.0, 0.24)	(25.0, 0.22)	(8.0, 0.10)	(11.0, 0.13)	(12.0, 0.17)	(12.0, 0.18)	(13.0, 0.18)	(22.0, 0.28)	(15.0, 0.21)	(13.0, 0.22)	(21.0, 0.30)	(16.0, 0.24)	(15.0, 0.23)
	179	176	173	174	171	173	171	167	179	173	169	166	170	171	166
B		1.00	0.66	0.74	0.76	0.84	0.79	0.74	0.68	0.36	0.73	0.81	0.66	0.33	0.77
		(0.0, 0.00)	(23.0, 0.23)	(23.0, 0.21)	(14.0, 0.17)	(12.0, 0.15)	(13.0, 0.18)	(17.0, 0.23)	(16.0, 0.19)	(22.0, 0.24)	(16.0, 0.19)	(18.0, 0.27)	(23.0, 0.31)	(19.0, 0.25)	(20.0, 0.26)
		1077	173	1040	171	173	171	173	179	1041	169	166	170	1033	166
C			1.00	0.63	0.72	0.74	0.64	0.62	0.62	0.19	0.49	0.66	0.39	0.27	0.61
			(0.0, 0.00)	(26.0, 0.23)	(21.0, 0.21)	(18.5, 0.19)	(19.0, 0.21)	(22.0, 0.27)	(23.0, 0.20)	(26.5, 0.28)	(24.0, 0.23)	(29.0, 0.37)	(33.0, 0.40)	(26.0, 0.26)	(31.0, 0.35)
			176	171	169	170	168	164	176	170	166	163	167	168	163
D				1.00	0.79	0.85	0.79	0.74	0.70	0.23	0.69	0.82	0.61	0.29	0.76
				(0.0, 0.00)	(27.0, 0.21)	(19.0, 0.17)	(23.0, 0.19)	(27.0, 0.28)	(20.0, 0.19)	(32.0, 0.29)	(24.0, 0.23)	(31.0, 0.36)	(36.0, 0.39)	(31.0, 0.29)	(31.0, 0.33)
				1058	169	171	169	171	177	1022	168	166	168	1020	164
E					1.00	0.93	0.84	0.86	0.74	0.17	0.70	0.89	0.53	0.34	0.73
					(0.0, 0.00)	(9.0, 0.10)	(13.0, 0.16)	(10.0, 0.16)	(13.0, 0.16)	(22.0, 0.26)	(15.0, 0.19)	(15.0, 0.25)	(22.0, 0.33)	(17.0, 0.22)	(18.0, 0.25)
					174	168	166	163	174	168	164	161	166	166	163
F						1.00	0.84	0.86	0.77	0.21	0.75	0.89	0.62	0.32	0.80
						(0.0, 0.00)	(12.0, 0.15)	(13.0, 0.19)	(12.0, 0.14)	(23.0, 0.25)	(16.0, 0.17)	(18.0, 0.28)	(25.0, 0.34)	(20.0, 0.23)	(20.0, 0.27)
						176	169	165	176	170	166	163	167	168	163
G							1.00	0.77	0.69	0.28	0.74	0.86	0.52	0.33	0.70
							(0.0, 0.00)	(15.0, 0.22)	(14.0, 0.18)	(23.0, 0.26)	(14.0, 0.18)	(19.0, 0.31)	(24.0, 0.36)	(19.0, 0.24)	(22.0, 0.30)
							174	162	174	168	165	161	165	166	163
H								1.00	0.71	0.18	0.66	0.83	0.59	0.36	0.76
								(0.0, 0.00)	(16.0, 0.23)	(27.0, 0.30)	(18.0, 0.25)	(13.0, 0.23)	(19.0, 0.29)	(17.0, 0.25)	(14.0, 0.22)
								176	170	169	161	157	161	168	157
I									1.00	0.24	0.69	0.75	0.50	0.39	0.68
									(0.0, 0.00)	(22.0, 0.24)	(12.0, 0.15)	(20.0, 0.32)	(26.0, 0.37)	(16.0, 0.21)	(21.0, 0.30)
			LEGEND						182	176	172	169	173	174	169
J			**R**							1.00	0.49	0.38	0.22	0.48	0.22
			(P90, COD)							(0.0, 0.00)	(15.0, 0.20)	(25.0, 0.34)	(28.0, 0.36)	(22.0, 0.21)	(27.0, 0.33)
			N							1059	166	163	168	1018	164
K											1.00	0.80	0.54	0.49	0.65
											(0.0, 0.00)	(17.0, 0.32)	(24.0, 0.35)	(14.0, 0.19)	(21.0, 0.31)
											172	161	165	164	162
L												1.00	0.60	0.33	0.78
												(0.0, 0.00)	(15.0, 0.26)	(19.0, 0.31)	(10.0, 0.20)
												169	161	161	158
M													1.00	0.24	0.84
													(0.0, 0.00)	(21.0, 0.35)	(8.0, 0.16)
													173	165	161
N														1.00	0.31
														(0.0, 0.00)	(19.0, 0.29)
														1051	161
O															1.00
															(0.0, 0.00)
															169

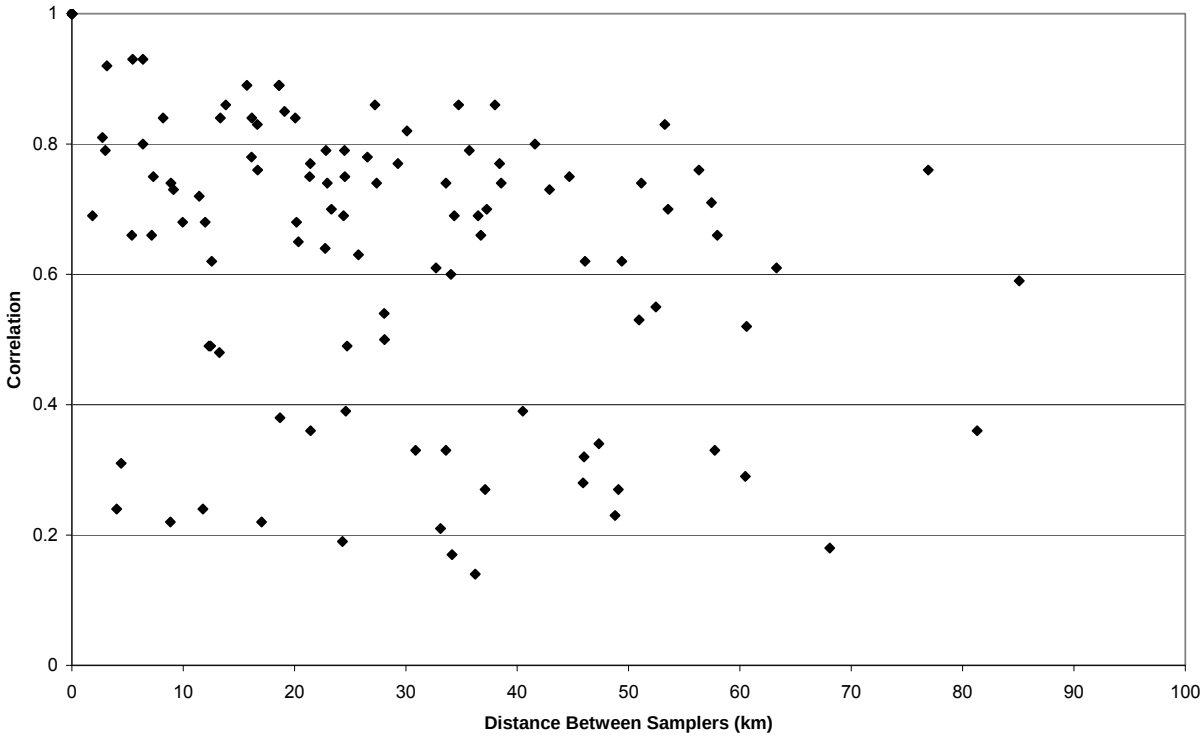


Figure A-93. PM_{10} inter-sampler correlations as a function of distance between monitors for Chicago, IL.

Figure A-94. PM_{10} monitor distribution and major highways, Denver, CO.

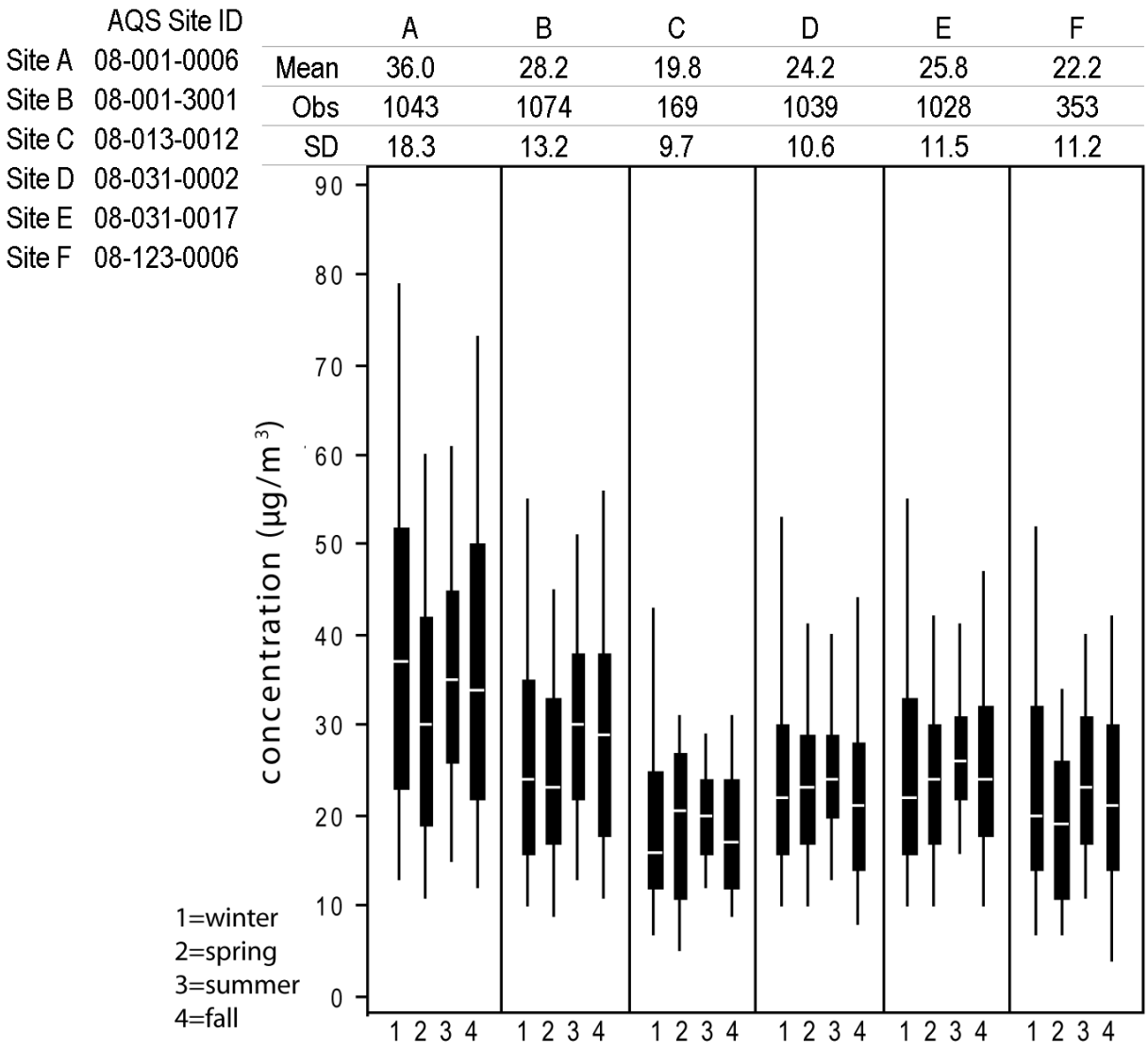


Figure A-95. Box plots illustrating the seasonal distribution of 24-h avg PM_{10} concentrations for Denver, CO.

Table A-39. Inter-sampler correlation statistics for each pair of PM_{10} monitors reporting to AQS for Denver, CO.

Site	A	B	C	D	E	F
A	1.00	0.84	0.43	0.70	0.72	0.67
	(0.0, 0.00)	(20.0, 0.16)	(36.0, 0.34)	(29.0, 0.24)	(26.0, 0.21)	(27.0, 0.28)
	1043	1022	164	987	980	339
B		1.00	0.57	0.72	0.74	0.72
		(0.0, 0.00)	(28.0, 0.27)	(17.0, 0.18)	(15.0, 0.16)	(18.0, 0.22)
		1074	169	1019	1007	348
C			1.00	0.75	0.72	0.51
			(0.0, 0.00)	(17.0, 0.23)	(16.0, 0.23)	(16.0, 0.23)
	LEGEND		169	169	156	164
D	**R**			1.00	0.89	0.52
	(P90, COD)			(0.0, 0.00)	(9.0, 0.13)	(17.0, 0.22)
	N			1039	976	341
E					1.00	0.58
					(0.0, 0.00)	(17.0, 0.23)
					1028	330
F						1.00
						(0.0, 0.00)
						353

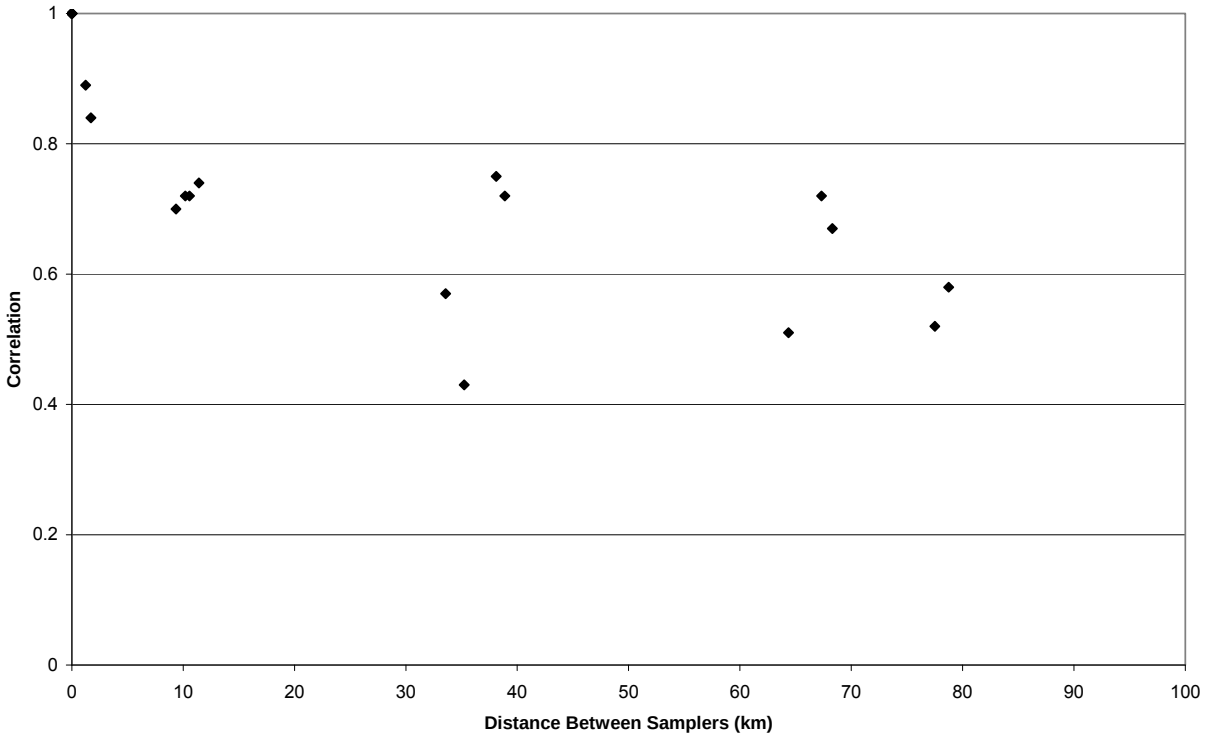


Figure A-96. PM_{10} inter-sampler correlations as a function of distance between monitors for Denver, CO.

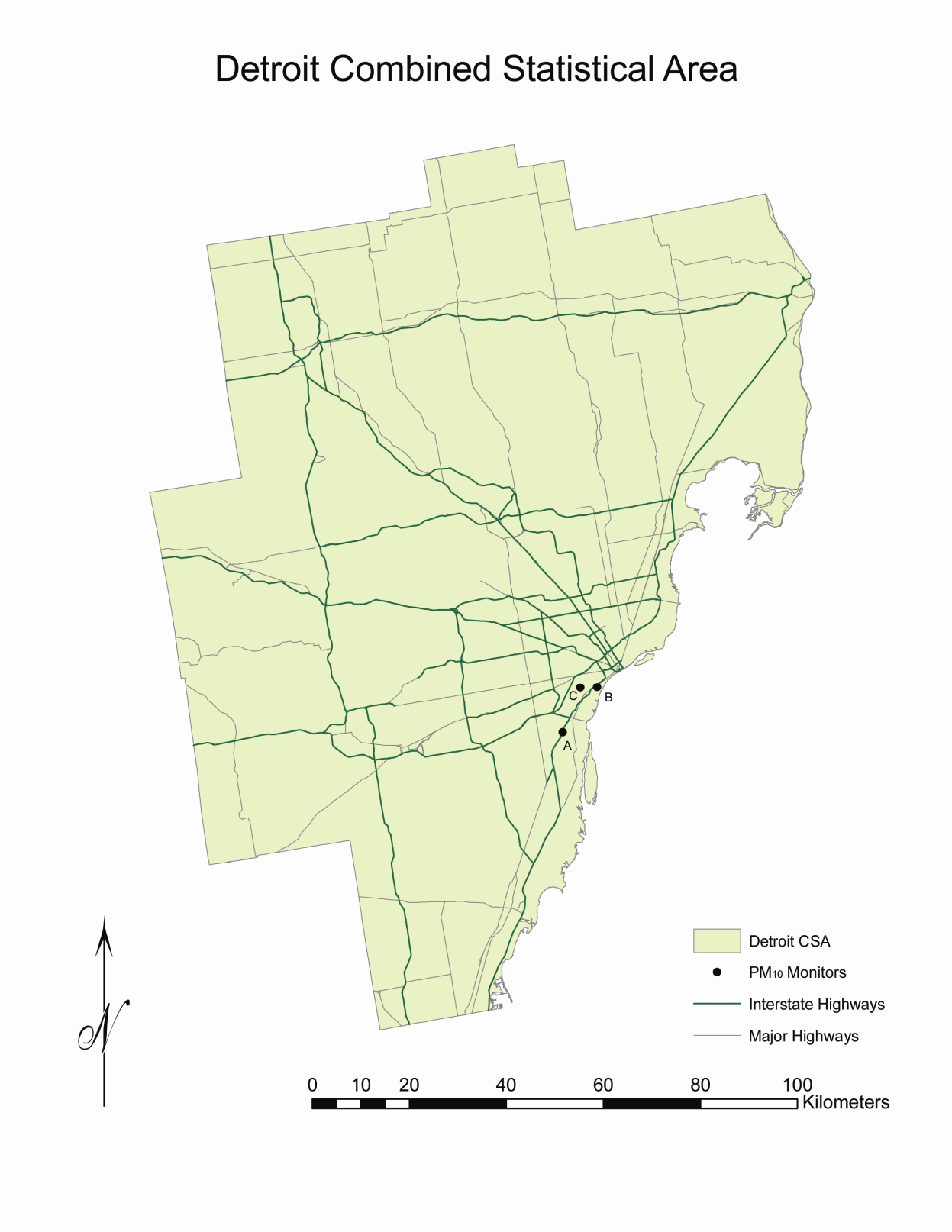


Figure A-97. PM_{10} monitor distribution and major highways, Detroit, MI.

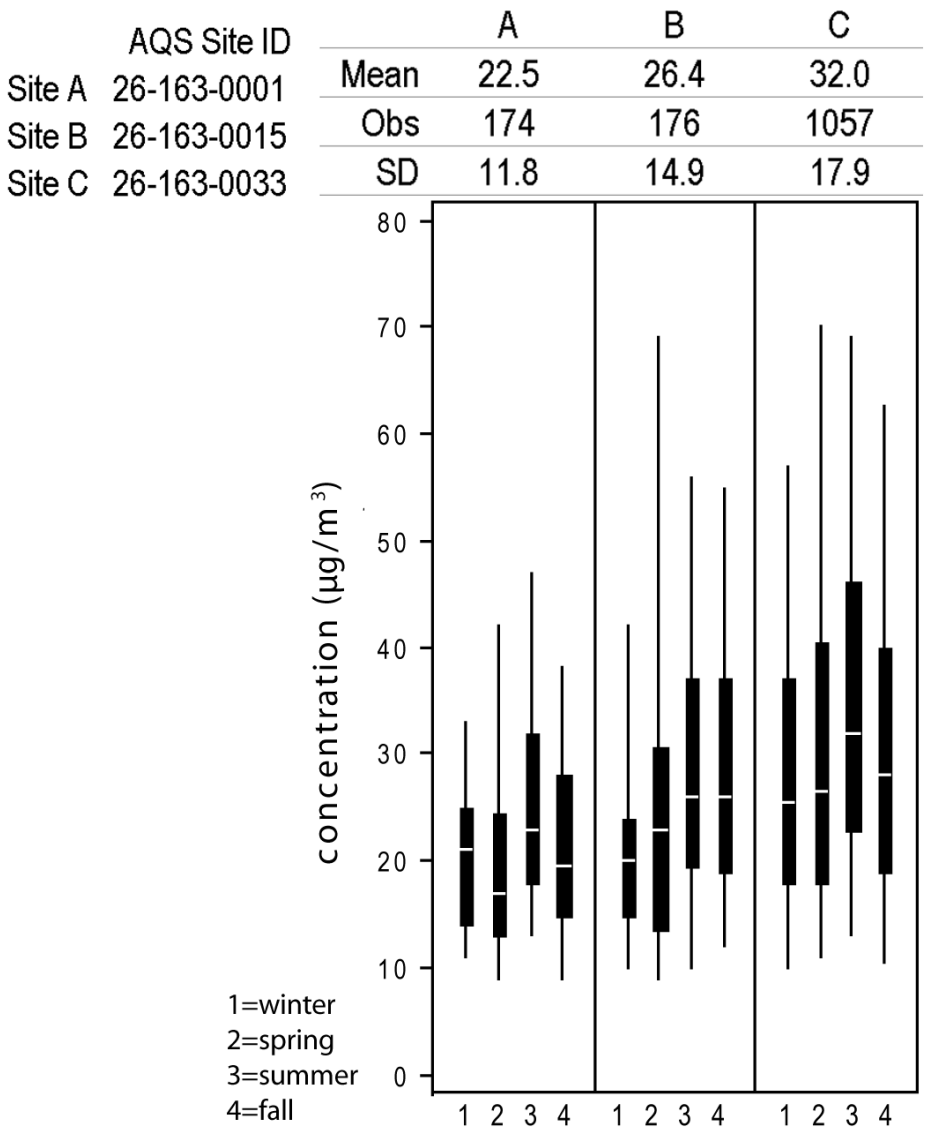


Figure A-98. Box plots illustrating the seasonal distribution of 24-h avg PM_{10} concentrations for Detroit, MI.

Table A-40. Inter-sampler correlation statistics for each pair of PM_{10} monitors reporting to AQS for Detroit, MI.

Site	A	B	C
A	1.00	0.77	0.74
	(0.0, 0.00)	(14.0, 0.18)	(28.0, 0.26)
	174	169	172
B		1.00	0.79
	LEGEND	(0.0, 0.00)	(21.0, 0.21)
	R	176	174
C	(P90, COD)		1.00
	N		(0.0, 0.00)
			1057

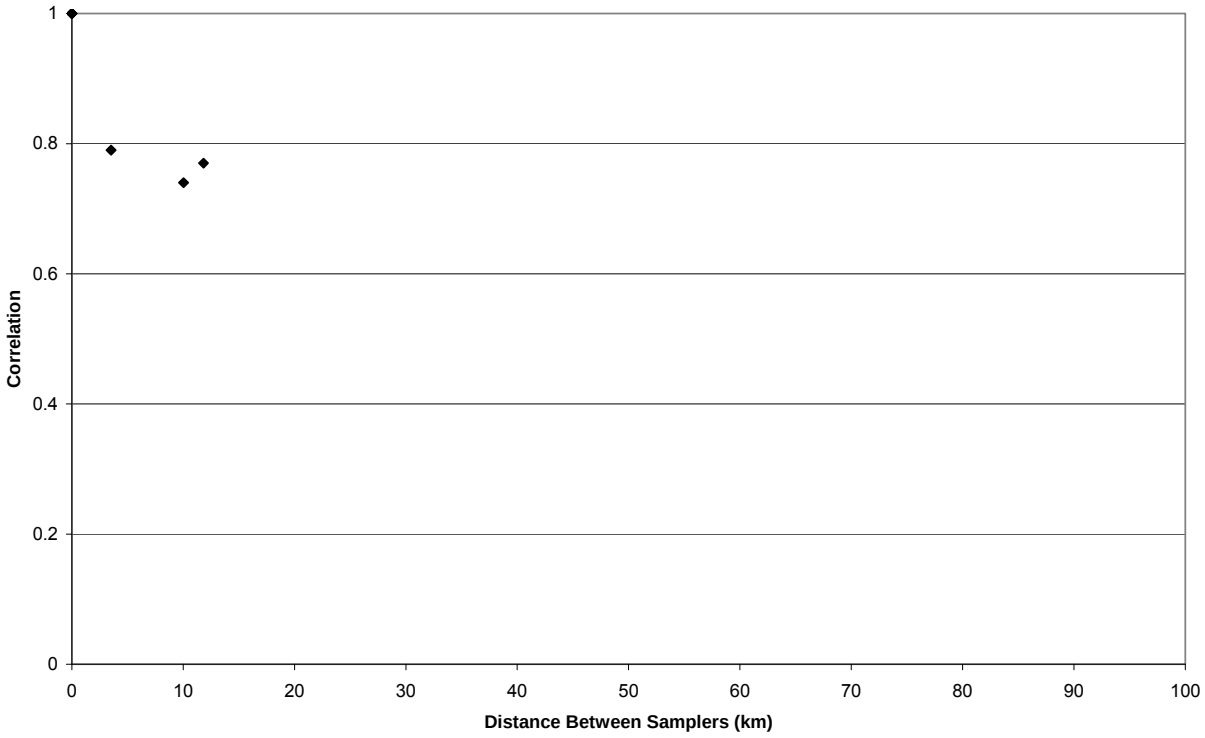


Figure A-99. PM_{10} inter-sampler correlations as a function of distance between monitors for Detroit, MI.

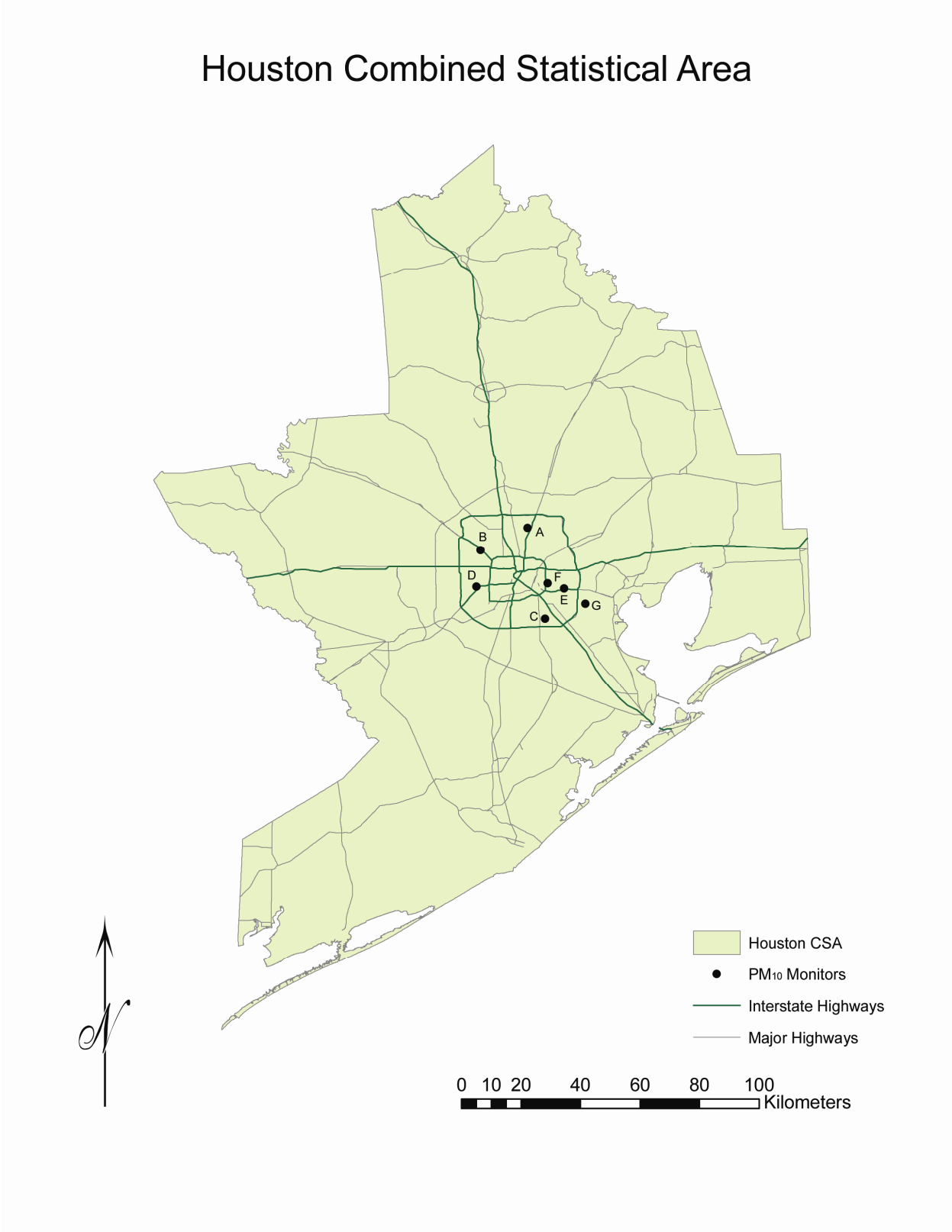


Figure A-100. PM_{10} monitor distribution and major highways, Houston, TX.

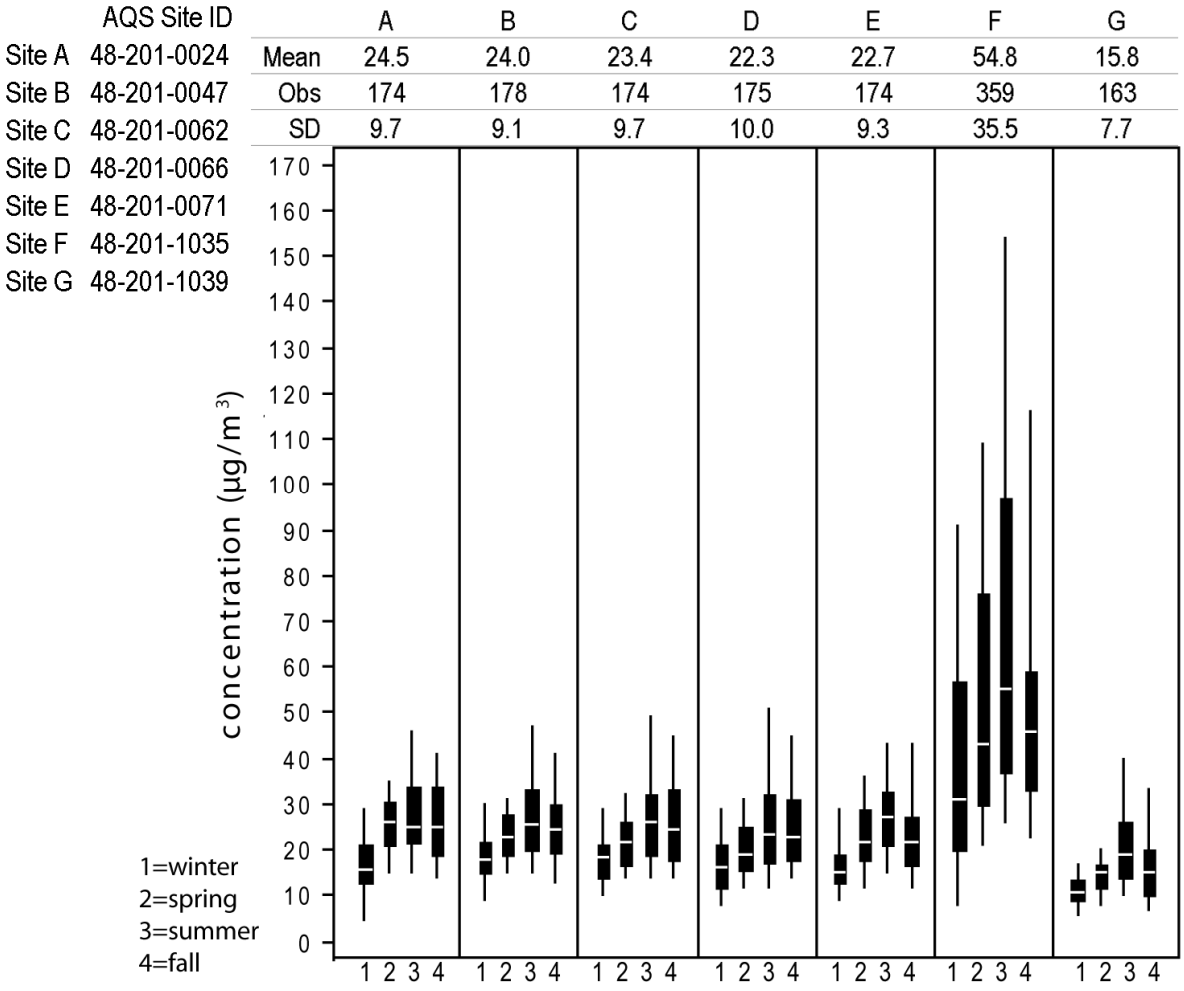


Figure A-101. Box plots illustrating the seasonal distribution of 24-h avg PM_{10} concentrations for Houston, TX.

Table A-41. Inter-sampler correlation statistics for each pair of PM_{10} monitors reporting to AQS for Houston, TX.

SITE	A	B	C	D	E	F	G
A	1.00	0.84	0.78	0.76	0.43	0.56	0.75
	(0.0, 0.00)	(9.0, 0.12)	(11.0, 0.16)	(12.0, 0.16)	(15.0, 0.20)	(77.0, 0.37)	(17.0, 0.28)
	174	163	158	165	167	159	156
B		1.00	0.86	0.86	0.38	0.52	0.79
		(0.0, 0.00)	(9.0, 0.11)	(9.0, 0.12)	(15.0, 0.19)	(74.0, 0.39)	(16.0, 0.26)
		178	156	160	163	158	152
C			1.00	0.83	0.41	0.38	0.85
			(0.0, 0.00)	(10.0, 0.14)	(17.0, 0.19)	(74.0, 0.40)	(14.5, 0.25)
			174	156	159	151	150
D				1.00	0.32	0.43	0.76
				(0.0, 0.00)	(18.0, 0.20)	(81.0, 0.43)	(16.0, 0.23)
				175	163	155	154
E					1.00	0.15	0.38
	LEGEND				(0.0, 0.00)	(78.0, 0.43)	(20.0, 0.28)
	R				174	158	157
F	**(P90, COD)**					1.00	0.37
	N					(0.0, 0.00)	(92.0, 0.54)
						359	149
G							1.00
							(0.0, 0.00)
							163

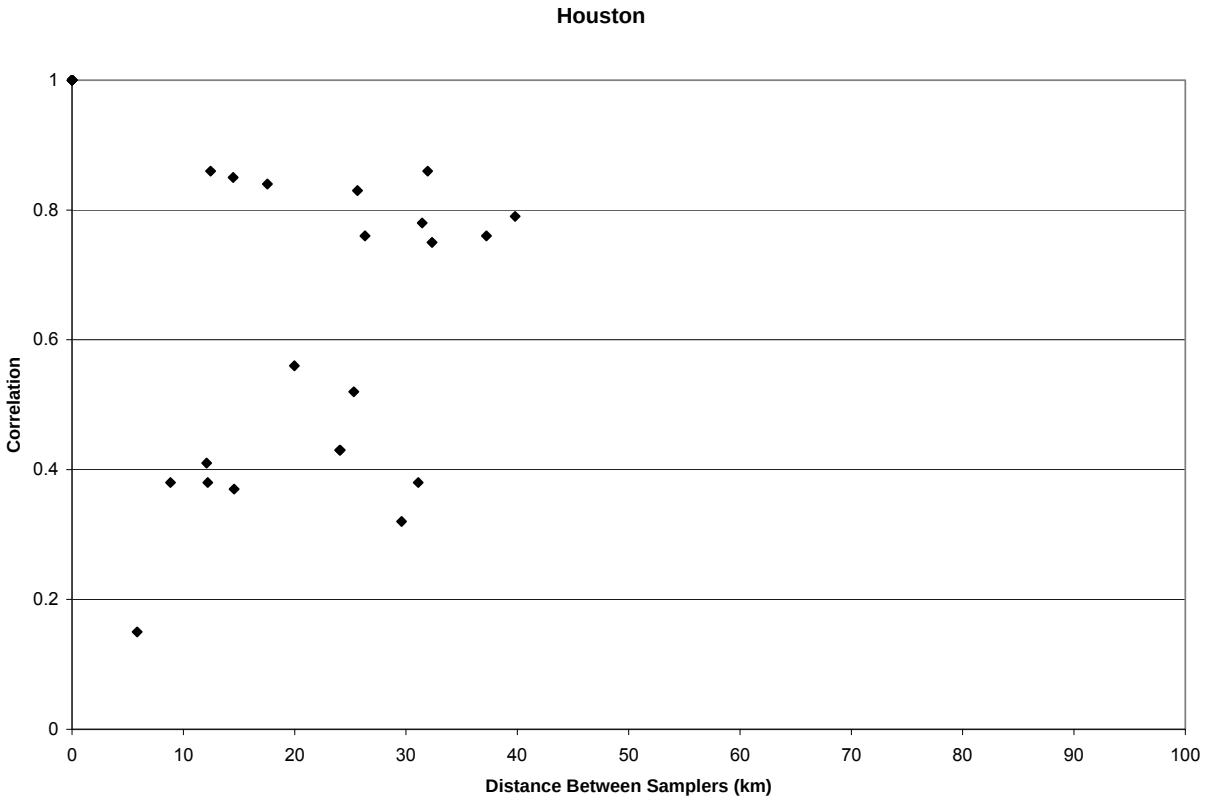


Figure A-102. PM_{10} inter-sampler correlations as a function of distance between monitors for Houston, TX.

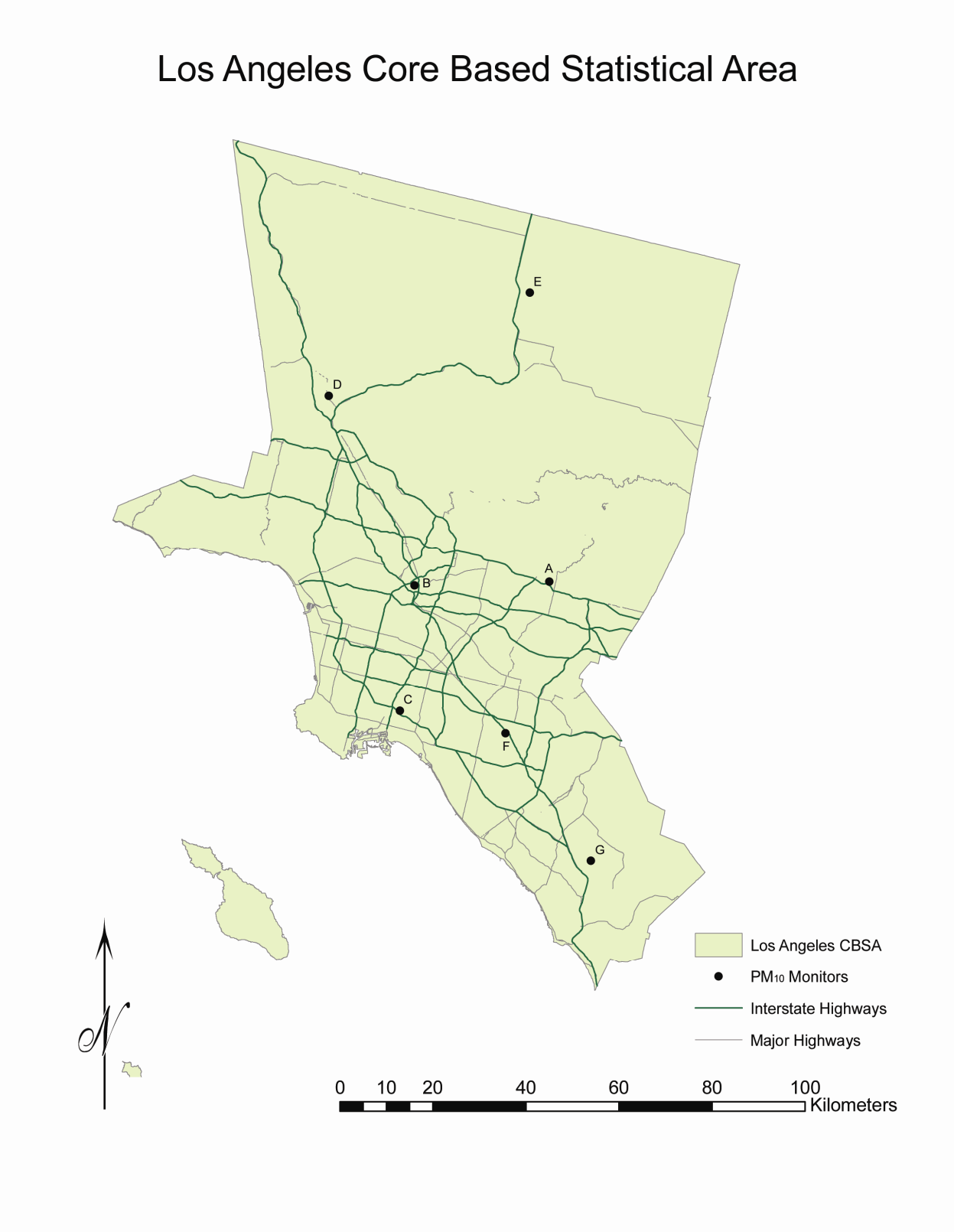


Figure A-103. PM_{10} monitor distribution and major highways, Los Angeles, CA.

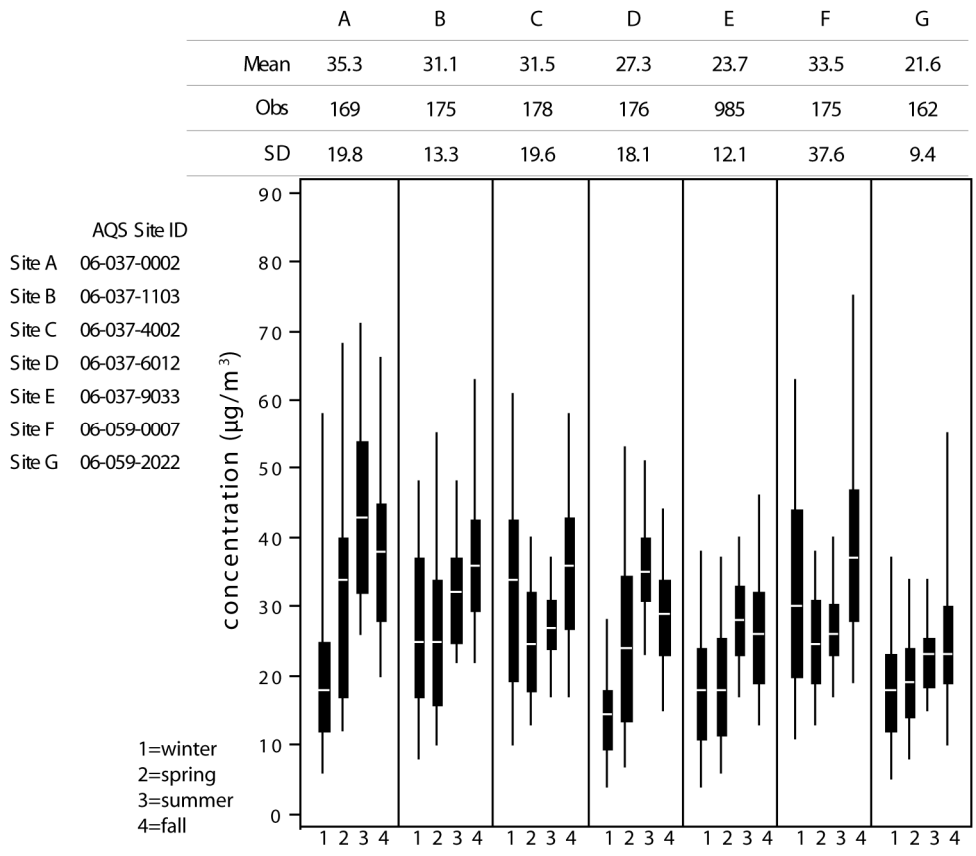


Figure A-104. Box plots illustrating the seasonal distribution of 24-h avg PM_{10} concentrations for Los Angeles, CA.

Table A-42. Inter-sampler correlation statistics for each pair of PM_{10} monitors reporting to AQS for Los Angeles, CA.

Site	A	B	C	D	E	F	G
A	1.00	0.73	0.44	0.73	0.47	0.41	0.65
	(0.0, 0.00)	(17.0, 0.17)	(27.0, 0.24)	(24.0, 0.22)	(28.0, 0.26)	(29.0, 0.24)	(30.0, 0.28)
	169	153	154	157	169	155	143
B		1.00	0.61	0.57	0.52	0.42	0.73
		(0.0, 0.00)	(14.0, 0.14)	(21.0, 0.24)	(23.0, 0.23)	(15.0, 0.16)	(20.0, 0.23)
		175	159	159	173	162	149
C			1.00	0.65	0.43	0.93	0.73
	LEGEND		(0.0, 0.00)	(27.0, 0.28)	(22.0, 0.24)	(11.0, 0.11)	(21.0, 0.22)
	Pearson R		178	158	176	159	148
D	**(P90,tCOD)**			1.00	0.70	0.65	0.57
				(0.0, 0.00)	(16.0, 0.20)	(26.0, 0.28)	(19.5, 0.24)
	n			176	175	161	150
E					1.00	0.29	0.38
					(0.0, 0.00)	(26.0, 0.25)	(20.0, 0.24)
					985	173	159
F						1.00	0.65
						(0.0, 0.00)	(21.5, 0.22)
						175	150
G							1.00
							(0.0, 0.00)
							162

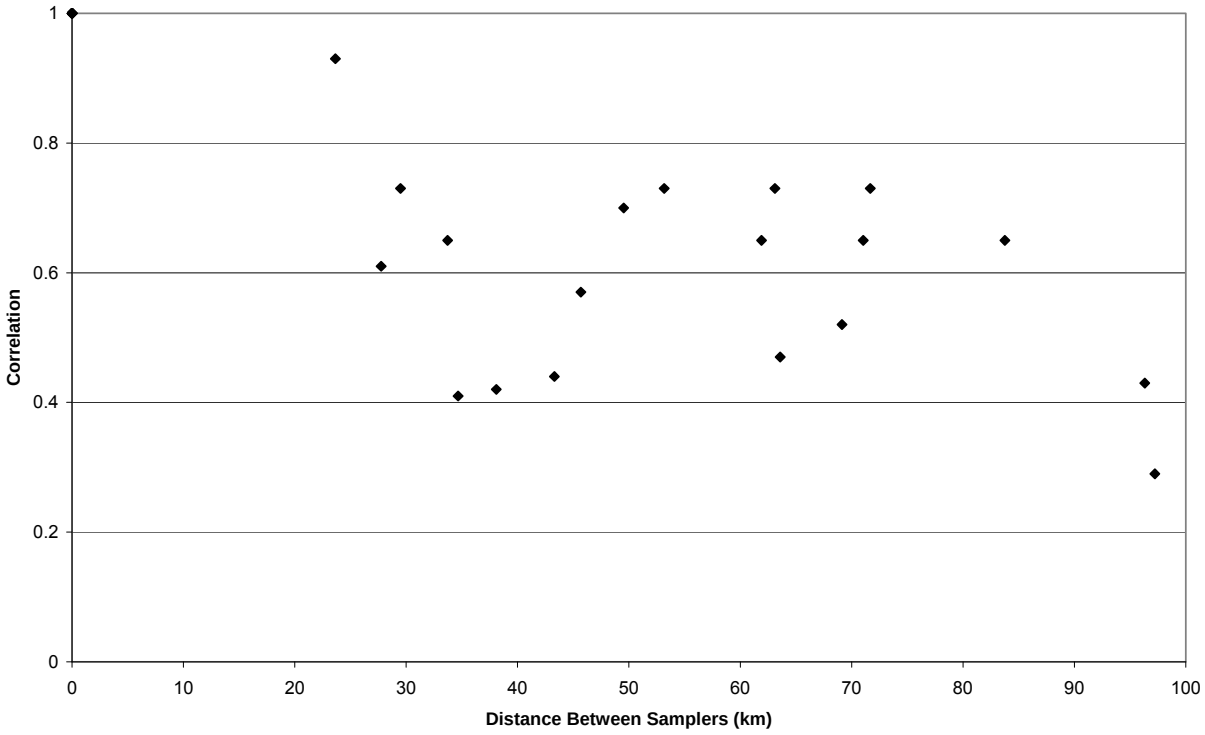


Figure A-105. PM_{10} inter-sampler correlations as a function of distance between monitors for Los Angeles, CA.

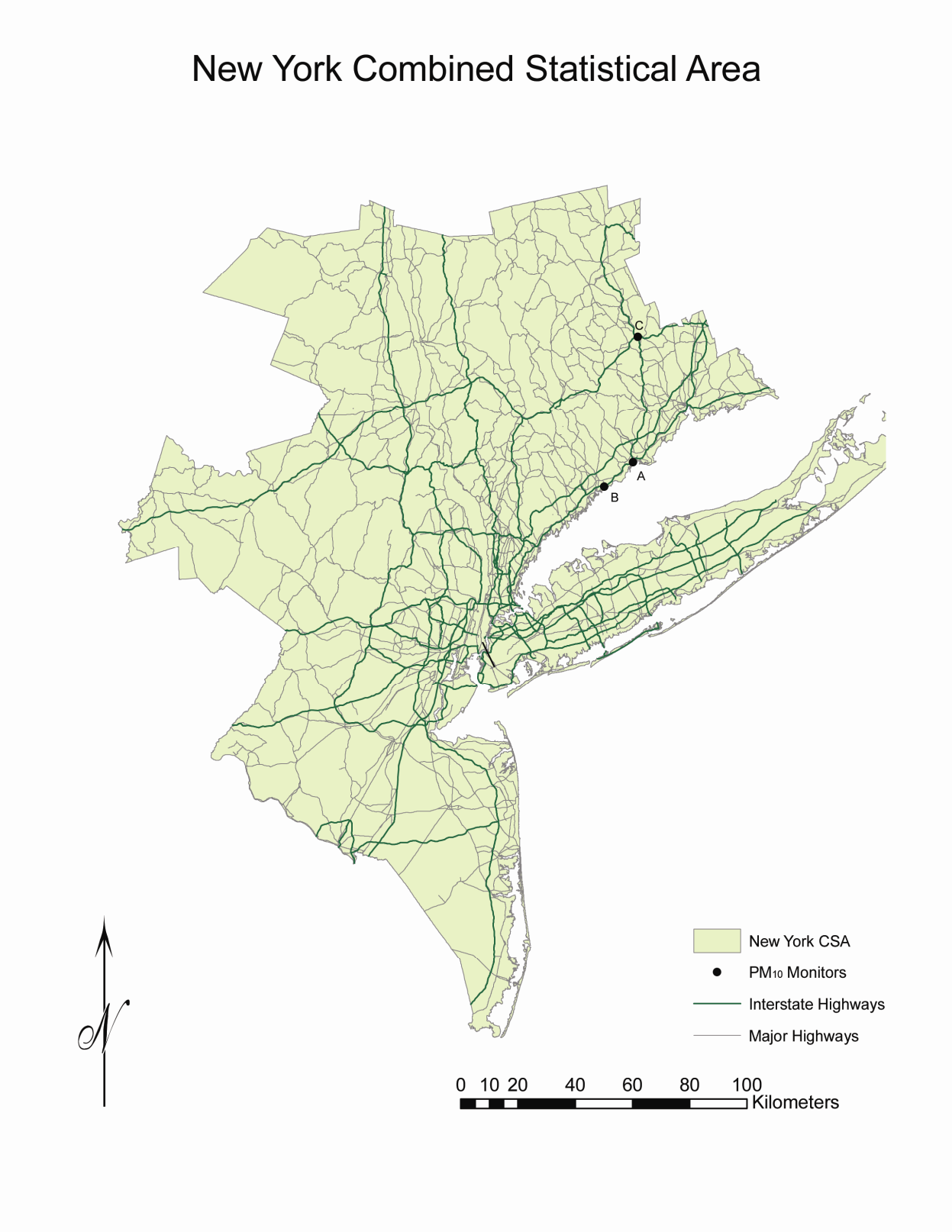


Figure A-106. PM_{10} monitor distribution and major highways, New York, NY.

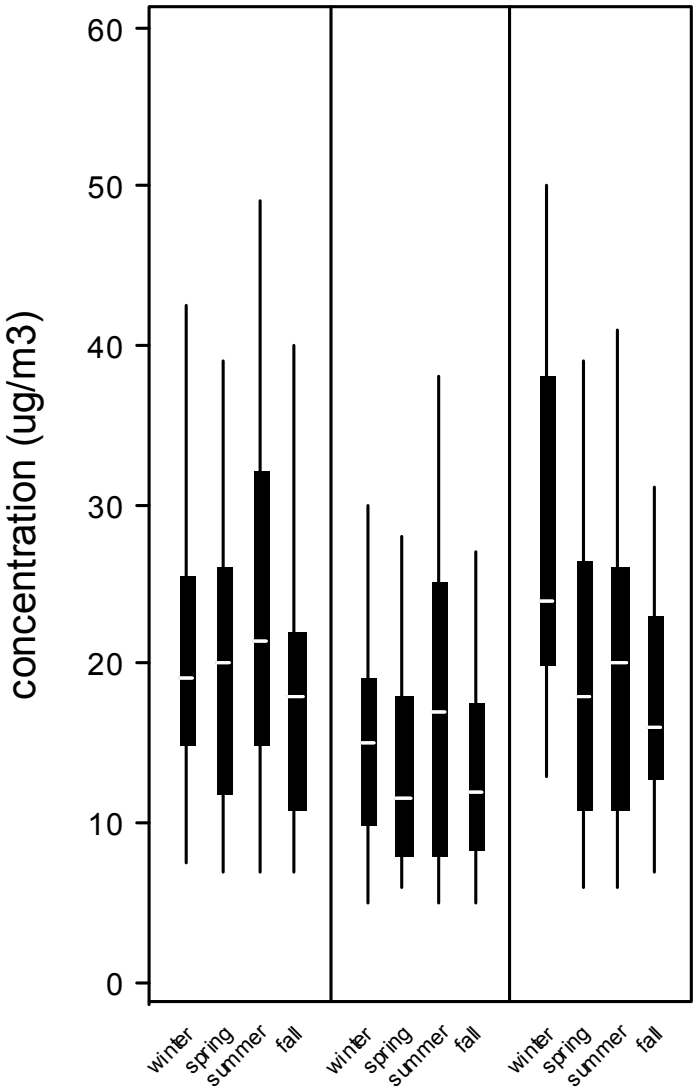


Figure A-107. Box plots illustrating the seasonal distribution of 24-h avg PM_{10} concentrations for New York, NY.

Table A-43. Inter-sampler correlation statistics for each pair of PM_{10} monitors reporting to AQS for New York, NY.

Site	A	B	C
A	1.00	0.88	0.82
	(0.0, 0.00)	(11.0, 0.20)	(12.0, 0.16)
	167	156	164
B		1.00	0.74
	LEGEND	(0.0, 0.00)	(18.0, 0.25)
	R	169	166
C	(P90, COD)		1.00
	N		(0.0, 0.00)
			178

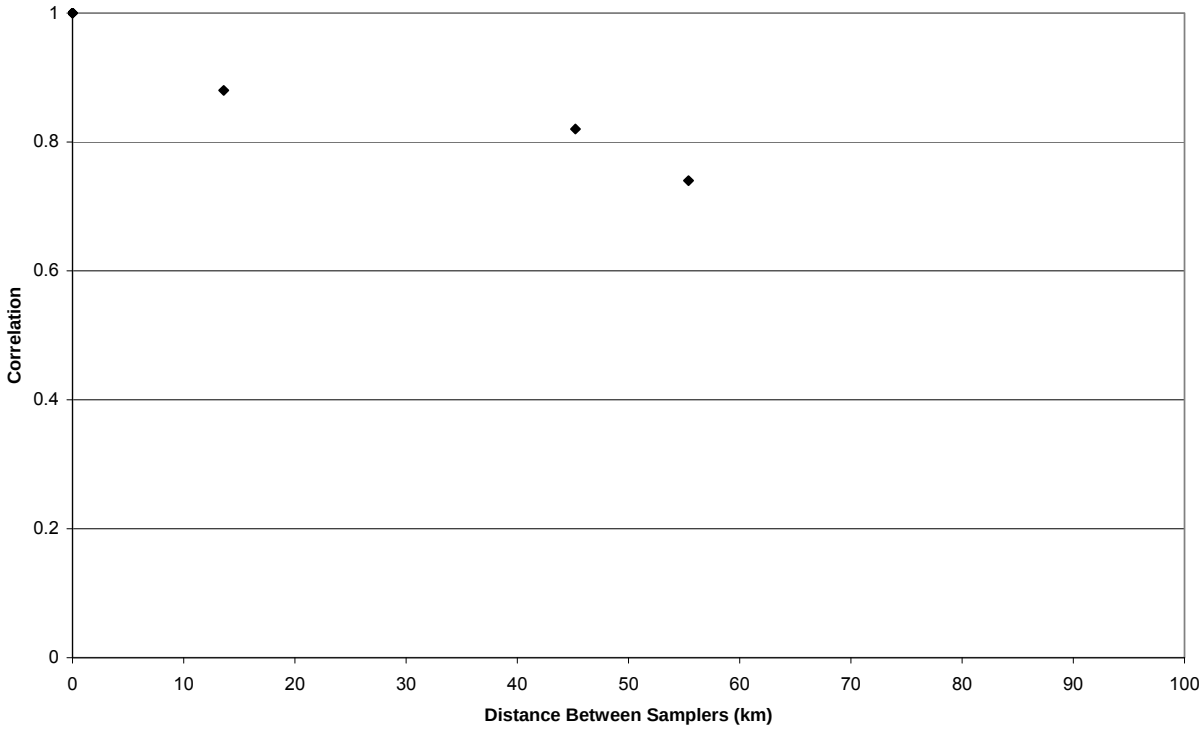


Figure A-108. PM_{10} inter-sampler correlations as a function of distance between monitors for New York, NY.

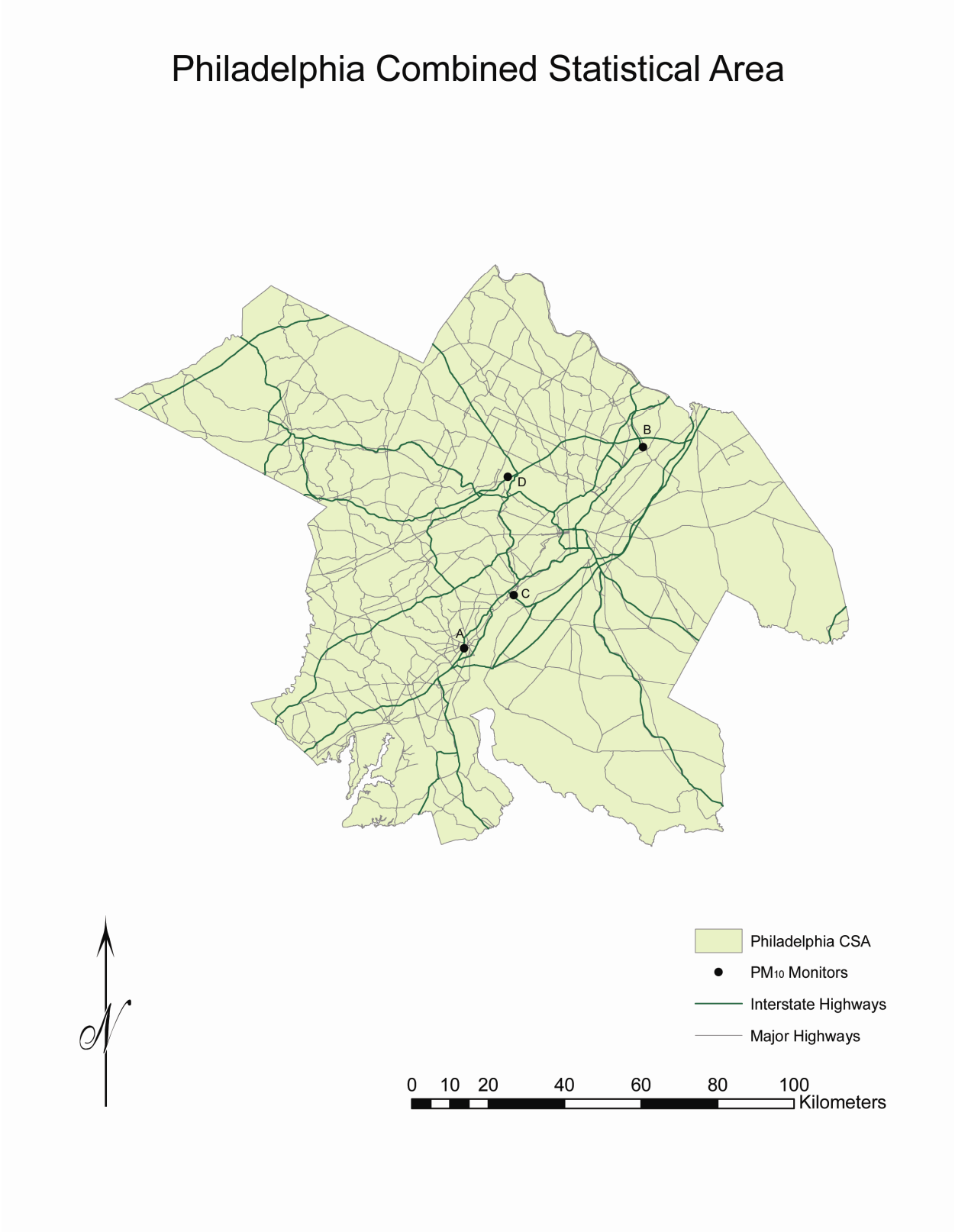


Figure A-109. PM_{10} monitor distribution and major highways, Philadelphia, PA.

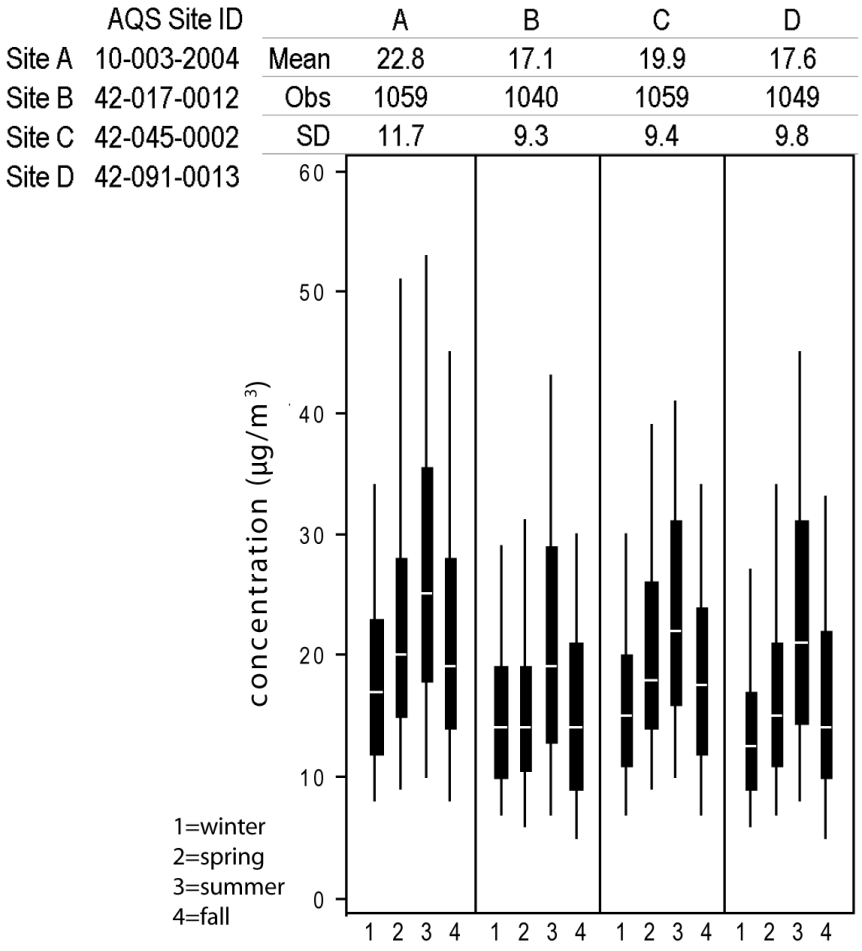


Figure A-110. Box plots illustrating the seasonal distribution of 24-h avg PM_{10} concentrations for Philadelphia, PA.

Table A-44. Inter-sampler correlation statistics for each pair of PM_{10} monitors reporting to AQS for Philadelphia, PA.

Site	A	B	C	D
A	1.00	0.81	0.64	0.84
	(0.0, 0.00)	(13.0, 0.21)	(14.0, 0.19)	(12.0, 0.20)
	1059	1005	1025	1013
B		1.00	0.71	0.93
		(0.0, 0.00)	(11.0, 0.20)	(6.0, 0.12)
		1040	1006	994
C			1.00	0.73
	LEGEND		(0.0, 0.00)	(11.0, 0.19)
	R		1059	1014
D	(P90, COD)			1.00
	N			(0.0, 0.00)
				1049

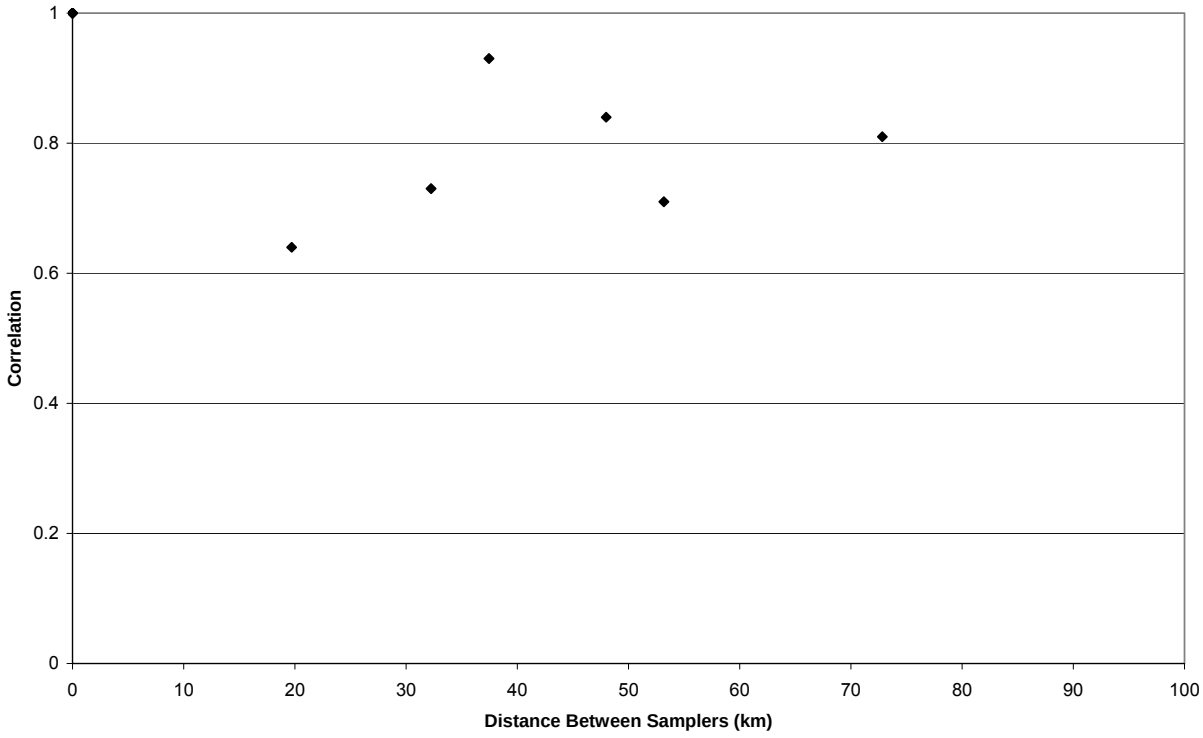


Figure A-111. PM_{10} inter-sampler correlations as a function of distance between monitors for Philadelphia, PA.

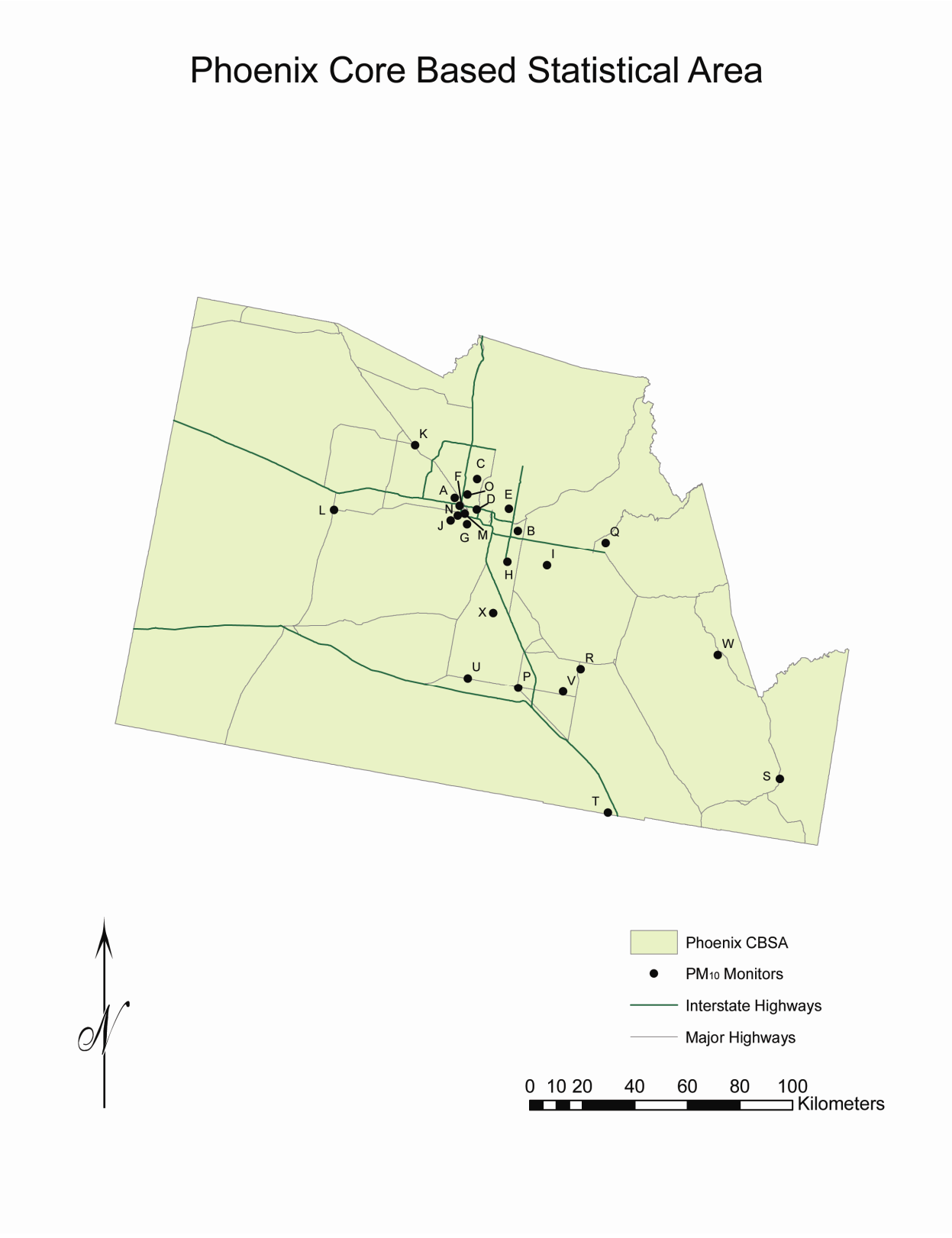
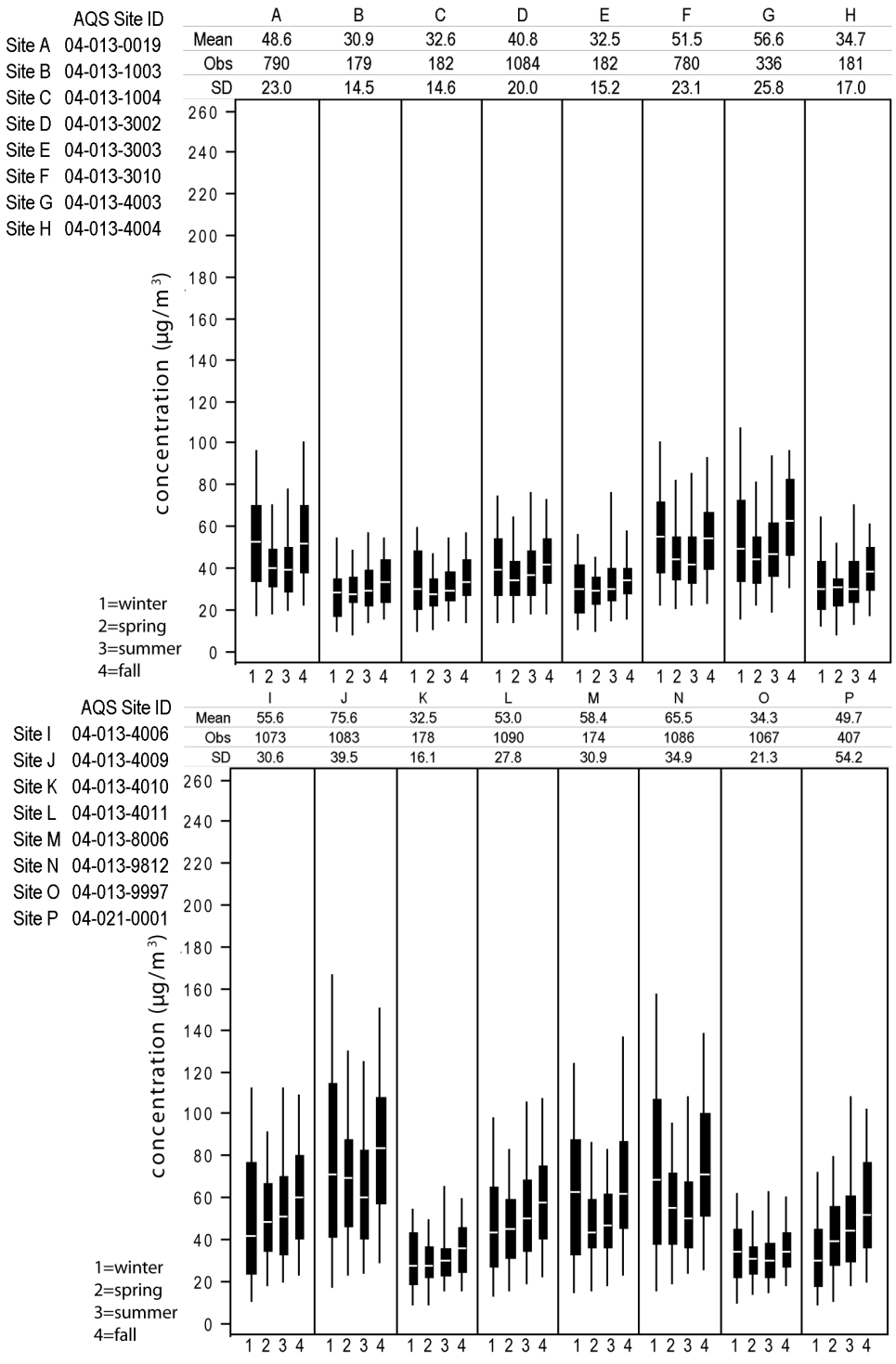


Figure A-112. PM_{10} monitor distribution and major highways, Phoenix, AZ.


AQS Site ID
Site A 04-013-0019
Site B 04-013-1003
Site C 04-013-1004
Site D 04-013-3002
Site E 04-013-3003
Site F 04-013-3010
Site G 04-013-4003
Site H 04-013-4004
A B C D E F G H
Mean 48.6 30.9 32.6 40.8 32.5 51.5 56.6 34.7
Obs 790 179 182 1084 182 780 336 181
SD 23.0 14.5 14.6 20.0 15.2 23.1 25.8 17.0
concentration (µg/m³)
1=winter
2=spring
3=summer
4=fall
AQS Site ID
Site I 04-013-4006
Site J 04-013-4009
Site K 04-013-4010
Site L 04-013-4011
Site M 04-013-8006
Site N 04-013-9812
Site O 04-013-9997
Site P 04-021-0001
I J K L M N O P
Mean 55.6 75.6 32.5 53.0 58.4 65.5 34.3 49.7
Obs 1073 1083 178 1090 174 1086 1067 407
SD 30.6 39.5 16.1 27.8 30.9 34.9 21.3 54.2
concentration (µg/m³)
1=winter
2=spring
3=summer
4=fall

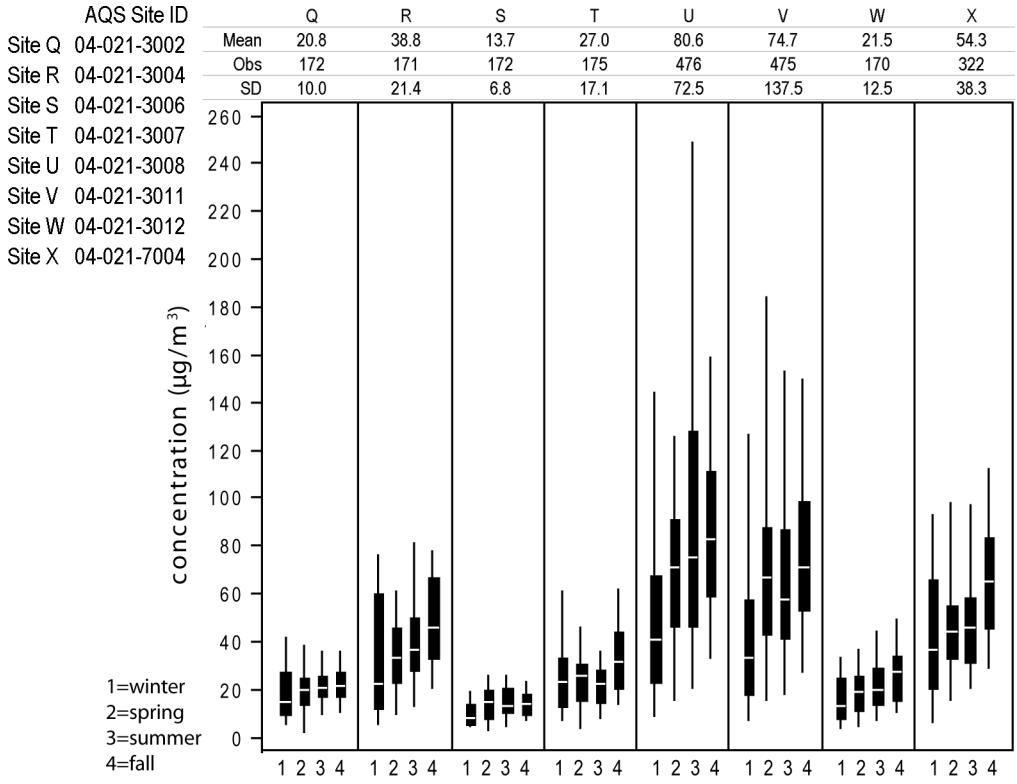


Figure A-113. Box plots illustrating the seasonal distribution of 24-h avg PM_{10} concentrations for Phoenix, AZ.

Table A-45. Inter-sampler correlation statistics for each pair of PM_{10} monitors reporting to AQS for Phoenix, AZ.

Site	A	B	C	D	E	F	G	H	I	J	K	L	M
A	1.00	0.71	0.85	0.85	0.67	0.94	0.86	0.77	0.73	0.83	0.77	0.70	0.87
	(0.0, 0.00)	(38.0, 0.25)	(33.0, 0.21)	(21.0, 0.12)	(38.0, 0.23)	(14.0, 0.09)	(22.0, 0.13)	(34.0, 0.21)	(35.0, 0.18)	(59.0, 0.24)	(34.0, 0.24)	(30.0, 0.17)	(28.5, 0.16)
	790	178	181	788	181	779	335	180	772	781	177	789	170
B		1.00	0.84	0.82	0.85	0.67	0.74	0.81	0.67	0.68	0.75	0.60	0.63
		(0.0, 0.00)	(13.0, 0.12)	(23.0, 0.19)	(11.0, 0.11)	(37.0, 0.29)	(47.0, 0.30)	(13.0, 0.13)	(49.0, 0.30)	(84.0, 0.43)	(16.0, 0.15)	(51.0, 0.31)	(56.0, 0.32)
		179	179	177	179	175	179	178	175	176	175	178	164
C			1.00	0.88	0.81	0.78	0.80	0.81	0.70	0.73	0.81	0.63	0.75
			(0.0, 0.00)	(20.0, 0.16)	(12.0, 0.11)	(38.0, 0.27)	(44.0, 0.28)	(13.0, 0.13)	(48.0, 0.29)	(84.0, 0.41)	(15.0, 0.14)	(49.0, 0.29)	(55.0, 0.30)
			182	180	182	178	182	181	178	179	178	181	167
D				1.00	0.76	0.88	0.81	0.82	0.76	0.78	0.79	0.65	0.83
				(0.0, 0.00)	(23.0, 0.17)	(22.0, 0.14)	(29.0, 0.16)	(18.0, 0.17)	(39.0, 0.20)	(71.0, 0.31)	(22.0, 0.19)	(35.0, 0.20)	(42.0, 0.21)
				1084	180	778	334	179	1062	1072	176	1080	172
E					1.00	0.64	0.68	0.74	0.66	0.59	0.67	0.51	0.61
					(0.0, 0.00)	(40.0, 0.27)	(47.0, 0.29)	(16.0, 0.14)	(48.0, 0.29)	(88.0, 0.42)	(15.0, 0.15)	(49.0, 0.30)	(58.0, 0.31)
					182	178	182	181	178	179	178	181	167
F						1.00	0.83	0.76	0.75	0.86	0.74	0.69	0.87
						(0.0, 0.00)	(22.0, 0.13)	(36.0, 0.25)	(32.0, 0.17)	(54.0, 0.21)	(41.0, 0.28)	(30.0, 0.17)	(25.0, 0.15)
						780	331	177	762	772	175	779	167
G							1.00	0.77	0.65	0.78	0.71	0.65	0.80
							(0.0, 0.00)	(44.0, 0.26)	(38.0, 0.19)	(48.0, 0.19)	(46.0, 0.30)	(36.0, 0.19)	(33.0, 0.16)
							336	181	326	333	178	335	169
H								1.00	0.79	0.81	0.79	0.69	0.72
								(0.0, 0.00)	(47.0, 0.26)	(79.0, 0.39)	(16.0, 0.14)	(43.0, 0.27)	(53.0, 0.29)
			LEGEND					181	177	178	177	180	167
I			**R (P90, COD) N**						1.00	0.79	0.76	0.69	0.68
									(0.0, 0.00)	(52.0, 0.22)	(48.0, 0.29)	(33.0, 0.17)	(38.0, 0.20)
									1073	1061	174	1068	171
J										1.00	0.78	0.73	0.80
										(0.0, 0.00)	(83.0, 0.42)	(57.0, 0.23)	(51.0, 0.22)
										1083	175	1078	171
K											1.00	0.72	0.68
											(0.0, 0.00)	(45.0, 0.29)	(56.0, 0.32)
											178	177	164
L												1.00	0.63
												(0.0, 0.00)	(42.0, 0.20)
												1090	173
M													1.00
													(0.0, 0.00)
													174

	N	O	P	Q	R	S	T	U	V	W	X
A	0.87	0.68	0.47	0.53	0.68	0.40	0.69	0.50	0.27	0.56	0.65
	(39.0, 0.18)	(28.0, 0.17)	(29.0, 0.19)	(49.0, 0.42)	(34.0, 0.27)	(64.0, 0.57)	(40.0, 0.34)	(82.0, 0.31)	(49.0, 0.27)	(48.0, 0.43)	(31.0, 0.20)
	784	783	406	171	171	171	174	475	474	169	262
B	0.59	0.75	0.75	0.73	0.63	0.55	0.59	0.53	0.66	0.65	0.64
	(67.0, 0.37)	(15.0, 0.15)	(22.0, 0.17)	(23.0, 0.27)	(30.0, 0.25)	(32.0, 0.43)	(21.0, 0.24)	(94.0, 0.41)	(62.0, 0.34)	(24.0, 0.30)	(46.0, 0.29)
	178	179	175	169	168	169	172	172	177	167	155
C	0.70	0.87	0.80	0.70	0.71	0.48	0.64	0.56	0.71	0.62	0.60
	(69.0, 0.35)	(11.0, 0.12)	(19.0, 0.15)	(24.0, 0.28)	(26.0, 0.24)	(36.0, 0.44)	(22.0, 0.24)	(91.0, 0.40)	(59.0, 0.32)	(28.0, 0.31)	(43.0, 0.28)
	181	182	178	172	171	172	175	175	180	170	157
D	0.78	0.86	0.73	0.63	0.68	0.49	0.65	0.66	0.45	0.58	0.70
	(57.0, 0.25)	(15.0, 0.12)	(30.0, 0.19)	(38.0, 0.38)	(27.0, 0.25)	(46.0, 0.53)	(31.0, 0.31)	(87.0, 0.34)	(59.0, 0.30)	(38.0, 0.39)	(32.0, 0.21)
	1075	1056	405	170	169	170	173	474	473	168	318
E	0.60	0.73	0.68	0.72	0.64	0.43	0.48	0.42	0.69	0.51	0.52
	(67.0, 0.35)	(14.0, 0.14)	(21.0, 0.17)	(21.0, 0.28)	(27.0, 0.24)	(33.0, 0.44)	(21.0, 0.25)	(93.0, 0.41)	(63.0, 0.32)	(25.0, 0.32)	(46.0, 0.28)
	181	182	178	172	171	172	175	175	180	170	157
F	0.91	0.68	0.46	0.48	0.63	0.38	0.63	0.47	0.28	0.42	0.66
	(35.0, 0.14)	(31.0, 0.21)	(30.0, 0.22)	(60.0, 0.46)	(37.0, 0.30)	(68.0, 0.60)	(45.0, 0.39)	(80.0, 0.31)	(50.0, 0.27)	(57.0, 0.47)	(34.0, 0.22)
	774	773	403	169	167	168	172	470	469	166	259
G	0.77	0.57	0.47	0.55	0.65	0.46	0.62	0.49	0.44	0.57	0.64
	(35.0, 0.16)	(41.0, 0.25)	(36.5, 0.24)	(61.0, 0.47)	(41.0, 0.30)	(73.0, 0.61)	(58.0, 0.41)	(78.0, 0.28)	(45.0, 0.24)	(59.0, 0.48)	(32.0, 0.22)
	332	336	330	172	171	172	175	329	334	170	185
H	0.70	0.75	0.82	0.63	0.74	0.55	0.62	0.60	0.76	0.64	0.76
	(66.0, 0.33)	(15.0, 0.14)	(18.0, 0.15)	(29.0, 0.31)	(24.5, 0.22)	(37.0, 0.46)	(24.0, 0.25)	(84.0, 0.38)	(58.0, 0.29)	(30.0, 0.33)	(39.0, 0.25)
	180	181	177	171	170	171	174	174	179	169	156
I	0.76	0.61	0.52	0.57	0.71	0.51	0.58	0.59	0.37	0.51	0.80
	(42.0, 0.18)	(49.0, 0.27)	(39.0, 0.22)	(66.0, 0.47)	(41.0, 0.27)	(77.0, 0.60)	(60.0, 0.40)	(72.0, 0.27)	(46.0, 0.23)	(63.0, 0.47)	(30.0, 0.16)
	1064	1045	397	169	168	168	171	461	461	167	314
J	0.91	0.58	0.41	0.48	0.65	0.48	0.65	0.51	0.28	0.46	0.74
	(29.0, 0.12)	(83.0, 0.38)	(68.0, 0.31)	(103.0, 0.58)	(75.0, 0.40)	(115.0, 0.69)	(92.0, 0.51)	(69.0, 0.26)	(59.0, 0.27)	(101.0, 0.58)	(62.0, 0.27)
	1074	1055	404	169	168	169	172	473	472	167	319
K	0.69	0.71	0.75	0.52	0.64	0.52	0.62	0.71	0.68	0.55	0.68
	(73.0, 0.36)	(16.0, 0.16)	(19.0, 0.18)	(28.0, 0.29)	(27.0, 0.23)	(34.0, 0.44)	(22.0, 0.24)	(89.0, 0.40)	(59.0, 0.33)	(28.0, 0.32)	(44.0, 0.29)
	177	178	174	168	167	168	171	171	176	166	153
L	0.68	0.55	0.51	0.47	0.57	0.48	0.49	0.59	0.33	0.50	0.68
	(48.0, 0.20)	(44.0, 0.26)	(37.0, 0.22)	(66.0, 0.47)	(44.5, 0.29)	(71.0, 0.60)	(62.0, 0.40)	(75.0, 0.27)	(53.0, 0.24)	(67.0, 0.48)	(29.0, 0.18)
	1081	1063	406	171	170	171	174	475	474	169	321
M	0.86	0.81	0.75	0.48	0.64	0.37	0.62	0.46	0.65	0.44	0.59
	(32.0, 0.16)	(53.0, 0.29)	(47.0, 0.30)	(74.0, 0.48)	(51.0, 0.32)	(80.0, 0.61)	(58.5, 0.41)	(62.0, 0.31)	(48.0, 0.26)	(68.0, 0.49)	(42.0, 0.24)
	173	174	165	157	158	158	160	165	168	156	145
N	1.00	0.58	0.41	0.48	0.67	0.42	0.63	0.42	0.26	0.40	0.60
	(0.0, 0.00)	(66.0, 0.32)	(51.0, 0.27)	(88.0, 0.53)	(62.5, 0.35)	(98.0, 0.65)	(75.0, 0.46)	(71.0, 0.29)	(55.0, 0.27)	(88.0, 0.54)	(48.0, 0.24)
	1086	1059	403	171	170	171	174	470	469	169	319
O		1.00	0.90	0.61	0.64	0.39	0.60	0.72	0.59	0.55	0.64
		(0.0, 0.00)	(35.0, 0.22)	(28.0, 0.31)	(25.0, 0.24)	(38.0, 0.47)	(22.0, 0.26)	(94.0, 0.39)	(69.0, 0.35)	(29.0, 0.33)	(44.0, 0.26)
		1067	407	172	171	172	175	475	473	170	317
P			1.00	0.67	0.81	0.58	0.78	0.82	0.64	0.71	0.67
			(0.0, 0.00)	(32.0, 0.29)	(22.0, 0.19)	(44.0, 0.45)	(21.0, 0.21)	(80.0, 0.30)	(52.0, 0.23)	(32.0, 0.31)	(39.0, 0.24)
			407	169	170	169	172	400	404	167	197
Q				1.00	0.72	0.65	0.57	0.36	0.58	0.68	0.47
				(0.0, 0.00)	(40.0, 0.33)	(15.0, 0.28)	(23.0, 0.24)	(104.0, 0.53)	(78.0, 0.46)	(15.0, 0.22)	(62.0, 0.43)
				172	162	163	167	165	171	161	148
R					1.00	0.66	0.68	0.53	0.82	0.68	0.68
					(0.0, 0.00)	(55.0, 0.48)	(32.0, 0.27)	(75.0, 0.35)	(47.0, 0.25)	(40.0, 0.34)	(39.0, 0.24)
					171	162	165	164	171	160	148
S						1.00	0.60	0.46	0.59	0.72	0.52
						(0.0, 0.00)	(28.0, 0.35)	(115.0, 0.65)	(86.0, 0.59)	(19.0, 0.28)	(74.0, 0.58)
						172	167	165	171	162	149
T							1.00	0.56	0.66	0.68	0.61
			LEGEND				(0.0, 0.00)	(94.0, 0.47)	(71.0, 0.39)	(18.0, 0.24)	(51.5, 0.37)
			R				175	169	174	165	150
U			**(P90, COD)**					1.00	0.54	0.52	0.71
			N					(0.0, 0.00)	(66.0, 0.24)	(101.0, 0.53)	(61.0, 0.25)
								476	464	165	204
V									1.00	0.60	0.64
									(0.0, 0.00)	(78.0, 0.47)	(35.0, 0.20)
									475	169	206
W										1.00	0.56
										(0.0, 0.00)	(63.0, 0.44)
										170	145
X											1.00
											(0.0, 0.00)
											322

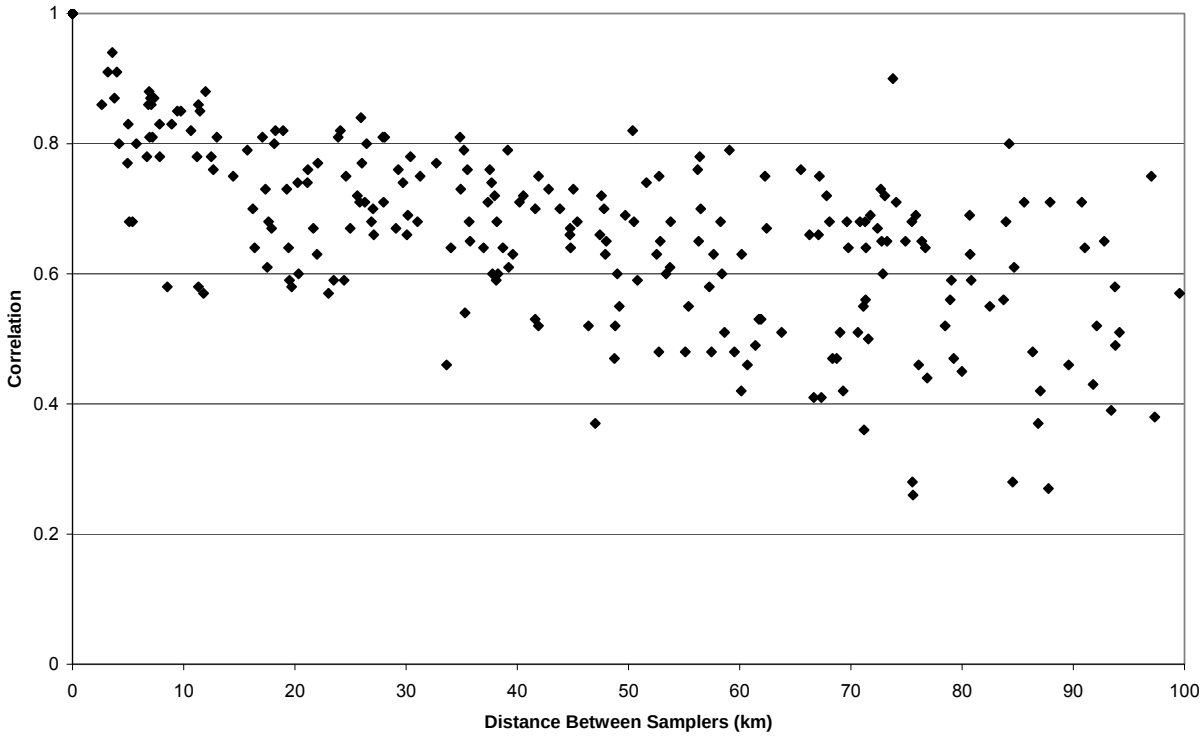


Figure A-114. PM_{10} inter-sampler correlations as a function of distance between monitors for Phoenix, AZ.

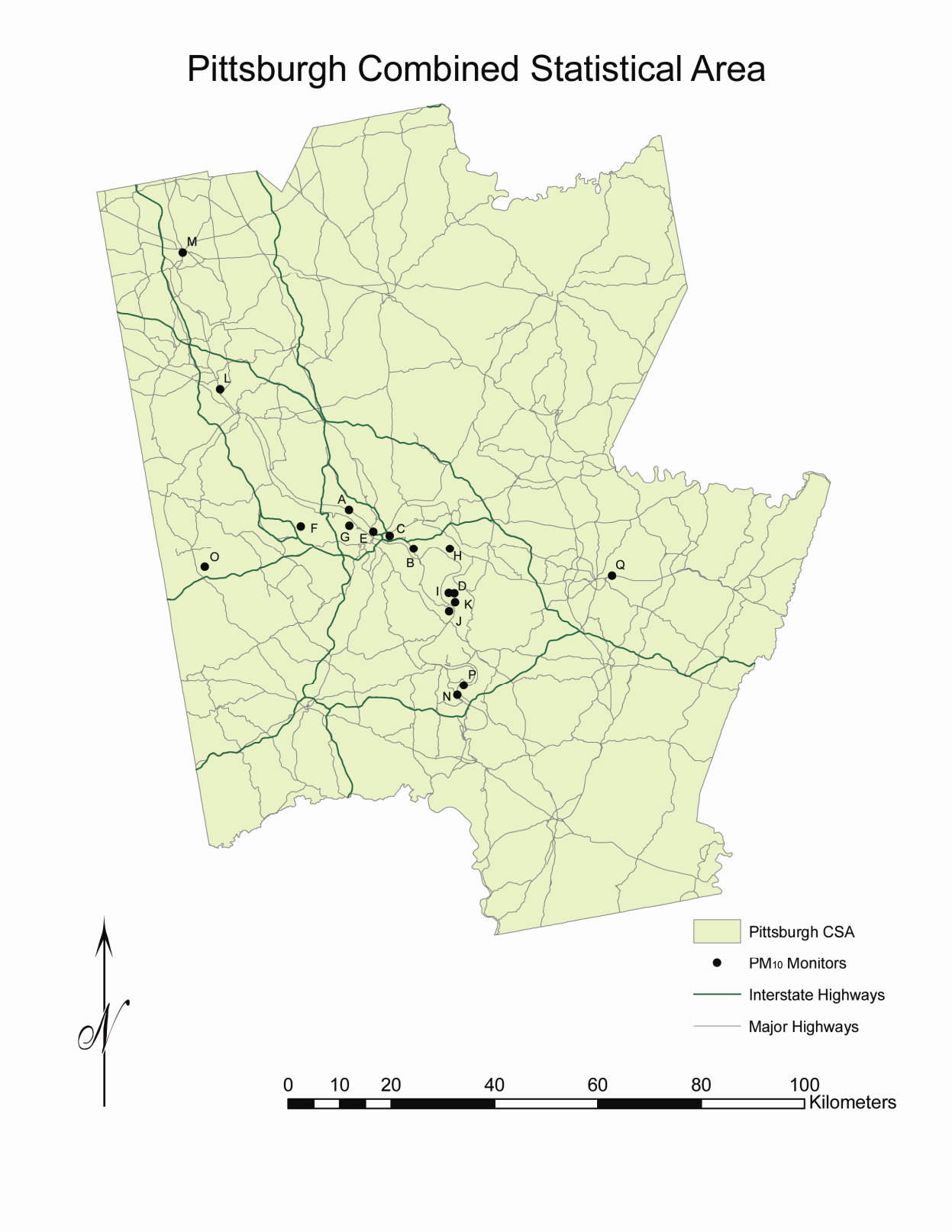


Figure A-115. PM_{10} monitor distribution and major highways, Pittsburgh, PA.

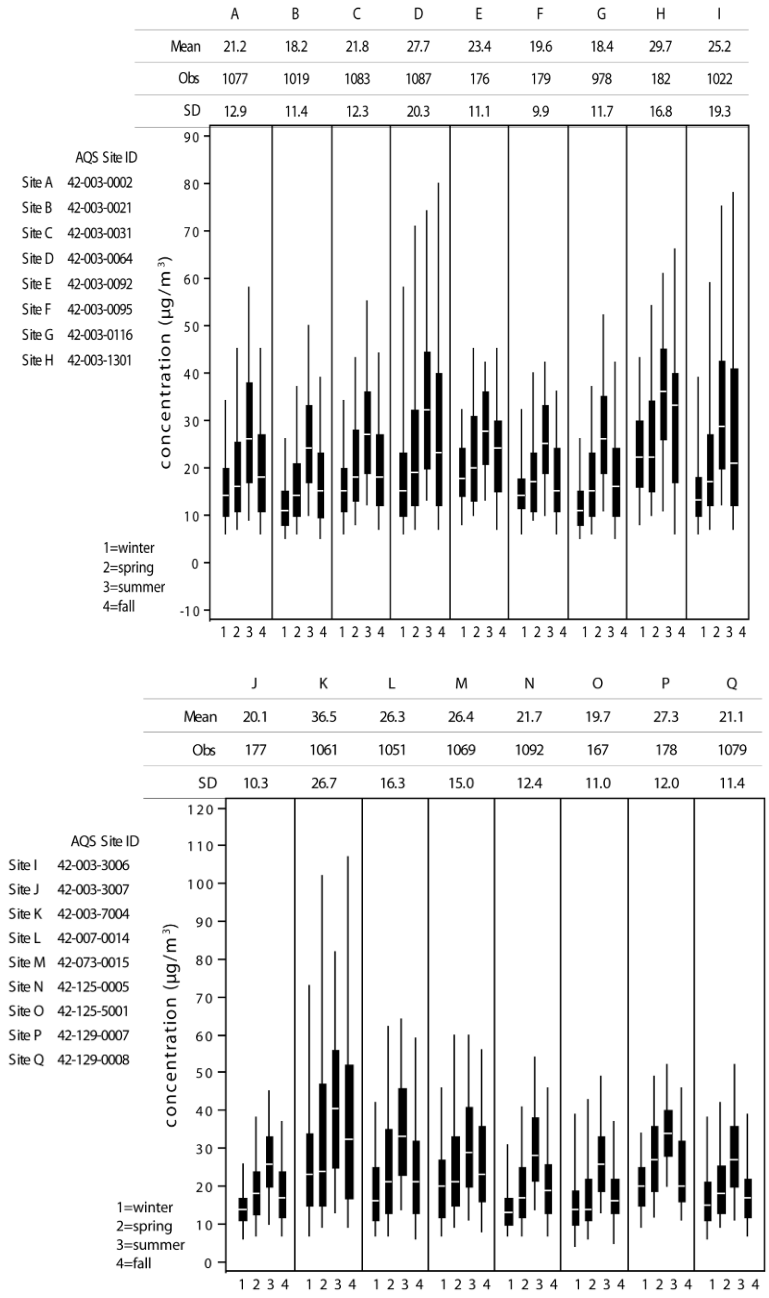


Figure A-116. Box plots illustrating the seasonal distribution of 24-h avg PM_{10} concentrations for Pittsburgh, PA.

Table A-46. Inter-sampler correlation statistics for each pair of PM_{10} monitors reporting to AQS for Pittsburgh, PA.

Site	A	B	C	D	E	F	G	H	I
A	1.00	0.93	0.93	0.80	0.92	0.89	0.93	0.79	0.86
	(0.0, 0.00)	(9.0, 0.15)	(8.0, 0.14)	(23.0, 0.21)	(8.0, 0.12)	(14.0, 0.18)	(8.0, 0.14)	(16.0, 0.17)	(18.0, 0.18)
	1077	1002	1065	1070	175	178	960	181	1005
B		1.00	0.96	0.80	0.91	0.92	0.97	0.81	0.89
		(0.0, 0.00)	(8.0, 0.15)	(29.0, 0.24)	(11.0, 0.20)	(6.0, 0.16)	(5.0, 0.10)	(25.0, 0.29)	(22.0, 0.20)
		1019	1007	1012	163	166	911	169	954
C			1.00	0.81	0.94	0.93	0.94	0.77	0.87
			(0.0, 0.00)	(23.0, 0.20)	(6.0, 0.11)	(7.0, 0.12)	(8.0, 0.13)	(21.0, 0.22)	(19.0, 0.17)
			1083	1075	173	176	966	179	1010
D				1.00	0.72	0.66	0.76	0.83	0.88
				(0.0, 0.00)	(21.0, 0.20)	(26.0, 0.24)	(27.0, 0.24)	(14.0, 0.18)	(16.0, 0.14)
				1087	176	179	970	182	1014
E					1.00	0.90	0.90	0.78	0.77
					(0.0, 0.00)	(10.0, 0.14)	(10.0, 0.17)	(20.0, 0.20)	(20.0, 0.19)
					176	173	154	175	166
F						1.00	0.94	0.70	0.74
						(0.0, 0.00)	(7.0, 0.12)	(25.0, 0.27)	(25.0, 0.22)
						179	157	178	168
G							1.00	0.70	0.87
							(0.0, 0.00)	(22.0, 0.28)	(20.0, 0.19)
							978	160	910
H								1.00	0.76
								(0.0, 0.00)	(17.0, 0.20)
								182	171
I									1.00
									(0.0, 0.00)
									1022

LEGEND
Pearson R
(P90, COD)
n

	J	K	L	M	N	O	P	Q
A	0.84	0.76	0.88	0.85	0.86	0.77	0.78	0.86
	(14.0, 0.20)	(40.0, 0.30)	(15.0, 0.18)	(16.0, 0.19)	(11.0, 0.16)	(16.0, 0.22)	(15.0, 0.19)	(11.0, 0.15)
	176	1044	1033	1052	1074	166	177	1061
B	0.93	0.76	0.88	0.81	0.91	0.76	0.83	0.88
	(7.0, 0.16)	(43.0, 0.36)	(19.0, 0.23)	(20.0, 0.26)	(10.0, 0.16)	(12.0, 0.19)	(18.0, 0.28)	(10.0, 0.18)
	164	986	982	994	1016	157	165	1003
C	0.90	0.75	0.88	0.83	0.89	0.78	0.88	0.90
	(8.0, 0.13)	(39.0, 0.30)	(14.0, 0.17)	(15.0, 0.19)	(9.0, 0.12)	(12.0, 0.18)	(13.0, 0.19)	(9.0, 0.12)
	174	1049	1039	1057	1080	164	175	1067
D	0.73	0.84	0.80	0.78	0.76	0.57	0.64	0.74
	(24.0, 0.22)	(24.0, 0.22)	(20.0, 0.18)	(20.0, 0.20)	(25.0, 0.20)	(28.0, 0.26)	(20.0, 0.25)	(26.0, 0.21)
	177	1055	1043	1061	1084	167	178	1071
E	0.86	0.65	0.83	0.80	0.84	0.77	0.84	0.85
	(10.0, 0.16)	(36.0, 0.29)	(16.0, 0.16)	(14.0, 0.17)	(12.0, 0.14)	(14.0, 0.19)	(13.0, 0.16)	(11.0, 0.15)
	171	169	169	172	176	161	172	174
F	0.90	0.57	0.82	0.75	0.86	0.83	0.84	0.86
	(7.0, 0.12)	(41.0, 0.34)	(20.0, 0.20)	(19.0, 0.22)	(11.0, 0.14)	(9.0, 0.15)	(16.0, 0.22)	(9.0, 0.14)
	174	172	172	175	179	164	175	177
G	0.92	0.73	0.87	0.78	0.89	0.81	0.84	0.86
	(7.0, 0.13)	(45.0, 0.35)	(18.0, 0.21)	(19.0, 0.24)	(9.0, 0.15)	(11.0, 0.17)	(17.0, 0.26)	(10.0, 0.16)
	156	955	938	952	975	146	157	967
H	0.74	0.68	0.77	0.78	0.74	0.60	0.65	0.76
	(23.0, 0.26)	(26.0, 0.22)	(15.0, 0.18)	(17.0, 0.18)	(21.0, 0.22)	(27.0, 0.29)	(19.0, 0.22)	(21.5, 0.24)
	176	175	175	178	182	167	177	180
I	0.79	0.83	0.82	0.78	0.81	0.66	0.69	0.78
	(22.0, 0.20)	(30.0, 0.25)	(16.0, 0.17)	(18.0, 0.20)	(20.0, 0.17)	(26.0, 0.24)	(21.0, 0.25)	(22.0, 0.19)
	166	992	978	998	1019	158	167	1009
J	1.00	0.66	0.79	0.72	0.88	0.78	0.86	0.86
	(0.0, 0.00)	(44.5, 0.33)	(18.0, 0.20)	(18.0, 0.22)	(8.0, 0.13)	(11.0, 0.17)	(16.0, 0.21)	(8.0, 0.15)
	177	170	170	173	177	163	173	175
K		1.00	0.74	0.75	0.70	0.47	0.58	0.68
		(0.0, 0.00)	(31.0, 0.26)	(33.0, 0.24)	(40.0, 0.30)	(44.0, 0.36)	(34.0, 0.30)	(43.0, 0.30)
		1061	1017	1035	1058	160	171	1048
L			1.00	0.87	0.85	0.70	0.74	0.80
			(0.0, 0.00)	(13.0, 0.16)	(16.0, 0.17)	(22.0, 0.24)	(17.0, 0.21)	(18.0, 0.19)
			1051	1025	1048	160	171	1035
M				1.00	0.74	0.64	0.67	0.77
				(0.0, 0.00)	(18.0, 0.21)	(19.0, 0.26)	(17.0, 0.22)	(18.0, 0.19)
				1069	1067	163	174	1053
N					1.00	0.72	0.86	0.86
					(0.0, 0.00)	(13.0, 0.18)	(14.0, 0.20)	(10.0, 0.14)
					1092	167	178	1076
O						1.00	0.75	0.69
						(0.0, 0.00)	(18.0, 0.25)	(14.0, 0.19)
						167	163	165
P							1.00	0.84
							(0.0, 0.00)	(15.0, 0.21)
							178	176
Q								1.00
								(0.0, 0.00)
								1079

LEGEND
Pearson R
(P90, COD)
n

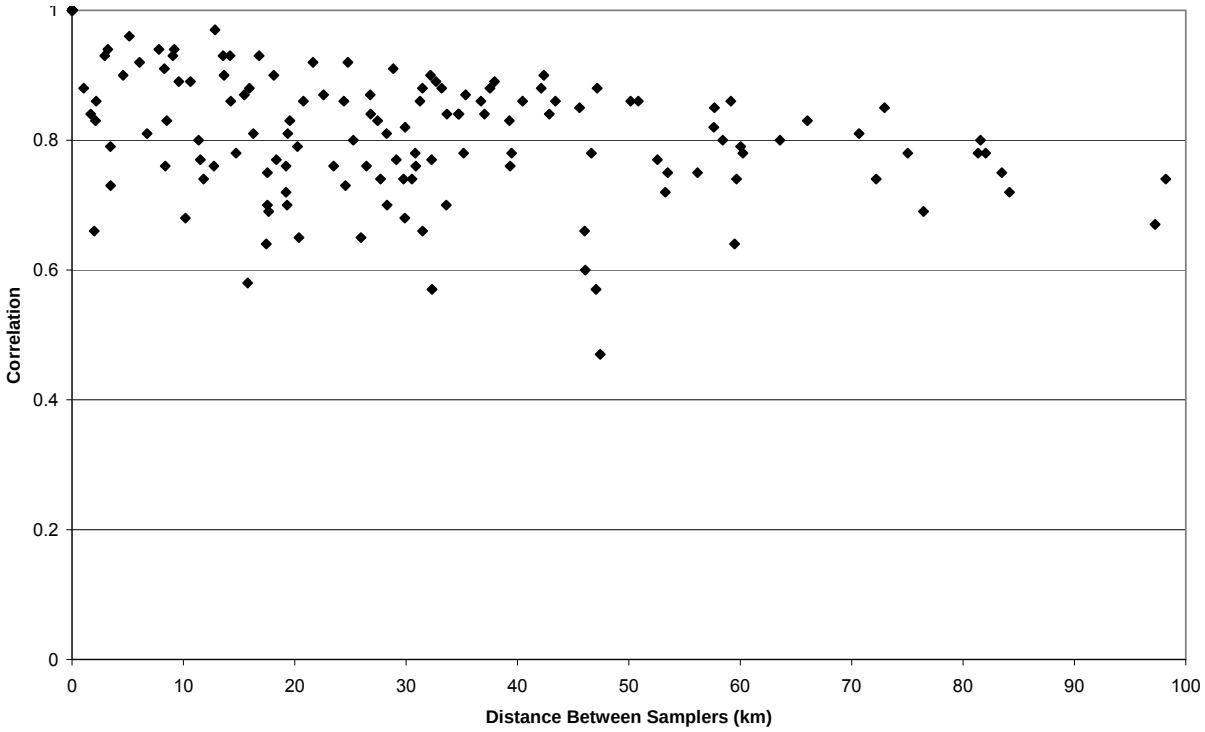


Figure A-117. PM_{10} inter-sampler correlations as a function of distance between monitors for Pittsburgh, PA.

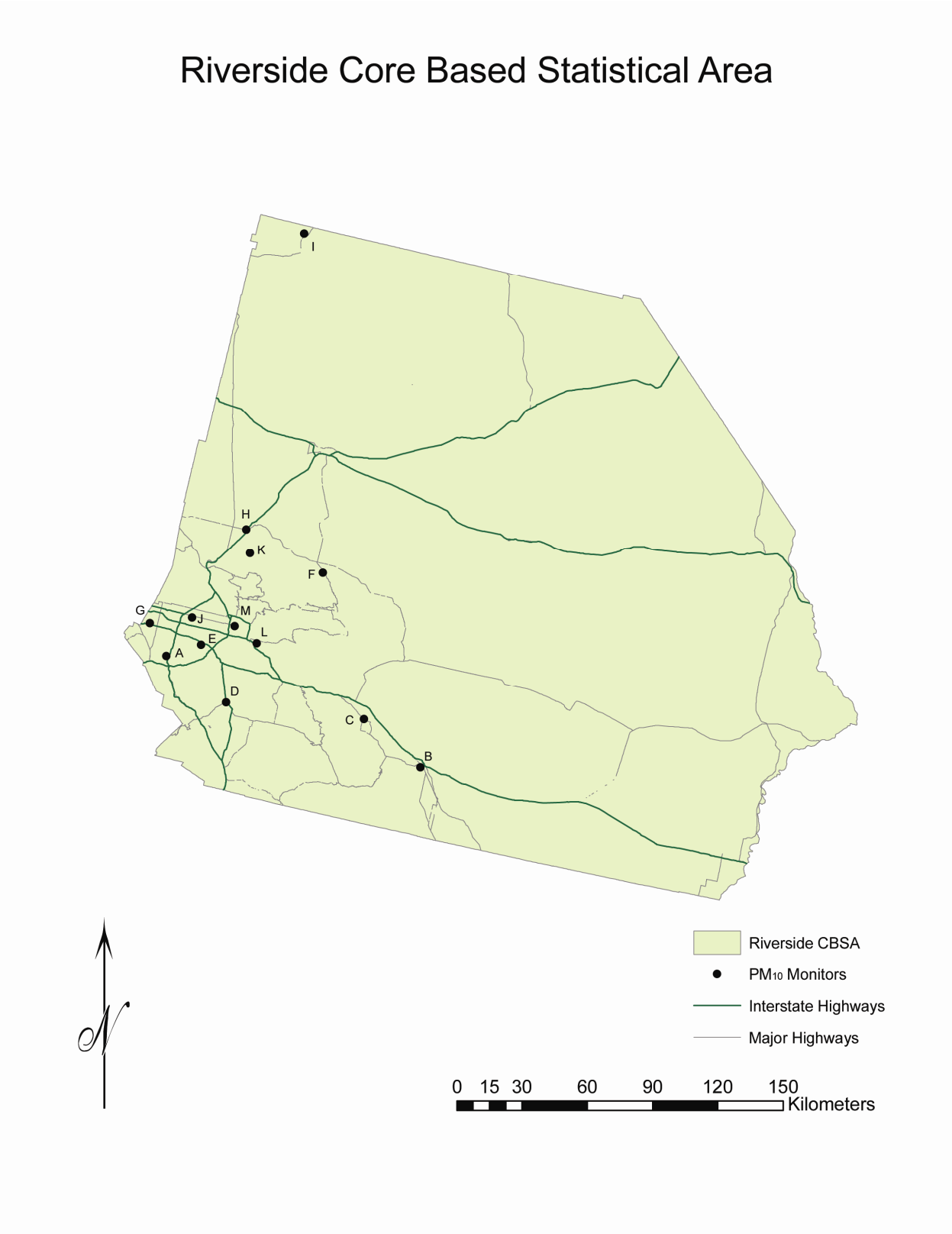


Figure A-118. PM_{10} monitor distribution and major highways, Riverside, CA.

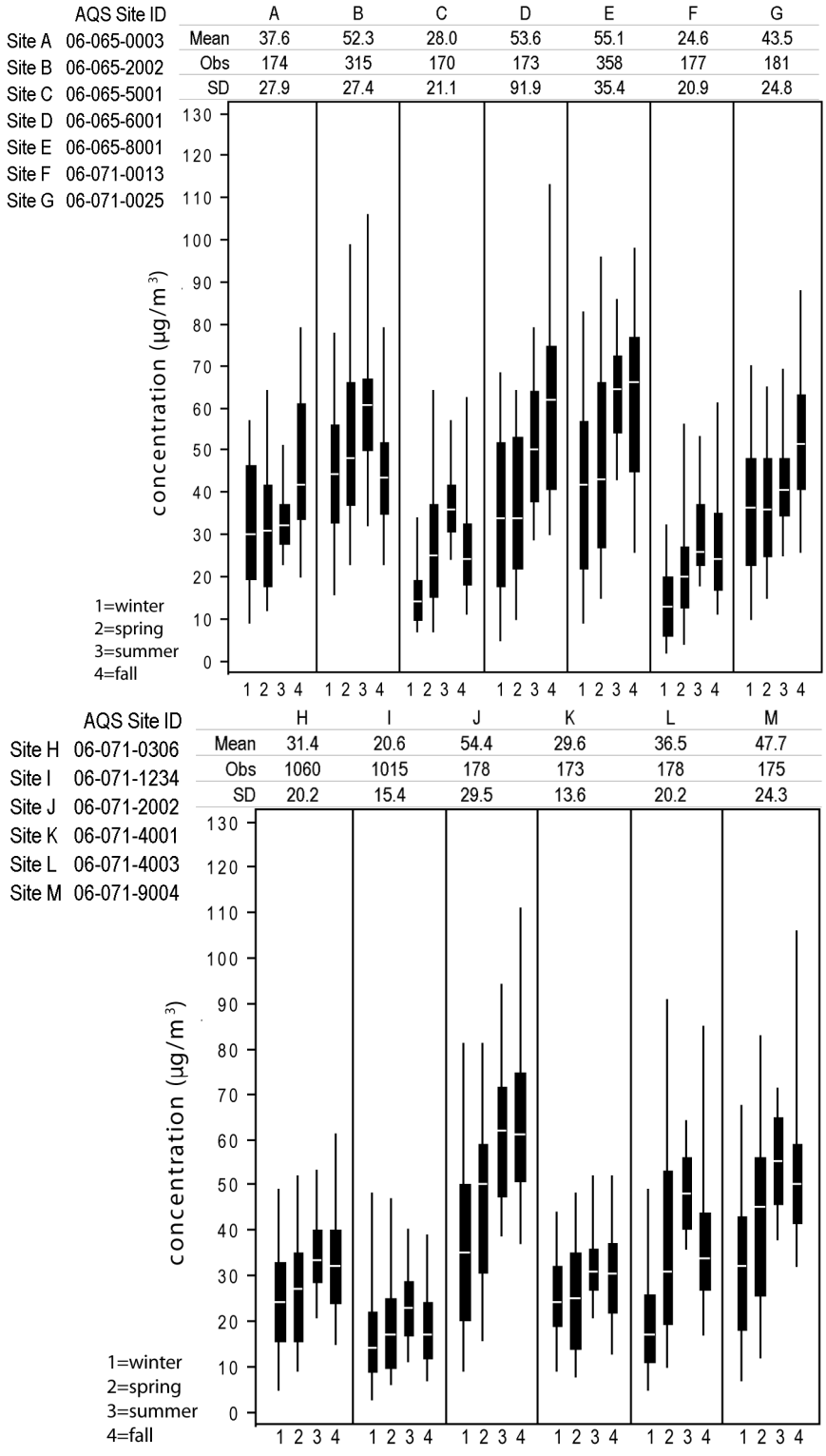


Figure A-119. Box plots illustrating the seasonal distribution of 24-h avg PM_{10} concentrations for Riverside, CA.

Table A-47. Inter-sampler correlation statistics for each pair of PM_{10} monitors reporting to AQS for Riverside, CA.

	A	B	C	D	E	F	G	H	I	J	K	L	M
A	1.00	0.09	0.15	0.90	0.94	0.25	0.94	0.24	0.12	0.83	0.27	0.46	0.78
	(0.0, 0.00)	(50.0, 0.31)	(36.0, 0.32)	(33.0, 0.19)	(37.0, 0.24)	(41.0, 0.38)	(16.0, 0.13)	(25.0, 0.22)	(40.0, 0.39)	(38.5, 0.24)	(30.0, 0.23)	(32.0, 0.25)	(33.0, 0.21)
	174	170	155	165	172	169	171	174	173	160	158	169	164
B		1.00	0.86	0.07	0.13	0.31	0.12	0.32	0.29	0.13	0.31	0.35	0.29
		(0.0, 0.00)	(48.0, 0.37)	(47.0, 0.28)	(45.0, 0.27)	(57.0, 0.47)	(49.0, 0.26)	(48.0, 0.33)	(55.0, 0.49)	(51.0, 0.25)	(49.0, 0.35)	(51.0, 0.31)	(44.0, 0.24)
		315	161	167	298	173	176	309	302	172	163	173	168
C			1.00	0.13	0.21	0.36	0.20	0.34	0.36	0.23	0.38	0.50	0.40
			(0.0, 0.00)	(49.0, 0.37)	(58.0, 0.42)	(24.0, 0.31)	(40.0, 0.35)	(27.0, 0.28)	(24.0, 0.30)	(57.5, 0.41)	(24.0, 0.27)	(30.0, 0.25)	(41.0, 0.34)
			170	151	162	156	160	170	168	150	147	159	154
D				1.00	0.93	0.19	0.83	0.11	0.05	0.73	0.13	0.38	0.69
				(0.0, 0.00)	(29.0, 0.17)	(52.0, 0.43)	(23.0, 0.17)	(38.0, 0.27)	(52.0, 0.46)	(26.0, 0.18)	(43.0, 0.30)	(40.0, 0.26)	(24.5, 0.16)
				173	169	167	168	173	172	157	155	165	160
E					1.00	0.23	0.93	0.26	0.16	0.86	0.27	0.57	0.82
					(0.0, 0.00)	(63.0, 0.48)	(27.0, 0.17)	(46.0, 0.33)	(63.5, 0.51)	(18.0, 0.13)	(54.0, 0.36)	(40.0, 0.28)	(26.0, 0.15)
					358	174	179	351	340	175	165	175	171
F						1.00	0.27	0.73	0.32	0.35	0.43	0.44	0.48
						(0.0, 0.00)	(44.0, 0.41)	(28.0, 0.33)	(27.0, 0.32)	(57.0, 0.46)	(24.5, 0.32)	(35.0, 0.35)	(46.0, 0.43)
						177	173	177	176	162	160	170	164
G							1.00	0.27	0.20	0.90	0.35	0.58	0.85
							(0.0, 0.00)	(30.0, 0.25)	(46.5, 0.45)	(25.0, 0.16)	(34.0, 0.27)	(29.0, 0.24)	(24.0, 0.15)
							181	181	180	165	163	174	168
H								1.00	0.26	0.47	0.48	0.40	0.44
								(0.0, 0.00)	(27.0, 0.33)	(45.0, 0.32)	(18.0, 0.18)	(29.0, 0.25)	(34.0, 0.26)
								1060	983	178	172	178	175
I									1.00	0.20	0.45	0.38	0.35
									(0.0, 0.00)	(62.0, 0.51)	(25.0, 0.32)	(41.0, 0.39)	(48.0, 0.46)
		LEGEND							1015	177	172	177	173
J		**R**								1.00	0.42	0.70	0.85
		(P90, COD)								(0.0, 0.00)	(49.0, 0.35)	(37.0, 0.27)	(20.0, 0.15)
		N								178	155	163	157
K											1.00	0.49	0.48
											(0.0, 0.00)	(30.0, 0.26)	(38.0, 0.29)
											173	162	157
L												1.00	0.84
												(0.0, 0.00)	(24.0, 0.20)
												178	167
M													1.00
													(0.0, 0.00)
													175

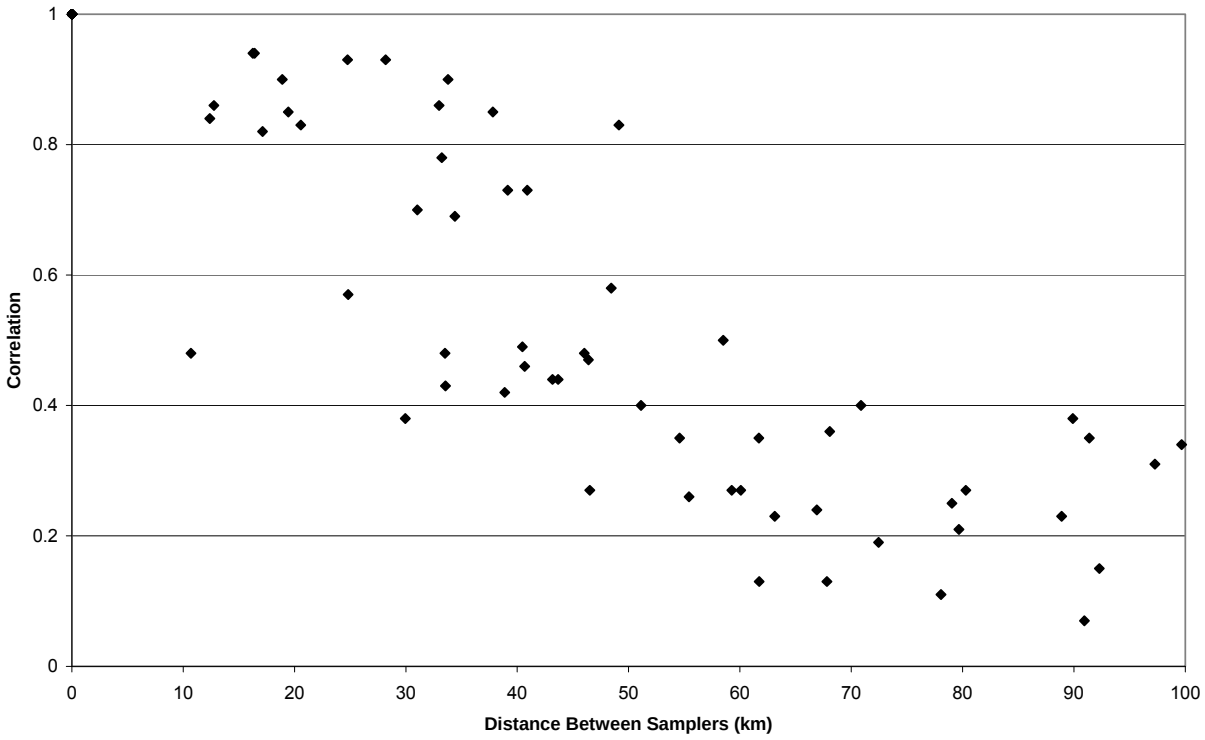


Figure A-120. PM_{10} inter-sampler correlations as a function of distance between monitors for Riverside, CA.

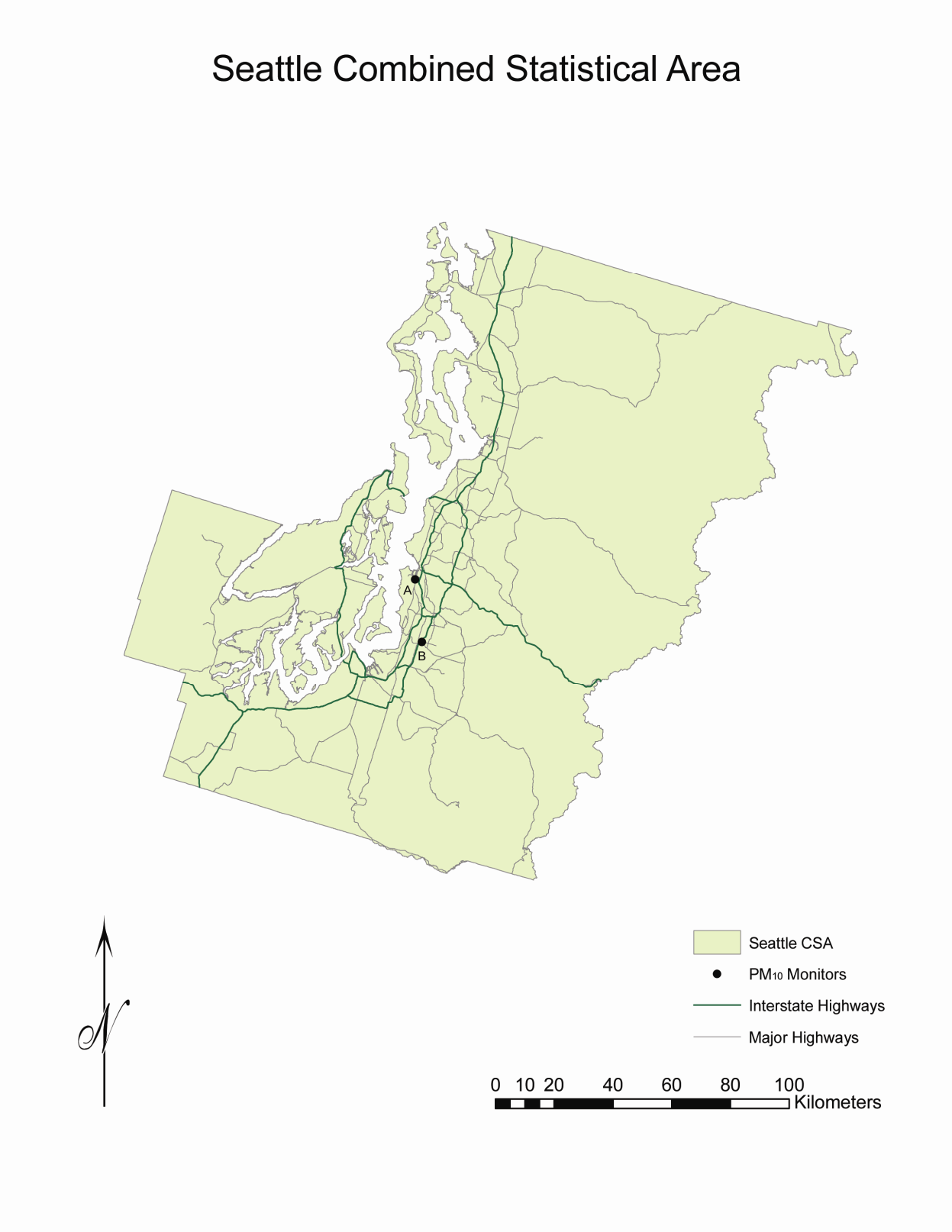


Figure A-121. PM_{10} monitor distribution and major highways, Seattle, WA.

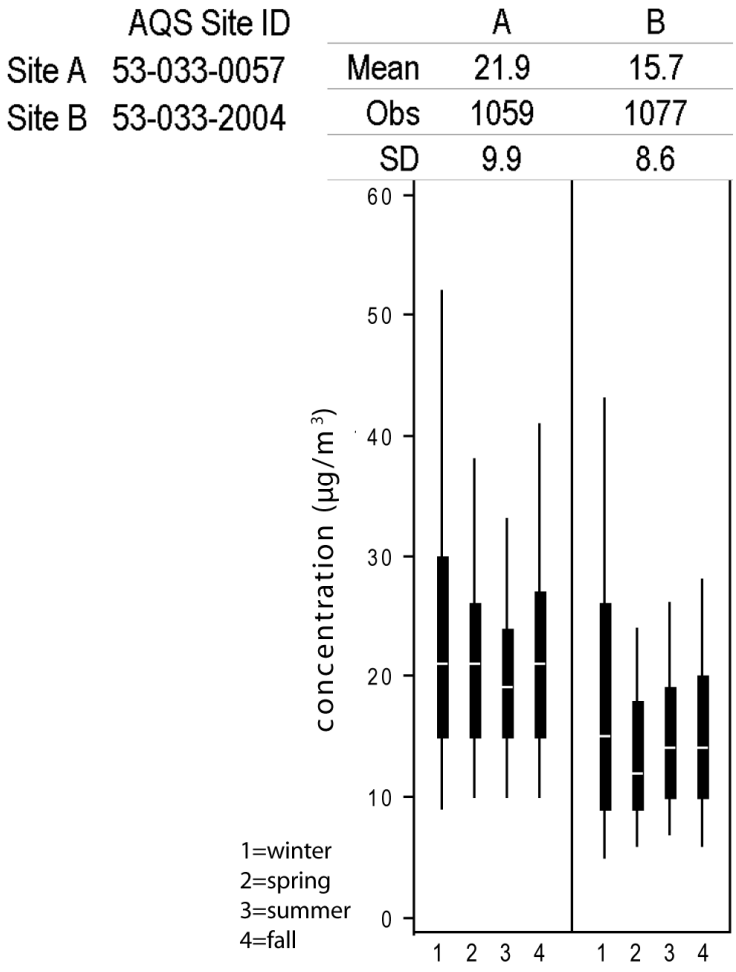


Figure A-122. Box plots illustrating the seasonal distribution of 24-h avg PM_{10} concentrations for Seattle, WA.

Table A-48. Inter-sampler correlation statistics for each pair of PM_{10} monitors reporting to AQS for Seattle, WA.

	A	B
A	1.00	0.77
	(0.0, 0.00)	(14.0, 0.24)
	1059	1041
B	**LEGEND**	1.00
	R	(0.0, 0.00)
	(P90, COD)	1077
	N	

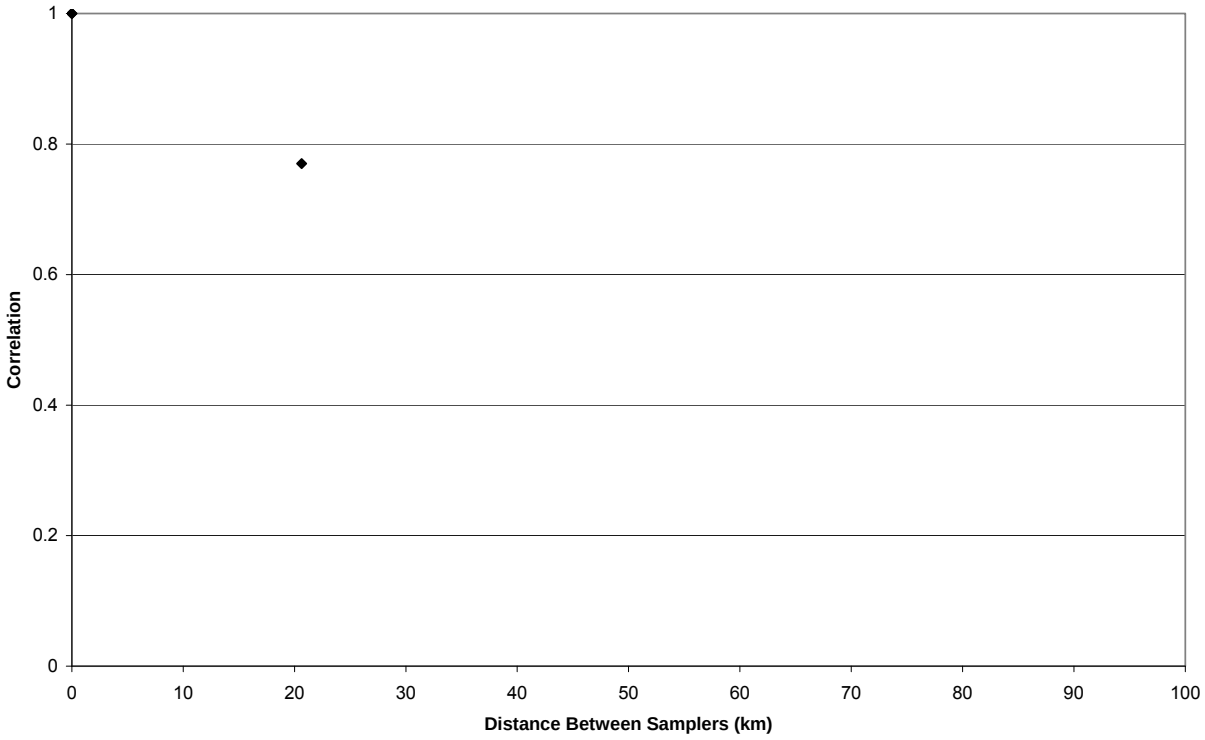


Figure A-123. PM_{10} inter-sampler correlations as a function of distance between monitors for Seattle, WA.

Figure A-124. PM_{10} monitor distribution and major highways, St. Louis, MO.

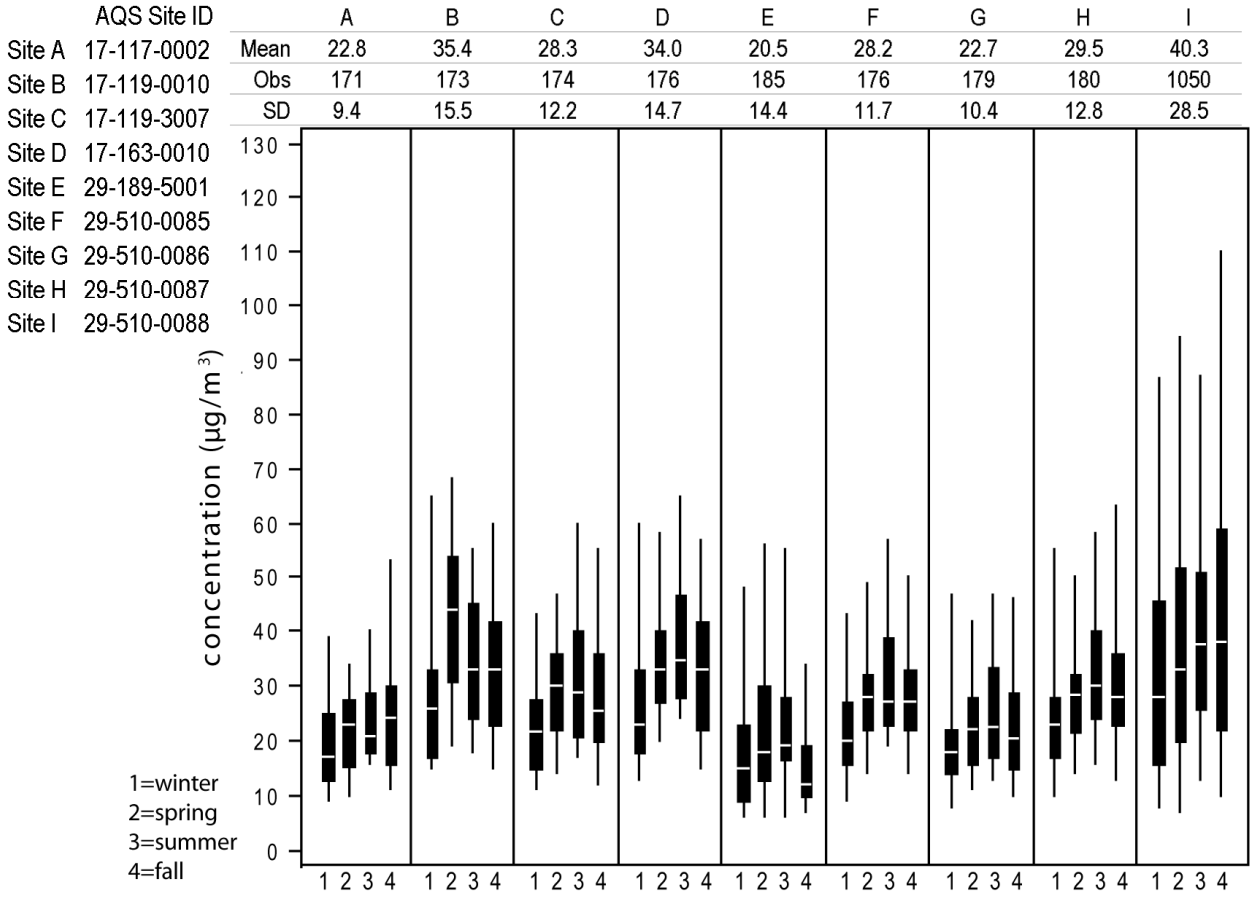


Figure A-125. Box plots illustrating the seasonal distribution of 24-h avg PM_{10} concentrations for St. Louis, MO.

Table A-49. Inter-sampler correlation statistics for each pair of PM_{10} monitors reporting to AQS for St. Louis, MO.

	A	B	C	D	E	F	G	H	I
A	1.00	0.50	0.75	0.67	0.47	0.65	0.67	0.73	0.55
	(0.0, 0.00)	(30.0, 0.28)	(14.0, 0.17)	(23.0, 0.24)	(16.0, 0.29)	(16.0, 0.18)	(13.0, 0.17)	(18.0, 0.19)	(52.0, 0.33)
	171	161	158	156	158	163	166	168	164
B		1.00	0.65	0.63	0.46	0.68	0.68	0.64	0.52
		(0.0, 0.00)	(20.0, 0.21)	(20.0, 0.19)	(37.0, 0.42)	(23.0, 0.20)	(28.0, 0.28)	(22.0, 0.20)	(36.0, 0.28)
		173	161	158	160	167	169	170	166
C			1.00	0.75	0.57	0.80	0.76	0.82	0.65
			(0.0, 0.00)	(17.0, 0.17)	(23.0, 0.33)	(12.0, 0.13)	(13.0, 0.18)	(12.0, 0.13)	(41.0, 0.27)
			174	157	158	165	169	169	168
D				1.00	0.44	0.82	0.81	0.80	0.59
				(0.0, 0.00)	(30.0, 0.40)	(16.0, 0.15)	(21.0, 0.24)	(14.0, 0.15)	(36.0, 0.27)
				176	157	163	165	166	169
E					1.00	0.53	0.62	0.56	0.34
					(0.0, 0.00)	(22.0, 0.34)	(17.0, 0.26)	(25.0, 0.35)	(55.0, 0.42)
					185	164	166	167	179
F						1.00	0.89	0.86	0.67
						(0.0, 0.00)	(11.0, 0.16)	(12.0, 0.11)	(41.0, 0.27)
		LEGEND				176	173	174	169
G		**R**					1.00	0.83	0.65
		(P90, COD)					(0.0, 0.00)	(16.0, 0.19)	(47.0, 0.32)
		N					179	177	173
H								1.00	0.64
								(0.0, 0.00)	(41.0, 0.27)
								180	173
I									1.00
									(0.0, 0.00)
									1050

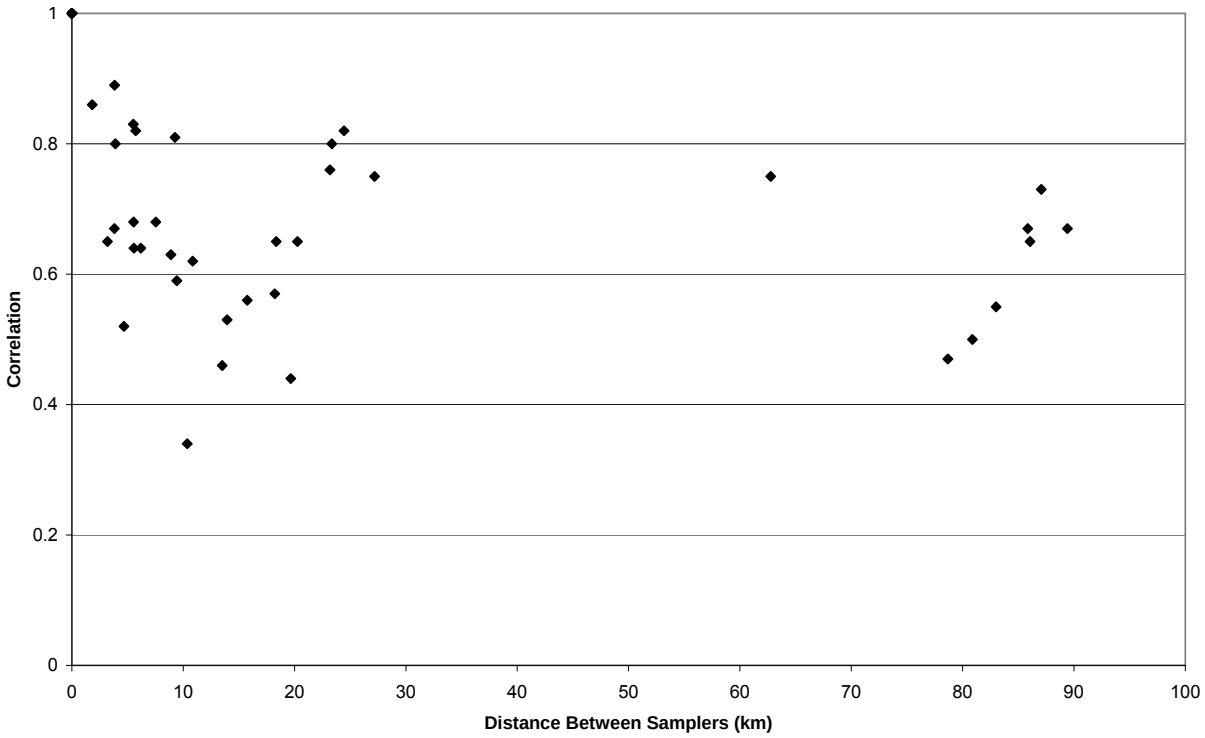


Figure A-126. PM_{10} inter-sampler correlations as a function of distance between monitors for St. Louis, MO.

Table A-50. Correlation coefficients of hourly and daily average particle number, surface and volume concentrations in selected particle size ranges.

Size range (nm)	Hourly averages					Daily avg
	All days (N = 5481)	Sundays (N = 701)	Weekdays (N = 3227)	Event days (N = 577)	No events (N = 4904)	All days (N = 263)
3-10	0.40	0.24	0.42	0.73	0.37	0.32
10-30	0.35	0.22	0.31	0.57	0.33	0.27
30-50	0.38	0.42	0.29	0.56	0.36	0.36
50-100	0.46	0.56	0.39	0.57	0.45	0.46
100-500	0.55	0.65	0.49	0.62	0.55	0.55
500-800	0.73	0.75	0.70	0.76	0.72	0.71
10-100	0.31	0.28	0.24	0.52	0.29	0.24
10-800	0.55	0.65	0.49	0.62	0.55	0.55
Total number	0.30	0.24	0.24	0.58	0.28	0.20
Total surface	0.57	0.63	0.51	0.65	0.56	0.57
Total volume	0.66	0.69	0.62	0.73	0.65	0.67

Source: Tuch et al. (2006)

A.2.3. Speciation

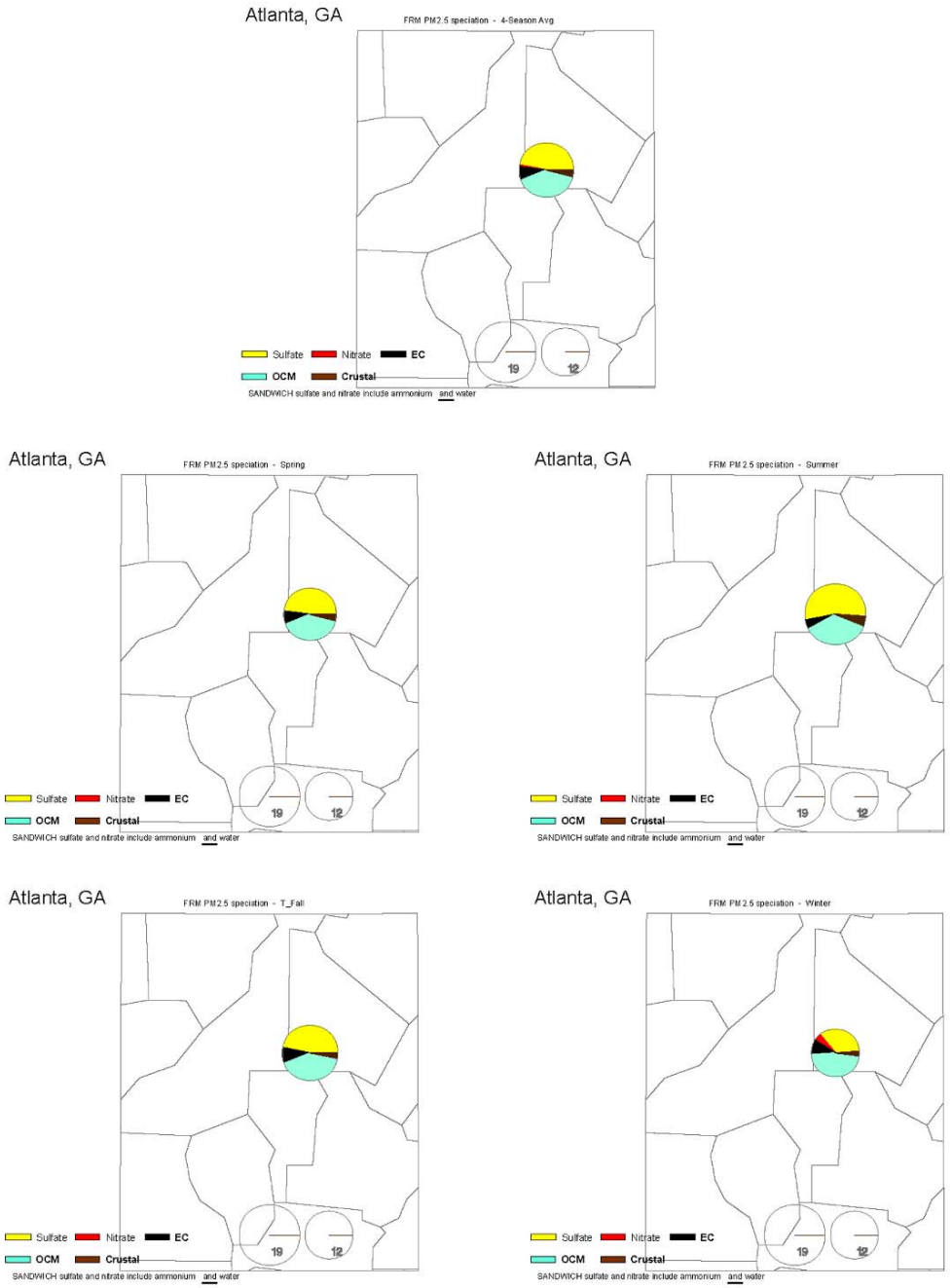


Figure A-127. Seasonally averaged $PM_{2.5}$ speciation data for 2005-2007 for a) annual, b) spring, c) summer, d) fall and e) winter derived using the SANDWICH method in Atlanta, GA.

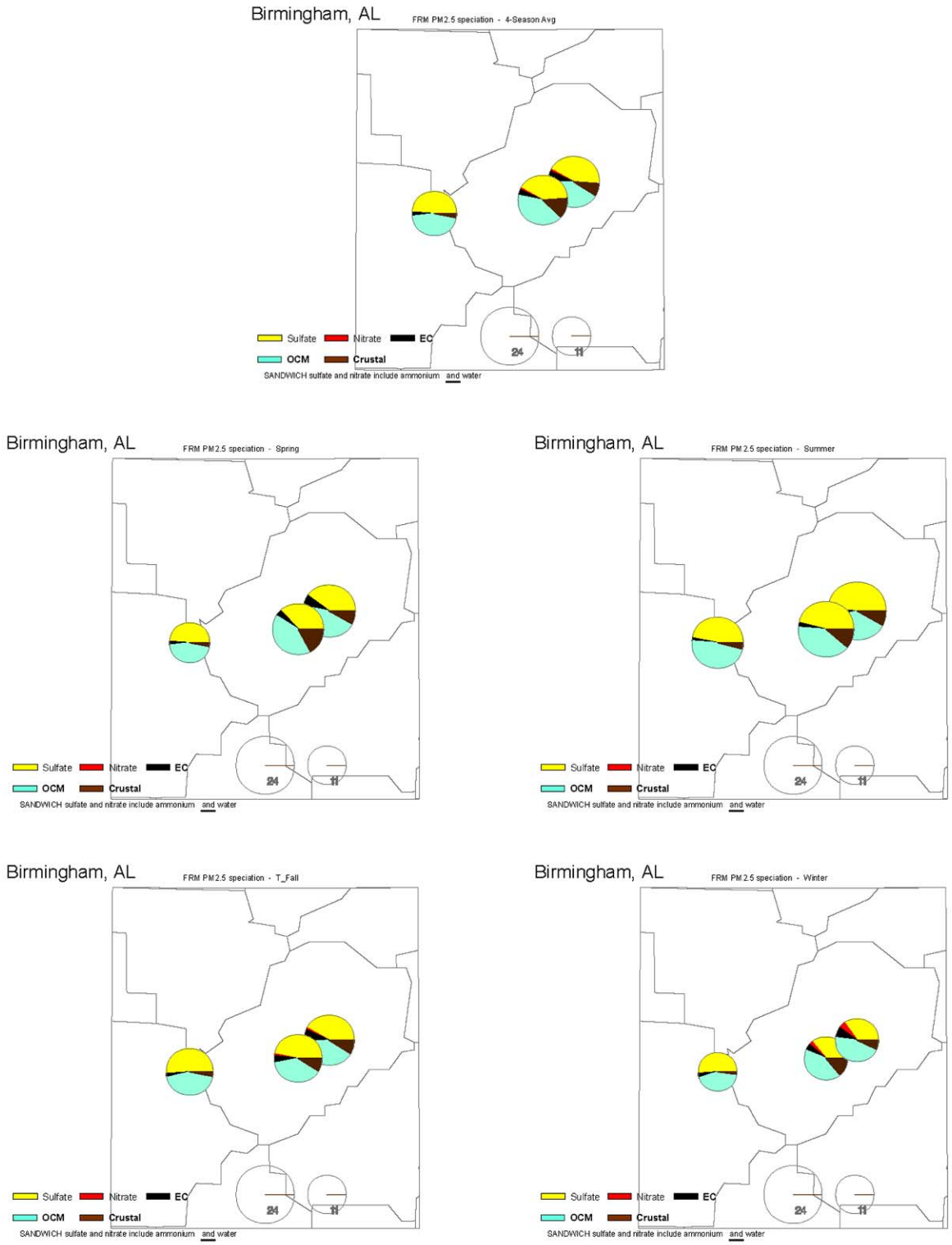


Figure A-128. Seasonally averaged $PM_{2.5}$ speciation data for 2005-2007 for a) annual, b) spring, c) summer, d) fall and e) winter derived using the SANDWICH method in Birmingham, AL.

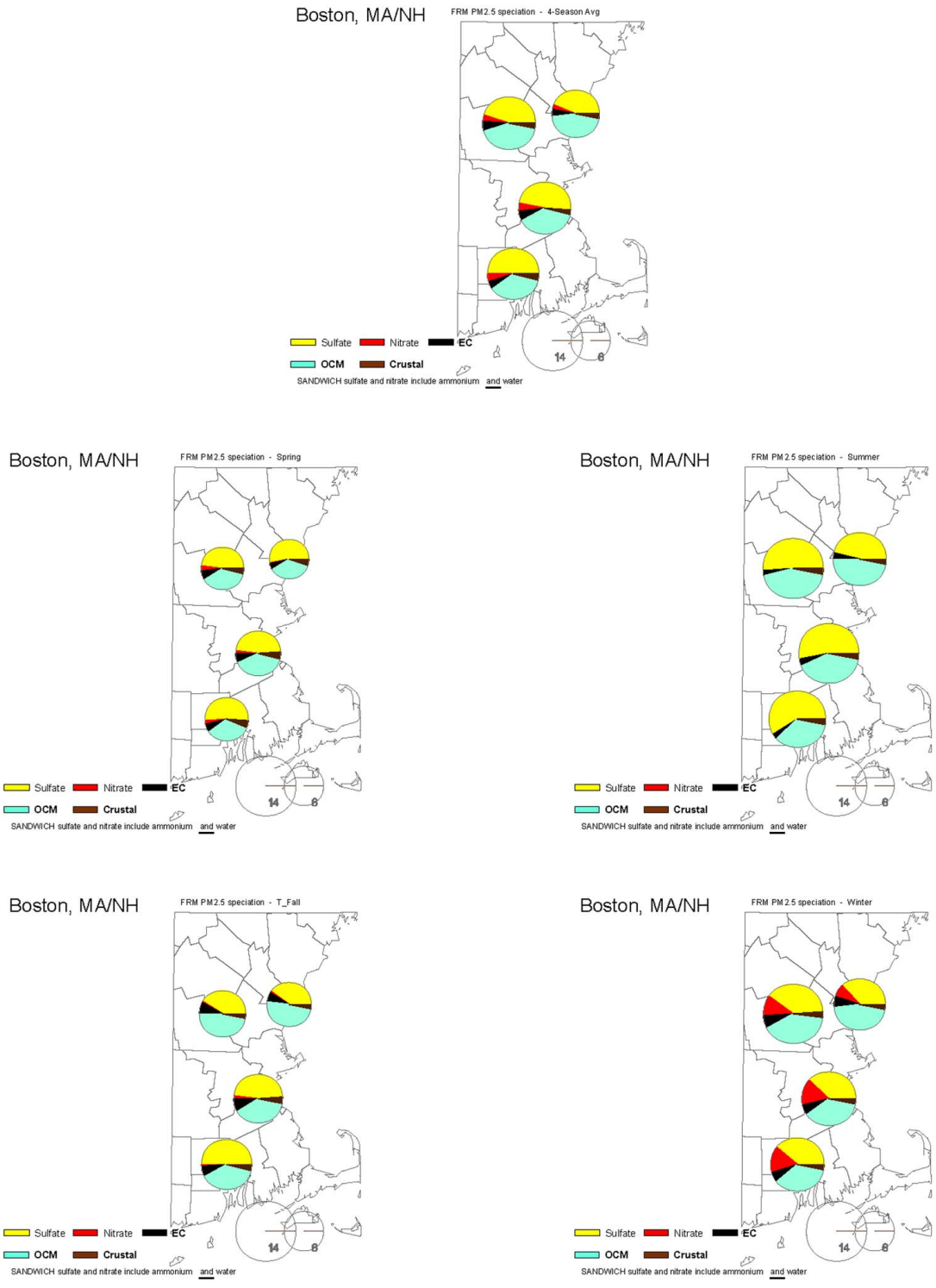


Figure A-129. Seasonally averaged $PM_{2.5}$ speciation data for 2005-2007 for a) annual, b) spring, c) summer, d) fall and e) winter derived using the SANDWICH method in Boston, MA.

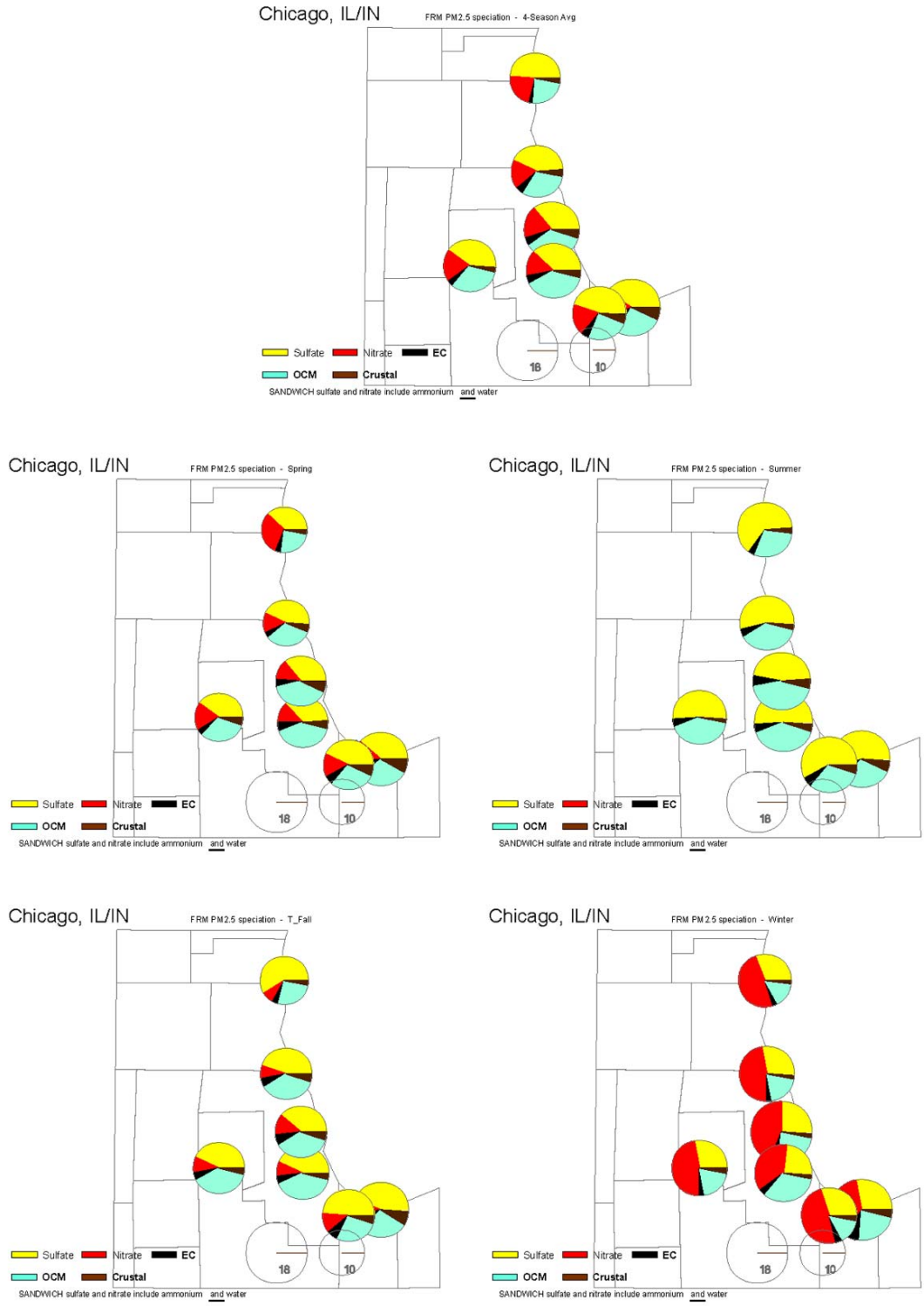


Figure A-130. Seasonally averaged $PM_{2.5}$ speciation data for 2005-2007 for a) annual, b) spring, c) summer, d) fall and e) winter derived using the SANDWICH method in Chicago, IL.

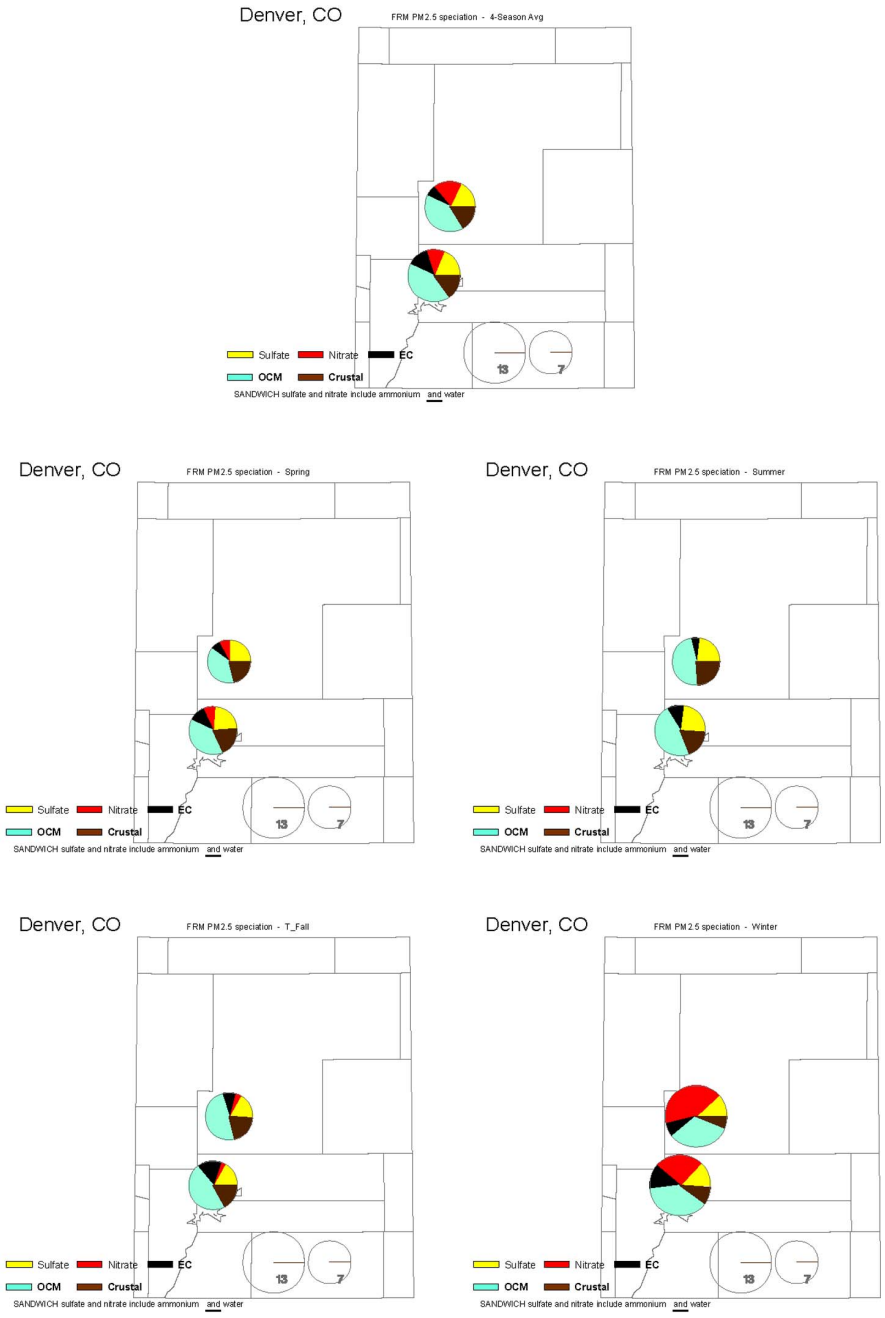


Figure A-131. Seasonally averaged $PM_{2.5}$ speciation data for 2005-2007 for a) annual, b) spring, c) summer, d) fall and e) winter, derived using the SANDWICH method in Denver, CO.

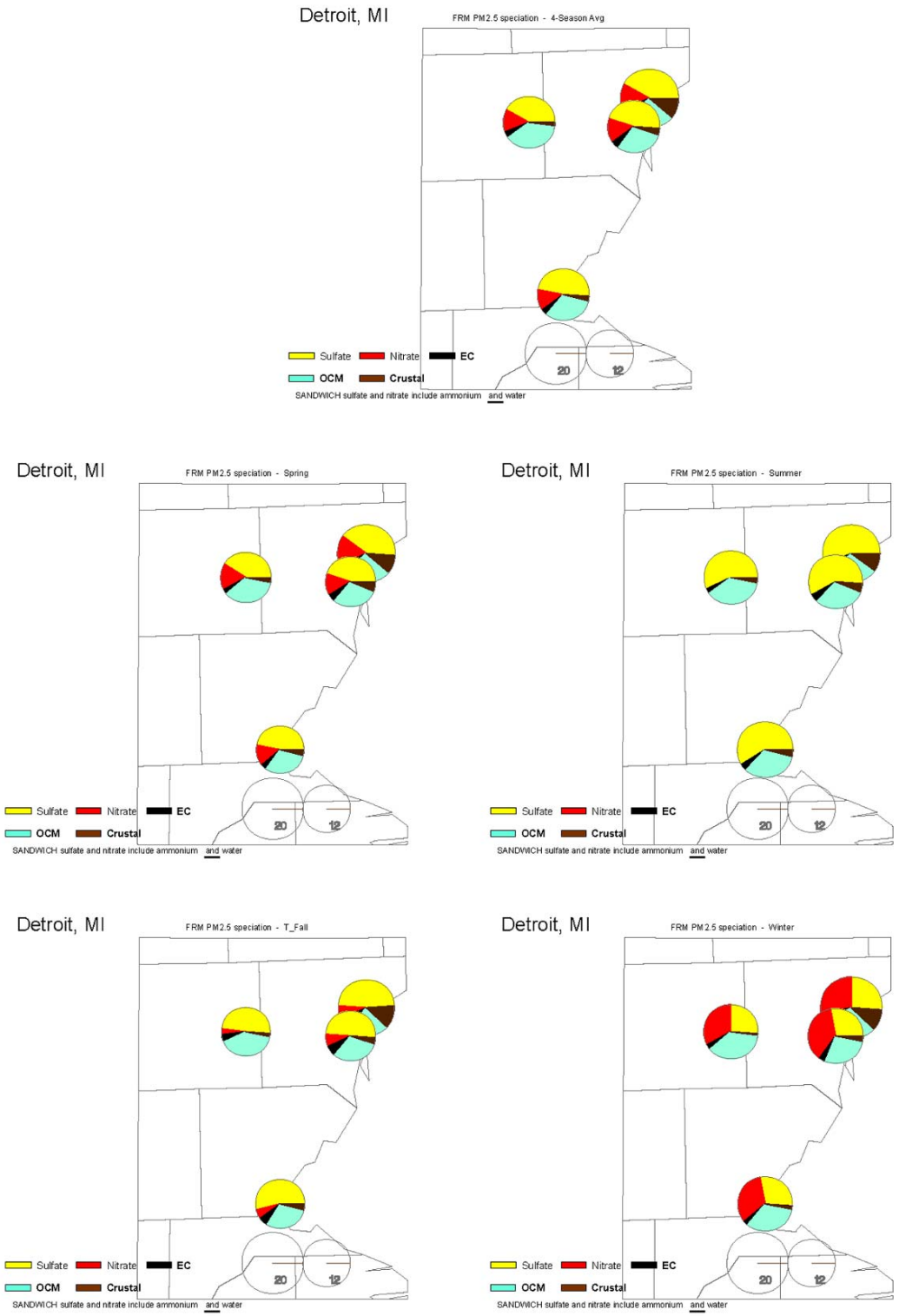


Figure A-132. Seasonally averaged $PM_{2.5}$ speciation data for 2005-2007 for a) annual, b) spring, c) summer, d) fall and e) winter derived using the SANDWICH method in Detroit, MI.

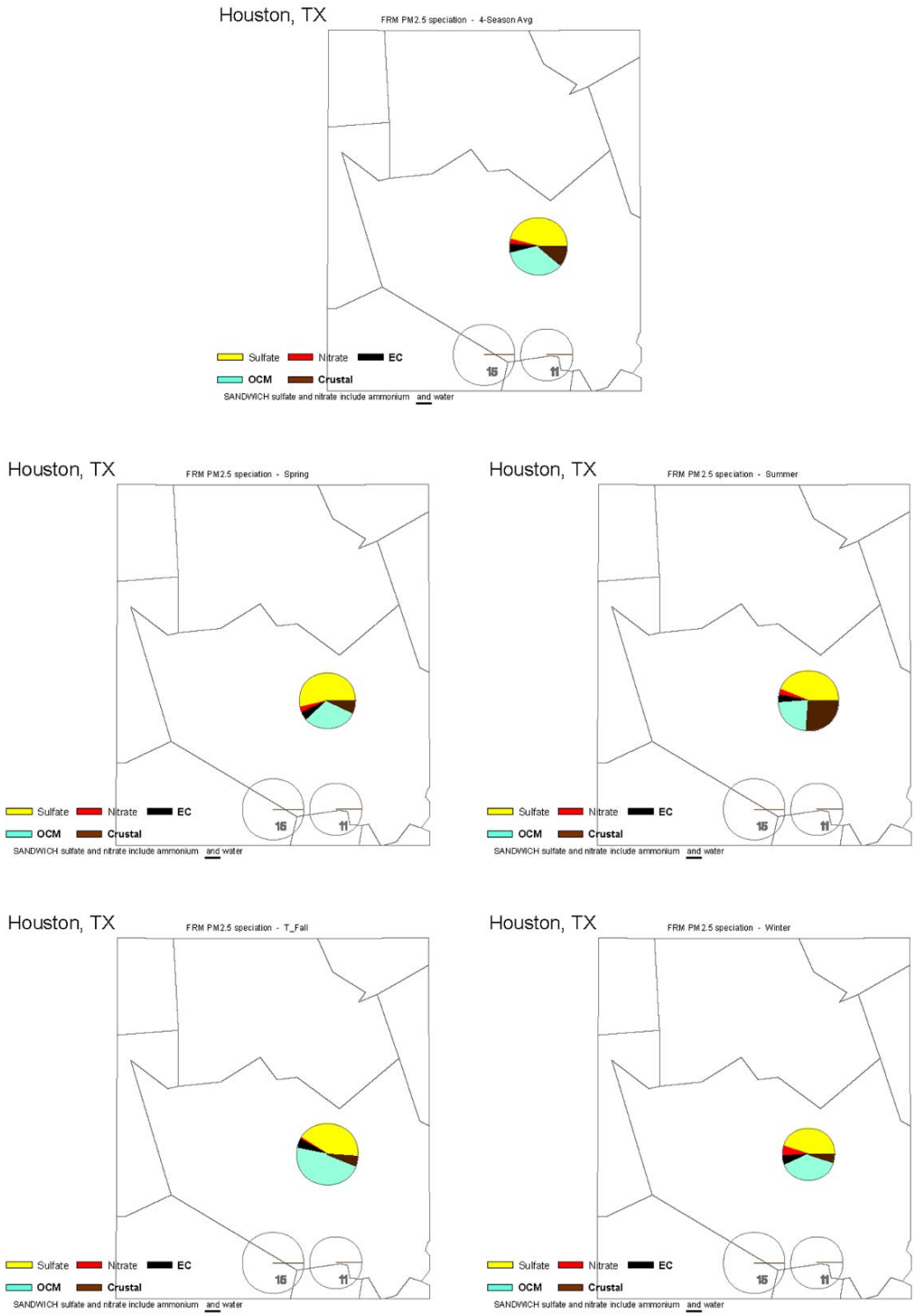


Figure A-133. Seasonally averaged $PM_{2.5}$ speciation data for 2005-2007 for a) annual, b) spring, c) summer, d) fall and e) winter derived using the SANDWICH method in Houston, TX.

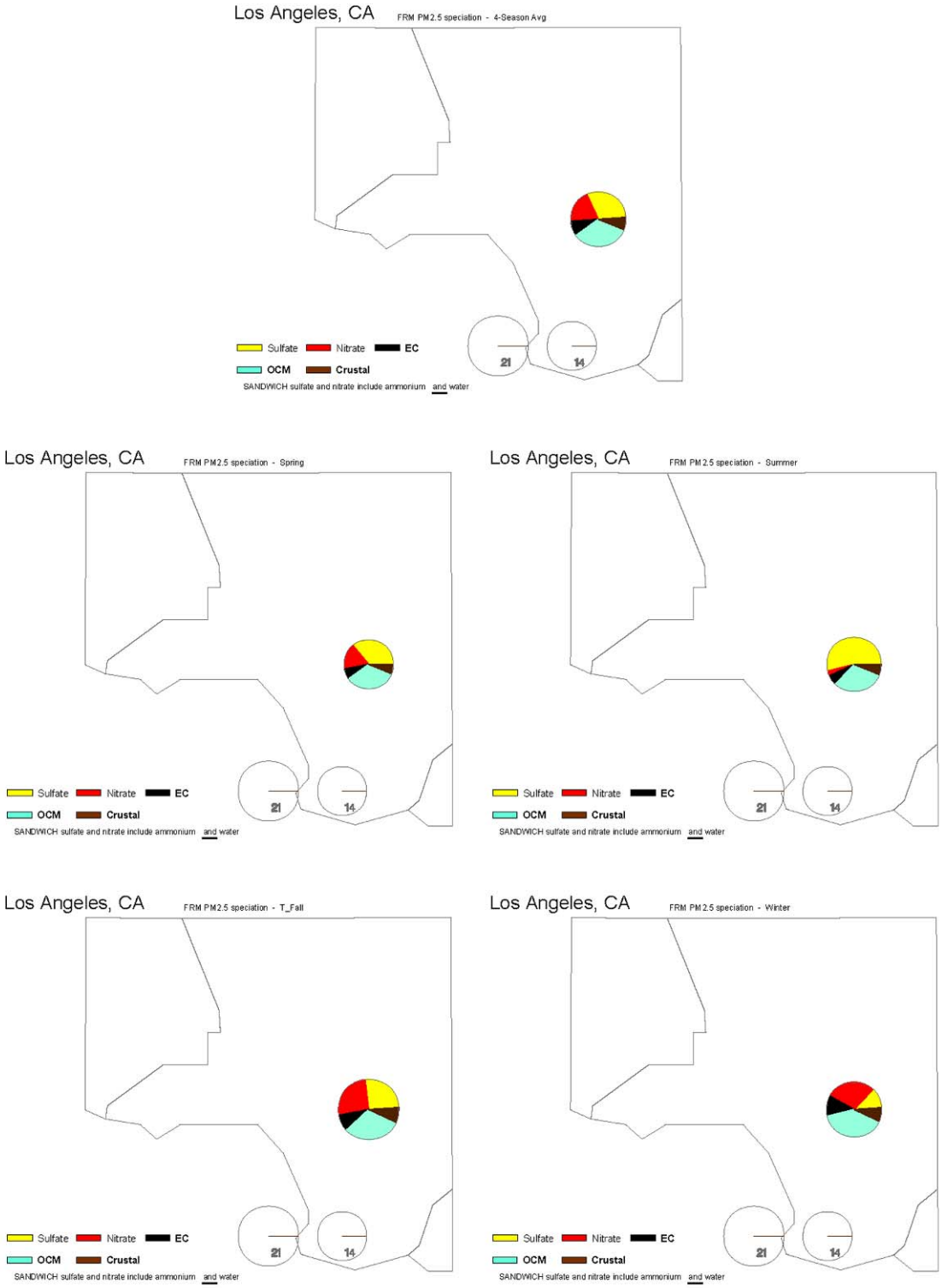


Figure A-134. Seasonally averaged $PM_{2.5}$ speciation data for 2005-2007 for a) annual, b) spring, c) summer, d) fall and e) winter derived using the SANDWICH method in Los Angeles, CA.

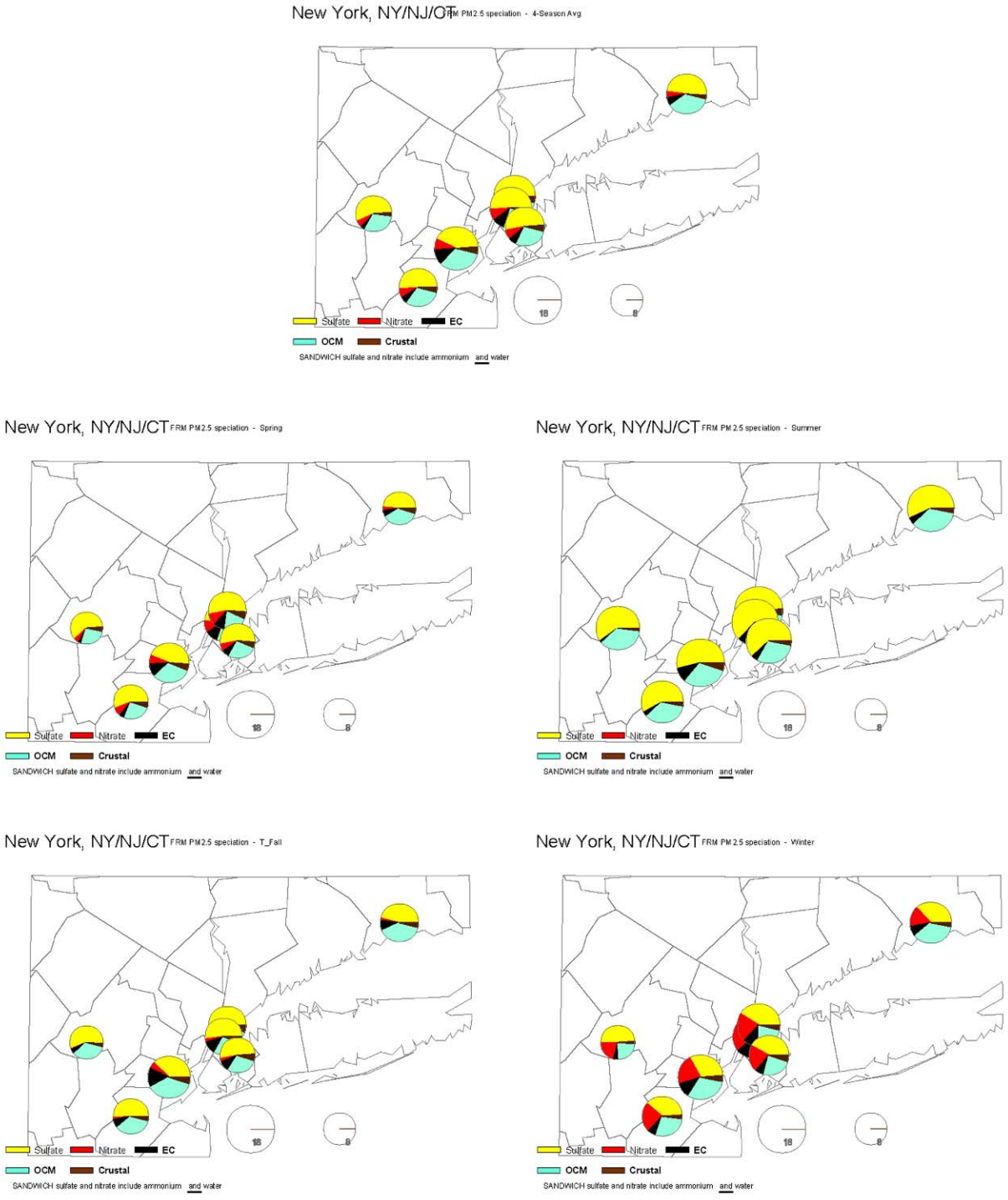


Figure A-135. Seasonally averaged $PM_{2.5}$ speciation data for 2005-2007 for a) annual, b) spring, c) summer, d) fall and e) winter derived using the SANDWICH method in New York, NY.

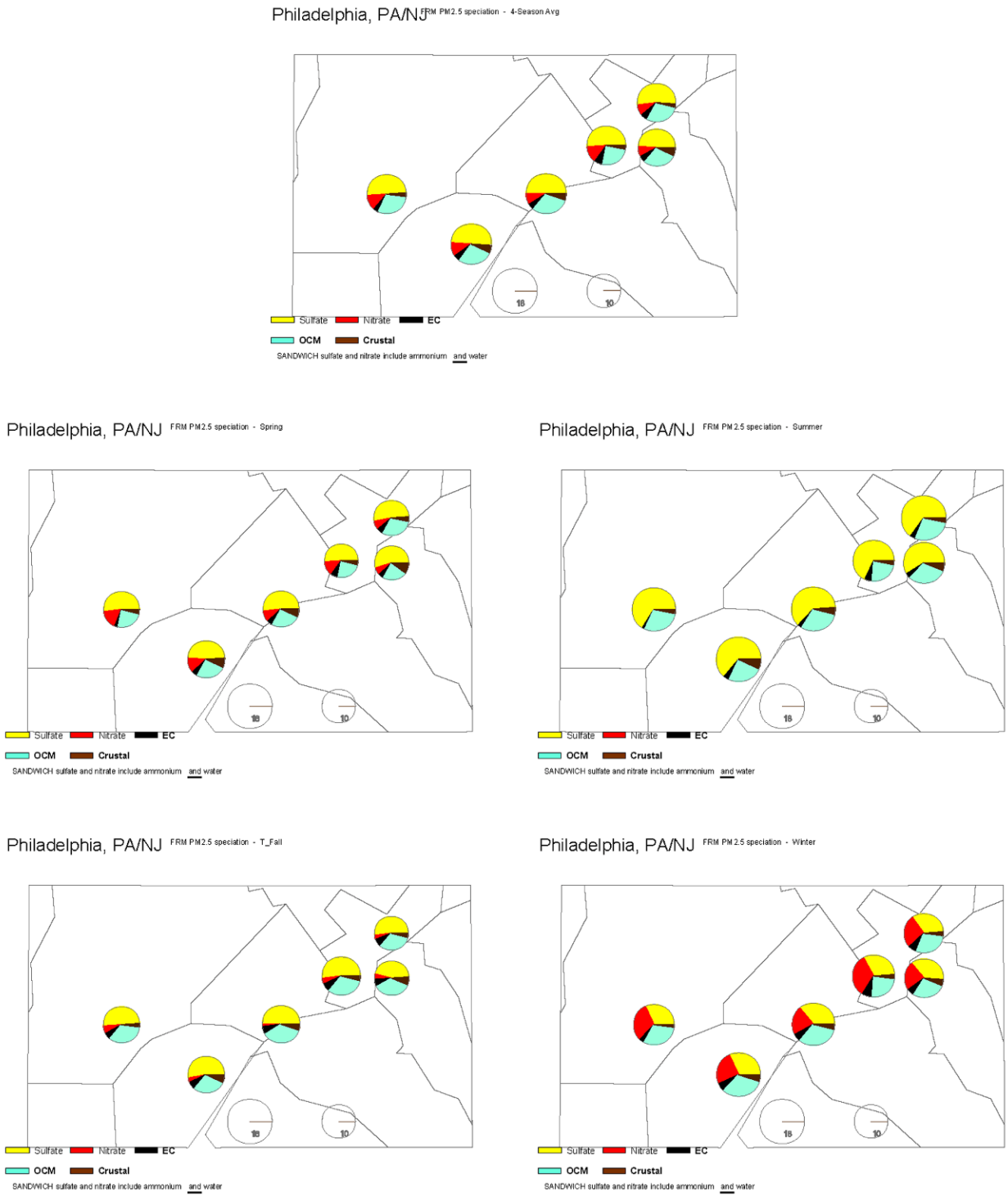


Figure A-136. Seasonally averaged $PM_{2.5}$ speciation data for 2005-2007 for a) annual, b) spring, c) summer, d) fall and e) winter derived using the SANDWICH method in Philadelphia, PA.

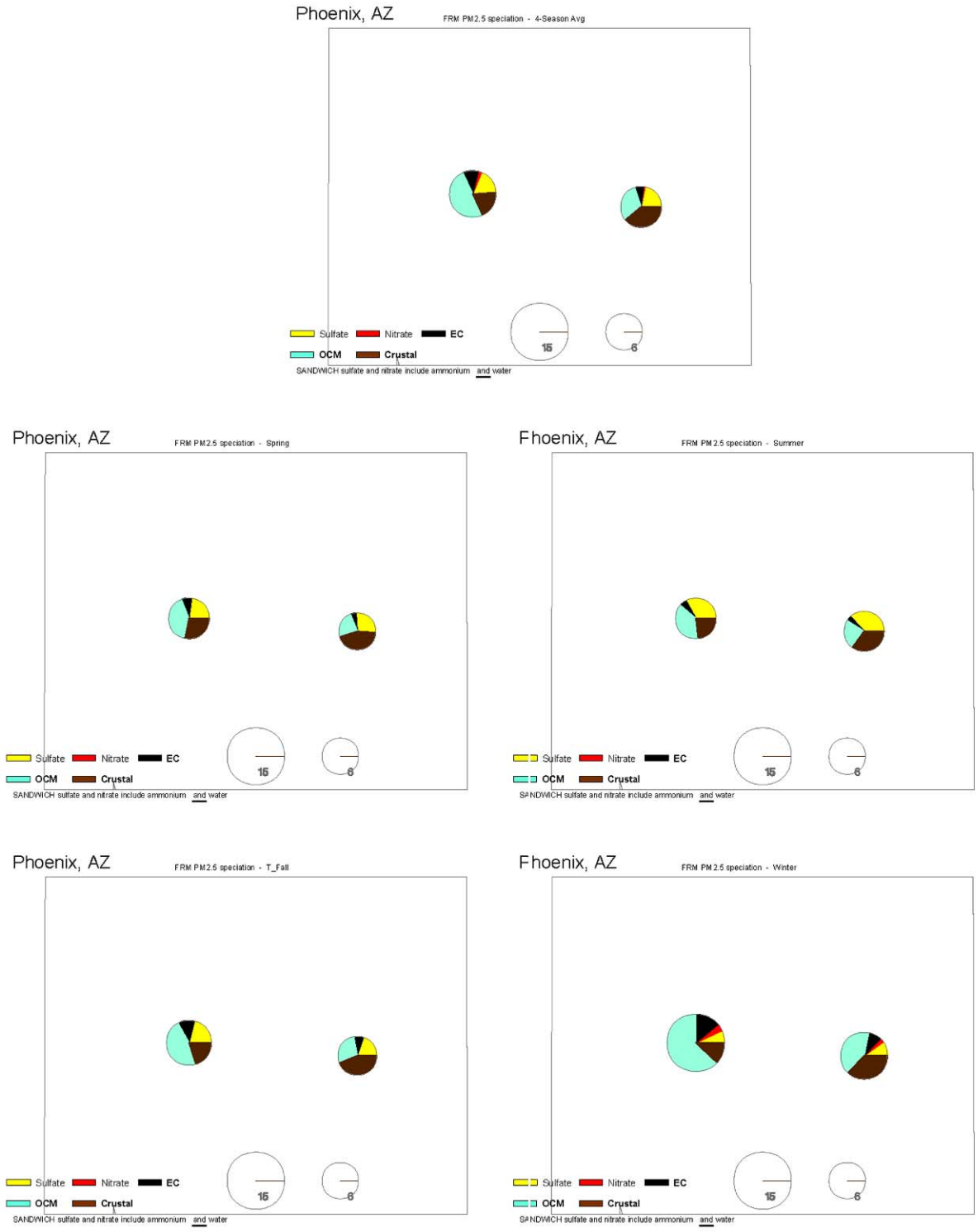


Figure A-137. Seasonally averaged $PM_{2.5}$ speciation data for 2005-2007 for a) annual, b) spring, c) summer, d) fall and e) winter derived using the SANDWICH method in Phoenix, AZ.

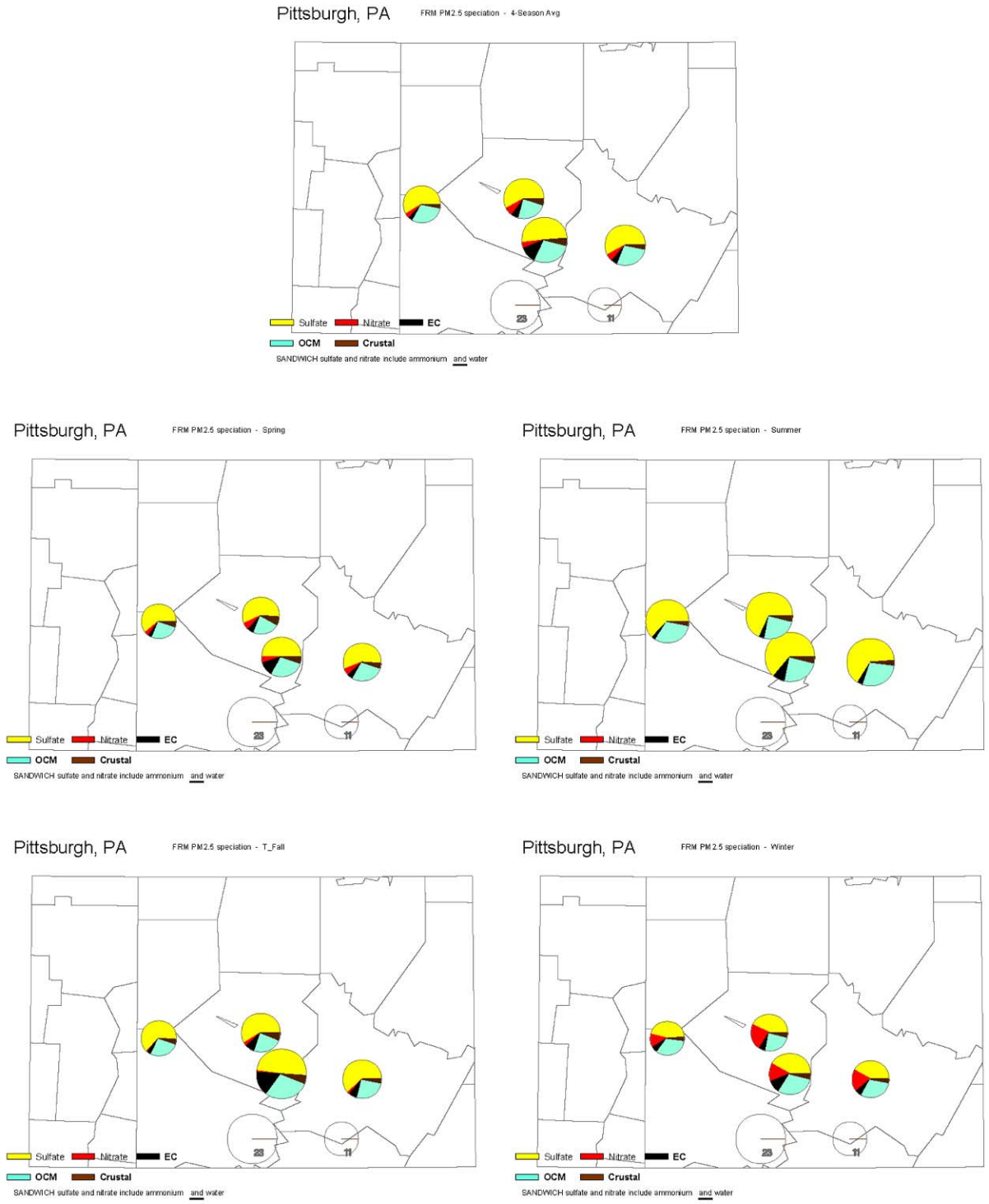


Figure A-138. Seasonally averaged $PM_{2.5}$ speciation data for 2005-2007 for a) annual, b) spring, c) summer, d) fall and e) winter derived using the SANDWICH method in Pittsburgh, PA.

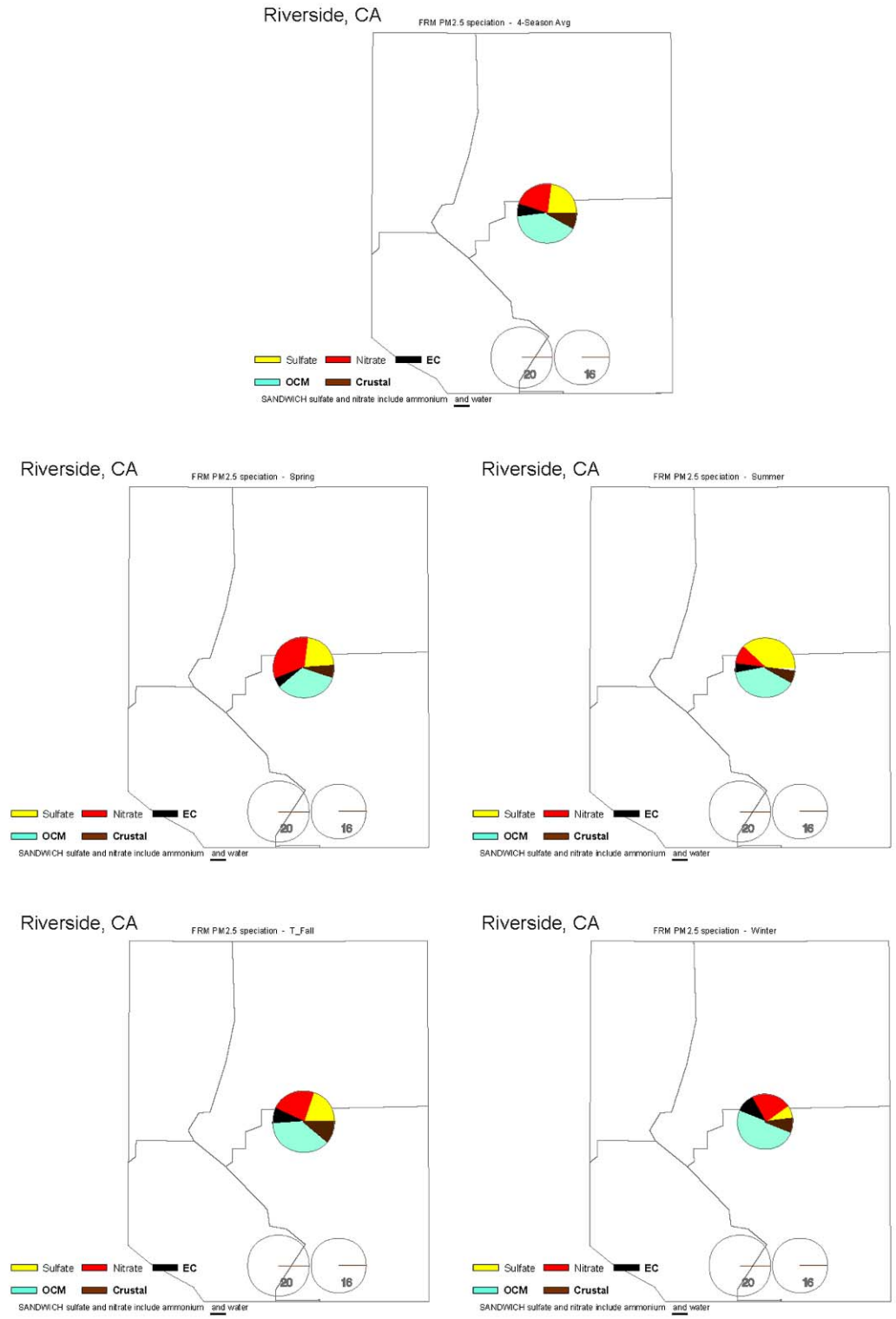


Figure A-139. Seasonally averaged $PM_{2.5}$ speciation data for 2005-2007 for a) annual, b) spring, c) summer, d) fall and e) winter derived using the SANDWICH method in Riverside, CA.

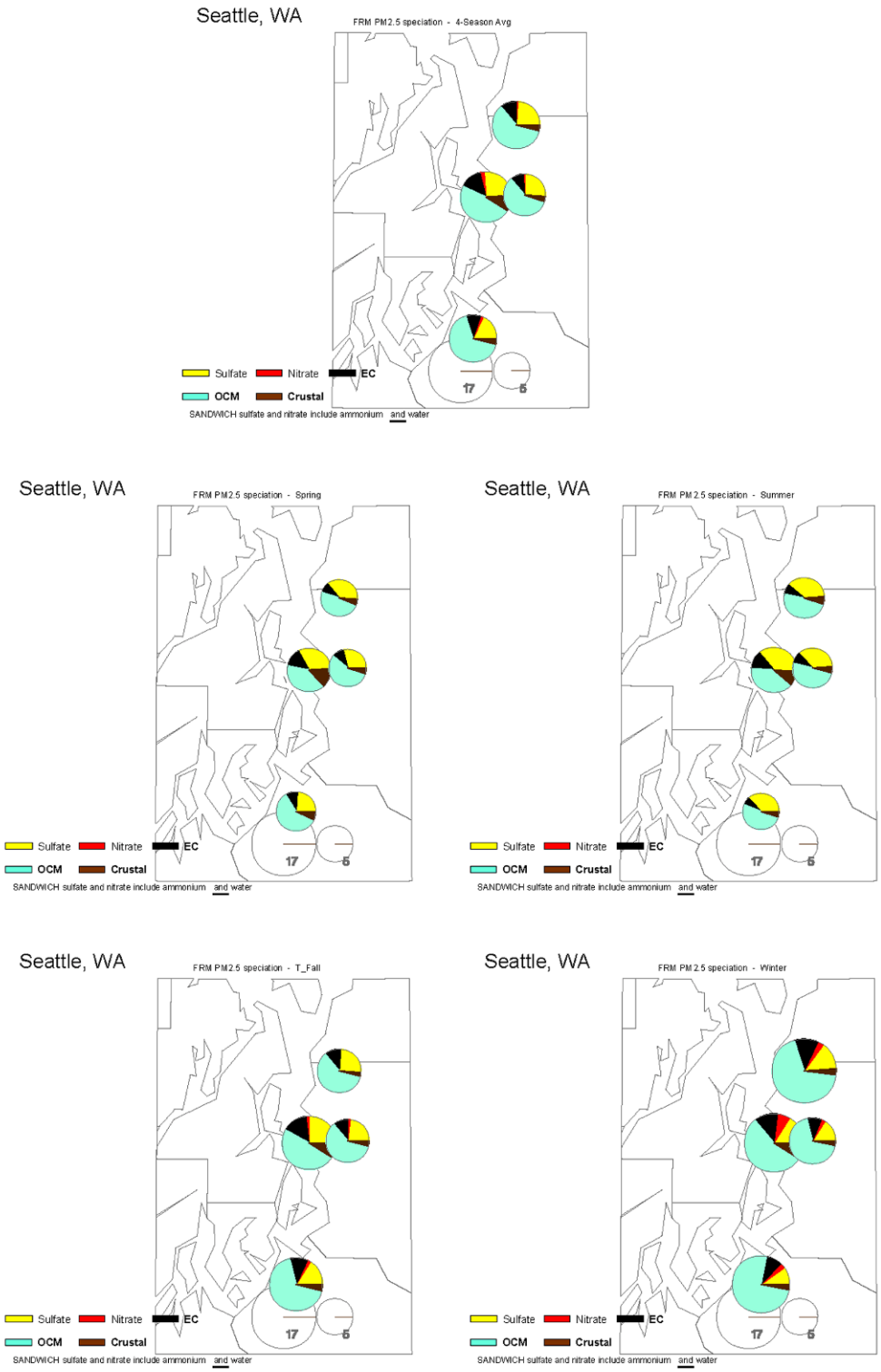


Figure A-140. Seasonally averaged $PM_{2.5}$ speciation data for 2005-2007 for a) annual, b) spring, c) summer, d) fall and e) winter derived using the SANDWICH method in Seattle, WA.

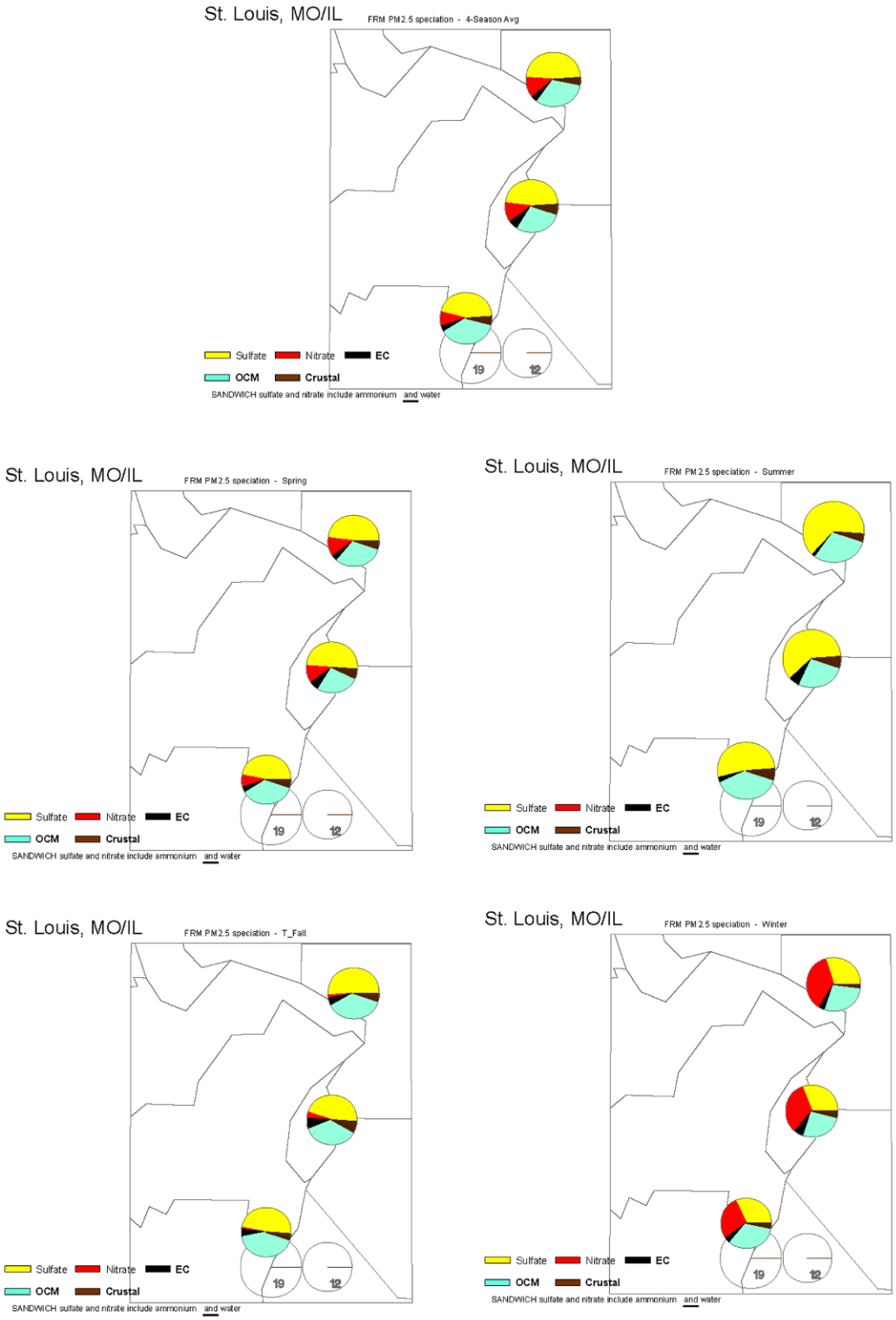


Figure A-141. Seasonally averaged $PM_{2.5}$ speciation data for 2005-2007 for a) annual, b) spring, c) summer, d) fall and e) winter derived using the SANDWICH method in St. Louis, MO.

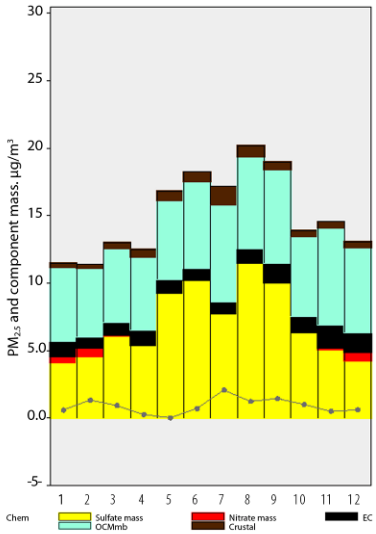


Figure A-142. Seasonal patterns in $PM_{2.5}$ chemical composition from city-wide monthly average values for Atlanta, GA, 2005-2007. The gray line represents the difference in OCM calculated using material balance and blank corrected OC×1.4.

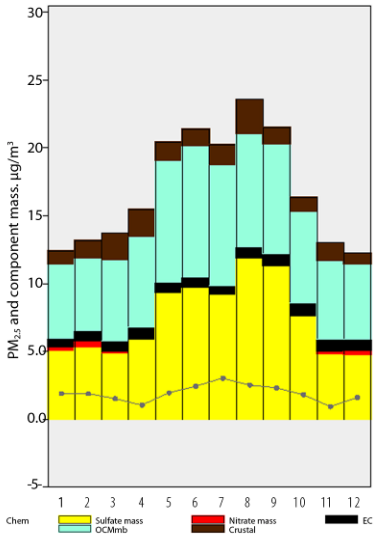


Figure A-143. Seasonal patterns in $PM_{2.5}$ chemical composition from city-wide monthly average values for Birmingham, AL, 2005-2007. The gray line represents the difference in OCM calculated using material balance and blank corrected OC×1.4.

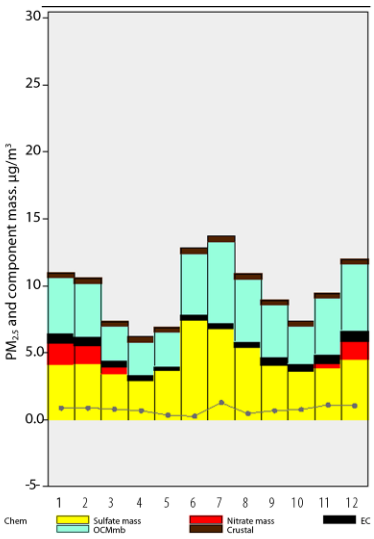


Figure A-144. Seasonal patterns in $PM_{2.5}$ chemical composition from city-wide monthly average values for Boston, MA, 2005-2007. The gray line represents the difference in OCM calculated using material balance and blank corrected OC×1.4.

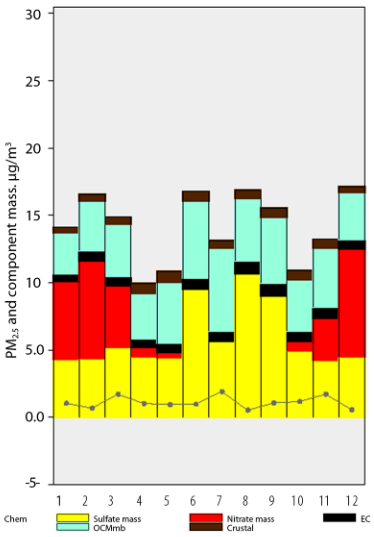


Figure A-145. Seasonal patterns in $PM_{2.5}$ chemical composition from city-wide monthly average values for Chicago, IL, 2005-2007. The gray line represents the difference in OCM calculated using material balance and blank corrected OC×1.4.

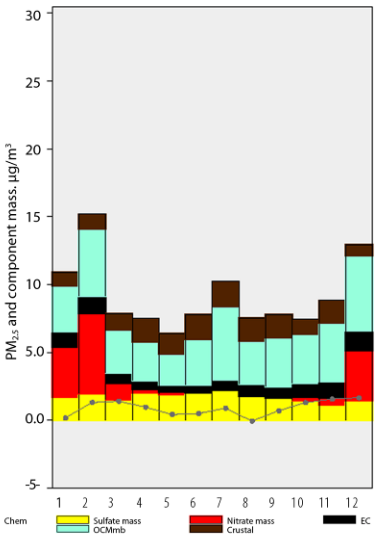


Figure A-146. Seasonal patterns in $PM_{2.5}$ chemical composition from city-wide monthly average values for Denver, CO, 2005-2007. The gray line represents the difference in OCM calculated using material balance and blank corrected OC×1.4.

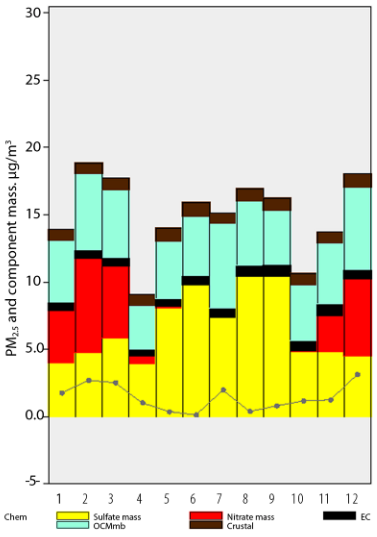


Figure A-147. Seasonal patterns in $PM_{2.5}$ chemical composition from city-wide monthly average values for Detroit, MI, 2005-2007. The gray line represents the difference in OCM calculated using material balance and blank corrected OC x 1.4.

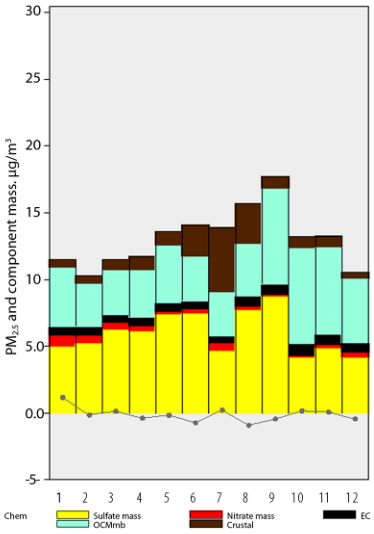


Figure A-148. Seasonal patterns in $PM_{2.5}$ chemical composition from city-wide monthly average values for Houston, TX, 2005-2007. The gray line represents the difference in OCM calculated using material balance and blank corrected OC×1.4.

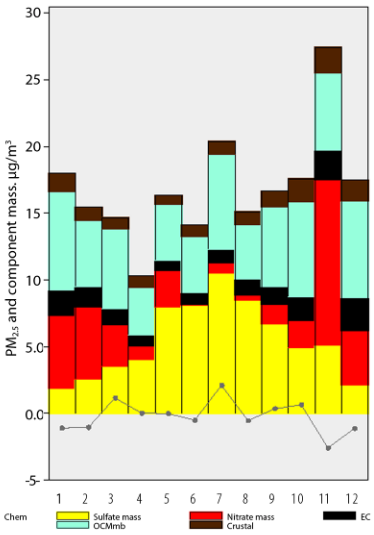


Figure A-149. Seasonal patterns in $PM_{2.5}$ chemical composition from city-wide monthly average values for Los Angeles, CA, 2005-2007. The gray line represents the difference in OCM calculated using material balance and blank corrected OC×1.4.

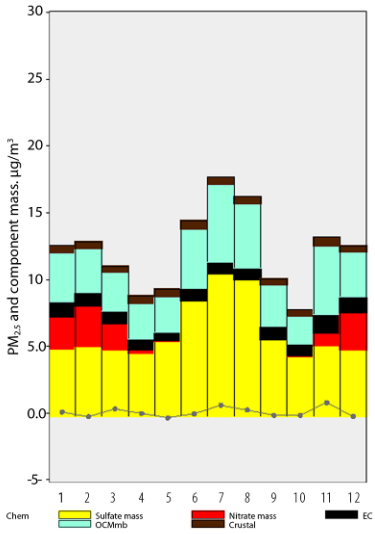


Figure A-150. Seasonal patterns in $PM_{2.5}$ chemical composition from city-wide monthly average values for New York, NY, 2005-2007. The gray line represents the difference in OCM calculated using material balance and blank corrected OC×1.4.

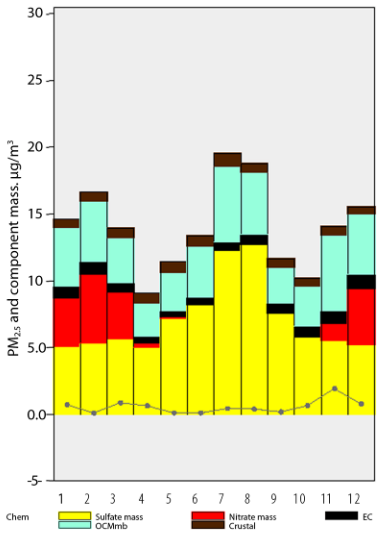


Figure A-151. Seasonal patterns in $PM_{2.5}$ chemical composition from city-wide monthly average values for Philadelphia, PA, 2005-2007. The gray line represents the difference in OCM calculated using material balance and blank corrected OC×1.4.

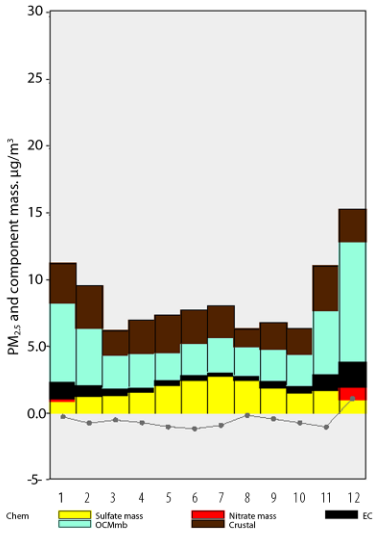


Figure A-152. Seasonal patterns in $PM_{2.5}$ chemical composition from city-wide monthly average values for Phoenix, AZ, 2005-2007. The gray line represents the difference in OCM calculated using material balance and blank corrected OC×1.4.

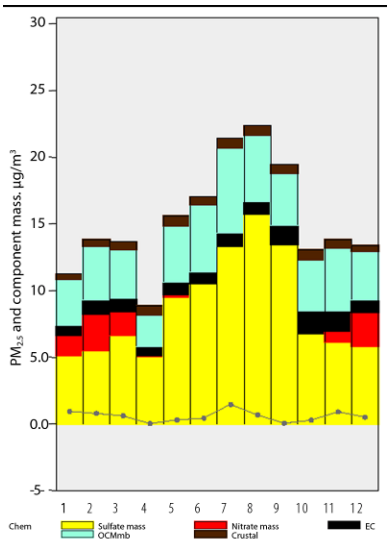


Figure A-153. Seasonal patterns in $PM_{2.5}$ chemical composition from city-wide monthly average values for Pittsburgh, PA, 2005-2007. The gray line represents the difference in OCM calculated using material balance and blank corrected OC×1.4.

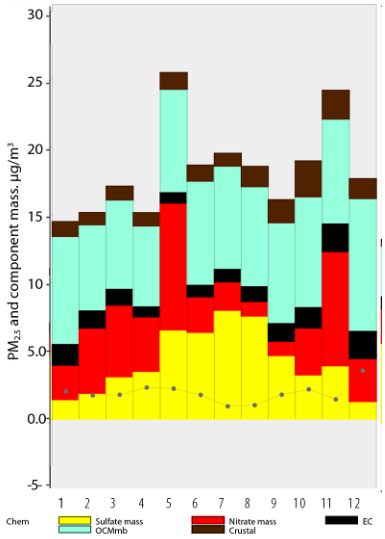


Figure A-154. Seasonal patterns in $PM_{2.5}$ chemical composition from city-wide monthly average values for Riverside, CA, 2005-2007. The gray line represents the difference in OCM calculated using material balance and blank corrected OC×1.4.

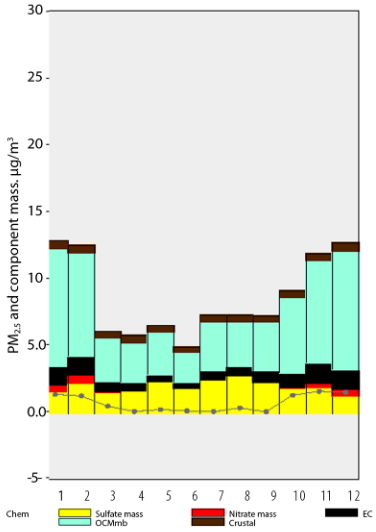


Figure A-155. Seasonal patterns in $PM_{2.5}$ chemical composition from city-wide monthly average values for Seattle, WA, 2005-2007. The gray line represents the difference in OCM calculated using material balance and blank corrected OC×1.4.

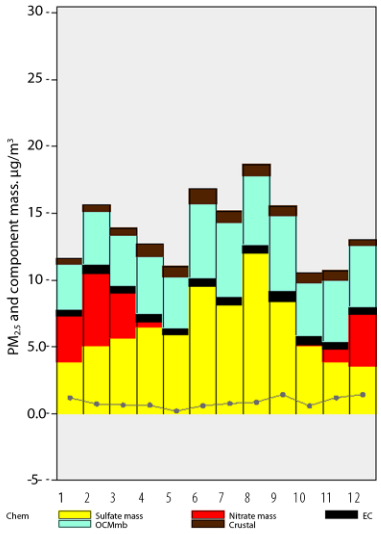


Figure A-156. Seasonal patterns in $PM_{2.5}$ chemical composition from city-wide monthly average values for St. Louis, MO, 2005-2007. The gray line represents the difference in OCM calculated using material balance and blank corrected OC×1.4.

A.2.4. Diel Trends

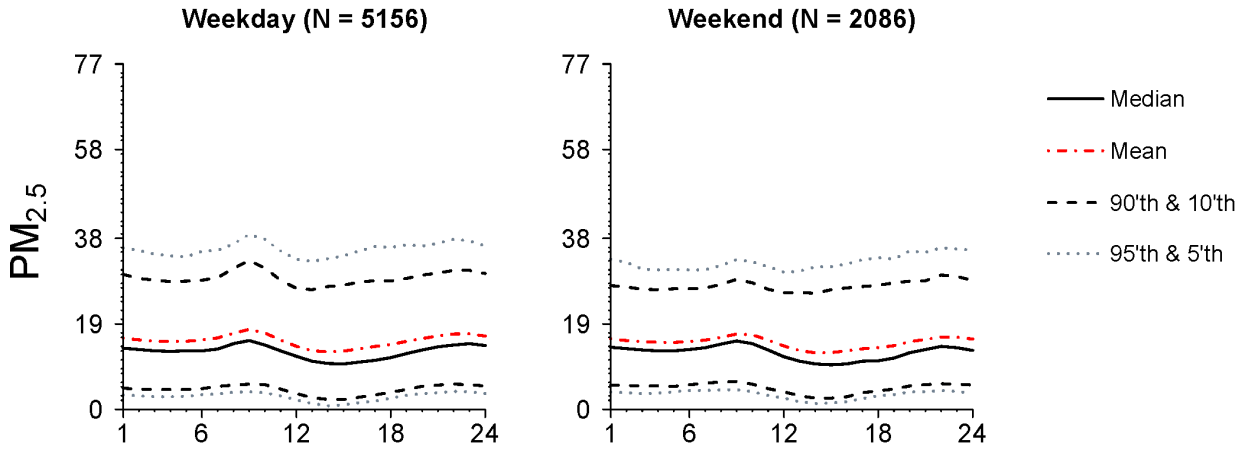


Figure A-157. Diel plots generated from all available hourly FRM-like $PM_{2.5}$ data, stratified by weekday (left) and weekend (right), in Atlanta, GA. Included are the number of monitor days (N) and the median, mean, 5th, 10th, 90th and 95th percentiles for each hour.

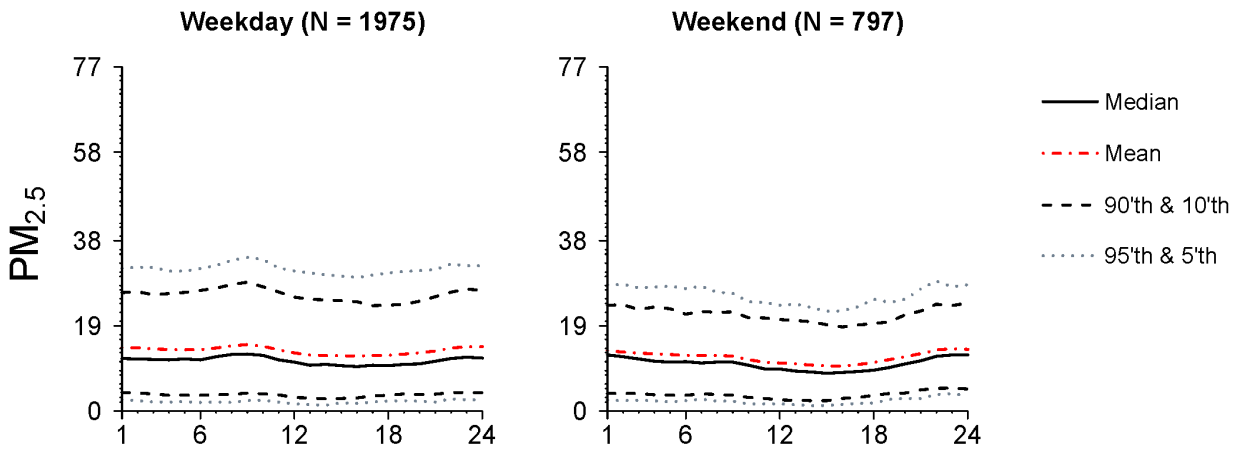


Figure A-158. Diel plots generated from all available hourly FRM-like $PM_{2.5}$ data, stratified by weekday (left) and weekend (right), in Chicago, IL. Included are the number of monitor days (N) and the median, mean, 5th, 10th, 90th and 95th percentiles for each hour.

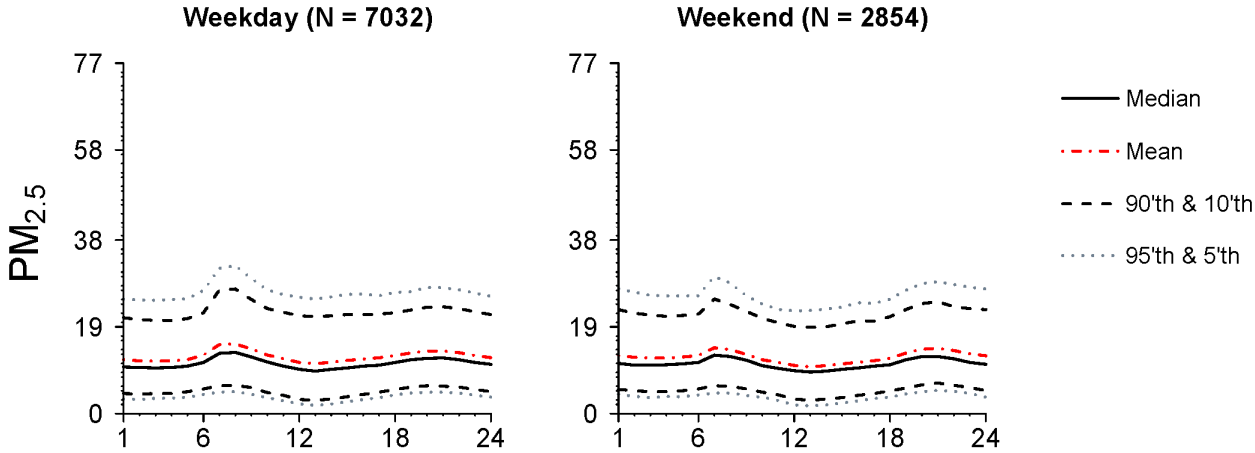


Figure A-159. Diel plots generated from all available hourly FRM-like $PM_{2.5}$ data, stratified by weekday (left) and weekend (right), in Houston, TX. Included are the number of monitor days (N) and the median, mean, 5th, 10th, 90th and 95th percentiles for each hour.

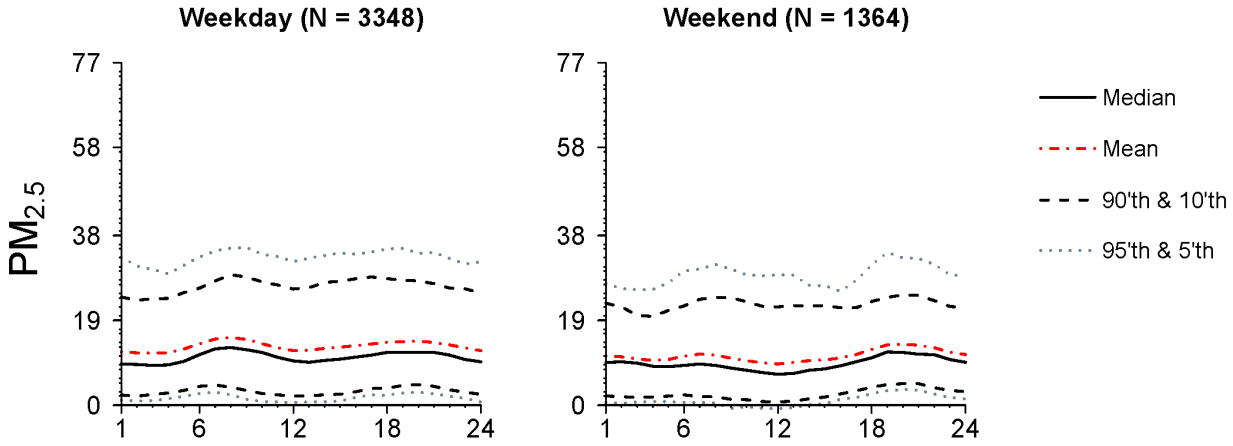


Figure A-160. Diel plots generated from all available hourly FRM-like $PM_{2.5}$ data, stratified by weekday (left) and weekend (right), in New York, NY. Included are the number of monitor days (N) and the median, mean, 5th, 10th, 90th and 95th percentiles for each hour.

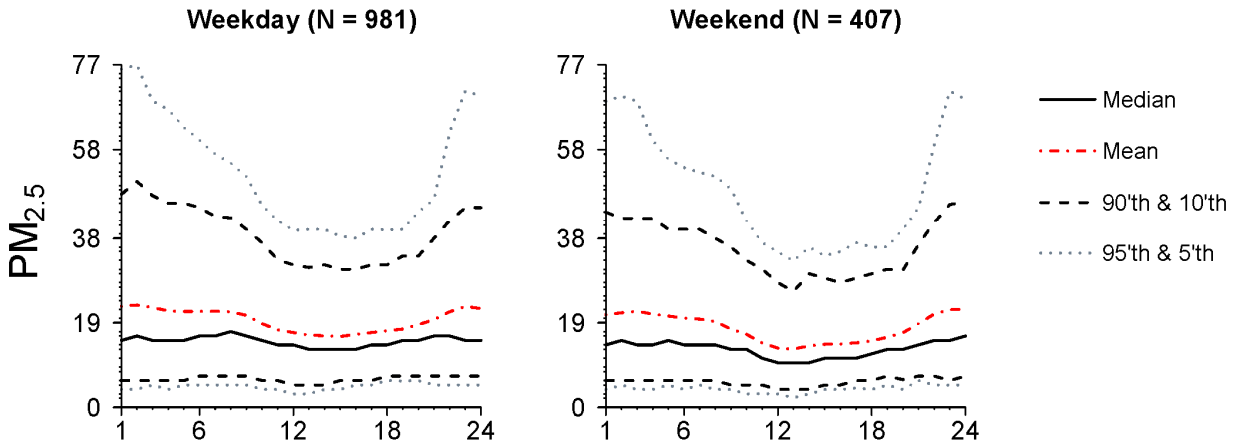


Figure A-161. Diel plots generated from all available hourly FRM-like $PM_{2.5}$ data, stratified by weekday (left) and weekend (right), in Pittsburgh, PA. Included are the number of monitor days (N) and the median, mean, 5th, 10th, 90th and 95th percentiles for each hour.

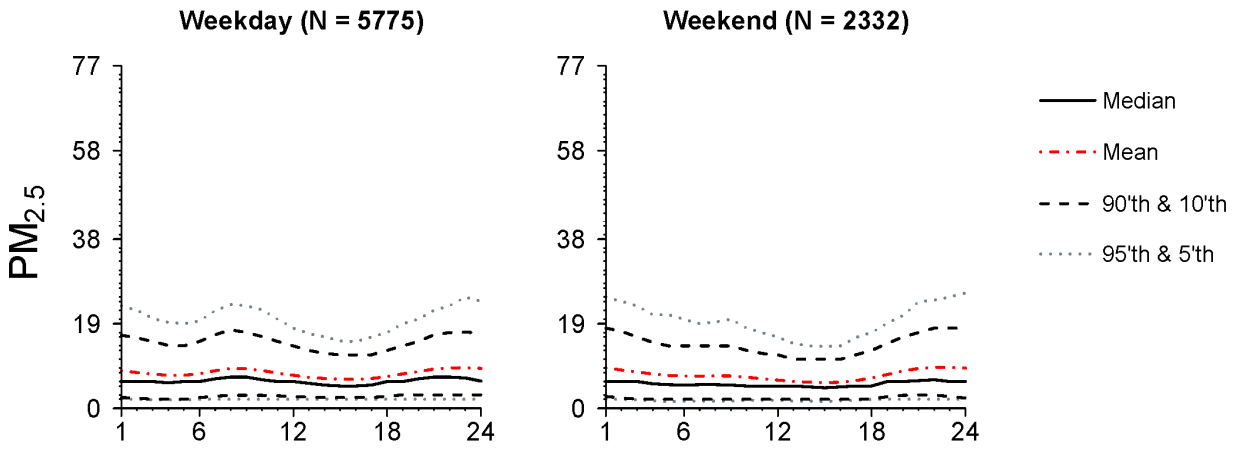


Figure A-162. Diel plots generated from all available hourly FRM-like $PM_{2.5}$ data, stratified by weekday (left) and weekend (right), in Seattle, WA. Included are the number of monitor days (N) and the median, mean, 5th, 10th, 90th and 95th percentiles for each hour.

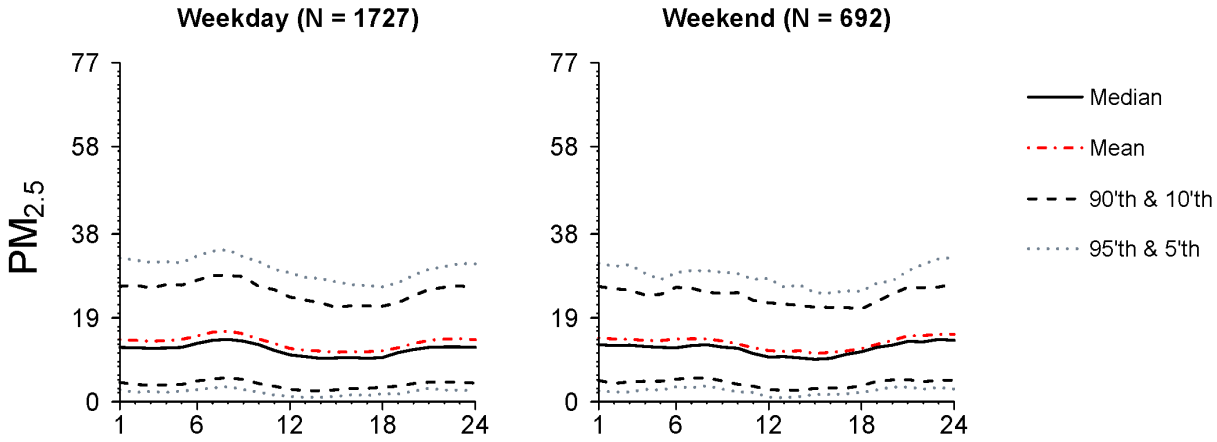


Figure A-163. Diel plots generated from all available hourly FRM-like $PM_{2.5}$ data, stratified by weekday (left) and weekend (right), in St. Louis, MO. Included are the number of monitor days (N) and the median, mean, 5th, 10th, 90th and 95th percentiles for each hour.

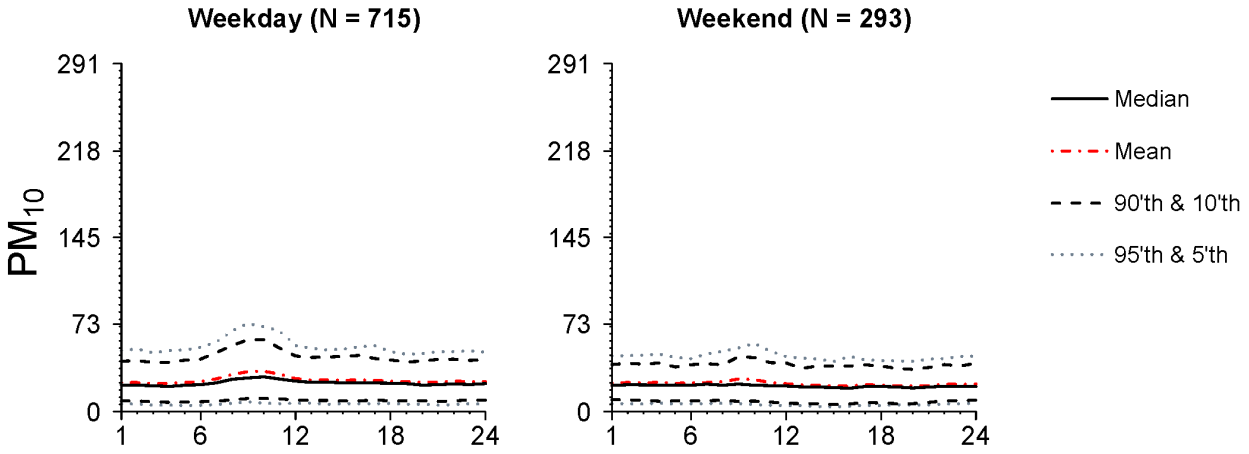


Figure A-164. Diel plot generated from all available hourly FRM/FEM PM_{10} data, stratified by weekday (left) and weekend (right), in Atlanta, GA. Included are the number of monitor days (N) and the median, mean, 5th, 10th, 90th and 95th percentiles for each hour.

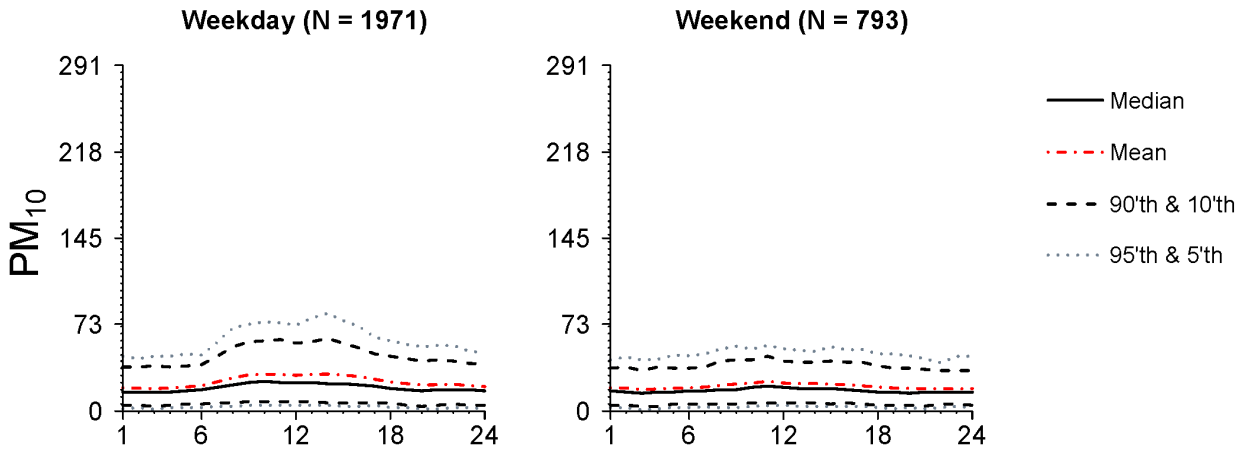


Figure A-165. Diel plot generated from all available hourly FRM/FEM PM_{10} data, stratified by weekday (left) and weekend (right), in Chicago, IL. Included are the number of monitor days (N) and the median, mean, 5th, 10th, 90th and 95th percentiles for each hour.

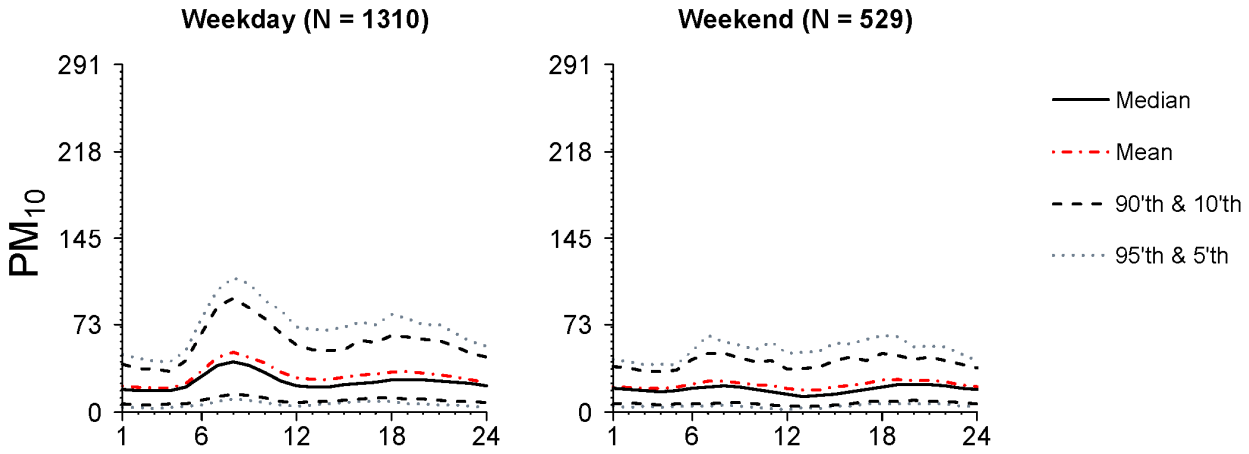


Figure A-166. Diel plot generated from all available hourly FRM/FEM PM_{10} data, stratified by weekday (left) and weekend (right), in Denver, CO. Included are the number of monitor days (N) and the median, mean, 5th, 10th, 90th and 95th percentiles for each hour.

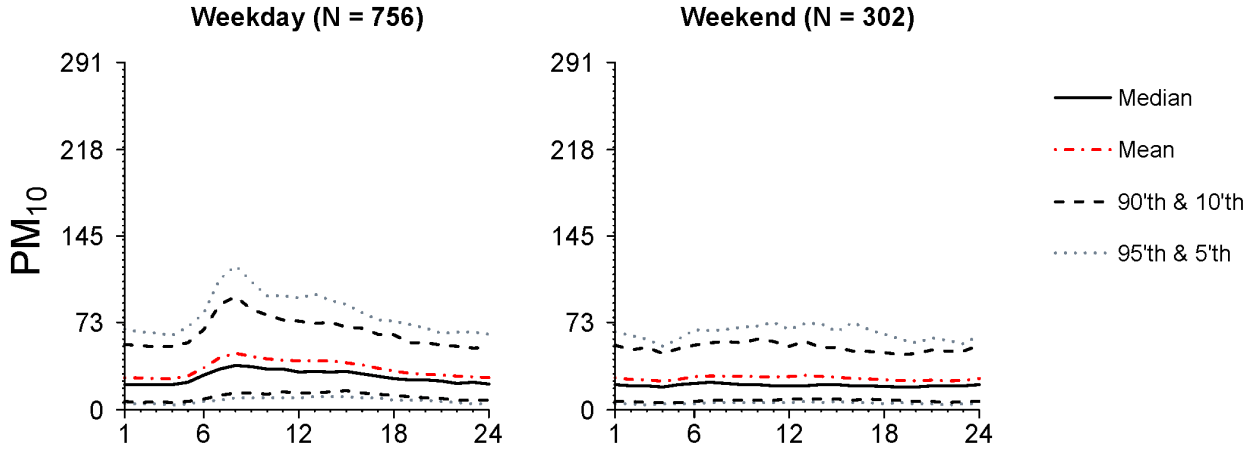


Figure A-167. Diel plot generated from all available hourly FRM/FEM PM_{10} data, stratified by weekday (left) and weekend (right), in Detroit, MI. Included are the number of monitor days (N) and the median, mean, 5th, 10th, 90th and 95th percentiles for each hour.

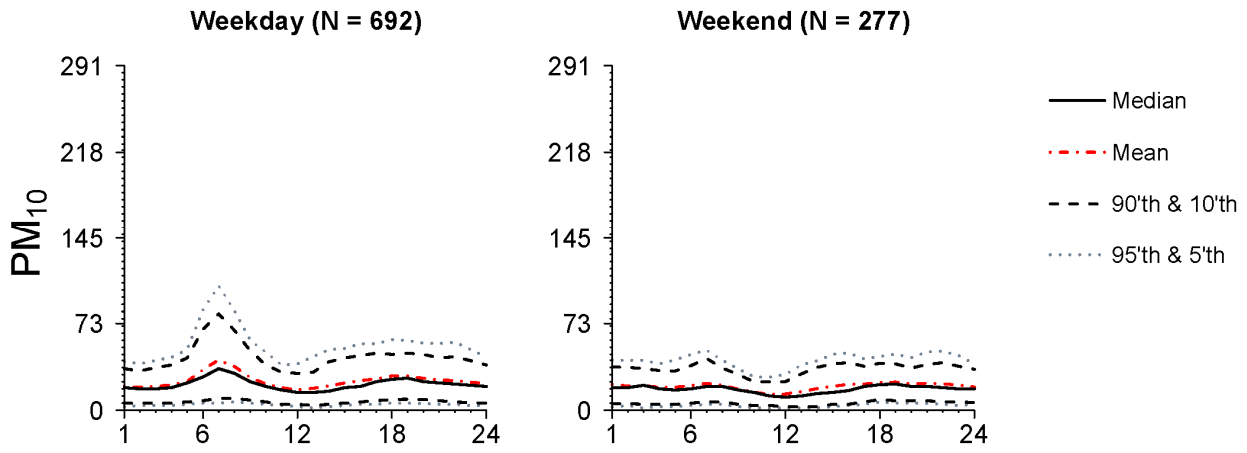


Figure A-168. Diel plot generated from all available hourly FRM/FEM PM_{10} data, stratified by weekday (left) and weekend (right), in Los Angeles, CA. Included are the number of monitor days (N) and the median, mean, 5th, 10th, 90th and 95th percentiles for each hour.

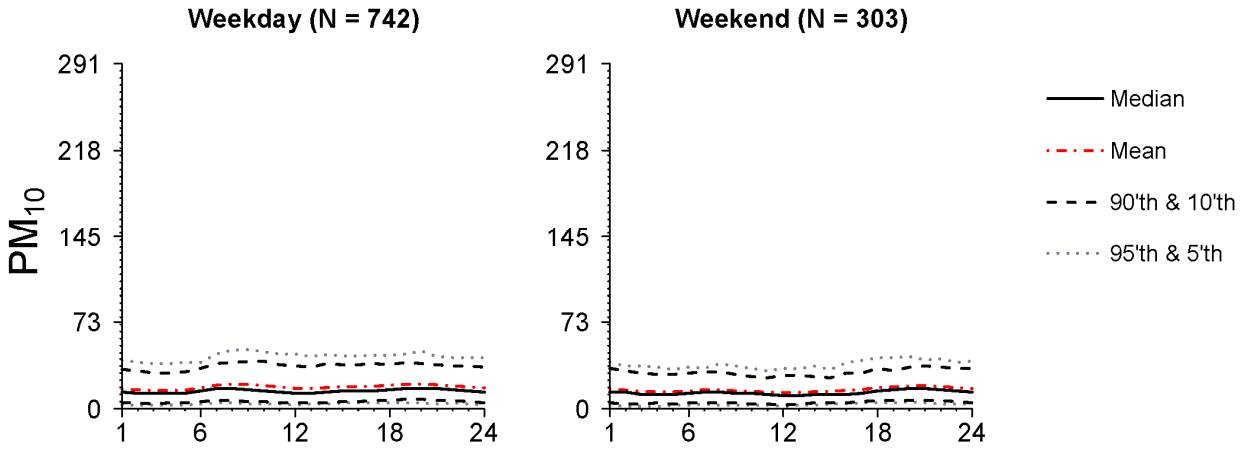


Figure A-169. Diel plot generated from all available hourly FRM/FEM PM_{10} data, stratified by weekday (left) and weekend (right), in Philadelphia, PA. Included are the number of monitor days (N) and the median, mean, 5th, 10th, 90th and 95th percentiles for each hour.

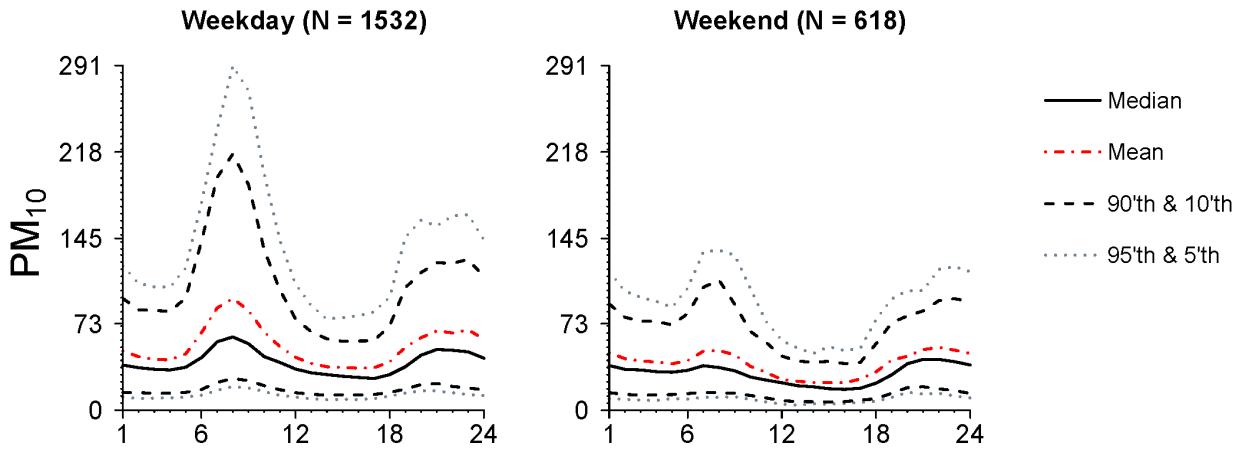


Figure A-170. Diel plot generated from all available hourly FRM/FEM PM_{10} data, stratified by weekday (left) and weekend (right), in Phoenix, AZ. Included are the number of monitor days (N) and the median, mean, 5th, 10th, 90th and 95th percentiles for each hour.

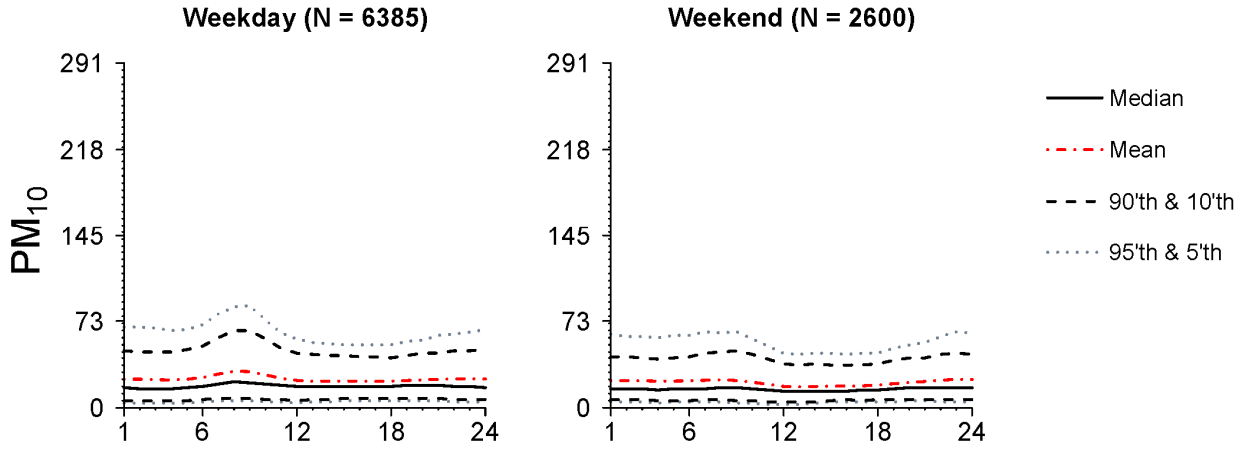


Figure A-171. Diel plot generated from all available hourly FRM/FEM PM_{10} data, stratified by weekday (left) and weekend (right), in Pittsburgh, PA. Included are the number of monitor days (N) and the median, mean, 5th, 10th, 90th and 95th percentiles for each hour.

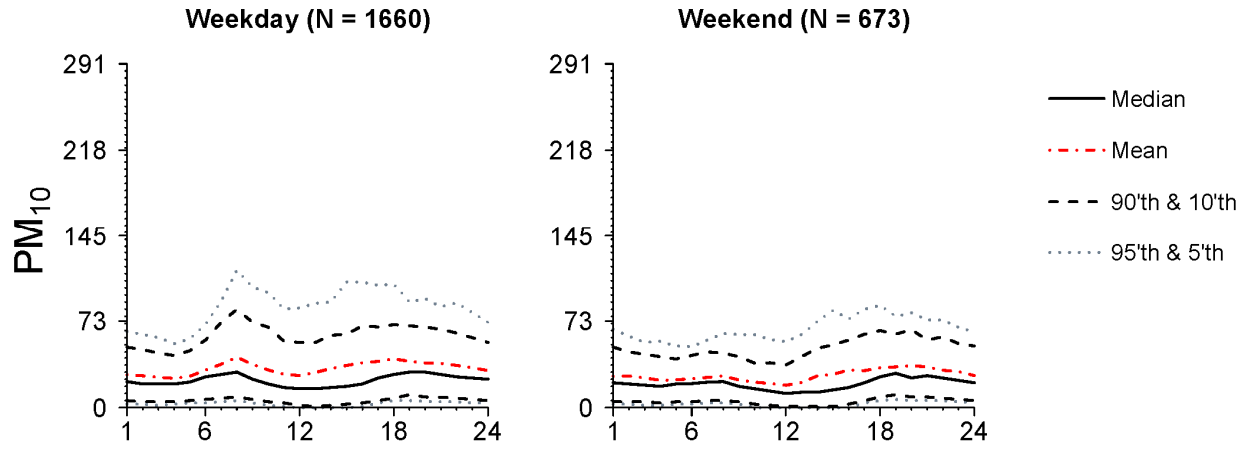


Figure A-172. Diel plot generated from all available hourly FRM/FEM PM_{10} data, stratified by weekday (left) and weekend (right), in Riverside, CA. Included are the number of monitor days (N) and the median, mean, 5th, 10th, 90th and 95th percentiles for each hour.

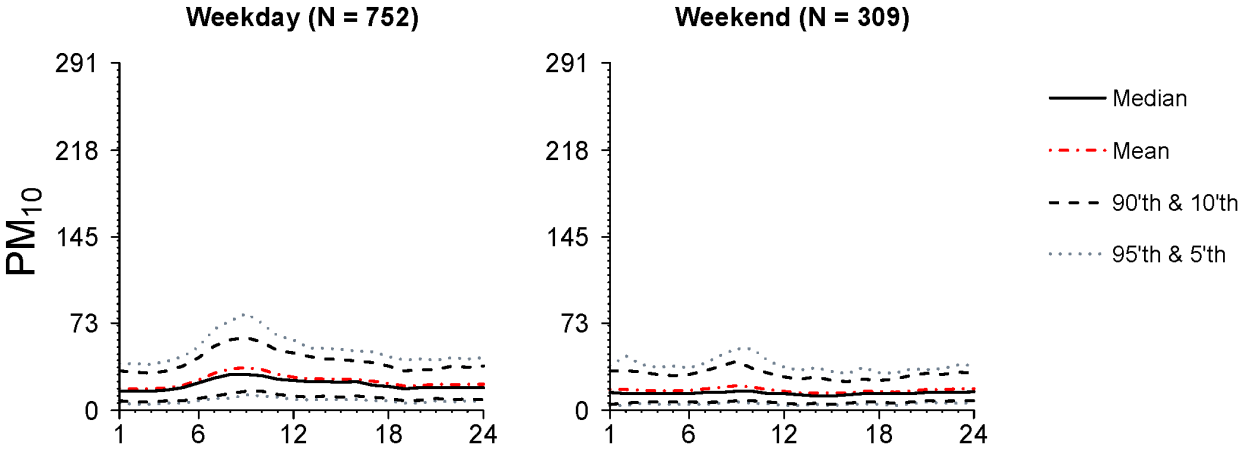


Figure A-173. Diel plot generated from all available hourly FRM/FEM PM_{10} data, stratified by weekday (left) and weekend (right), in Seattle, WA. Included are the number of monitor days (N) and the median, mean, 5th, 10th, 90th and 95th percentiles for each hour.

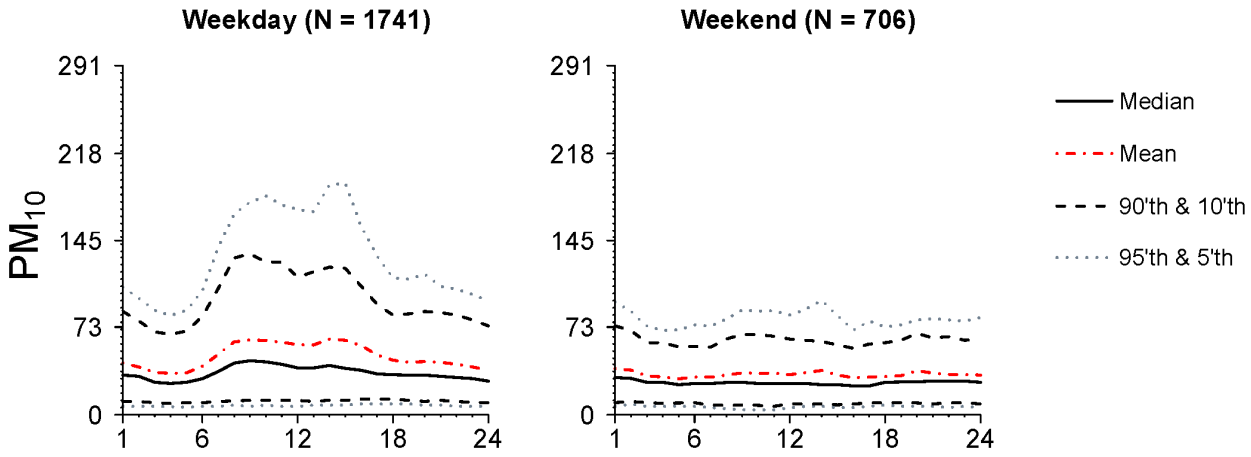


Figure A-174. Diel plot generated from all available hourly FRM/FEM PM_{10} data, stratified by weekday (left) and weekend (right), in St. Louis, MO. Included are the number of monitor days (N) and the median, mean, 5th, 10th, 90th and 95th percentiles for each hour.

A.2.5. Copollutant Measurements

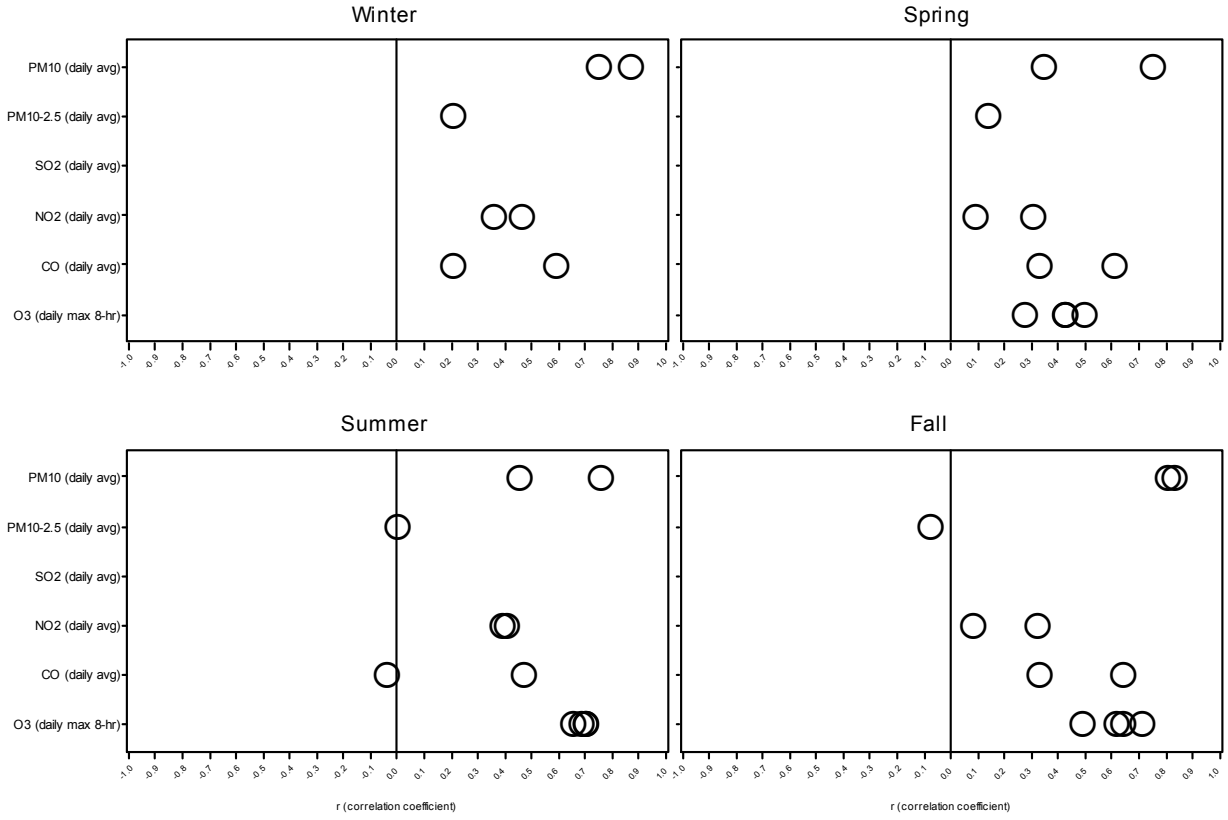


Figure A-175. Correlations between 24-h $PM_{2.5}$ and co-located 24-h avg PM_{10}, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Atlanta, GA, stratified by season (2005-2007). One point is included for each available monitor pair.

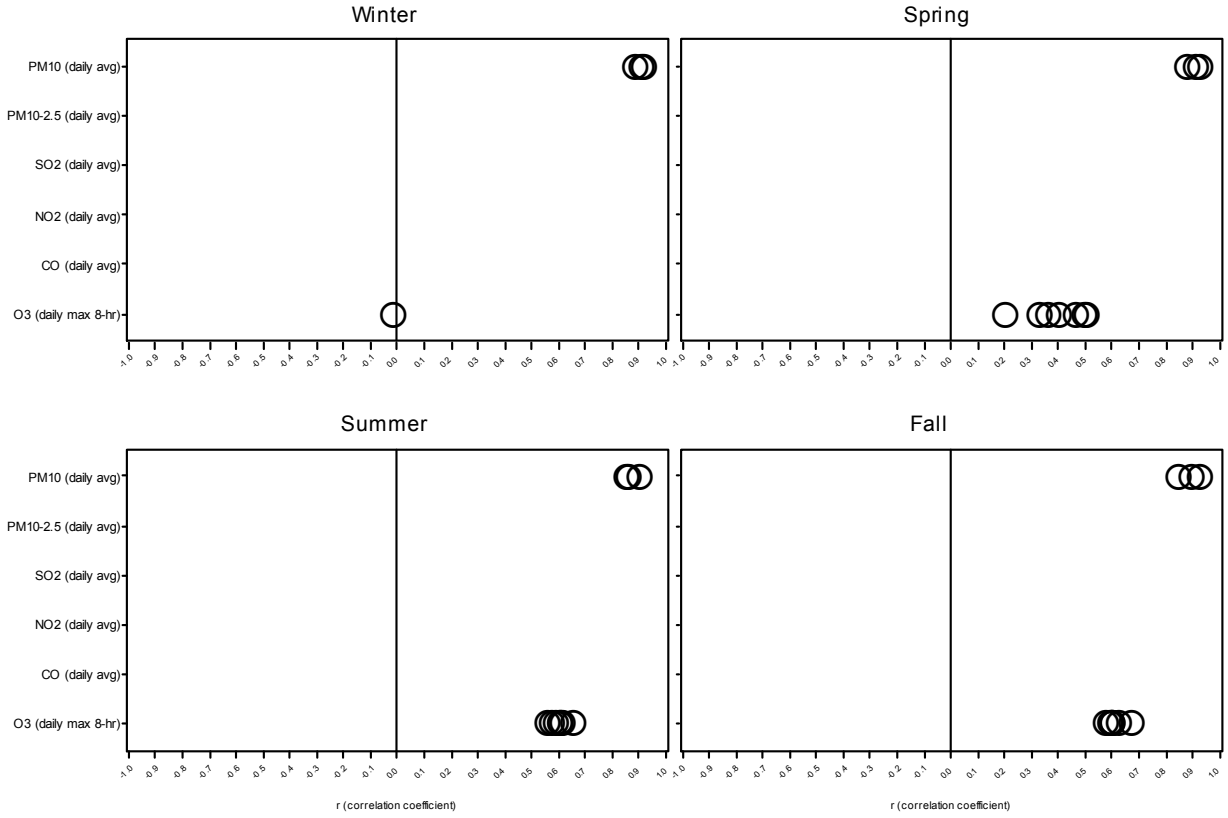


Figure A-176. Correlations between 24-h $PM_{2.5}$ and co-located 24-h avg PM_{10}, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Birmingham, AL, stratified by season (2005-2007). One point is included for each available monitor pair.

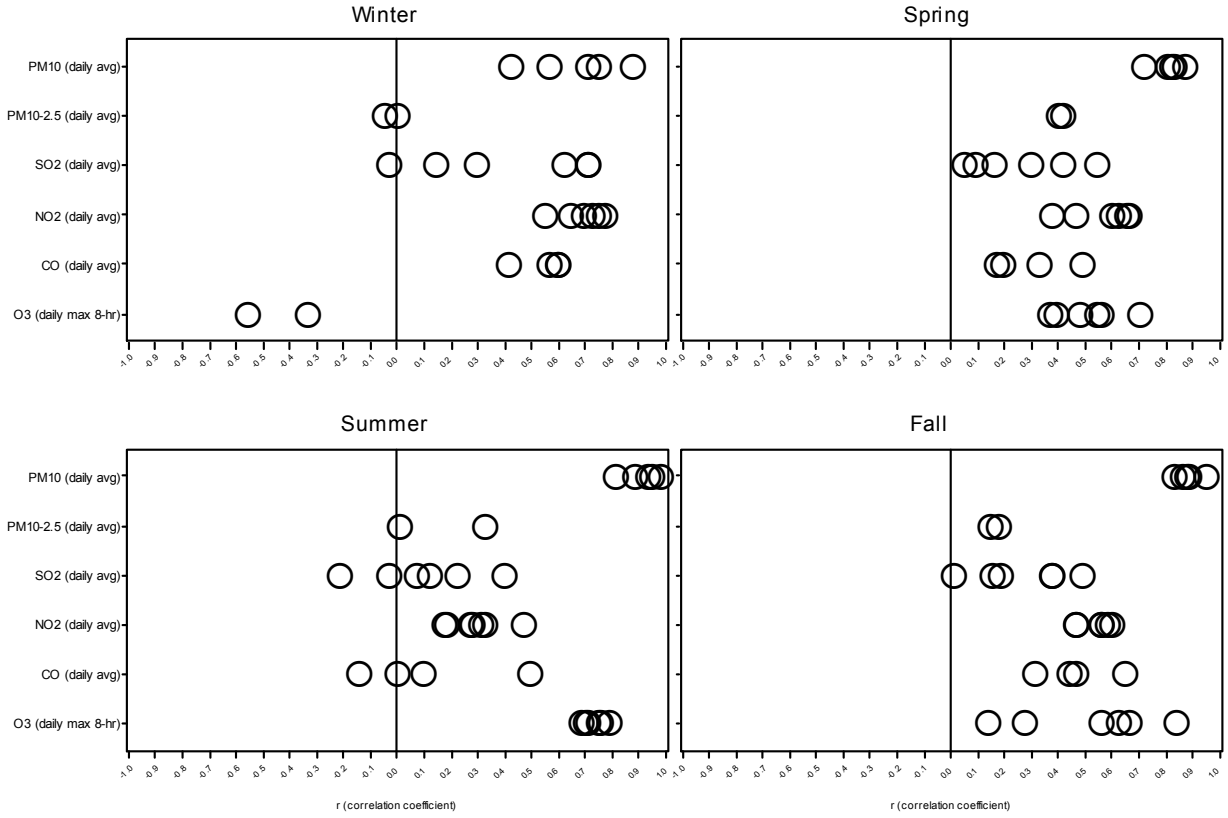


Figure A-177. Correlations between 24-h $PM_{2.5}$ and co-located 24-h avg PM_{10}, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Boston, MA, stratified by season (2005-2007). One point is included for each available monitor pair.

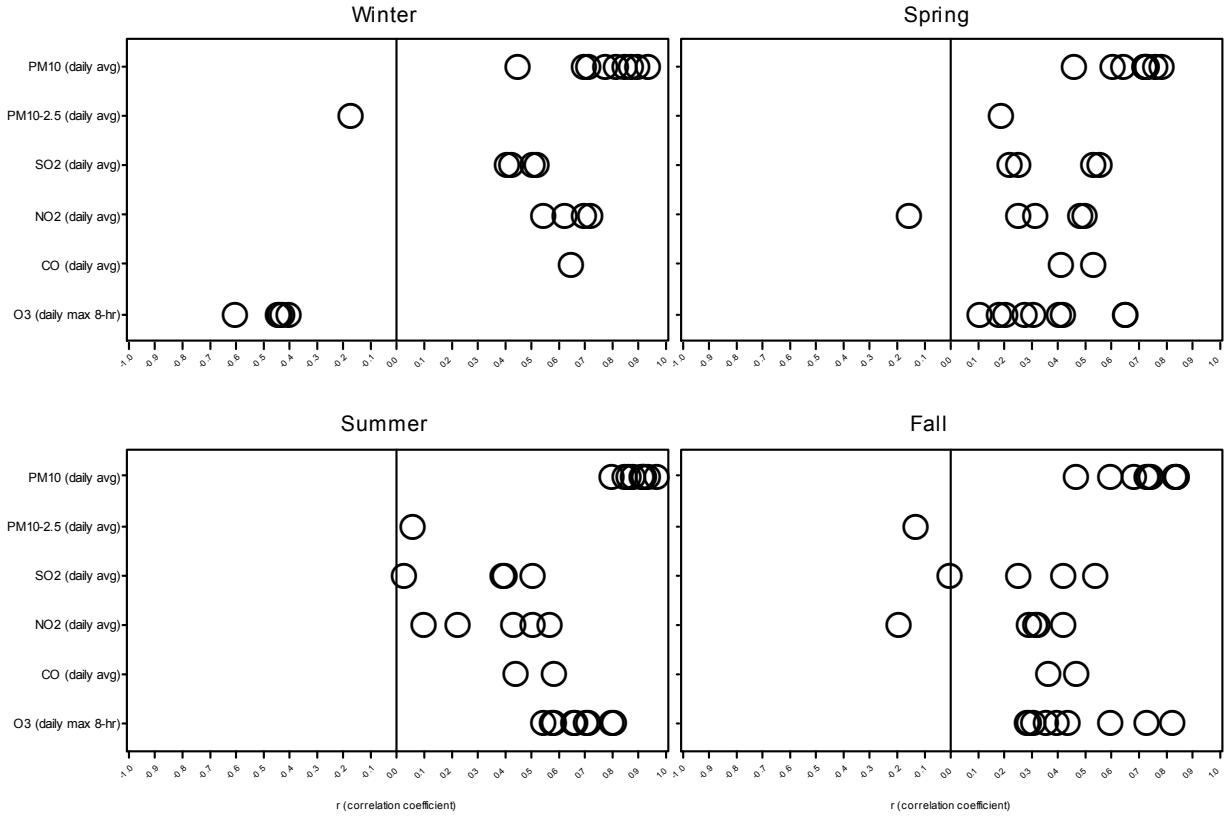


Figure A-178. Correlations between 24-h $PM_{2.5}$ and co-located 24-h avg PM_{10}, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Chicago, IL, stratified by season (2005-2007). One point is included for each available monitor pair.

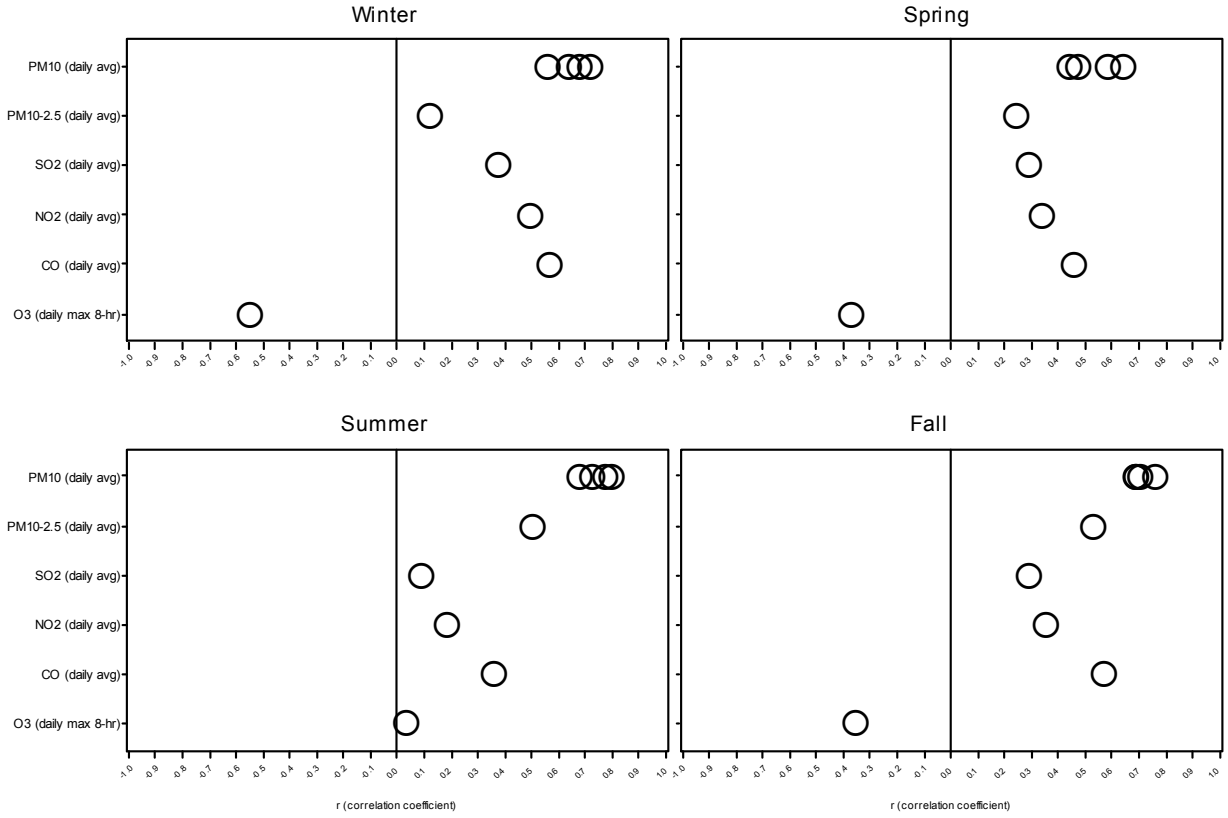


Figure A-179. Correlations between 24-h $PM_{2.5}$ and co-located 24-h avg PM_{10}, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Denver, CO, stratified by season (2005-2007). One point is included for each available monitor pair.

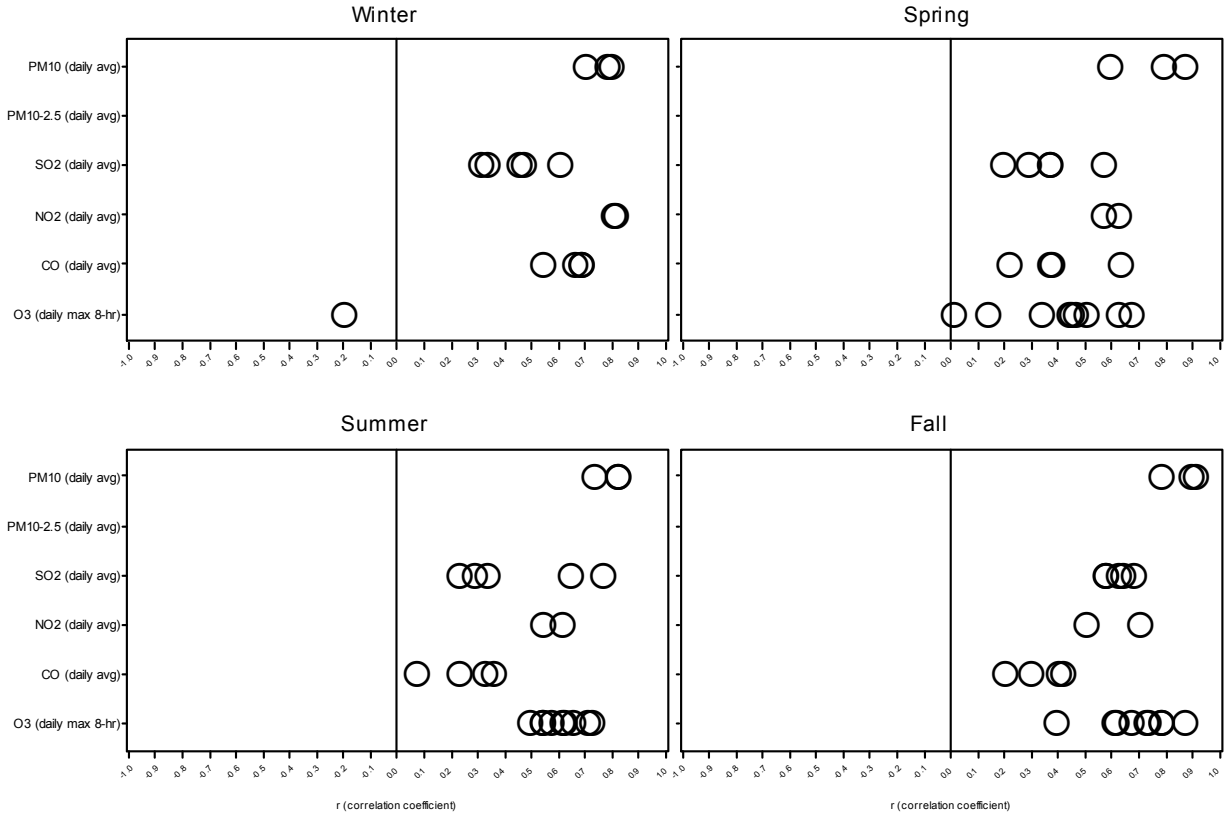


Figure A-180. Correlations between 24-h $PM_{2.5}$ and co-located 24-h avg PM_{10}, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Detroit, MI, stratified by season (2005-2007). One point is included for each available monitor pair.

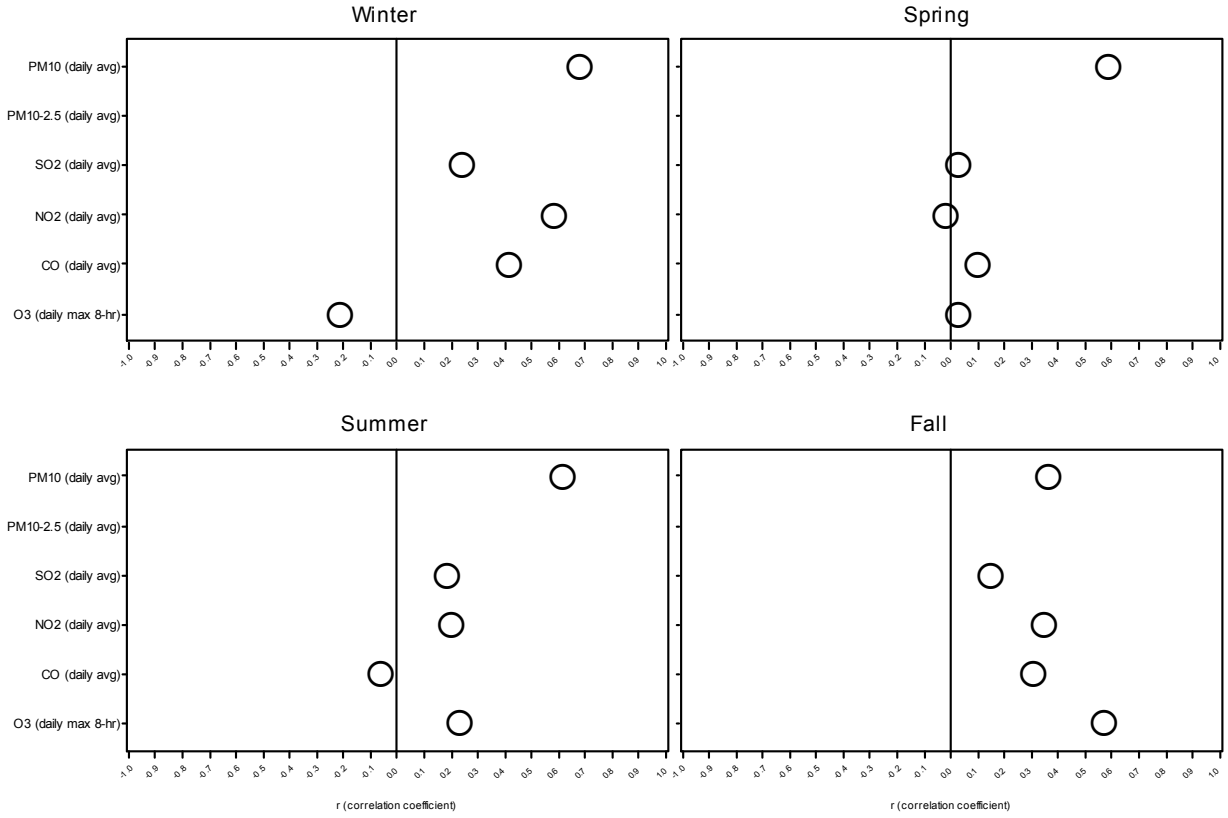


Figure A-181. Correlations between 24-h $PM_{2.5}$ and co-located 24-h avg PM_{10}, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Houston, TX, stratified by season (2005-2007). One point is included for each available monitor pair.

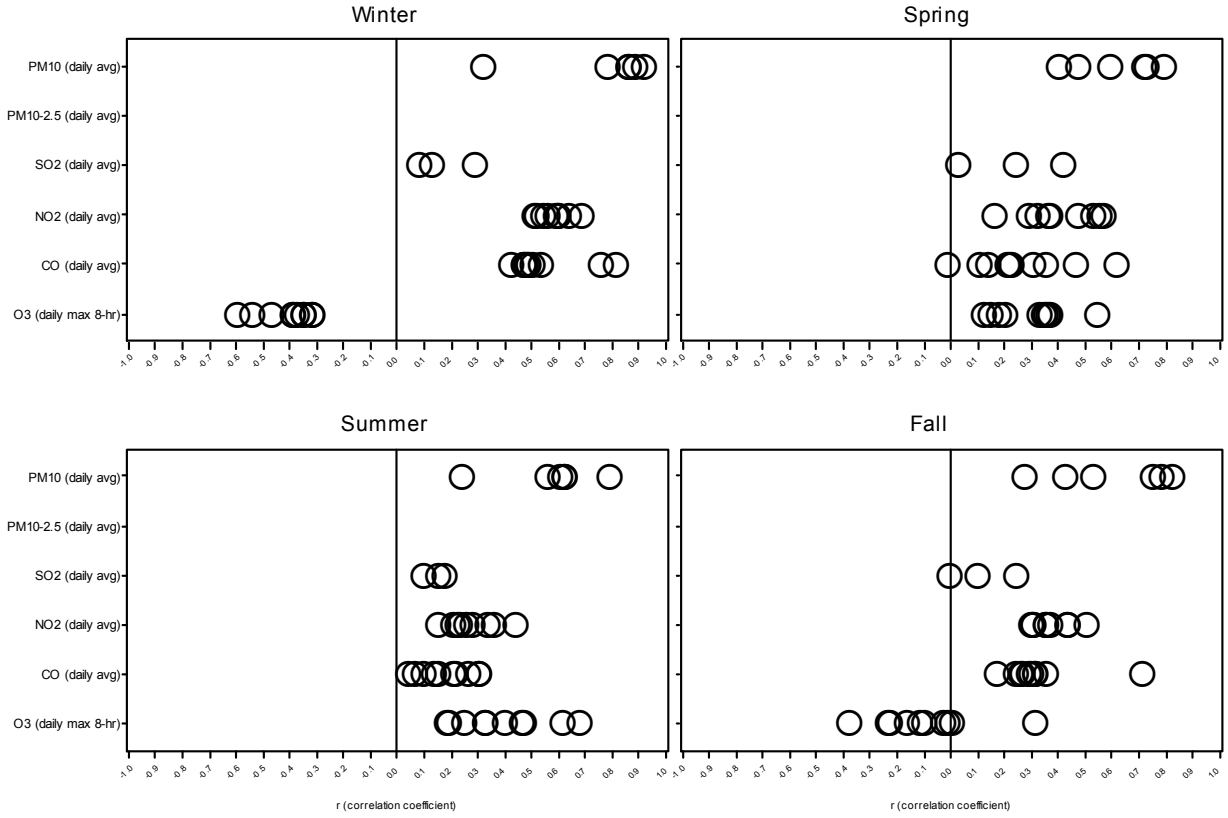


Figure A-182. Correlations between 24-h $PM_{2.5}$ and co-located 24-h avg PM_{10}, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Los Angeles, CA, stratified by season (2005-2007). One point is included for each available monitor pair.

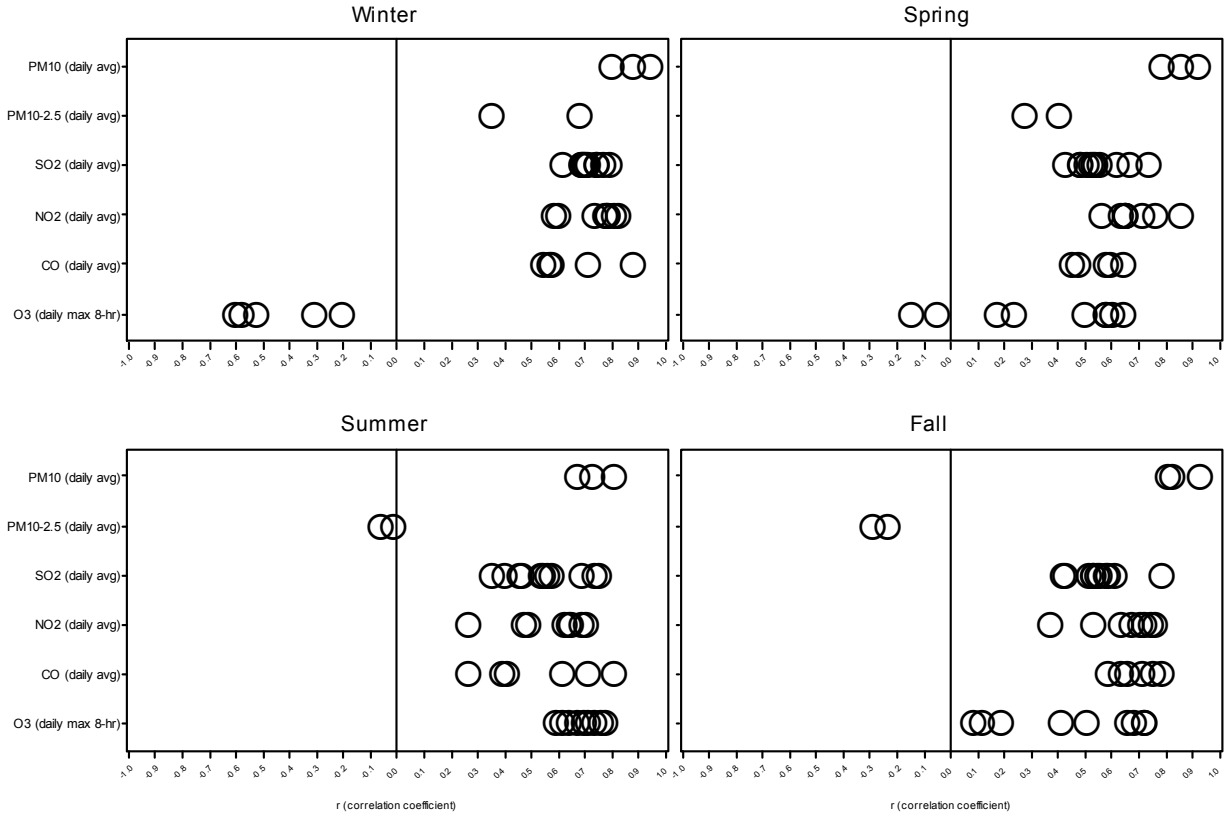


Figure A-183. Correlations between 24-h $PM_{2.5}$ and co-located 24-h avg PM_{10}, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for New York, NY, stratified by season (2005-2007). One point is included for each available monitor pair.

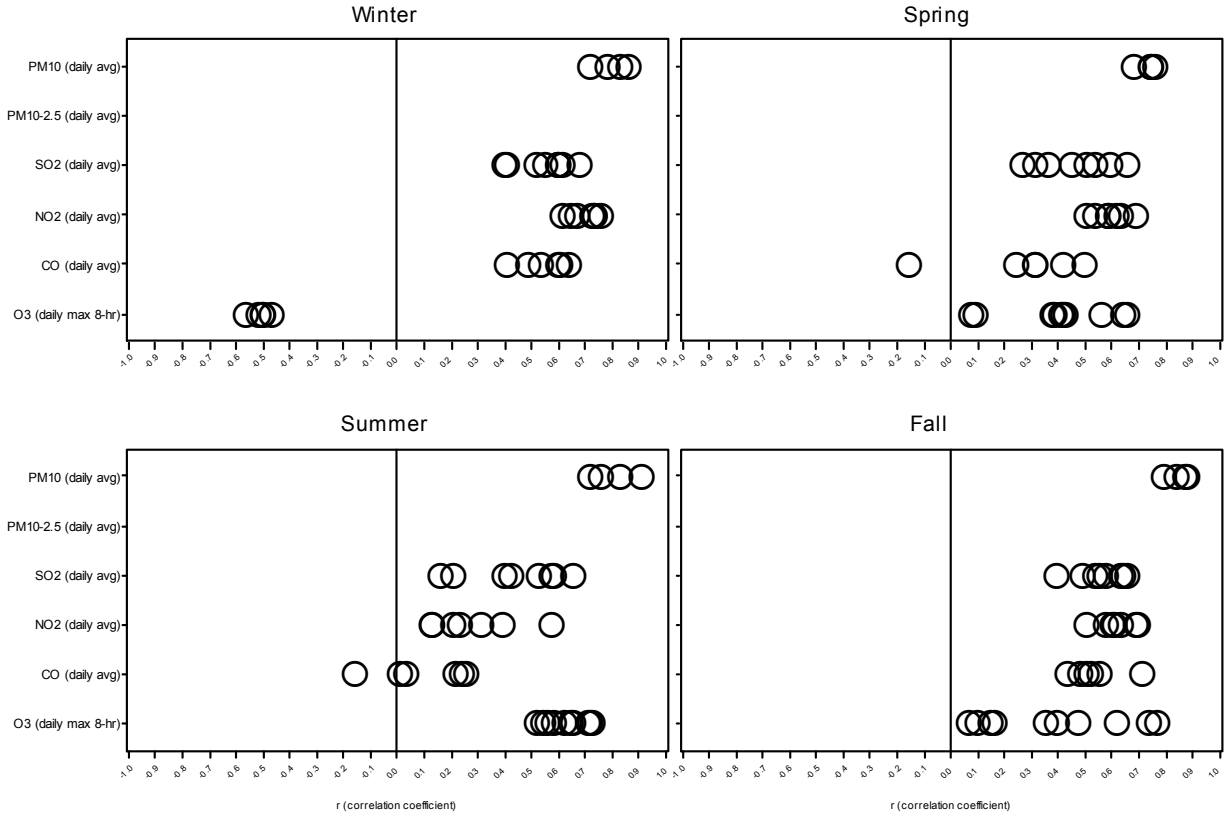


Figure A-184. Correlations between 24-h $PM_{2.5}$ and co-located 24-h avg PM_{10}, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Philadelphia, PA, stratified by season (2005-2007). One point is included for each available monitor pair.

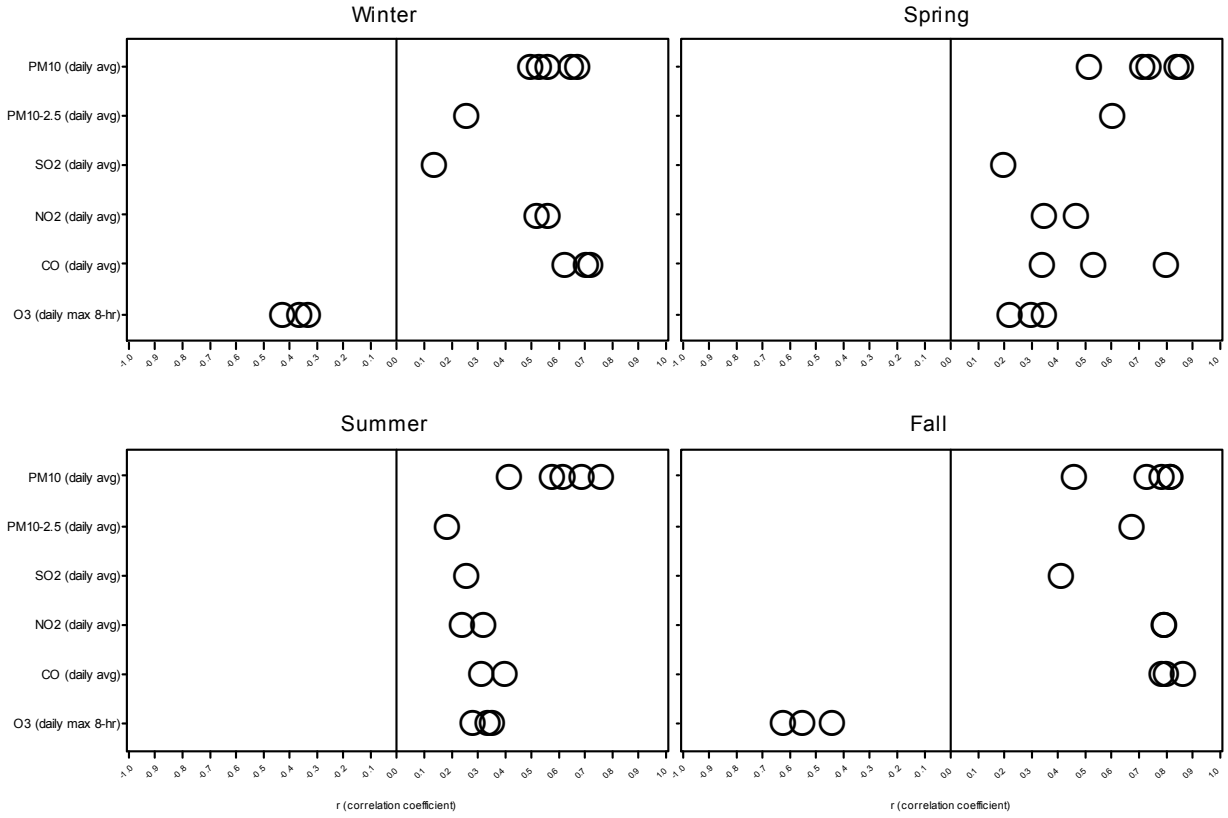


Figure A-185. Correlations between 24-h $PM_{2.5}$ and co-located 24-h avg PM_{10}, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Phoenix, AZ, stratified by season (2005-2007). One point is included for each available monitor pair.

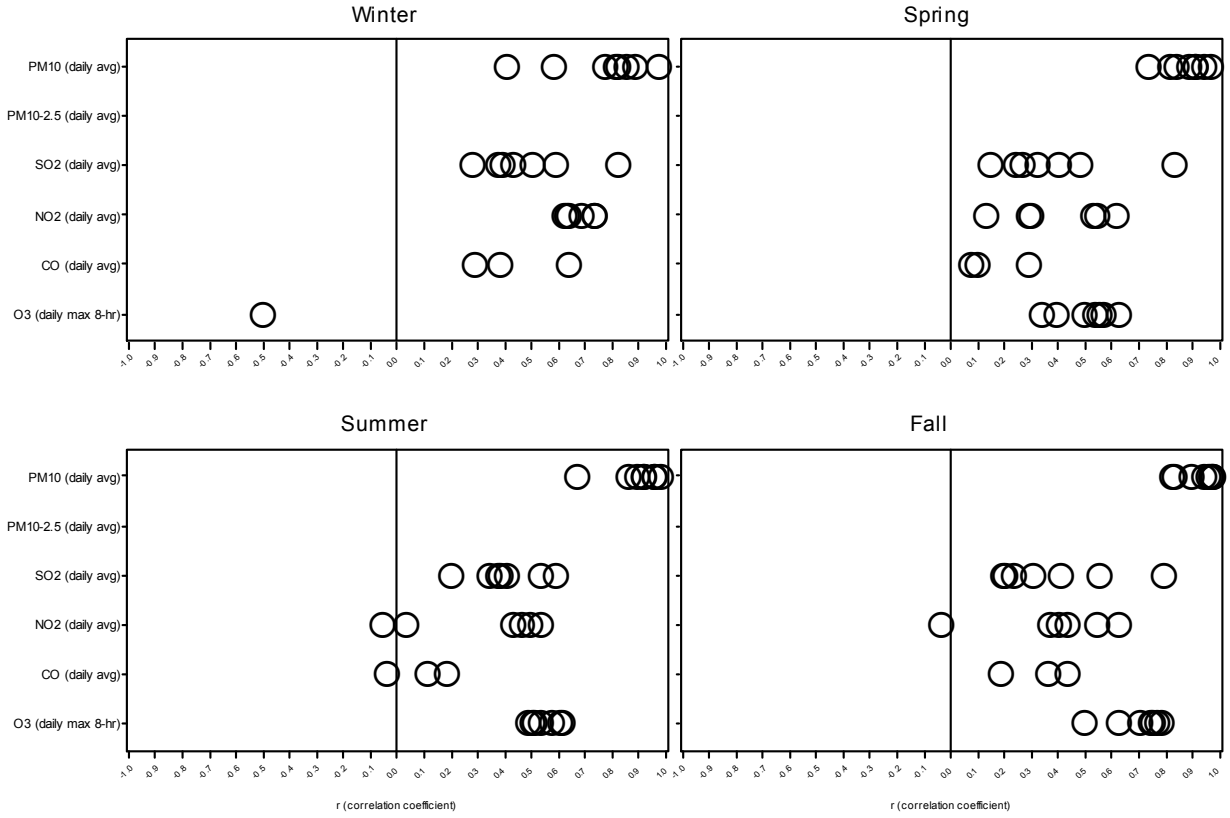


Figure A-186. Correlations between 24-h $PM_{2.5}$ and co-located 24-h avg PM_{10}, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Pittsburgh, PA, stratified by season (2005-2007). One point is included for each available monitor pair.

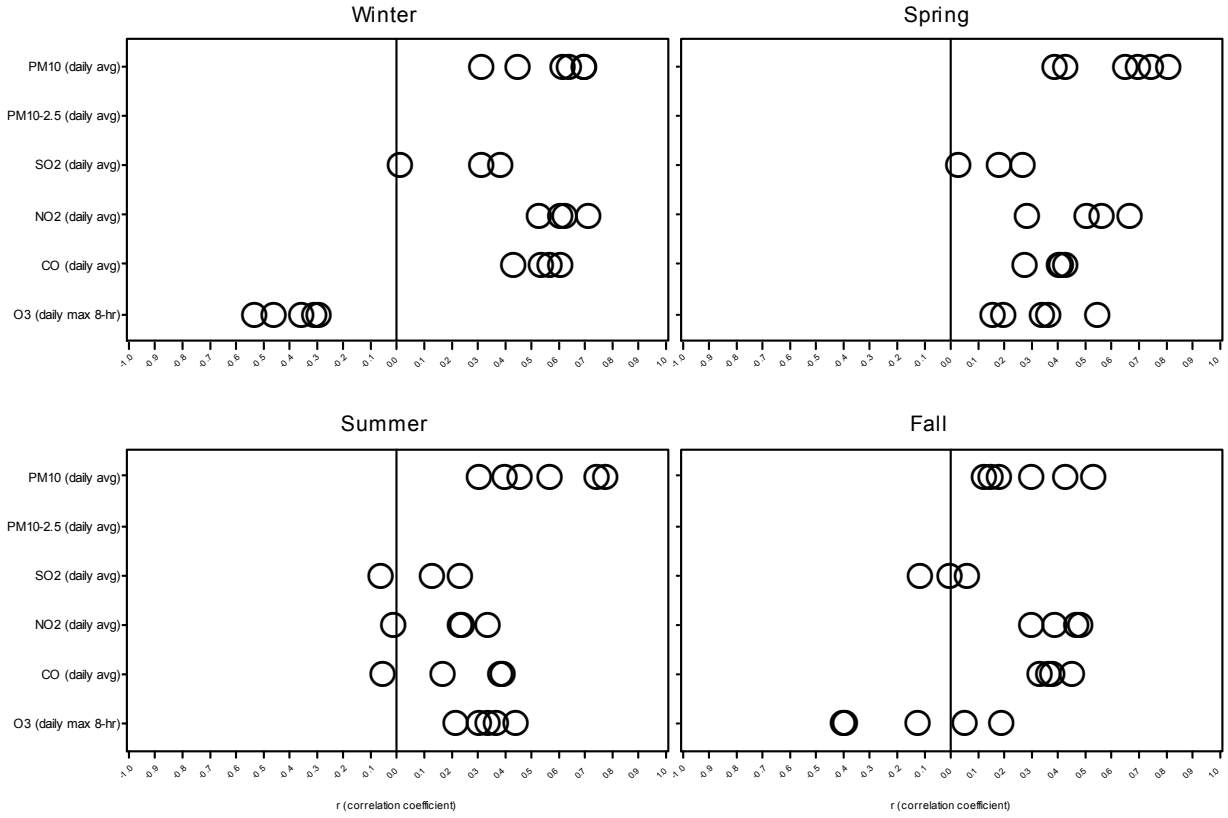


Figure A-187. Correlations between 24-h $PM_{2.5}$ and co-located 24-h avg PM_{10}, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Riverside, CA, stratified by season (2005-2007). One point is included for each available monitor pair.

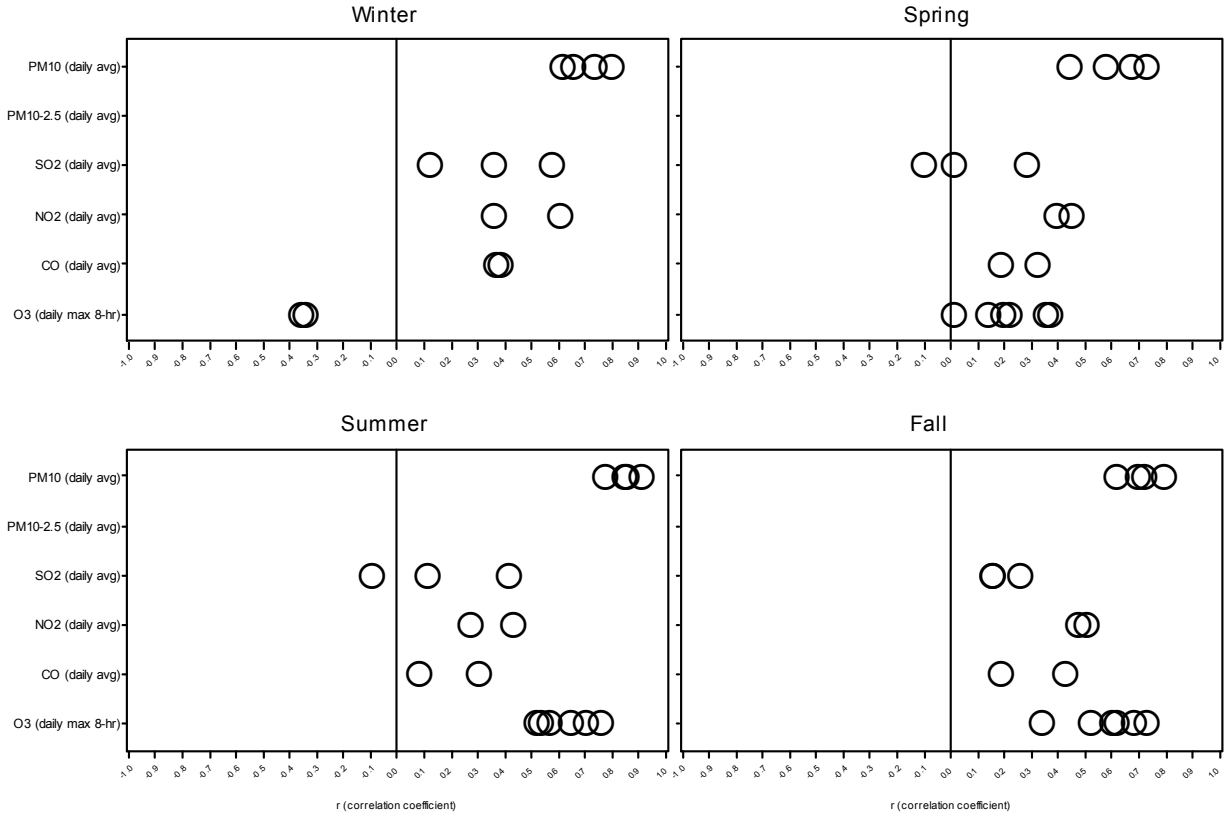


Figure A-188. Correlations between 24-h $PM_{2.5}$ and co-located 24-h avg PM_{10}, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for St. Louis, MO, stratified by season (2005-2007). One point is included for each available monitor pair.

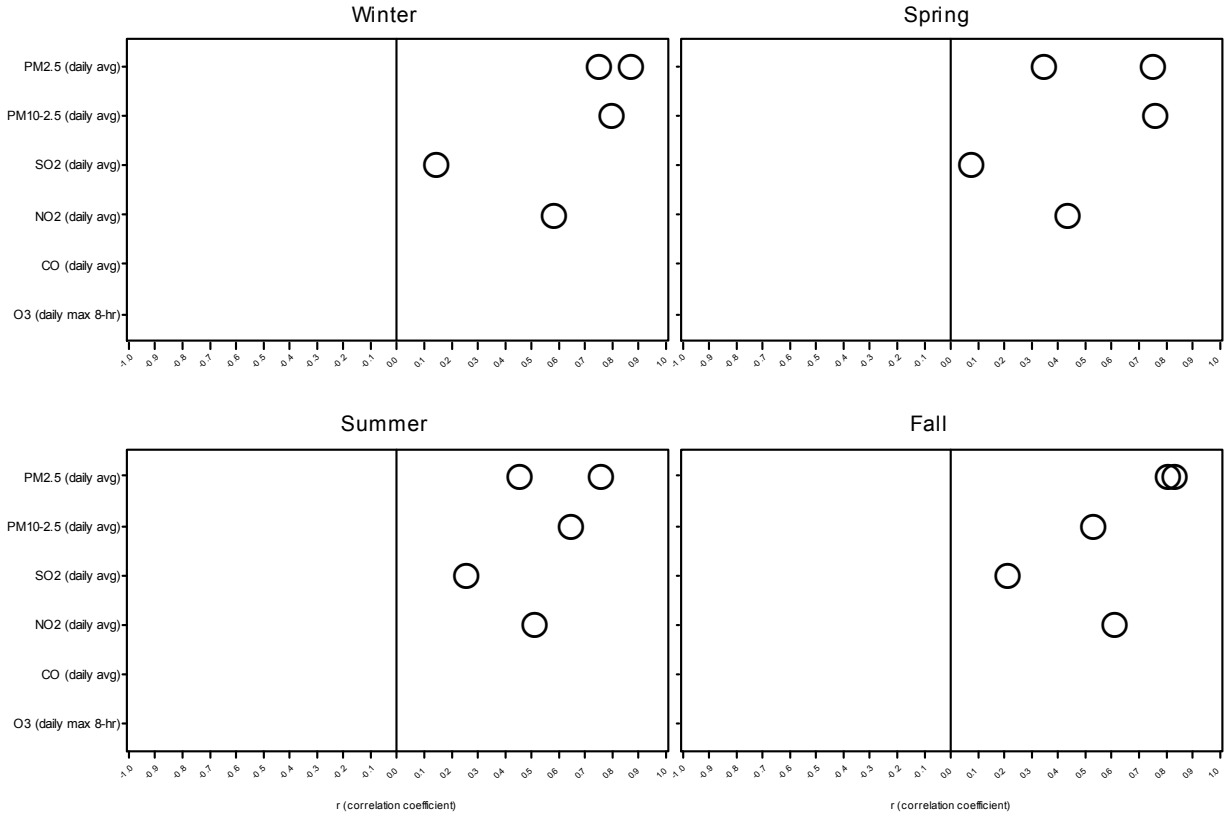


Figure A-189. Correlations between 24-h PM_{10} and co-located 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Atlanta, GA, stratified by season (2005-2007). One point is included for each available monitor pair.

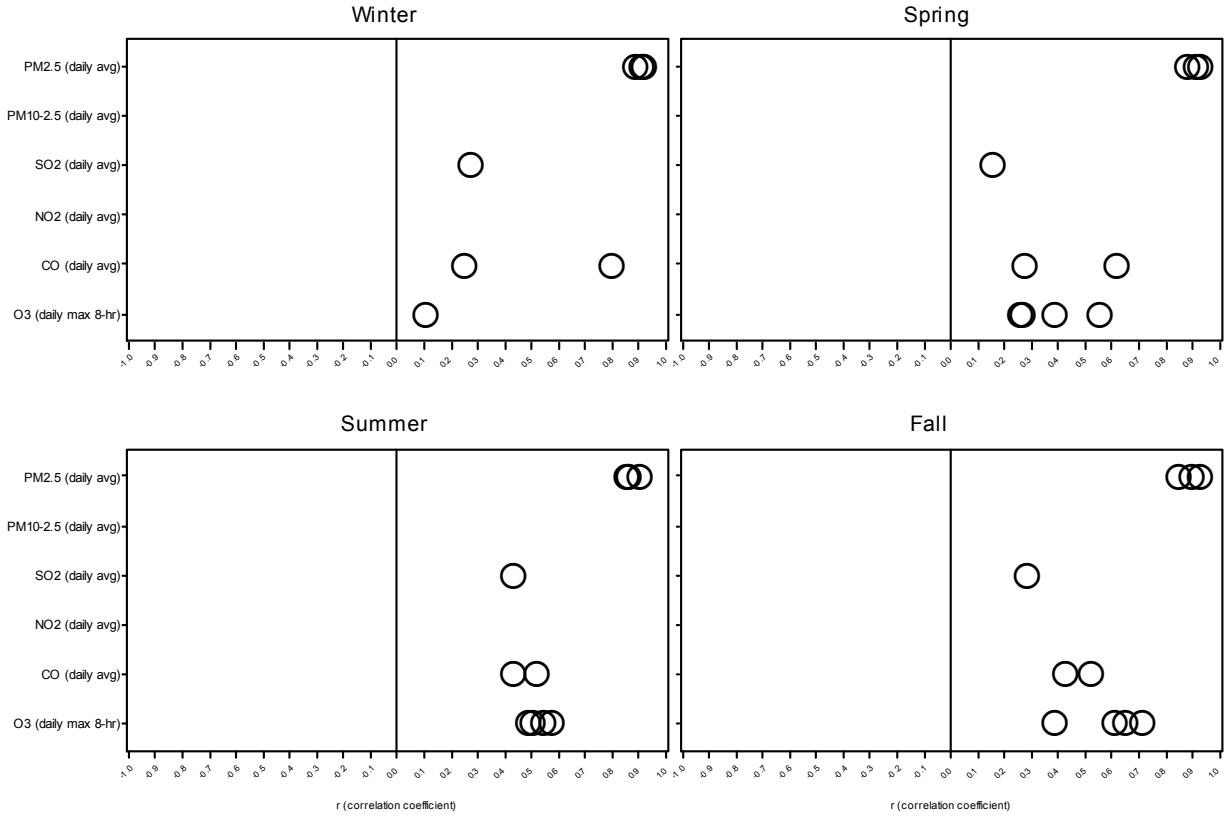


Figure A-190. Correlations between 24-h PM_{10} and co-located 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Birmingham, AL, stratified by season (2005-2007). One point is included for each available monitor pair.

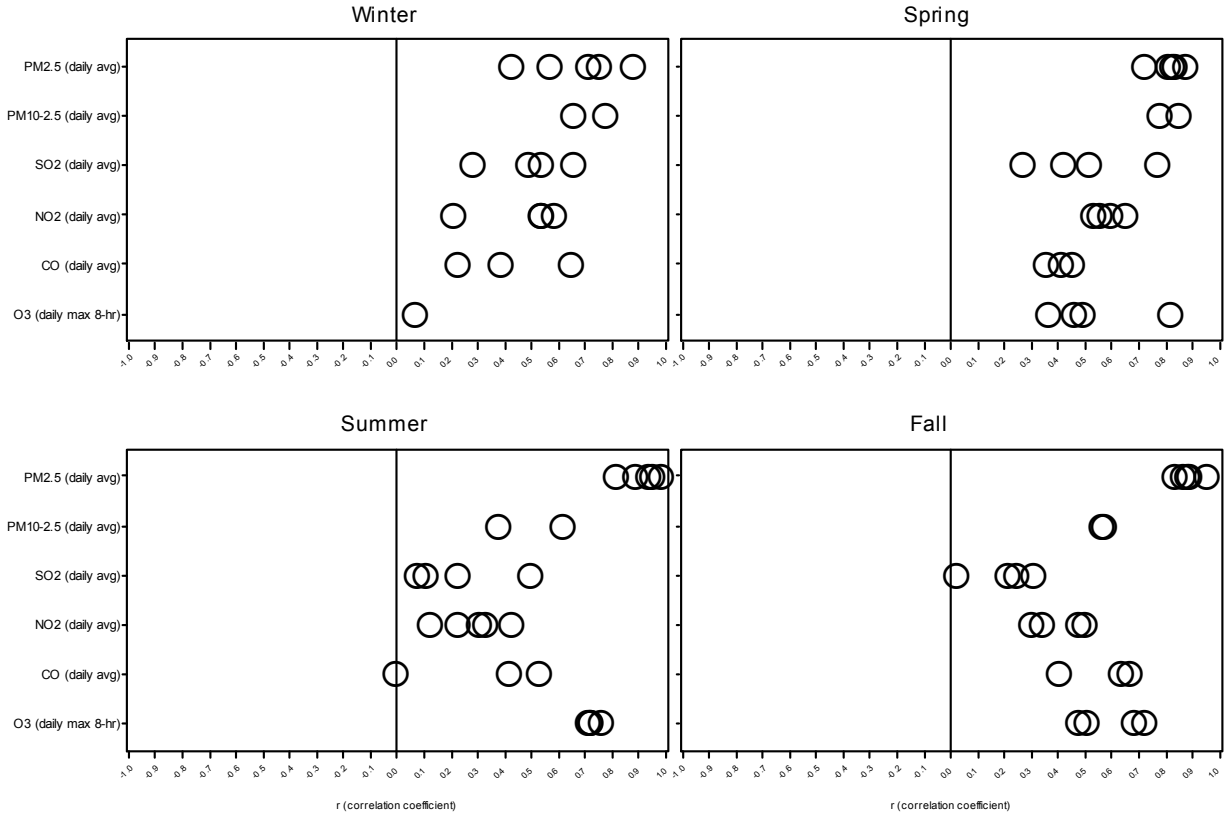


Figure A-191. Correlations between 24-h PM_{10} and co-located 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Boston, MA, stratified by season (2005-2007). One point is included for each available monitor pair.

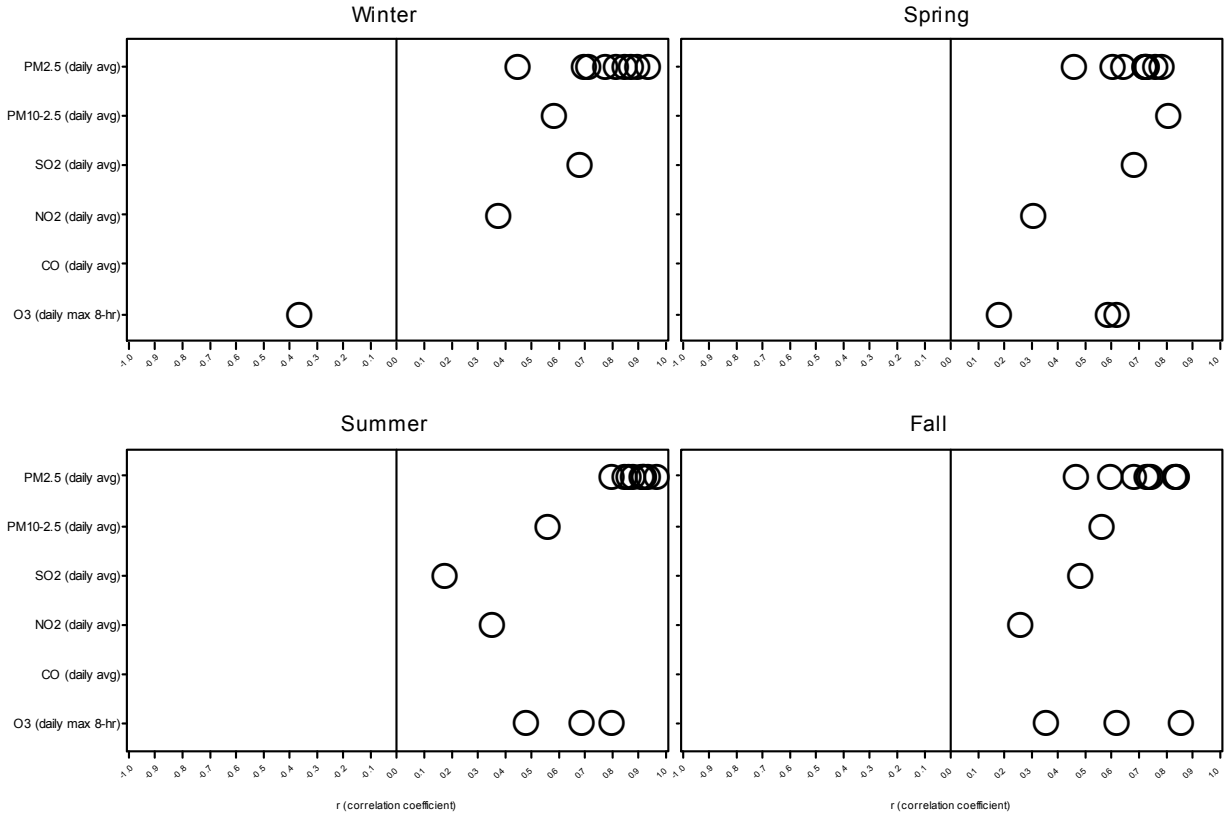


Figure A-192. Correlations between 24-h PM_{10} and co-located 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Chicago, IL, stratified by season (2005-2007). One point is included for each available monitor pair.

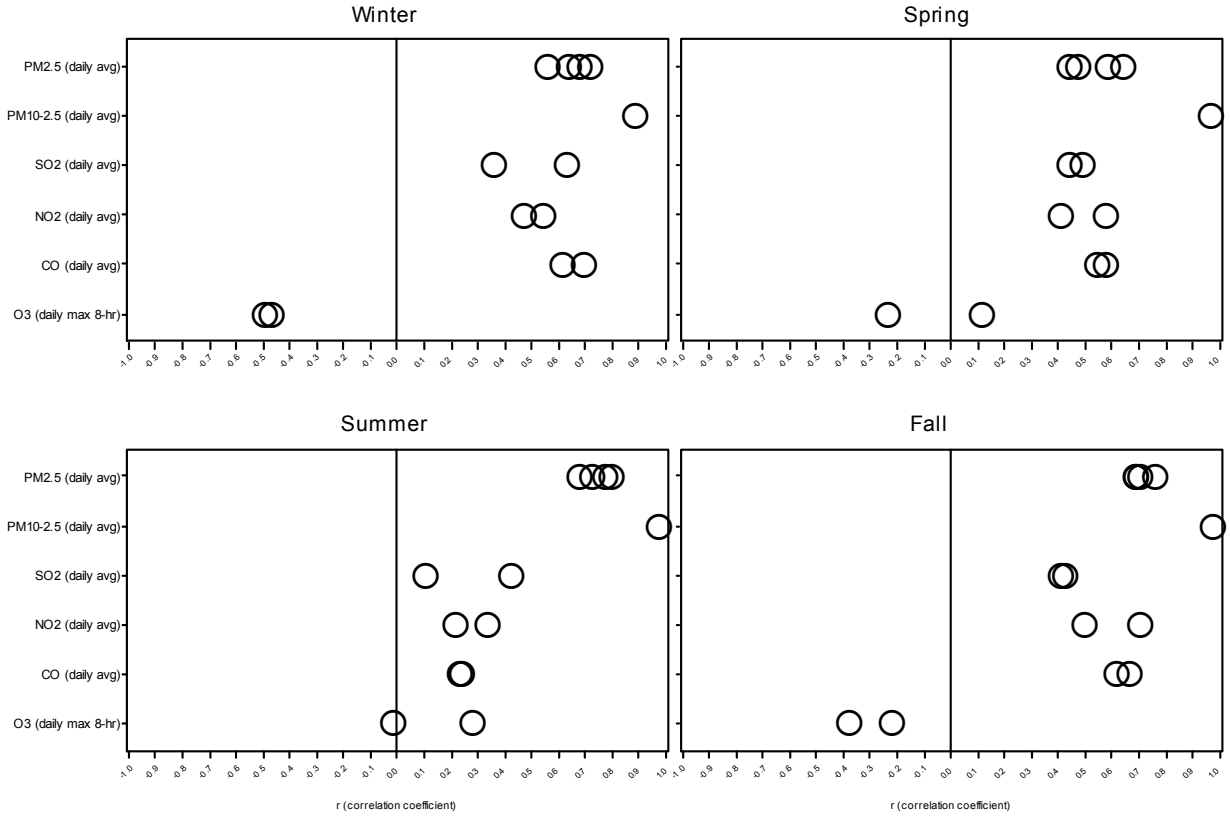


Figure A-193. Correlations between 24-h PM_{10} and co-located 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Denver, CO, stratified by season (2005-2007). One point is included for each available monitor pair.

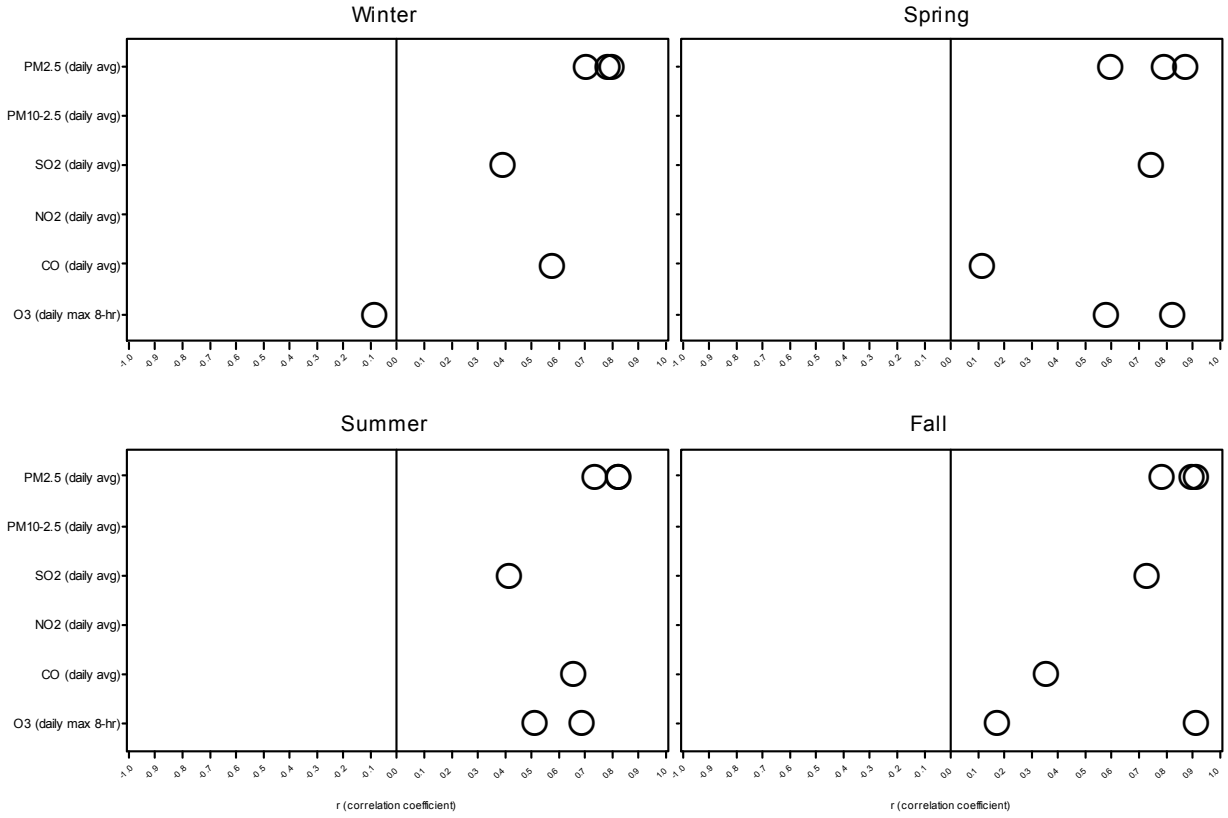


Figure A-194. Correlations between 24-h PM_{10} and co-located 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Detroit, MI, stratified by season (2005-2007). One point is included for each available monitor pair.

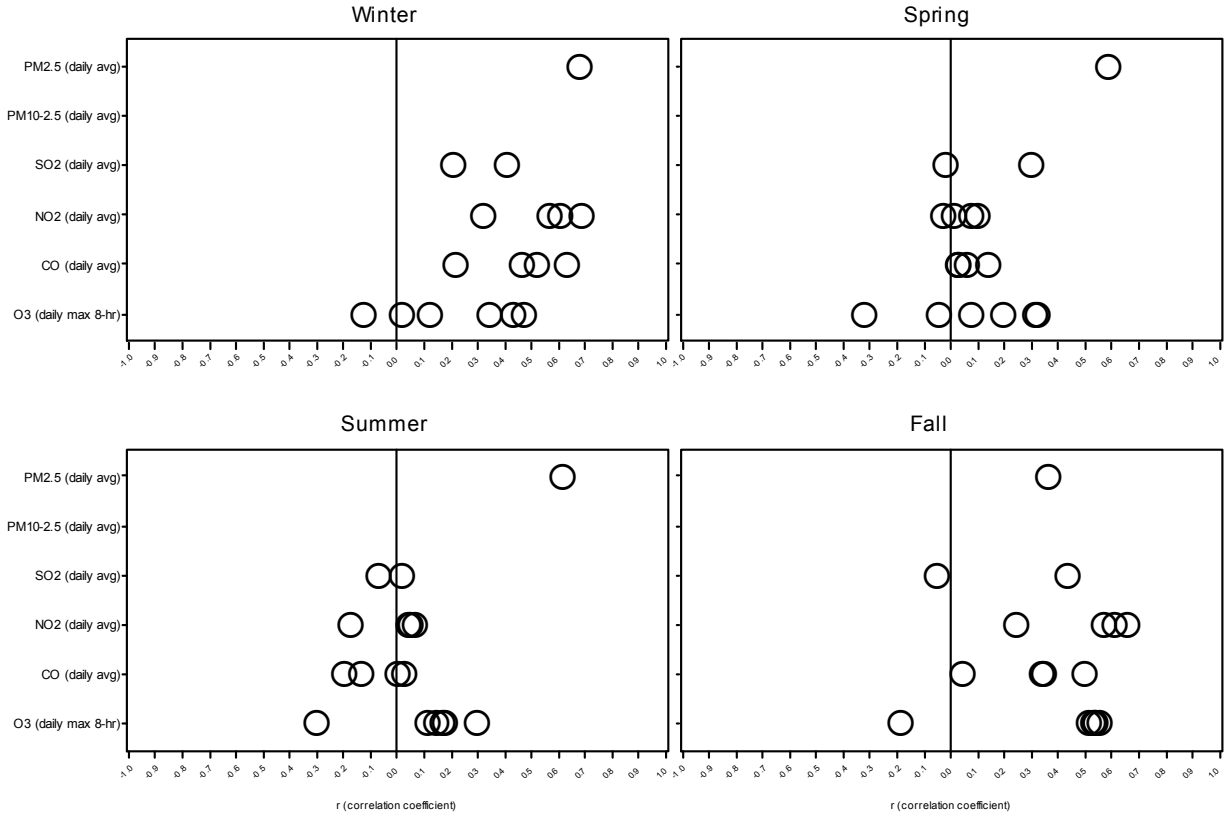


Figure A-195. Correlations between 24-h PM_{10} and co-located 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Houston, TX, stratified by season (2005-2007). One point is included for each available monitor pair.

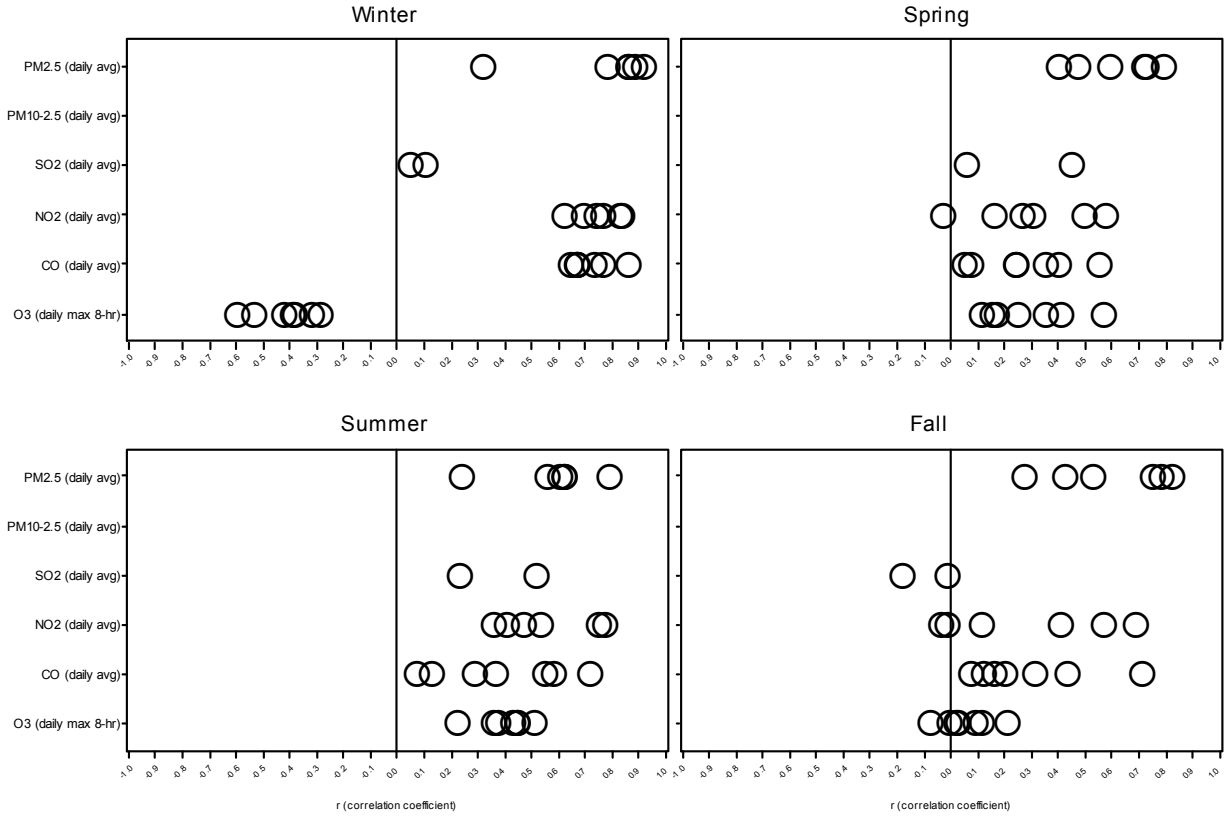


Figure A-196. Correlations between 24-h PM_{10} and co-located 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Los Angeles, CA, stratified by season (2005-2007). One point is included for each available monitor pair.

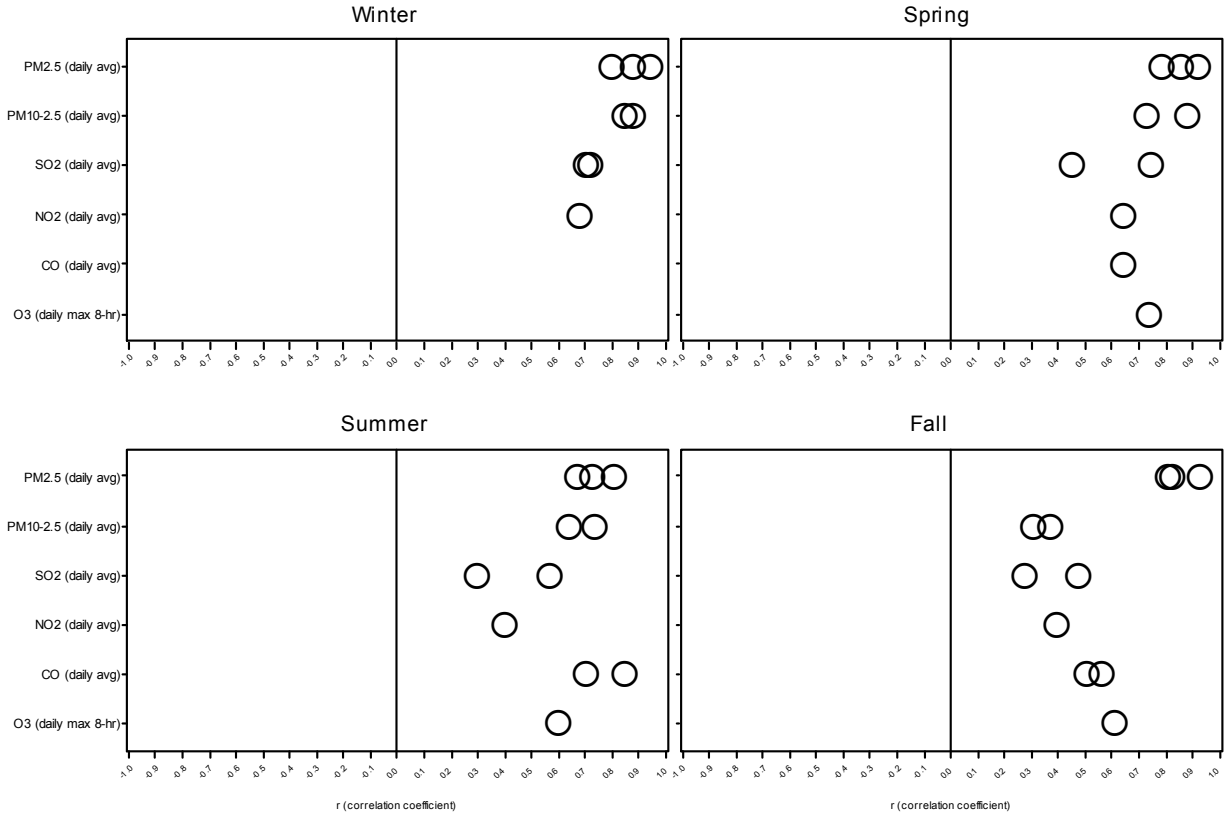


Figure A-197. Correlations between 24-h PM_{10} and co-located 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for New York, NY, stratified by season (2005-2007). One point is included for each available monitor pair.

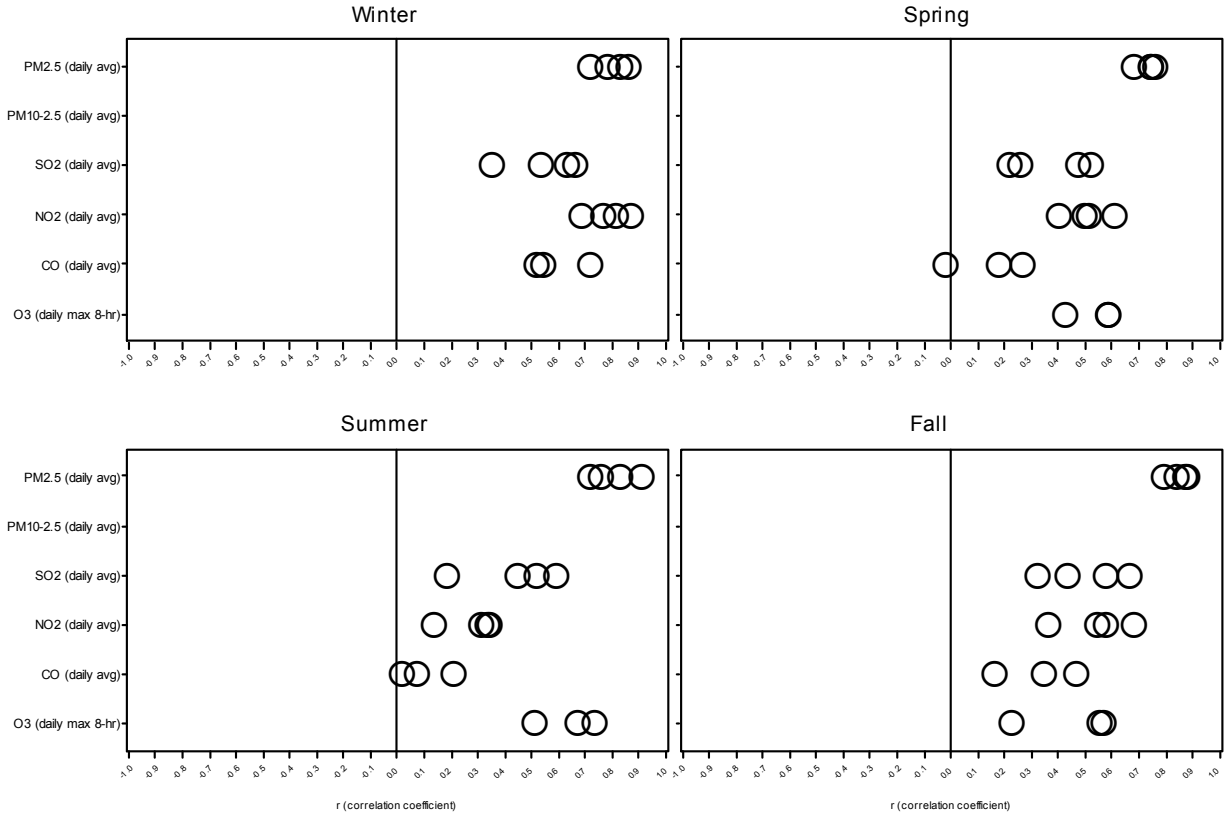


Figure A-198. Correlations between 24-h PM_{10} and co-located 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Philadelphia, PA, stratified by season (2005-2007). One point is included for each available monitor pair.

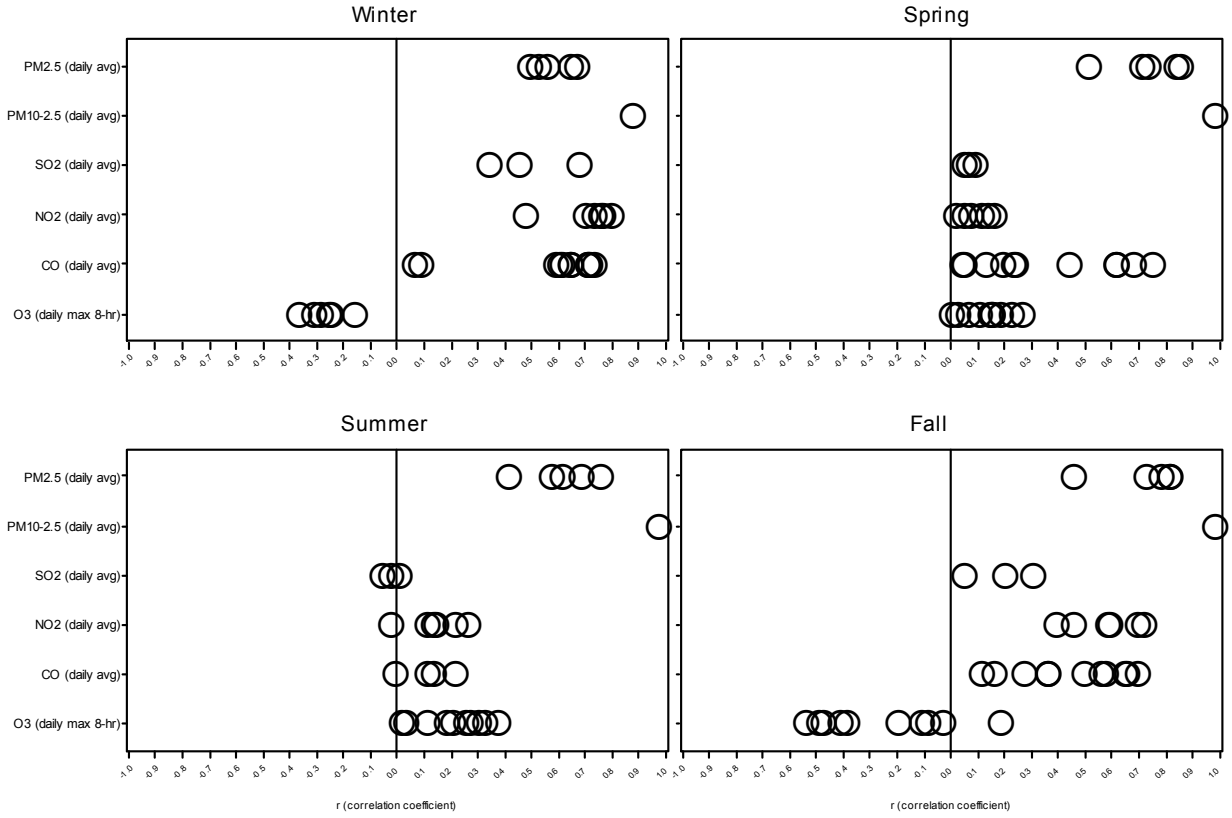


Figure A-199. Correlations between 24-h PM_{10} and co-located 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Phoenix, AZ, stratified by season (2005-2007). One point is included for each available monitor pair.

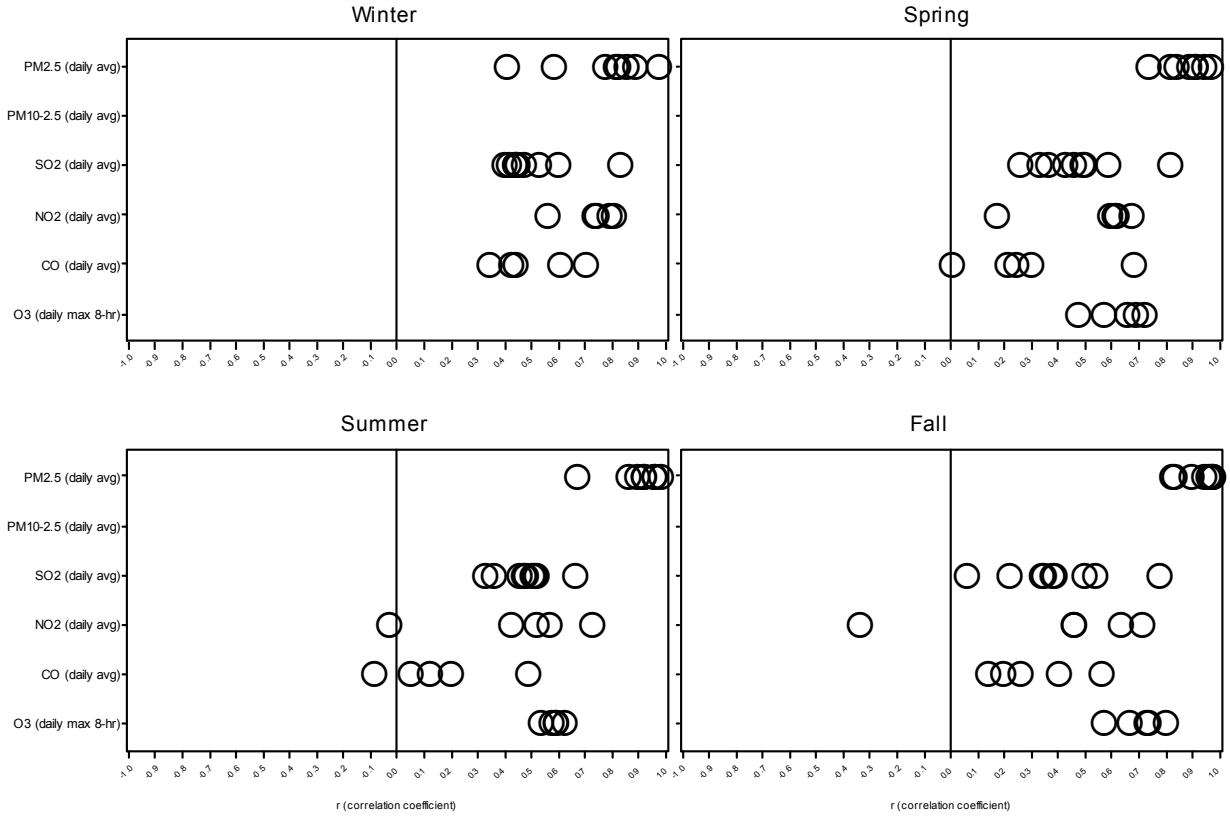


Figure A-200. Correlations between 24-h PM_{10} and co-located 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Pittsburgh, PA, stratified by season (2005-2007). One point is included for each available monitor pair.

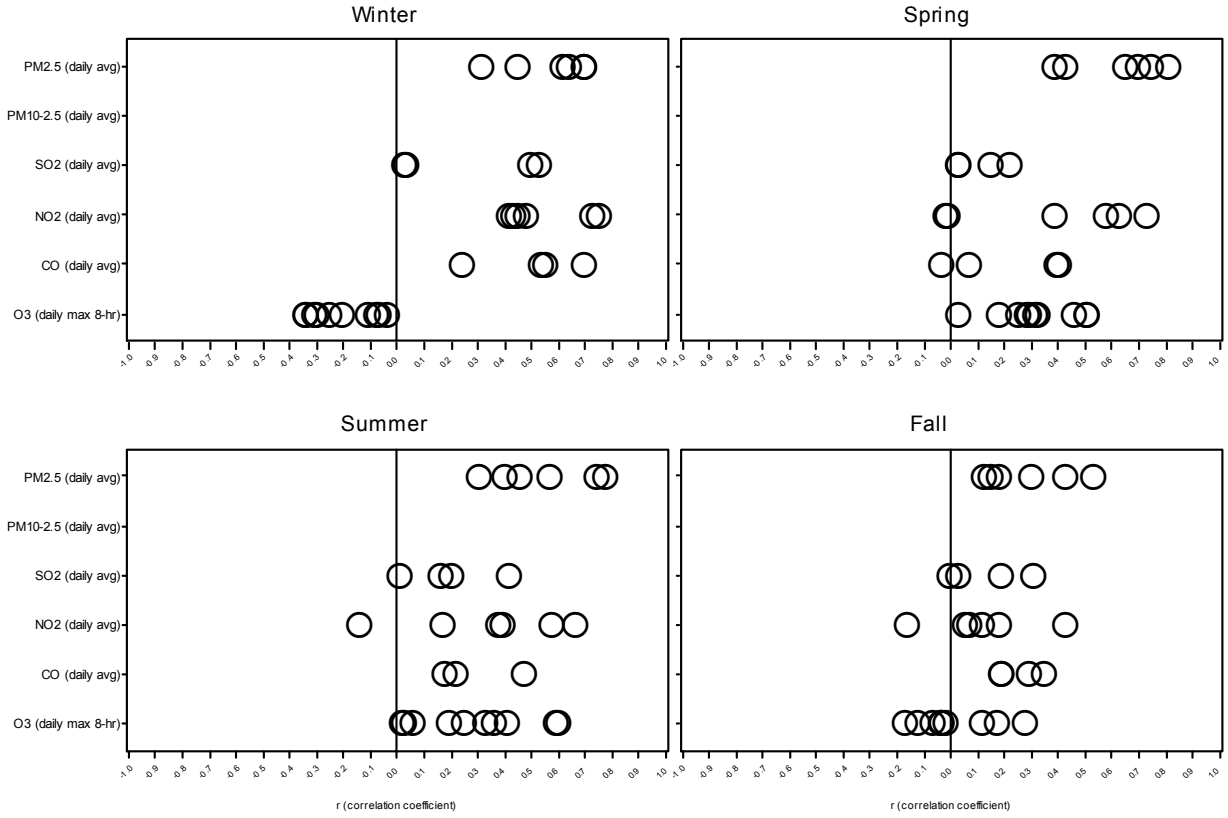


Figure A-201. Correlations between 24-h PM_{10} and co-located 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for Riverside, CA, stratified by season (2005-2007). One point is included for each available monitor pair.

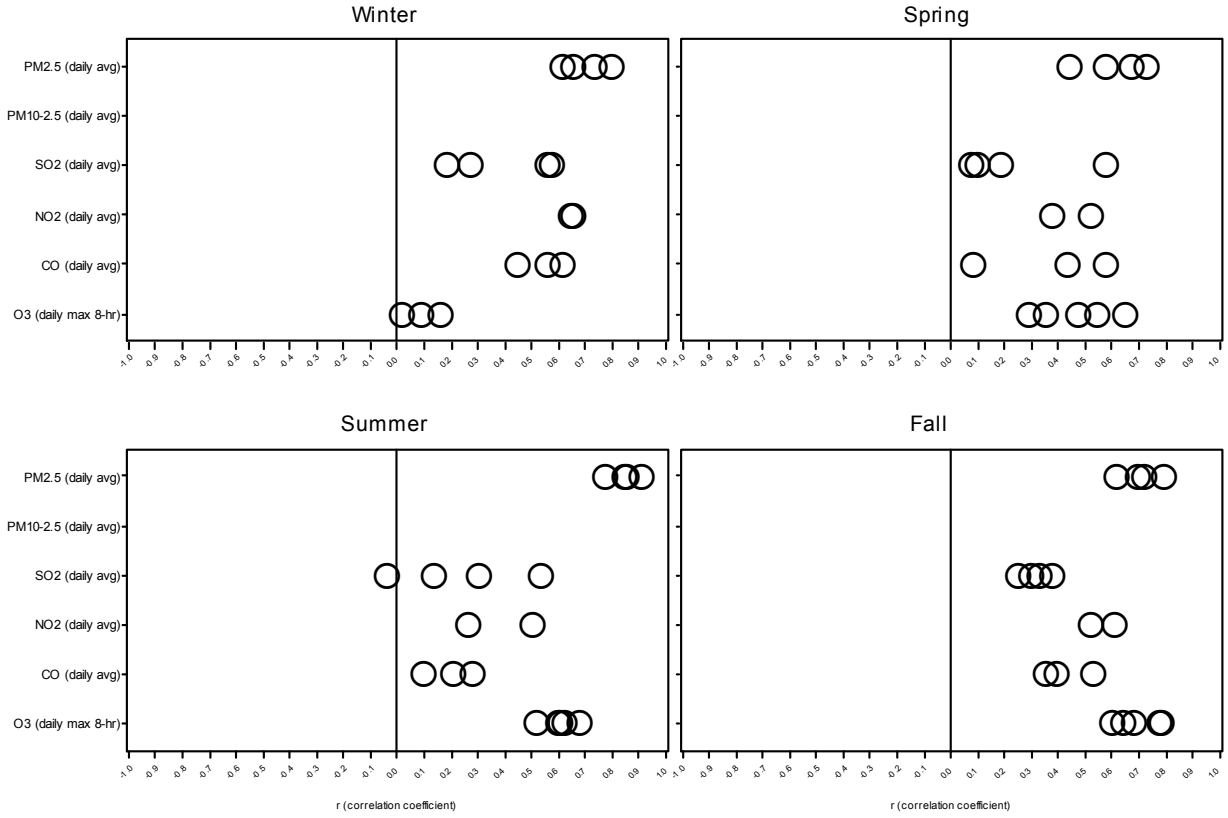


Figure A-202. Correlations between 24-h PM_{10} and co-located 24-h avg $PM_{2.5}$, $PM_{10-2.5}$, SO_2, NO_2 and CO and daily maximum 8-h avg O_3 for St. Louis, MO, stratified by season (2005-2007). One point is included for each available monitor pair.

A.3. Source Apportionment

A.3.1. Type of Receptor Models

Table A-51. Different receptor models used in the Supersite source apportionment studies: chemical mass balance.

Receptor Model	Description	Strengths and Weaknesses
Effective Variance CMB [42,121] (Note that all models based on eq 1 or 2 are CMB equations. The term CMB used here reflects the historical solution in which source profiles are explicitly used as model input and a single sample effective variance solution is reported.) CMB software is currently distributed by EPA. The most recent version is the CMB 8.2, which is run in the Microsoft Windows system.	**Principle** Ambient chemical concentrations are expressed as the sum of products of species abundances in source emissions and source contributions (Equations A-1 or A-2). These equations are solved for the source contribution estimates when ambient concentrations and source profiles are input. The single-sample effective variance least squares is the most commonly used solution method because it incorporates uncertainties of ambient concentrations and source profiles in the estimate of source contributions and their uncertainties. This reduced to the tracer solution when it is assumed that there is one unique species for each source. Choices of source profiles should avoid collinearity, which occurs when chemical compositions of various source emissions are not sufficiently different.[121] $$C_{iklmn} = \sum_{j=1}^{J} F_{ijm} T_{ijklmn} S_{iklmn}$$ **for i = 1 to I** **Equation A-1** $$C_{it} = \sum_{j} F_{ij} S_{jt} + E_{it}$$ **Equation A-2** **Data Needs** CMB requires source profiles, which are the mass fractions of particulate or gas species in source emissions. The species and particle size fraction measured in source emissions should match those in ambient samples to be apportioned. Several sampling and analysis methods provide time-integrated speciation of $PM_{2.5}$ and volatile organic compounds (VOCs) for CMB. Source profiles are preferably obtained in the same geographical region as the ambient samples, although using source profiles from different regions is commonly practiced in the literature. The practitioner needs to decide the source profiles and species being included in the model, on the basis of the conceptual model and model performance measures. **Output** Effective variance CMB determines, if converged, source contributions to each sample in terms of PM or VOC mass. CMB also generates various model performance measures, including correlation R^2, deviation X^2, residue/ uncertainty ratio, and MPIN matrix that are useful for refining the model inputs to obtain the best and most meaningful source apportionment resolution.	**Strengths** Software available providing a good user interface. Provides quantitative uncertainties on source contribution estimates based on input concentrations, measurement uncertainties, and collinearity of source profiles. Quantifies contributions from source types with single particle and organic compound measurements. **Weaknesses** Completely compatible source and receptor measurements are not commonly available. Assumes all observed mass is due to the sources selected in advance, which involves some subjectivity. Chemically similar sources may result in collinearity without more specific chemical markers. Typically does not apportion secondary particle constituents to sources. Must be combined with profile aging model to estimate secondary PM.

[42] Hidy and Friedlander (1972, 156546)
[121] Watson et al. (1997, 157121) [122] (1984, 045693)

Source: Watson et al. (2008, 157128)

Table A-52. Different receptor models used in the Supersites source apportionment studies: factor analysis.

Receptor Model	Description	Strengths and Weaknesses
PMF PMF_x (PMF_2 and PMF_3) software is available from Dr. Pentti Paatero at the University of Helsinki, Finland. This software is a Microsoft DOS application. EPA distributes EPA PMF76 version 1.1 as a Microsoft Windows application with better user interface.	**Principle** PMFx contains PMF_2 and PMF_3. PMF_2 solves the CMB equations (i.e., Equations A-2 and A-3) using an iterative minimization algorithm. Source profiles F_{ij} and contribution S_{jt} are solved simultaneously. The non-negativity constraint is implemented in the algorithm to decrease the number of possible solutions (local minimums) in the PMF analyses, because both source profile and contribution should not contain negative values. There is rotational ambiguity in all two-way factor analyses (i.e.,F_{jt} and S_{jt} matrices may be rotated and still fit the data). PMF2 allows using the FPEAK parameter to control the rotation. A positive FPEAK value forces the program to search such solutions where there are many zeros and large values but few intermediate values in the source matrix $F_{jt}.F_{key}$ can further bind individual elements in F_{jt} to zero On the basis of a similar algorithm, PMF3 solves a three-way problem. PMFx and UNMIX estimate F_{ij} and S_{jt} by minimizing: $$Q \text{ or } \chi^2 = \sum_i \sum_t [E_{it}/\sigma_{it}]^2 = \sum_i \sum_t [(C_{it} - \sum_j F_{ij} S_{jt})/\sigma_{it}]^2 \quad \textbf{Equation A-3}$$ Where the weighing factor, σit, represents the magnitude of Eit, PMFx limits solutions of Equation A-2 to non-negative F_{ij} and S_{jt}. **Data Needs** A large number of ambient samples (usually much more than the number of factors in the model) are required to produce a meaningful solution. Species commonly used in PMF are also those in CMB. Weighting factors associated with each measurement need to be assigned before analysis. The practitioner also needs to decide the number of factors, FPEAK, and Fkey in the model. **Output** PMFx reports all the elements in F_{ij} and S_{jt} matrices (PMF2). It also calculates model performance measures such as deviation X^2 and standard deviation of each matrix element. The practitioner needs to interpret the results linking them to source profiles and source contributions.	**Strengths** Software available. Can handle missing or below-detection-limit data. Weights species concentrations by their analytical precisions. Downweight outliers in the robust mode. Derives source profiles from ambient measurements as they would appear at the receptor (does not require source measurements). **Weaknesses** Requires large (>100) ambient datasets. Need to determine the number of retaining factors. Requires knowledge of source profiles or existing profiles to verify the representativeness of calculated factor profiles and uncertainties of factor contributions. Relies on many parameters/initial conditions adjustable to model input; sensitive to the preset parameters.
ME2[125] ME2 code is available from Dr. Pentti Paatero at the University of Helsinki, Finland as a Microsoft DOS application.	**Principle** The PMFx algorithm is derived from ME2. Unlike PMFx that is limited to questions in the form of Equation A-1 or A-2, ME2 solves all models in which the data values are fitted by sums of products of unknown (and known) factor elements. The first part of the algorithm interprets instructions from the user and generates a table that specifies the model. The second part solves the model using an iterative minimization approach. Additional constraints could be programmed into the model to reduce the ambiguity in source apportionment. These constraints may include known source profiles and/or contributions (e.g., contributions are known to be zero in some cases). **Data Needs** Data needs are similar to those of PMFx but are more flexible. In theory, any measured or unknown variables may be included in the model as long as they satisfy linear relationships. The users need to specify the model structure, the input, and the output. **Output** ME2 calculates and reports all unknown variables in the model.	**Strengths** Software available. Can handle user-specified models. Possibility to include all measured variables into the model, such as speciated concentration over different time scales, size distributions, meteorological variables, and noise parameters. **Weaknesses** Require substantial training to access the full feature of the software and develop a model. Generally requires large ambient datasets. Need to assume linear relationships between all variables. Relies on many parameters/initial conditions adjustable to model input; sensitive to the preset parameters.

Receptor Model	Description	Strengths and Weaknesses
UNMIX [29,44,126] UNMIX code is available from Dr. Ron Henry at the University of Southern California as an MatLab application. A stand-alone version (UNMIX version 6) is also available from EPA.	**Principle** UNMIX views each sample as a data point in a multidimensional space with each dimension representing a measured species. UNMIX solves Equations A-2 and A-3 by using a principle component analysis (PCA) approach to reduce the number of dimensions in the space to the number of factors that produce the data, followed by an unique "edge detection" technique to identify "edges" defined by the data points in the space of reduced dimension (e.g., Figures 1 and 3). The number of factors is estimated by the NUMFACT algorithm in advance[127], which reports the R^2 and signal-to-noise (S/N) ratio associated with the first N principle components (PCs) in the data matrix. The number of factors should coincide with the number of PCs with S/N ratio >2. Once the data are plotted on the reduced space, an edge is actually a hyperplan that signifies missing or small contribution from one or more factors. Therefore, UNMIX searches all the edges and uses them to calculate the vertices of the simplex, which are then converted back to source composition and contributions. Geometrical concepts of self-modeling curve resolution are used to ensure that the results obey (to within error) non-negativity constraints on source compositions and contributions. **Data Needs** A large number of ambient samples (usually much more than the number of factors in the model) are required to achieve a meaningful solution. Species commonly used in UNMIX are also those in CMB. The measurement precision is not required. The practitioner needs to specify the number of factors on the basis of the NUMFACT results. **Output** UNMIX determines all the elements in the factor (F_{ij}) and contribution (S_{it}) matrices. It also calculates the uncertainty associated with the factor elements and model performance measures including: (1) R^2, (2) S/N ratio, and (3) strength.	**Strengths** Software available with graphical user interface. Does not require source measurements. Provide graphical problem diagnostic tools (e.g., species scatter plot). Provide evaluation tools (e.g., R^2, S/N ratio). **Weaknesses** Requires large (>100) ambient datasets. Need to assume or predetermine number of retained factors. Does not make explicit use of errors or uncertainties in ambient measurements. Cannot use samples containing missing data in any species. Limited to a maximum of 7 or 14 (UNMIX version 6) factors. Can report multiple or no solutions. Requires knowledge of existing source profiles to evaluate the solutions.

Receptor Model	Description	Strengths and Weaknesses
PDRM[97] PDRM was developed under the Supersites Program and requires MatLab or equivalent software to perform the calculation.	**Principle** PDRM estimates contributions from selected stationary sources for a receptor site using high time-resolution measurements and meteorological data. In PDRM, Equation A-2 is modified to: $$C_k = \sum_j ER_{ij}\left(\frac{\chi}{Q}\right)_{j,t} + E_k$$ **Equation A-4** where $ER_{i,j}$ is interpreted as the emission rate of species i from stationary source j and (X/Q,t is the meteorological dispersion factor averaged over the time interval t. Equation A-4 is solved for ERi,j and (X/Q,t simultaneously by a nonlinear fit minimizing the objective function, FUN: $$FUN = \sum_{i=1}^{l}\sum_{t=1}^{m}\sum_{j=1}^{n}\left[ER_{ij}\left(\frac{\chi}{Q}\right)_{j,t}^{PDRM} - C_k\right]^2$$ **Equation A-5** Because the number of solutions for a product of unknowns is infinite, additional constraints are set up for (X/Q,t on the basis of the Gaussian plume model, thus: $$LB\left(\frac{\chi}{Q}\right)_{j,t}^{Met} \le \left(\frac{\chi}{Q}\right)_{j,t}^{PDRM} \le UB\left(\frac{\chi}{Q}\right)_{j,t}^{Met}$$ $$\left(\frac{\chi}{Q}\right)_{j,t}^{Met} = \frac{1}{2\pi\sigma_y\sigma_z u}\exp\left(-\frac{1}{2}\frac{y^2}{\sigma_y^2}\right)\left\{\exp\left[-\frac{1}{2}\left(\frac{z-h}{\sigma_z}\right)^2\right] + \exp\left[-\frac{1}{2}\left(\frac{z+h}{\sigma_z}\right)^2\right]\right\}$$ **Equations A-6 & A-7** Equations A-6 and A-7 limit the solution of Equation A-5 within the lower (LB) and upper (UB) bound of those predicted by the Gaussian plume model using different parameterizations. **Data Needs** PDRM requires speciated measurements at a higher time-resolution than typical CMB or PMF applications because of the fast-changing meteorological parameters. PDRM also requires data for Equation A-7: transport speed (u), lateral and vertical dispersion parameters (σy and σz), and stack height (h). **Output** PDRM determines emission rates and contributions from each point source considered in the model at the same time resolution as the measurement.	**Strengths** Explicitly include meteorological information and stack configuration of stationary sources into the model. Do not require source measurements. Do not need to interpret the relations between factors and sources. Commercial software (e.g., MatLab) available for performing nonlinear fit. Suitable for high time-resolution measurement. **Weaknesses** Can only handle stationary sources but not area or mobile sources. Need to assume that only stationary sources are considered in the model contribute significantly for a measurement at the receptor site. Do not account for uncertainty in the measurement. Meteorological data may not be always available or accurate. Gaussian plume model may not be representative of the actual atmospheric dispersion. Sensitive to the imposed constraints (UB and LB).

Receptor Model	Description	Strengths and Weaknesses
PLS[128]	**Principle** PLS examines the relationships between a set of predictor (independent) and response (dependent) variables. It assumes that the predictor and response variables are controlled by independent "latent variables" less in number than either the predictor or the response variables. In recent applications, [96] PM chemical composition and size distribution are used as predictor (X) and response (Y) variables, respectively. Equation A- 2 is modified to: $$X_k = \sum_i T_i P_{ik} + E_k$$ **Equation A-8** $$Y_n = \sum_i U_i C_{in} + D_k$$ **Equation A-9** where T and U are matrices of so-called "latent variables," and P and C are loading matrices. If X and Y are correlated to some degree, T and U would show some similarity. Equations A-8 and A-9 are solved by an iterative algorithm "NIPALS," which attempts to minimize E,D, and the difference between T and U simultaneously. If T and U end up being close enough, the X and Y variables can be explained by the same latent variables. These latent variables may then be interpreted as source or source categories. **Data Needs** Typical applications of PLS require both chemical speciated and size-segregated measurements. The practitioner needs to decide the number of latent variables on the basis of the correlation of resulting T and U matrices. **Output** PLS calculates latent variables, which are common factors best explaining the predictor and response variables, and the residues from fitting. Rx and Ry, $$R_x = 1 - \text{var}(E)/\text{var}(X)$$ **Equation A-10** $$R_y = 1 - \text{var}(D)/\text{var}(Y)$$ **Equation A-11** indicate the degree to which variables X and Y are explained by the latent variables.	**Strengths** Fit two types of measurements (e.g., chemistry and size) with common factors. Provide more information to identify sources. Analyze strongly collinear and noisy dataset. Do not require source measurements. **Weaknesses** Requires large (>100) ambient datasets. Difficult to relate latent variables to any physical quantities. Do not provide quantitative source contribution estimates. Need to decide the number of latent variables. Do not explicitly make use of measurement uncertainties. Can result in no solution.

Henry (1997, 020941)
Lewis et al. (2003, 088413)
Ogulei et al. (2006, 119975)
Park et al. (2005, 156844)
Paatero (1997, 087001)
Paatero et al. (2002, 156836)
Paatero (1999, 156835)
Henry (2003, 156540)

Source: Watson et al. (2008, 157128)

Table A-53. Different receptor models used in the Supersites source apportionment studies: tracer-based methods.

Receptor Model	Description	Strengths and Weaknesses
EF [129,130] The EF method may use a MLR algorithm, which is available in most statistical and spreadsheet software	**Principle** A tracer (or marker) for a particular source or source category is a species enriched heavily in the source emission against other species and other sources. Using EFs-, concentration of the ith pollutant at a receptor site at time t (i.e., Ci,t) can be expressed as: $$C_{i,t} = \sum_{j} \frac{1}{EF_{i,pj}} C_{pj,t} + Z_{i,t} = \sum_{j} \left(\frac{F_{ij}}{F_{pj}}\right) C_{pj,t} + Z_{i,t}$$ **Equation A-12** where the enrichment factor $EF_{i,pj}$ is the ratio of emission rate of the pollutant of interest (F_{ij}) and tracer species (F_{pj}) from source j. $C_{pj,t}$ is the concentration of tracer species for source j at time t, and Zi,t represents contributions from all other sources (including the background level). The solution for eq 12 is situation-dependent. $EF_{i,pj}$ is usually unknown but may be estimated from source profiles, edges of a two-way scatter plot or the ratio of $C_{i,t}$ to $C_{pj,t}$ for a particular period when it is believed that a single source is dominant. In cases where $Z_{i,t}$ is a constant, $EF_{i,pj}$ may be derived from MLR. **Data Needs** The minimum data needs include concentrations of all primary tracers at the receptor site. Known EFs or background levels are helpful. **Output** The EF method determines contributions to species i from each source considered in the model.	**Strengths** No special software needed. Indicate presence or absence of particular emitters. Provides evidence of secondary PM formation and changes in source impacts by changes in ambient composition. Could use a large (>100) dataset or a small (e.g., < 10) dataset. **Weaknesses** Semiquantitative method, not specific especially when the EFs are unknown in advance. Limited to sources with unique markers. Tracer species must be exclusively from the sources or source categories examined. Provide very limited error estimates. More useful for source/process identification than for quantification.
NNLS [131,132] The MatLab Optimization Toolbox provides a function "lsqnonneg" for performing the NNLS calculation.	**Principle** NNLS also solves the EF equation (Equation A-12 or equivalent) with known target species and tracer concentrations. Conventional MLR solutions to eq 12 may lead to negative EFs due to the uncertainty in measurements or colinearity in source contributions. This is avoided in the NNLS approach since additional non-negative constraints are built into the algorithm, i.e.: $$EF_{i,pj} \geq 0$$ **Equation A-13** Utilizing orthogonal decomposition, a NNLS problem can be reduced to the more familiar least-distance programming and solved by a set of iterative subroutines developed and tested by Lawson and Hanson.131 In a more general sense, NNLS linearly relates a response variable to a set of independent variables with only non-negative coefficients. **Data Needs** When applied to EF or MLR problems, NNLS requires the concentration of target (response) and tracer (independent) species. **Output** NNLS generates non-negative regression coefficients for an EF/MLR problem and these coefficients can be related to the source contributions.	**Strengths** Implemented by many statistical software packages. Generate only non-negative EFs or regression coefficients. Do not require source measurements. Possible to include meteorological or other (besides chemistry) data into the model. **Weaknesses** Require a large (>100) set of ambient measurements. Semiquantitative method, not specific. Do not explicitly consider measurement uncertainties. Tracer species must be exclusively from the sources or source categories examined. Non-negative constraints may not be appropriate in some cases.

Receptor Model	Description	Strengths and Weaknesses
FAC	**Principle** FAC provides a simple mean of estimating the SOA production rate using the emission inventories of primary precursor VOCs. FAC is actually a source-oriented modeling technique but it does not take into account all the atmospheric processes. FAC is defined as the fraction of SOA that would result from the reactions of a particular VOC: $$[\text{SOA}] = \sum_i FAC_i \times ([\text{VOC}_i]_0 \times \text{Fraction of VOC } i \text{ reacted})$$ **Equation A-14** where $[\text{VOC}_i]_0$ is the emission rate of VOC_i and [SOA] is the formation rate of SOA. Equation A-14 can be viewed as an extension of Equation -12 but concentrations are replaced with emission rates and EFs are replaced with FACs. FAC and the fraction of VOC reacted under typical ambient conditions have been developed for a large number of hydrocarbons $>C_6$ [111]. The most significant SOA precursors are aromatic compounds (especially toluene, xylene, and trimethylbenzenes) and terpenes. In most applications, these FACs are used directly to estimate SOA. **Data Needs** FAC requires the VOC emission inventory in the region of interest. The knowledge of O_3 and radiation intensity is also helpful for slight modifications of the FACs. **Output** FAC method estimates the total production rate of SOA.	**Strengths** Link SOA to primary VOC emissions so that SOA can also be treated as primary particles in the PM modeling. Simple and inexpensive. **Weaknesses** Ignore the influence of aerosol concentration and temperature-dependent gas-particle partitioning on SOA yield. Limited by the accuracy of VOC emission inventory. Do not directly infer the contribution of each source to ambient SOA concentration. Difficult to verify.

Grosjean and Seinfeld (1989, 045643)
Darns et al. (1970, 156379)
Reimann and De Caritat (2000, 013269)
Lawson and Hanson (1974, 156673)
Wang and Hopke (1989, 157105)

Source: Watson et al. (2008, 157128)

Table A-54. Different receptor models used in the Supersites source apportionment studies: meteorology-based methods.

Receptor Model	Description	Strengths and Weaknesses
CPF [134,135]	**Principle** CPF estimates the probability that a given source contribution from a given wind direction will exceed a predetermined threshold criterion (e.g., upper 25th percentile of the fractional contribution from the source of interest). The calculation of CPF uses source contributions (i.e., O_3 in Equation A-2) determined for the receptor site and local wind direction data matching each of the source contributions in time. These data are then segregated to several sectors according to wind direction and the desired resolution (usually 36 sectors at a 10° resolution). Data with very low wind speed (e.g., < 0.1 m/sec) are usually excluded from analysis because of the uncertain wind direction. CPF is then determined by: $$CPF(\theta) = \frac{m_{\Delta\theta}}{n_{\Delta\theta}}$$ **Equation A-15** where $m\Delta\theta$ is the number of occurrences in the direction sector $\theta \rightarrow \theta + \Delta\theta$ that exceeds the specified threshold, and $n\Delta\theta$ is the total number of wind occurrences in that sector. Because wind direction is changing rapidly, high-time resolution measurements (e.g., minutes to hours) are preferred for a CPF analysis. If the calculated source contributions represent long-term averages, wind direction needs to be averaged over the same duration. In addition to source contribution, CPF can be applied directly to pollutant concentration measurements at a receptor site. **Data Needs** CPF requires the time series of source contributions at a receptor site, which is usually determined by CMB or factor analysis methods using speciated measurements at the site. CPF also requires wind direction and wind speed data averaged over the same time resolution as the sampling duration. **Output** CPF reports the probability of "high" contribution from a particular source or factor occurring within each wind direction sector. The results are often presented in a wind rose plot.	**Strengths** Infer the direction of sources or factors relative to the receptor site. Provide verification for the source identification made by factor analysis method. Easy to implement. **Weaknesses** Criterion for the threshold is subjective. Absolute source contribution (or fractional contribution) may be influenced by other factors besides wind direction (e.g., wind speed, mixing height). Local and near-surface wind direction only has a limited implication for long-range transport. Easy to be biased by a small number of wind occurrences in a particular sector. Work better for stationary sources than area or mobile sources.

Receptor Model	Description	Strengths and Weaknesses
NPR [136,137]	**Principle** NPR calculates the expected (averaged) source contribution as a function of wind direction following: $$S(\theta) = \frac{\sum_i K\left(\frac{\theta - W_i}{\Delta\theta}\right) \times S_i}{\sum_i K\left(\frac{\theta - W_i}{\Delta\theta}\right)}$$ **Equation A-16** where Wi is the wind direction for the ith sample and Si is the contribution from a specific source to that sample, determined from measurements at the receptor site. K is a weighting function called the kernel estimator. There are many possible choices for K. Henry et al.[136] recommend either Gaussian or Epanechnikov functions. The most important decision in NPR is the choice of the smoothing parameter Δθ. If Δθ is too large, S(θ) will be too smooth and meaningful peaks could be lost. If it is too small, S(θ) will have too many small, meaningless peaks. Δθ needs to be chosen according to the project-specific spatial distribution of sources. NPR also estimates the confidence intervals of S(θ) based on the asymptotic normal distribution of the kernel estimates, thus: $$\Delta S(\theta) = \frac{\sum_i K\left(\frac{\theta - W_i}{\Delta\theta}\right) \times (S_i - S(\theta))^2}{\left(\sum_i K\left(\frac{\theta - W_i}{\Delta\theta}\right)\right)^2}$$ **Equation A-17** **Data Needs** NPR requires the same data as the CPF method, including the time series of source/factor contributions (or fractional contributions) at the receptor site and local wind direction data matching the sampling duration in time. **Output** NPR reports the distribution of source contribution as a function of wind direction and the confidence level associated with it.	**Strengths** Infer the direction of sources or factors relative to the receptor site. Provide verification for the source identification made by factor analysis method. Require no assumption about the function form of the relationship between wind direction and source contribution. Provide uncertainty estimates. Easy to implement. **Weaknesses** Choices for the kernel estimator and smoothing factor are subjective. Absolute source contribution (or fractional contribution) may be influenced by other factors besides wind direction (e.g., wind speed, mixing height). Local and near-surface wind direction only has a limited implication for long-range transport. Easy to be biased by a small number of wind occurrences in a particular sector. Work better for stationary sources than area or mobile sources.

Receptor Model	Description	Strengths and Weaknesses
TSA [138] TSA requires the calculation of air parcel back trajectory, which is often accomplished using the HY-SPLIT model.[115,139] HY-SPLIT version 4.5 is available at http://www.arl.noaa.gov/-ready/hysplit4.html.	**Principle** Similar to CPF, TSA clusters the measured pollutant concentration or calculated source contribution according to the wind pattern. However, air parcel back trajectory, rather than local wind direction, is used. A back trajectory traces the air parcel backward in time from a receptor. The initial height is often between 200 and 1000 m above ground level where the wind direction could differ from the surface wind direction substantively. For each sample i, TSA obtains one or more trajectories and calculates their total residence time in the jth directional sector ($\tau_{i,j}$, i.e., the total number of 1-h trajectory end points that fall into the sector). The pollutant concentration or source contribution in the sample, S_i, is then linearly apportioned into each directional sector according to $\tau_{i,j}$ and averaged over all samples to produce the directional dependent pollutant concentration/source contribution for the period of interest: $$\overline{S_j} = \sum_i S_i \left(\frac{\tau_{ij}}{\sum_i \tau_{ij}} \right) / N$$ **Equation A-18** where N is the number of samples. Compared with CPF and NPR, TSA considers the entire air mass history rather than just the wind direction at the receptor. **Data Needs** TSA requires the time series of pollutant concentration or source contribution at the receptor site, and back trajectories initiated over the site during the sampling duration. Trajectory is usually calculated once every hour so TSA is more suitable for analyzing measurements of >1-h resolution. **Output** TSA reports the avg pollutant concentration or source contribution as a function of wind direction based on back trajectory calculations.	**Strengths** Infer the direction of sources or factors relative to the sampling site. Provide verification for the source identification made by factor analysis method. Account for air mass transport over hundreds to thousands of kilometers and on the order of several days. Can represent plume spread from vertical wind shear at different hours of day by adjusting the initial height of back trajectories. **Weaknesses** Need to generate and analyze the back trajectory data. Uncertainty in back trajectory calculation increases with its length in time. Source contribution depends on not only trajectory residence time but also entrainment efficiency, dispersion, and deposition. Difficult to resolve the direction of more localized sources.

Receptor Model	Description	Strengths and Weaknesses
PSCF [140] PSCF requires the calculation of air parcel back trajectory, which is often accomplished using the HY-SPLIT model.[115,139] HY-SPLIT version 4.5 is available at http://www.arl.noaa.gov/-ready/hysplit4.html.	**Principle** Ensemble air parcel trajectory analysis refers to the statistical analysis on a group of trajectories to retrieve useful patterns regarding the spatial distribution of sources. Uncertainties associated with individual trajectory calculations largely cancel out for a sufficient number of trajectories or trajectory segments. As a popular ensemble back trajectory analysis, PSCF estimates the probability that an upwind area contributes to high pollutant concentration or source contribution. Back trajectories are first calculated for each sample at the receptor site. To determine the PSCF, a study domain containing the receptor site is divided into an array of grid cells. Trajectory residence time (the time it spends) in each grid cell is calculated for all back trajectories and for a subset of trajectories corresponding to "high" pollutant concentration or source contribution at the site. PSCF in cell (i,j) is then defined as: $$PSCF_{ij} = \frac{\text{Sum of "high" residence time in cell } (i, j)}{\text{Sum of all residence time in cell } (i, j)}$$ **Equation A-19** The criterion for high pollutant concentration or source contribution is critical for the PSCF calculation. The 75th or 90th percentile of the concentration or factor is often used.[113,141,142] Residence time can be represented by the number of trajectory end points in a cell. **Data Needs** Similar to TSA, PSCF calculation requires the time series of pollutant concentration or source contribution at the receptor site, and back trajectories initiated over the site during the sampling period. Trajectories should be calculated with 1-to 3-h segment to reduce the uncertainty from interpolation (if needed). **Output** PSCF reports the probability that an upwind area contributes to high pollutant concentrations or source contribution at the downwind receptor site. The results are often presented as a contour plot on the map. A high probability usually suggests potential source region.	**Strengths** Infer the location of sources or factors relative to the sampling site. Provide verification for the source identification made by factor analysis method Account for air mass transport over hundreds to thousands of kilometers and on the order of several days. Resolve the spatial distribution of source strength (qualitatively). **Weaknesses** Need to generate and analyze the back trajectory data. Need to correct for the central tendency (residence time always increases toward the receptor site regardless of source contribution). Uncertainty in back trajectory calculation increases with its length in time. Source contribution depends on not only trajectory residence time but also entrainment efficiency, dispersion, and deposition. Difficult to resolve the location of more localized sources.

Receptor Model	Description	Strengths and Weaknesses
SQTBA [117, 143] SQTBA requires the calculation of air parcel back trajectory, which is often accomplished using the HY-SPLIT model.[115,139] HY-SPLIT version 4.5 is available at http://www.arl.noaa.gov/-ready/hysplit4.html.	**Principle** SQTBA is another type of ensemble air parcel trajectory analysis. The concept of SQTBA is to estimate the "transport field" for each trajectory ignoring the effects of chemical reactions and deposition. Back trajectories are first calculated for each sample at the receptor site, and a study domain containing the receptor site is divided into an array of grid cells. SQTBA assumes that the transition probability that an air parcel at (x',y',t'), where x' and y' are spatial coordinates and t' means time, will reach a receptor site at (x,y,t) is approximately normally distributed along the trajectory with a standard deviation that increases linearly with time upwind[144,145], thus: $$Q(x, y, t|x', y', z') = \frac{1}{2\pi(at')^2}\exp\left[-\frac{1}{2}\left(\left(\frac{X - x'(t')}{at'}\right)^2 + \left(\frac{Y - y'(t')}{at'}\right)^2\right)\right]$$ **Equation A-20** where (X,Y) is the coordinate of the grid center, a is the dispersion speed, and x'(t') and x' (t') represent the trajectory. The probability field, Q, for a given trajectory is then integrated over the upwind period, τ, to produce a two-dimensional "natural" (nonweighted) transport field: $$T_k(x, y|x', y') = \frac{\int_{-\tau}^{0} Q(x, y, t|x', y', z')}{\int_{-\tau}^{0} dt'}$$ **Equation A-21** After the transport field for each trajectory is established, they are weighted by the corresponding pollutant concentration or source contribution at the receptor site and summed to yield the overall SQTBA field.[117] **Data Needs** SQTBA requires the time series of pollutant concentration or source contribution at the receptor site, and back trajectories initiated over the site during the sampling period. Trajectories should be calculated with 1to 3-h segment to reduce the uncertainty from interpolation (if needed). **Output** SQTBA put more weight on trajectories associated higher pollutant concentration or source contribution and therefore the resulting field may imply the major transport path.	**Strengths** Imply the location of sources or factors relative to the sampling site. Account for air mass transport over hundreds to thousands of kilometers and on the order of several days. Resolve the spatial distribution of source strength (qualitatively). **Weaknesses** Need to generate and analyze the back trajectory data. Need to correct for the central tendency (residence time always increases toward the receptor site regardless of source contribution). Need to estimate dispersion velocity. Involve complicated calculations. Physical meaning of the SQTBA field is unclear. Difficult to resolve the location of more localized sources.

Receptor Model	Description	Strengths and Weaknesses
RTWC [146] RTWC requires the calculation of air parcel back trajectory, which is often accomplished using the HY-SPLIT model.[115,139] HY-SPLIT version 4.5 is available at http://www.arl.noaa.gov/ready/hysplit4.html	**Principle** As an ensemble air parcel trajectory analysis, RTWC requires back trajectories calculated for each sample at the receptor site, and a study domain containing the receptor site divided into an array of grid cells. RTWC assumes that no major pollutant sources are located along "clean" (associated with low pollutant concentrations) trajectories and that "polluted" trajectories picked up emissions along their paths. In practice, RTWC distributes pollutant concentrations at the receptor to upwind grid cells along the back trajectories according to the trajectory residence times in those cells.[117,146] $$S_{i,k} = S_k \frac{\text{resident time in cell } i}{\text{average residence time in each cell}}$$ **Equation A-22** where S_k is the pollutant concentration or source contribution determined upon the arrival of trajectory k and $S_{i,k}$ is the redistributed pollutant concentration or source contribution for cell i upwind. RTWC is known for the problem of "tailing effect," i.e., spurious source areas can be identified when cells are crossed by a very small number of trajectories. Although some corrections were proposed147 these approaches are purely empirical.	**Strengths** Imply the location of sources or factors relative to the sampling site. Account for air mass transport over hundreds to thousands of kilometers and on the order of several days. Resolve the spatial distribution of source strength (qualitatively). **Weaknesses** Need to generate and analyze the back trajectory data. Need to correct for the central tendency and tailing effect. The amount of emission entrainment should not be proportional to the residence time of trajectories (so there is no linear relationship between RTWC field and source strength). Physical meaning of the RTWC field is unclear. Difficult to resolve the location of more localized sources.

[113] (Pekney et al., 2006, 086115)
[117] (Zhou et al., 2004, 157190)
[134] (Ashbaugh, 1983, 156229)
[135] (Ashbaugh et al., 1984, 045148)
[136] (Henry et al., 2002, 136097)
[137] (Yu et al., 2004, 101779)
[138] (Parekh and Husain, 1981, 156840)
[140] (Hopke et al., 1995, 156566)
[143] (Keeler and Samson, 1989, 156633)
[144] (Samson, 1978, 188974)
[145] (Samson, 1980, 073010)
[146] (Stohl, 1996, 157014)
[147] (Cheng et al., 1993, 052294)

Source: (Watson et al., 2008, 157128)

A.3.2. Source Profiles

Table A-55. Source Profiles: Part I

Element	Symbol	Motor Vehicle Exhaust - Gasoline		Coal Combustion		Highway Road Dust		Unpaved Road Dust		Refinery	
		Weight %	Uncertainty	Weight %	Uncertainty	Weight %	Uncertainty	Weight %	Uncertainty	Weight %	Uncertainty
Aluminum	Al	0.1	N/A	5.968	0.5247	5.729	0.4058	7.4822	0.9315	8.4853	2.3478
Antimony	Sb	0.01	N/A	0	0.0625	0	0.0335	0	0.1601	0	0.0285
Arsenic	As			0	0.0164	0	0.0123	0	0.0226	0	0.0045
Barium	Ba	0.01	N/A	1.3315	1.0801	0.1377	0.1027	0	0.5473	0	0.0979
Cadmium	Cd			0	0.0341	0	0.019	0	0.0881	0	0.0155
Calcium	Ca	0.42	N/A	3.4536	1.0411	2.5657	0.1388	2.163	1.0444	0.1236	0.056
Chloride ion	Cl-	0.39	N/A								
Chromium	Cr	0.01	N/A	0.0176	0.0041	0.0271	0.0023	0.0312	0.0161	0.0443	0.0127
Cobalt	Co			0	0.0432	0	0.0668	0	0.0869	0	0.0218
Copper	Cu	0.02	N/A	0.0179	0.0112	0.0219	0.0101	0.0474	0.0307	0.0299	0.0082
Total carbon	TC			4.2763	4.2579	14.3927	2.3449	4.2671	3.7193	0	1.6175
Gallium	Ga			0.014	0.014	0	0.005	0	0.0233	0	0.0059
Gold	Au										
Indium	In	0	N/A	0	0.0404	0	0.022	0	0.1041	0	0.0183
Iron	Fe	1.27	N/A	2.916	0.3827	4.5713	0.2661	5.5128	2.1152	1.4708	0.2216
Lanthanum	La	0	N/A	0	0.2462	0	0.1341	0	0.6521	0	0.1146
Lead	Pb	0.08	N/A	0.068	0.0336	0.067	0.0074	0.0288	0.0284	0.0097	0.0063
Magnesium	Mg	0.14	N/A								
Manganese	Mn	0.01	N/A	0.0284	0.0139	0.087	0.009	0.1372	0.0509	0.016	0.002
Mercury	Hg	0	N/A	0	0.0154	0	0.0083	0	0.0383	0	0.0073
Molybdenum	Mo			0	0.0134	0	0.0071	0	0.0331	0.0079	0.0088
Nickel	Ni	0.01	N/A	0.0072	0.0019	0.0081	0.0015	0.0091	0.0057	0.04	0.0065
Nitrate	NO_3^-	0.06	N/A	0	0.2116	0	0.094	0	0.6371	0	0.0772
Organic carbon	OC	59.37	N/A	0	2.9263	12.7127	2.1296	4.2671	2.2637	0	1.5288
Palladium	Pd			0	0.0263	0	0.0151	0	0.0701	0	0.0127
Phosphorus	P	0.27	N/A	0.9372	0.6322	0	0.0324	0.1603	0.044	0.0689	0.0144
Potassium	K	0.01	N/A	0.4644	0.0602	2.7161	0.3069	2.8299	0.4949	0.0825	0.0234
Rubidium	Rb			0.0053	0.0043	0.0184	0.0023	0.0184	0.0093	0	0.002
Selenium	Se			0.0406	0.0407	0	0.0024	0	0.0108	0	0.0021
Silicon	Si	1.61	N/A	9.0112	0.5675	17.596	1.4183	24.2969	4.0089	17.9733	5.1834
Silver	Ag			0	0.0312	0	0.0175	0	0.083	0	0.0151
Sodium	Na	0.01	N/A								
Strontium	Sr			0.1964	0.0686	0.0395	0.0078	0.0313	0.0112	0.0094	0.0031
Sulfate	SO_4^-			10.1716	8.9405	1.1604	0.2003	0.8688	1.3788	2.3243	3.4523
Sulfur	S	0.37	N/A	2.948	2.729	0.598	0.0509	0.2808	0.3884	0.6304	0.9627

		Motor Vehicle Exhaust - Gasoline		Coal Combustion		Highway Road Dust		Unpaved Road Dust		Refinery	
Thallium	Tl										
Tin	Sn			0	0.0527	0	0.0298	0	0.1464	0	0.0254
Titanium	Ti			0.4315	0.0651	0.3612	0.0313	0.5258	0.1289	0.6178	0.0711
Uranium	U										
Vanadium	V			0	0.0734	0.0288	0.0074	0	0.0646	0.0432	0.0084
Yttrium	Y			0	0.006	0.0046	0.0012	0	0.0146	0	0.0029
Zinc	Zn	0.49	N/A	0.0797	0.0341	0.0932	0.0256	0.0502	0.021	0.0166	0.003
Zirconium	Zr			0.0247	0.0043	0.0128	0.0025	0.0219	0.0168	0.0166	0.0022
Ammonium	NH4+	0.34	N/A	0.3476	0.1352	0	0.025	0	0.1317	0.3281	0.5565
Sodium ion	Na+										
Carbonate	CO_3^-										
Organic carbon II	OC2										
Organic carbon III	OC3										
Organic carbon IV	OC4										
EC I	EC1										
Chlorine atom	Cl-			0.0629	0.0221	3.4403	0.5505	0.1519	0.0755	0.0186	0.0074
EC III	EC3										
EC	EC	16.44	N/A	4.2763	3.0931	1.68	0.9817	0	2.9512	0	0.5283
Bromine Atom	Br			0.0147	0.0154	0.0037	0.0011	0	0.0078	0	0.0017
Organic carbon I	OC1										
EC II	EC2										
Sulfur dioxide	SO_2			7262.6687	7677.5681						
Potassium ion	K+			0.1109	0.0571	0.2295	0.1046	0.1263	0.0744	0.0115	0.0059

Source: USA EPA Speciate database http://www.epa.gov/ttnchie1/software/speciate/index.html

Part II

Element	Symbol	Residential Wood Burning		Oil Combustion		DE		Fly Ash		Incinerator	
		Weight %	Uncertainty	Weight %	Uncertainty	Weight %	Uncertainty	Weight %	Uncertainty	Weight %	Uncertainty
Aluminum	Al	0.0034	0.0103	0	0.05	0	0.01	1.5708	0.4755	1.15	0.83
Antimony	Sb	0.0002	0.0108	0	0.01	0	0.01	0.007	0.0218	0.01	0.15
Arsenic	As	0.0003	0.0016	0.02	0	0	0	0.001	0.0023	0	0.04
Barium	Ba	0.0093	0.0369	0	0.03	0.01	0.04	0.0303	0.0655	0.14	0.55
Cadmium	Cd	0.0013	0.0058	0	0.01	0	0.01	0	0.0154	0.01	0.08
Calcium	Ca	0.0664	0.0165	0	0.04	0.01	0.01	10.1398	1.7825	2.37	0.62
Chloride ion	Cl-	0.0028	0.0004					17.5498	1.5419		
Chromium	Cr	0.0003	0.0012	0.01	0.01	0	0	0.0054	0.001	0.02	0.02
Cobalt	Co	0.0005	0.0005	0.05	0.01	0	0	0.0015	0.0128	0	0.03
Copper	Cu	0.0002	0.0007	0.01	0.01	0	0	0.017	0.0013	0.08	0.1
Total carbon	TC	70.6416	7.1435	3.55	1.0855	98.94	17.859	1.4329	0.2009	55.79	27.5948
Gallium	Ga	0	0.0016	0.01	0	0	0	0.0013	0.0018	0	0.02
Gold	Au							0.0008	0.0033		
Indium	In	0.0021	0.0069	0	0.01	0	0.01	0	0.0164	0.01	0.1
Iron	Fe	0.0038	0.0017	0.68	0.1	0	0	0.8306	0.059	1.72	0.31
Lanthanum	La	0.0086	0.0431	0	0.04	0.02	0.05	0.0046	0.0868	8.43	61.15
Lead	Pb	0.0031	0.0018	0	0	0	0	0.0031	0.0031	14.56	11.69
Magnesium	Mg							0.4455	0.0465		
Manganese	Mn	0.003	0.0013	0	0	0	0	0.0426	0.0033	0.04	0.01
Mercury	Hg	0.0004	0.0027	0	0	0	0	0.0008	0.0025	27.63	47.27
Molybdenum	Mo	0	0.0024	0	0	0	0	0.0041	0.001	0.01	0.04
Nickel	Ni	0.0002	0.0005	2.36	0.23	0	0	0.0028	0.0004	0.01	0
Nitrate	NO_3^-	0.2025	0.0156	0	0	0.06	0.01	0	0.2192	5.5	4.55
Organic carbon	OC	49.4961	5.481	1.71	0.56	90.8	14.79	1.4329	0.1592	37.21	18.03
Palladium	Pd	0.0006	0.0047	0	0	0	0	0	0.0126	0.02	0.07
Phosphorus	P	0	0.0051	0	0.65	0.01	0.02	0.5808	0.2447	0.05	0.16
Potassium	K	0.6346	0.1008	0	0	0	0	24.4341	5.0076	1.28	0.86
Rubidium	Rb	0.0007	0.0007	0	0	0	0	0.0351	0.0026	0	0.02
Selenium	Se	0.0001	0.0008	0.03	0	0	0	0.0018	0.0003	0.01	0.01
Silicon	Si	0.0443	0.0167	0	0.09	0.01	0.01	4.0201	1.2886	4.42	1.82
Silver	Ag	0.0023	0.0054	0	0	0	0.01	0	0.0143	0.02	0.08
Sodium	Na							2.8137	0.2174		
Strontium	Sr	0.0006	0.0009	0	0	0	0	0.0406	0.0029	0.02	0.01
Sulfate	SO_4^{2-}	0.4553	0.0359	25.29	5.62	0.53	0.07	8.0717	0.6409	10.46	2.6
Sulfur	S	0.1533	0.0173	16.48	1.62	0.59	0.21	2.6349	0.1873	3.16	0.63
Thallium	Tl							0.0011	0.0025		
Tin	Sn	0.0006	0.0092	0	0.01	0	0.01	0.0067	0.0198	0.04	0.14
Titanium	Ti	0.001	0.012	0.01	0.01	0	0.01	0.058	0.0093	0.11	0.17
Uranium	U							0.0021	0.0052		

		Residential Wood Burning		Oil Combustion		DE		Fly Ash		Incinerator	
Vanadium	V	0.0007	0.005	0.4	0.04	0	0.01	0.0038	0.011	0.01	0.07
Yttrium	Y	0.0001	0.0011	0	0	0	0	0.0013	0.0021	0	0.02
Zinc	Zn	0.0762	0.0054	0.01	0	0.02	0.02	0.031	0.0023	0.57	0.39
Zirconium	Zr	0	0.0014	0	0	0	0	0.0039	0.0008	0	0.02
Ammonium	NH4+	0.1132	0.014	0.84	0.24	0.03	0.01	0.0234	0.022	7.41	7.81
Sodium ion	Na+			0.11	0.02	0	0.01	4.7518	0.3438	1.81	2.63
Carbonate	CO_3^-			0	0.0214	0.2577	0.4463				
Organic carbon II	OC2	7.513	0.6675								
Organic carbon III	OC3	8.9627	1.4665								
Organic carbon IV	OC4	2.7683	1.1919								
EC I	EC1	20.342	2.9324								
Chlorine atom	Cl^-	0.2874	0.0404	0.05	0.01	0.03	0.01	27.5797	8.1193	6.35	10.46
EC III	EC3	2.2878	0.4252								
EC	EC	21.1455	4.5813	1.84	0.93	8.14	10.01	0	0.1227	18.58	20.89
Bromine Atom	Br	0.0029	0.0011	0	0	0	0	0.0441	0.0032	0.19	0.3
Organic carbon I	OC1	25.1452	4.6648								
EC II	EC2	2.9362	1.2422								
Sulfur dioxide	SO_2										
Potassium ion	K^+	0.5208	0.0795	0.01	0.01	0	0.01	14.5473	1.3393	1.01	0.42

Source: U.S. EPA SPECIATE database http://www.epa.gov/ttnchie1/software/speciate/index.html

A.3.3. Receptor Model Results

Table A-56. $PM_{2.5}$ receptor model results ($\mu g/m^3$)

Sampling Site	Measured $PM_{2.5}$ Concentration	Vegetative Burning	Road Dust, Soil	$(NH_4)_2SO_4$	NH_4NO_3	Tailpipe	Brake Wear
Albany, NY 2000-2001	20.9	5.5	1.9	2.4	4.6	2.9	0.0
Birmingham, AL, 2000-2001	16.2	3.3	1.4	3.7	2.4	5.7	0.0
Houston, TX, 2000-2001	12.4	3.1	2.6	1.6	2.2	2.6	0.0
Long Beach, CA, 2000-2001	30.0	4.6	1.3	2.1	16.3	4.1	0.4
Las Vegas, NV, 2000-2001	2.5	1.0	2.0	0.5	0.3	1.5	0.0
El Paso, TX, 2000-2001	5.5	0.7	2.8	0.7	0.3	2.0	0.3
Westbury, NY, 2000-2001	11.5	1.7	0.7	5.2	2.2	5.3	0.0

Source: Abu-Allaban et al. (2007, 098575)

Table A-57. PM_{10} receptor model results (mass percent)

Sampling Site	Wood Smoke	Diesel	Gasoline Vehicles	Natural Gas Combustion	Vegetative Detritus	Tire Wear Debris
Apline, CA, 1994-1995	15.00	33.19	46.46		5.31	
Apline, CA, 1995	9.92	58.78	11.47		19.63	
Apline, CA, 1995	10.97	65.64	10.81		12.66	
Atascadero, CA, 1994-1995	44.22	22.16	26.44			6.91
Atascadero, CA, 1995	21.36	38.99	12.41		17.89	9.43
Atascadero, CA, 1995	73.45	18.11			3.14	5.31
Lake Arrowhead, CA, 1994-1995	6.86	46.55	33.92	2.73	9.85	
Lake Arrowhead, CA, 1995	4.85	65.20	7.40	4.95	17.65	
Lake Arrowhead, CA, 1995	9.91	38.90	46.70	0.79	3.66	
Lake Elsinore, CA, 1994-1995	12.72	44.01	18.61		4.21	20.42
Lake Elsinore, CA, 1995	17.13	74.72		0.26	7.81	
Lake Elsinore, CA, 1995[2]	6.84	38.48	10.85	0.21	15.55	28.01
Lancaster, CA, 1994-1995	22.49	43.14	20.56	0.45	3.73	9.78
Lancaster, CA, 1995	3.69	46.18	12.66	0.20	8.21	29.17
Lancaster, CA, 1995	34.89	37.30	7.33	0.61	7.78	11.93
Lompoc, CA, 1994-1995		18.16	49.65		5.89	26.38
Lompoc, CA, 1995	13.09	51.27	14.73		20.73	
Lompoc, CA, 1995		79.42	10.19		10.87	
Long Beach, CA, 1994-1995	10.12	43.24	16.49	0.13	3.97	26.00
Long Beach, CA, 1995	2.38	70.25	5.47	0.86	6.79	14.11
Long Beach, CA, 1995	14.32	56.80	6.15	0.72	5.34	16.61
Mira Loma, CA, 1994-1995	4.68	48.87	18.10		8.82	19.52
Mira Loma, CA, 1995	5.20	53.72	6.65		18.79	15.71
Mira Loma, CA, 1995	27.97	41.88	8.87		11.50	9.85
Riverside, CA, 1994-1995	14.14	46.67	12.03		6.83	20.31
Riverside, CA, 1995	6.20	52.15	7.93	0.16	14.54	19.06
Riverside, CA, 1995	25.28	47.65			6.91	20.17
San Dimas, CA, 1995	7.62	71.35	4.87	0.15	8.35	
San Dimas, CA, 1995	22.01	61.34	4.48	0.23	3.70	7.85
Santa Maria, CA, 1994-1995	18.66	23.99	22.03		5.58	8.15
Santa Maria, CA, 1995	12.94	52.57	11.87	0.27	9.63	12.78
Santa Maria, CA, 1995	12.24	48.13	10.79	0.47	18.04	15.05
Upland, CA, 1994-1995	20.33	46.39	14.08		4.49	14.70
Upland, CA, 1995	7.33	68.69	3.50	0.17	9.19	11.25
Upland, CA, 1995	28.10	46.52	4.90	0.33	10.30	9.81

Source: Manchester-Neesvig et al. (2003, 098102)

A.4. Exposure Assessment

A.4.1. Exposure Assessment Study Findings

Table A-58. Exposure Assessment Study Summaries

Adar et al. (2007, 098635)

Study Design	Cohort
Period	March 2002-June 2002
Location	St. Louis, Missouri
Population	Senior citizens exposed to traffic-related PM
Age Groups	60
Indoor Source	NR
Personal Method	Samples of FeNO were collected between 8:00 and 9:00 a.m. on the mornings before and after each trip. In the hours surrounding these samples, group-level measurements of particle concentrations also were collected using several continuous instruments installed on two portable carts. These carts were first positioned in a central location inside the participants' living facilities 24-h before each trip. The carts remained at the facilities until it was time for the trips, at which point they followed the participants from the health testing room, onto the bus, to the group activity, and to lunch. After the trip home aboard the bus, the carts were returned to the central location in the living facility where they remained until the conclusion of the health testing on the following morning. Continuous measurements of ambient particles and gases also were collected from a central monitoring station in East St. Louis, Illinois. Two portable carts containing continuous air pollution monitors were used to measure group-level micro-environmental exposures to traffic related pollutants, including $PM_{2.5}$, BC, and size-specific particle counts. $PM_{2.5}$ concentrations were measured continuously using a DustTrak aerosol monitor model 8520 with a Nafion diffusion dryer. Integrated samples of $PM_{2.5}$ mass also were collected using a Harvard Impactor for daily calibration of the trip and facility.
Periods	Continuous BC concentrations were measured using a portable aethalometer with a 2.5-µm impaction inlet. Particle counts were measured using a model CI500 optical particle counter with a modified flow rate of 0.1 cubic feet per minute.
Personal Size	NR
Microenvironment Size	$PM_{2.5}$
Ambient Size	$PM_{2.5}$, PM_{10}
Component(s)	BC, pollen and mold also assessed
Primary Findings	$PM_{2.5}$ exposures resulted in increased levels of FeNO in elderly adults, suggestive of increased airway inflammation. These associations were best assessed by microenvironmental exposure measurements during periods of high personal particle exposures. In pre-trip samples, both microenvironmental and ambient exposures to $PM_{2.5}$ were positively associated with FeNO. For example, an interquartile increase of 4 µg/m^3 in the daily microenvironmental $PM_{2.5}$ concentration was associated with a 13% [95% CI: 2-24) increase in FeNO. After the trips, however, FeNO concentrations were associated predominantly with microenvironmental exposures, with significant associations for concentrations measured throughout the whole day. Associations with exposures during the trip also were strong and statistically significant with a 24% (95% CI: 15-34) increase in FeNO predicted per interquartile increase of 9 µg/m^3 in $PM_{2.5}$. Although pre-trip findings were generally robust and the post-trip findings were generally robust, the post-trip findings were sensitive to several influential days.

Adgate et al. (2002, 030676)

Study Design	Comparison of outdoor, indoor and personal $PM_{2.5}$ in three communities.
Period	April-June, June-August, September-November, 1999
Location	Battle Creek, East St. Paul, and Phillips, Minnesota, constituting the Minneapolis-St. Paul metropolitan area.
Population	Adults in urban areas
Age Groups	Mean age 42 ± 10, range 24-64 yr
Indoor Source	No
Personal Method	Inertial impactors (PEM) in a foam-insulated bag with shoulder strap with the inlet mounted on the front.
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$
Ambient Size	$PM_{2.5}$
Component(s)	NR
Primary Findings	The relative level of concentrations report in other studies was duplicated. Outdoor < indoor < personal. On days with paired samples (n = 29), outdoor concentrations were significantly lower (mean difference 2.9 µg/m^3, p = 0.026) than outdoor at home.

Adgate et al. (2007, 156196)

Study Design	NR
Period	1999-; April 26-June 20, June 21-August 11, September 23-November 21
Location	Minneapolis-St. Paul metropolitan area
Population	NR
Indoor Source	Cigarette smoke, resuspension of house dust from carpets, furniture and clothes, and emissions from stoves and kerosene heaters (Leaderer et al., 1993; Ferro et al., 2004).
Personal Method	Personal monitoring was conducted for two consecutive days, and was conducted so that the two 24-h averages matched indoor (I) and personal (P) measurements were collected in concert with outdoor (O) samples in each community. Gravimetric concentrations for P and I were collected using inertial impactor environmental monitoring inlets and air sampling pumps. To obtain I measurements, monitors were placed inside each residence in a room where the participants reported spending the most waking hours. P measurements were obtained by carrying personal pumps in small bags. O samples were collected near the approximate geographic center of each neighborhood and monitors ran from midnight to midnight for two consecutive 24-h periods, followed by a day to change filters. Gravimetric O $PM_{2.5}$ concentrations were obtained using a federal reference method sampler.
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$
Ambient Size	$PM_{2.5}$
Component(s)	Ag, Al, Ca, Cd, Co, Cr, Cs, Cu, Fe, K, La, Mg, Mn, Na, Ni, Pb, S, Sb, Sc, Ti, Tl, V, Zn
Primary Findings	The relationships among P, I, and O concentrations varied across trace elements (TE). Unadjusted mixed-model results demonstrated that O monitors are more likely to underestimate than overestimate exposure to many of the TEs that are suspected to play a role in the causation of air pollution related health effects. These data also support the conclusion that TE exposures are more likely to be underestimated in a lower income and centrally located community than in a comparatively higher income community. Within the limits of statistical power for this sample size, the adjusted models indicated clear seasonal and community related effects that should be incorporated in long-term exposure estimates for this population.

Adgate et al. (2003, 040341)

Study Design	Time-series epidemiologic study
Period	April-November 1999; spring: 26 April-20 June; summer: 21 June-11 August; fall: 23 September-21 November
Location	Minneapolis-St. Paul, Minnesota
Population	Healthy non-smoking results
Age Groups	24-64 yr (mean age 42 ± 10)
Indoor Source	NR
Personal Method	Personal and indoor gravimetric PM concentrations were collected using $PM_{2.5}$ inertial impactor environmental monitoring inlets and air sampling pumps. Monitors were placed inside each participant's residence in the room where he/she reported spending the majority of their waking hours to obtain I measurements. Participants also carried personal pumps in small bags to obtain P measurements. Start times for indoor and personal monitors were always within a few minutes of each other. Gravimetric O and central site $PM_{2.5}$ concentrations were obtained using a federal reference method sampler and EPA site requirements for ambient sampling. Gravometric samples were collected near the approximate geographic center of each neighborhood, and monitors ran from midnight to midnight for 2 consecutive 24-h periods, followed by a day to change filters.
Personal Size	NR
Microenvironment Size	NR
Ambient Size	NR
Component(s)	NR
Primary Findings	$PM_{2.5}$ concentrations were higher than I concentrations, which were higher than O concentrations. In healthy non-smoking adults, moderate median for correlation between P and I; modest median for correlation between I and O; and minimal median correlation between P and O longitudinal were observed for $PM_{2.5}$ measurements. A sensitivity analysis indicated that correlations did not increase if the days with exposures to environmental tobacco smoke or occupational exposures were excluded. In the sample population neither P nor I monitors provided a highly correlated estimate of exposure to O $PM_{2.5}$ over time. These results suggest that the studies showing relatively strong longitudinal correlation coefficients between P and O $PM_{2.5}$ for individuals sensitive to air pollution health effects do not necessarily predict exposure to $PM_{2.5}$ in the general population.

Allen et al. (2003, 053578)

Study Design	Use of continuous light scattering data to separate indoor PM into indoor- and outdoor-generated components to enhance knowledge of the outdoor contribution to total indoor and personal PM exposures.
Period	November 1999-May 2001
Location	Seattle, WA
Population	Elderly people and children spending most of their time (up to 70%) indoors. The study included healthy elderly subjects, elderly with COPD and coronary heart disease (CHD), and child subjects with asthma.
Age Groups	Age n; 0-29 25; 30-59 36; >60 22; unknown 2
Indoor Source	Suggested (not identified)
Personal Method	NR. Indoor and outdoor sampling conducted
Personal Size	NR
Microenvironment Size	$PM_{2.5}$

Ambient Size	$PM_{2.5}$
Component(s)	S
Primary Findings	A recursive mass balance model can be successfully used to attribute indoor PM to its outdoor and indoor components and to estimate an avg Penetration, air exchange rate, deposition rate, and NH^{4+} for each residence.

Allen et al. (2007, 154226)

Period	Heating seasonOctober-February; Non-heating season March-September
Location	Seattle, WA
Population	NR
Age Groups	NR
Indoor Source	NR
Personal Method	Indoor and outdoor $PM_{2.5}$ was measured using a 10-l/min single-stage Harvard Impactor (HI) with 37-mm Teflon filters. The relationship between particle mass concentration and light scattering coefficient (bsp) was also measured on a continuous basis indoors and outdoors using nephelometers (model 902 and 903).
Personal Size	NR
Microenvironment Size	$PM_{2.5}$
Ambient Size	$PM_{2.5}$
Component(s)	S (measured by XRF)
Primary Findings	The authors showed that RM can reliably estimate F_{inf}. Simulation results suggest that the RM F_{inf} estimates are minimally impacted by measurement error. In addition, the average light scattering response per unit mass concentration was greater indoors than outdoors. Results show that the RM method is unable to provide satisfactory estimates of the individual components of F_{inf}. Individual homes vary in their infiltration efficiencies, thereby contributing to exposure misclassification in epidemiologic studies that assign exposures using ambient monitoring data. This variation across homes indicates the need for home-specific estimation methods, such as RM or S, instead of techniques that give average estimates of infiltration across homes.

Annesi-Maesano et al. (2007, 093180)

Study Design	Population based
Period	March 1999 to October 2000
Location	Bordeaux, France; Clermont-Ferrand, France; Créteil, France; Marseille, France; Strasbourg, France; Reims, France
Population	School children
Age Groups	10.4 ± 0.7 yr
Indoor Source	NR
Personal Method	$PM_{2.5}$ was monitored simultaneously in both schoolyards (proximity level) and fixed-site monitoring stations (city level) using 4L/min battery operated pumps attached to polyethylene filter sampling cartridges.
Personal Size	NR
Microenvironment Size	NR
Ambient Size	$PM_{2.5}$
Component(s)	NR
Primary Findings	Results show an increased risk for EIB and flexural dermatitis at the period of the survey, past year atopic asthma and SPT positivity to indoor allergens in children exposed to high levels of traffic-related air pollution ($PM_{2.5}$ concentrations exceeding 10 $\mu g/m^3$). Population based findings are also consistent with experimental data that have demonstrated that inhalation of traffic-related air pollutants either individually or in combination, can enhance the immune responses and airway response to inhaled allergens, such as pollens or house dust mites, in atopic subjects.

Balasubramanian and Lee (2007, 156248)

Study Design	Case study of 3 rooms of 1 flat on the 8th floor, and "outside the home."
Period	May 12-23, 2004
Location	Singapore
Population	Residents of an urban area in a densely populated country.
Age Groups	NR
Indoor Source	Time-activity logs identified tobacco smoking, cooking, household cleaning and general resident movements.
Personal Method	NR
Personal Size	NR
Microenvironment Size	$PM_{2.5}$
Ambient Size	$PM_{2.5}$
Primary Findings	I/O suggest that chemicals such as Cl^-, Na^+, Al, Co, Cu, Fe, Mn, Ti, V, Zn, and EC were derived from the migration of outdoor particles (I/O <1 or ~1).

Barn et al. (2008, 156252)

Study Design	Measure indoor F_{inf} of $PM_{2.5}$ from forest fires/wood smoke, effectiveness of high-efficiency particulate air (HEPA) filter air cleaners in reducing indoor $PM_{2.5}$, and to analyze the home determinants of F_{inf} and air cleaner effectiveness (ACE).
Period	2004-2005 (summer 2004 and 2005, winter 2004)
Location	British Columbia, Canada
Population	Homes affected by either forest fire smoke or residential wood smoke
Age Groups	NR
Indoor Source	NR
Personal Method	Personal Data RAM for ambient air sampling
Personal Size	Indoor home $PM_{2.5}$
Microenvironment Size	NR
Ambient Size	Outdoor home $PM_{2.5}$
Component(s)	NR
Primary Findings	Use of HEPA filter air cleaners can dramatically reduce indoor $PM_{2.5}$ concentrations. Number of windows and season predict F_{inf} ($p< 0.001$).

Baxter et al. (2007, 092726)

Study Design	Part of a prospective birth cohort study performed by the Asthma Coalition for Community, Environment, and Social Stress (ACCESS)
Period	2003-2005. Non-heating season: May to October; Heating season: December to March
Location	Boston (urban)
Population	Lower socio-economic status (SES) households
Age Groups	NR
Indoor Source	NR
Personal Method	$PM_{2.5}$ samples were collected with Harvard personal environmental monitors (PEM). NO concentrations were measured using Yanagisawa passive filter badges.
Personal Size	NR
Microenvironment Size	$PM_{2.5}$
Ambient Size	$PM_{2.5}$
Component(s)	EC
Primary Findings	The authors' regression models indicated that $PM_{2.5}$ was influenced less by local traffic but had significant indoor sources, while EC was associated with local traffic and NO_2 was associated with both traffic and indoor sources. However, local traffic was found to be a larger contributor to indoor NO_2 where traffic density is high and windows are opened, whereas indoor sources are a larger contributor when traffic density is low or windows are closed. Similarly, traffic contributed up to 0.2 $\mu g/m^3$ to indoor EC for homes with open windows, with an insignificant contribution for homes where windows were closed.; Comparing models based on p-values and using a Bayesian approach yielded similar results, with traffic density volume within a 50 m buffer of a home and distance from a designated truck route as important contributors to indoor levels of NO_2 and EC, respectively. However, results from the Bayesian approach also suggested a high degree of uncertainty in selecting the best model. The authors concluded that by utilizing public databases and focused questionnaire data they could identify important predictors of indoor concentrations for multiple air pollutants in a high-risk population.

Baxter et al. (2007, 092725)

Study Design	Simultaneous indoor and outdoor samples taken in 43 low SES homes in heating and non-heating seasons. Homes were selected from a prospective birth cohort study of asthma etiology (n = 25). Non-cohort homes were in similar neighborhoods (n = 18).
Period	2003-2005
Location	Boston, Massachusetts
Population	Lower SES populations in urban areas
Indoor Source	Home type, year built, tobacco smoke, opening windows, time spent cooking, use of candles or air freshener, cleaning activities, air conditioner use.
Personal Method	NR
Personal Size	NR
Microenvironment Size	$PM_{2.5}$
Ambient Size	NR
Component(s)	EC (m-1 x 10^{-5}); Ca (ng/m^3); Fe (ng/m^3); K (ng/m^3); Si (ng/m^3); Na (ng/m^3); Cl (ng/m^3); Zn (ng/m^3); S (ng/m^3); V (ng/m^3)
Copollutant(s)	NO_2
Primary Findings	The effect of indoor sources may be more pronounced in high-density multi-unit dwellings. Cooking times, gas stoves, occupant density and humidifiers contributed to indoor pollutants.

BéruBé et al. (2004, 007894)

Study Design	6 homes in Wales and Cornwall were monitored four times per year, inside samples in the living areas and outside the home.
Period	NR but < 2003
Location	Wales and Cornwall, UK
Population	Urban, suburban, and rural homes
Indoor Source	ETS, pets, cleaning, traffic load
Personal Method	NR
Personal Size	NR
Microenvironment Size	PM_{10}
Ambient Size	NR
Component(s)	NR
Primary Findings	There are greater masses of PM_{10} indoors, and that the composition of the indoor PM_{10} is controlled by outdoor sources and to a lesser extent by indoor anthropogenic activities, except in the presence of tobacco smokers. The indoor and outdoor PM_{10} collected was characterized as being a heterogeneous mixture of particles (soot, fibers, sea salt, smelter, gypsum, pollen and fungal spores).

Branis et al. (2005, 156290)

Study Design	Human exposure assessment in a university lecture hall
Period	Oct. 8, 2001-Nov. 11, 2001
Location	Prague, Czech Republic
Population	University students
Age Groups	NR
Indoor Source	Presence of people identified as a source of coarse particles; outdoor air identified as a source of indoor fine particles ($PM_{1.0}$ and $PM_{2.5}$)
Personal Method	Harvard impactors (HI) with membrane Teflon filters
Personal Size	PM_1, $PM_{2.5}$, PM_{10}
Microenvironment Size	PM_1, $PM_{2.5}$, PM_{10}
Ambient Size	PM_{10}
Component(s)	NR
Primary Findings	Presence of people is an important source of coarse particles indoors; Outdoor air may be an important source of fine indoor particles.

Brunekreef et al. (2005, 090486)

Study Design	Exposure assessment
Period	Winter and spring 1998-1999
Location	Amsterdam and Helsinki
Population	Elderly
Age Groups	50-84 yr
Indoor Source	NR
Personal Method	Amsterdam Gillian with made to fit bags with belt with GK2.05 cyclone samplers 4L/min; Helsinki BGI with shoulder strap or backpack with GK2.05 cyclone samplers 4 L/min.
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$
Ambient Size	$PM_{2.5}$
Component(s)	SO_4^{2-}
Primary Findings	In both cities, personal and indoor $PM_{2.5}$ were highly correlated with outdoor concentrations.

Chillrud et al. (2004, 054799)

Study Design	Repeated measures on a cohort of high school students in New York City
Period	Summer and winter of 1999 (eight weeks each)
Location	Manhattan, Bronx, Queens, Brooklyn, NY
Population	Persons traveling the subway
Age Groups	14-18 yr
Indoor Source	No
Personal Method	Sampling packs carried by subjects
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$ (home indoor and home outdoor)
Ambient Size	$PM_{2.5}$. Urban fixed-site and upwind fixed site operated for three consecutive 48-h periods each week.
Component(s)	Elemental Fe, Mn, and Cr are reported in this study out of 28 elements sampled.
Primary Findings	Personal samples had significantly higher concentration of Fe, Mn, and Cr than home indoor and ambient samples. The ratios of Fe (ng/µg of $PM_{2.5}$) vs Mn (pg/µg $PM_{2.5}$) showed personal samples to be twice the ratio for crustal material. Similarly for the Cr/Mn ratio. The ratios and strong correlations between pairs of elements suggested steel dust as the source. Time-activity data suggested subways as a source of the elevated personal metal levels.

Conner and Williams (2004, 156364)

Study Design	This is part of the EPA Baltimore PM Study of the Elderly.
Period	July-August, 1998
Location	Towson, Maryland
Population	65+ adults
Age Groups	65+ yr
Indoor Source	Personal sampling devices (PEM)
Personal Method	$PM_{2.5}$
Personal Size	$PM_{2.5}$
Microenvironment Size	NR
Ambient Size	NR
Primary Finding(s)	A greater variety of particles was observed in the personal samples compared to the fixed-location apartment samples.

Cortez-Lugo et al. (2008, 156368)

Study Design	Cohort
Period	Feb-Nov 2000
Location	Mexico City, Mexico
Population	Ambulatory adults with moderate to severe COPD, active smokers excluded
Age Groups	Adults
Indoor Source	carpeting, aerosol sprays used, boiler use and location, animals, mold, tobacco smoking, windows closed
Personal Method	Personal pumps with 37-mm Teflon filters, flow rate 4 l/min in a bag with shoulder strap. The impactor was near the breathing zone
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$, PM_{10}
Ambient Size	$PM_{2.5}$, PM_{10}
Component(s)	NR
Primary Findings	Indoor $PM_{2.5}$ concentrations explained 40% of the variability of personal exposure. The best predictors of personal exposure were indoor contact with animals (12%), mold (27%), being present during cooking (27%), and aerosol use (17%).

Crist et al. (2008, 156372)

Study Design	Indoor, outdoor, and personal monitoring
Period	January 1999-August 2000
Location	Ohio
Population	Fourth & fifth-grade children
Age Groups	9-11 yr old
Indoor Source	Filter, portable pump
Personal Method	Filter, $PM_{2.5}$
Personal Size	Indoor school; Filter, $PM_{2.5}$
Microenvironment Size	Outdoor school; Filter, $PM_{2.5}$
Ambient Size	$PM_{2.5}$
Component(s)	NR
Primary Findings	Higher correlation was observed between P and I compared with the correlation between either P and ambient (A) or I and A.

Delfino et al. (2004, 056897)

Study Design	Panel study with repeated measures
Period	Sep-Oct 1999 or Apr-Jun 2000
Location	Alpine, California
Population	Children
Age Groups	9-17 yr
Indoor Source	No
Personal Method	Personal dataRAM (pDR) carried at waist level using a fanny pack, shoulder harness, or vest.
Personal Size	0.1-10 μm
Microenvironment Size	PM_{10} and $PM_{2.5}$; measured immediately outside the house and in the living room of the home.
Ambient Size	PM_{10}
Copollutant(s)	O_3 and NO_2 measured at central site
Primary Findings	Percent predicted FEV_1 was inversely associated with personal exposure to fine particles. Also with indoor, outdoor and central site gravimetric $PM_{2.5}$, PM_{10}, and with hourly TEOM PM_{10}.

Delfino et al. (2006, 090745)

Study Design	Cohort. Measured daily expired NO (FeNO)
Period	Aug-Dec 2003
Location	Riverside and Whittier, California
Population	Children with asthma exacerbations in previous 12 months, non-smokers, non-smoking households
Age Groups	9-18 yr
Indoor Source	No
Personal Method	Wore a backpack during waking hours for $PM_{2.5}$, EC and OC, NO_2, temperature, and relative humidity. Exhaled air collected in Mylar bags to analyze for NO.
Personal Size	24-h $PM_{2.5}$; 1-h max $PM_{2.5}$; 8-h max $PM_{2.5}$; 24-h NO_2
Microenvironment Size	NR
Ambient Size	24-h $PM_{2.5}$; 24-h PM_{10}; 8-h max O_3; 8-h max NO_2; 24-h NO_2; 8-h max CO
Component(s)	24-h $PM_{2.5}$ EC; 24-h $PM_{2.5}$ OC
Primary Findings	The strongest positive associations were between FeNO and 2-day average pollutant concentrations. Per IQR increases 1.1 ppb FeNO/24 μg/m^3 personal $PM_{2.5}$.; 0.7 ppb FeNO/0.6 μg/m^3 personal EC; 1.6 ppb FeNO / 17 ppb personal NO_2 Ambient $PM_{2.5}$ and personal and ambient EC were significant only when subjects were taking inhaled corticosteroids. Subjects taking both inhaled steroids and antileukotrienes had no significant associations. Distributed lag models showed personal $PM_{2.5}$ in the preceding 5 h was associated with FeNO.

Diapouli et al. (2007, 156397)

Study Design	Exposure assessment. Sampling of schools, residence, private vehicle
Period	Schools- 11/2003-02/2004 and 10/2004-12/2004.; Residence- 10/2004; Vehicle- 10/204-12/2004
Location	Athens, Greece
Population	Primary school children
Age Groups	NR
Indoor Source	NR
Personal Method	Handheld portable Condensation Particle Counters (TSI, Model 3007) were used for all sampling locations. Primary schools indoor measurements were primarily conducted inside classrooms, at table height. However, at three of the schools, rooms of different uses were selected. These included a teachers' office (where smoking was permitted), a computer day lab (used by students only part of the day), and a library and gymnasium (where intense activity took place almost all day long). Outdoor measurements took place in the yard of each school. Residence samples were taken in a bedroom at breathing height and on the terrace, for indoor and outdoor samples, respectively. In-vehicle samples were taken by placing the CPC 3700 on the passenger seat while the vehicle drove along predetermined routes.
Personal Size	NR
Microenvironment Size	0.01-1 μm
Ambient Size	0.01-1 μm
Component(s)	NR
Primary Findings	The results showed that children attending primary schools in the Athens area are exposed to significant PM concentration levels, both indoors and outdoors. Vehicular emissions seem to be a major contributor to the measured outdoor concentration levels at the studied sites. Indoor PM concentrations appeared to be influenced by both vehicular emissions and indoor sources including cleaning activities, smoking, a high number of people in relation to room volume and furniture material (i.e., carpet). UFPs concentrations diurnal variation, both outside the schools and the residence, supports the close relation of UFPs levels with traffic density. Indoor concentrations within schools exhibited variability during the school day only when there were significant changes in room occupancy. 24-h variation of indoor concentrations at the residence were well correlated with the outdoor concentration (R^2 = 0.89).

Diapouli et al. (2008, 190893)

Study Design	Indoor, outdoor air monitoring of PM. To determine children exposure in school environment. To evaluate relationship between indoor and outdoor levels.
Period	Athens, Greece
Location	Primary schools
Population	NR
Indoor Source	Indoor PM_1, $PM_{2.5}$, PM_{10}, presence of children and activities of children in classrooms, infiltrated vehicular exhaust
Personal Method	Harvard PEM, Teflon filters Dust Trak Condensation particle counter
Personal Size	NR
Microenvironment Size	PM_1, $PM_{2.5}$, PM_{10}
Ambient Size	PM_1, $PM_{2.5}$, PM_{10}
Component(s)	NO_3^-, SO_4^{2-}
Primary Findings	High levels of PM_{10} and $PM_{2.5}$ measured indoors and outdoors. PM_{10} more variable spatially than $PM_{2.5}$. I/O ratio for PM_{10} and $PM_{2.5}$ close to 1 at almost all sites. Ratio of PM_1 smaller than 1 in all cases. Vehicular traffic presumed to be the main source of PM_1. Indoor $PM_{2.5}$ and PM_{10} levels dependent on the amount of activity in classroom and outdoor levels. Indoor SO_4^{2-} concentrations strongly associated with outdoor levels. Result suggests that SO_4^{2-} can be used as a proper surrogate for indoor PM of outdoor origin.

Ebelt et al. (2005, 056907)

Study Design	Personal exposure assessment related to health outcomes for a sensitive sub-population
Period	Summer 1998
Location	Vancouver, British Columbia, Canada
Population	16 persons who had COPD
Age Groups	Mean subject age 74 yr, Range 54 to 86
Indoor Source	Separated total personal exposure into “ambient” and “non-ambient” based on sulfate results and modeling.
Personal Method	24-h integrated filter sample
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$, PM_{10}, $PM_{10-2.5}$
Ambient Size	$PM_{2.5}$, PM_{10}, $PM_{10-2.5}$
Component(s)	SO_4^{2-}
Primary Findings	Ambient exposures and (to a lesser extent) ambient concentrations were associated with health outcomes. Total and nonambient particle exposures were not.

Farmer et al. (2003, 089017)

Study Design	Case control molecular epidemiology studies of carcinogenic environmental pollutants, particularly PAHs
Period	12 months
Location	Prague, Czech Republic (2 sites); Košice, Slovak republic; Sofia, Bulgaria
Population	Policeman and busdrivers usually working through busy streets in 8-10 h shifts and a control population.
Age Groups	Variable, range not stated
Indoor Source	NR
Personal Method	Personal Monitoring Devices; Blood and Urine Samples; Stationary Versatile Air Pollution Samplers (VAPS)
Personal Size	PM_{10}
Microenvironment Size	NR
Ambient Size	PM_{10}; $PM_{2.5}$ (not reported)
Component(s)	Extractable organic matter (EOM), B[a]P, c-PAHs
Primary Findings	EOM per PM_{10} was at least 2-fold higher in winter than in summer, and c-PAHs over 10-fold higher in winter than in summer. Personal exposure to B[a]P and to total c-PAHs in Prague ca. was 2-fold higher in the exposed group compared to the control group, in Košice ca. 3-fold higher, and in Sofia ca. 2.5-fold higher.

Ferro et al. (2004, 055387)

Study Design	Case study, 1 home
Period	Redwood City, California
Location	NR
Population	NR
Age Groups	NR
Personal Method	Co-located real-time particle counters and integrated filter samplers (Met-One Model 237B) were used to measure personal (PEM), indoor (SIM) and outdoor (SAM) PM concentrations. The PEM was attached to a backpack frame and worn by the investigator while performing prescribed activities. The SIM was attached to a six foot step-ladder with the intake at breathing height. The SAM was located under a two-sided roofed shed in the backyard of the home with the filter samplers supported by a metal stand and the real-time particle counters sitting on a table.
Personal Size	PM_5
Microenvironment Size	$PM_{2.5}$; PM_5
Ambient Size	$PM_{2.5}$; PM_5
Component(s)	NR
Primary Findings	The results of this study indicate that house dust resuspended from a range of human activities increases personal PM concentrations and this resuspension effect significantly contributes to the personal cloud. The results of this study also suggest that normal human activities that resuspend house dust may contribute significantly to the strong correlations found between personal exposure and indoor PM concentrations in previous studies. The PEM/SIM ratios for human activity presented in this paper are also in the range of those reported by previous studies.

Gadkari and Pervez (2007, 156459)

Study Design	Evaluation of relative source contribution estimates of various routes of personal RPM in different urban residential environments.
Period	Summer 2004 (March 15-June 15)
Location	Chattisgarh, India
Population	All likely. Not specified
Age Groups	21-61 yr, average age 40 ± 15 yr
Indoor Source	No
Personal Method	Personal respirable dust samplers (RDS) with GFF
Personal Size	RPM
Microenvironment Size	NR
Ambient Size	RPM
Component(s)	Fe, Ca, Mg, Na K, Cd, Hg, Ni, Cr, Zn, As, Pb, Mn and Li
Primary Findings	Authors concluded that "(1) indoor activities and poor ventilation qualities are responsible for major portion of high level of indoor RPM, (2) majority of personal RPM is greatly correlated with residential indoor RPM, (3) time–activity diary of individuals has much impact on relationship investigations of their personal RPM with their respective indoor and ambient-outdoor RPM levels; as reported in earlier reports and (4) residential indoors, local road-traffic and soil-borne RPMs are the dominating routes of personal exposure compared to ambient outdoor RPM levels."

Gauvin et al. (2002, 034893)

Study Design	Fine particle exposure assessment for children in French urban environments, part of VESTA study
Period	March 1998-December 2000
Location	Paris, Grenoble, Toulouse, France
Population	Children aged 8-14 yr
Indoor Source	ETS from mother, rodents at home.
Personal Method	SKC pump 4 Lpm with $PM_{2.5}$ inlet and 37 mm, 2 micron Teflon filter
Personal Size	$PM_{2.5}$
Microenvironment Size	NR
Ambient Size	PM_{10}
Component(s)	NR
Primary Findings	The final model explains 36% of the between subjects variance in $PM_{2.5}$ exposure, with ETS contributing more than a third to this.

Graney et al. (2004, 053756)

Study Design	The study was designed to assess the trace metal quantification abilities of several analytical methods to measure the total as well as soluble amounts of metals with $PM_{2.5}$ collected from indoor and PM samples. (X-ray fluorescence and instrumental neutron activation analysis)
Location	Retirement facility in Towson, Maryland
Population	Retirement facility with subjects who spent 94% of their time indoors
Age Groups	Mean age = 84 yr
Indoor Source	NR
Personal Method	Measured using personal exposure monitors (MSP Inc) with nozzle to remove particles > 4 µm
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$
Ambient Size	NR
Component(s)	42 elements were analyzed for in the $PM_{2.5}$ samples collected from personal and well as indoor samples
Primary Findings	Most of the extractable components of the metals were in a water-soluble form suggesting a high potential for bioavailability of elements from respiratory exposure to $PM_{2.5}$. Based on comparison of trace metals in central I site vs. P samples, resident activities result in exposure to higher concentration of soluble trace metals.

Haverinen-Shaughnessy et al. (2007, 156526)

Study Design	Cross-sectional
Period	Winter, year not reported
Location	Eastern Sweden
Population	Elementary school teachers
Age Groups	NR
Personal Method	Button inhalable aerosol samplers
Personal Size	Particle mass
Microenvironment Size	Particle mass
Ambient Size	NR
Component(s)	Absorbance coefficient/m x 10^{-5}; Total fungi (spores/m^3); Total bacteria (cells/m^3); Viable fungi MEA (CFU/m^3); Viable fungi DG18 (CFU/m^3); Viable bacteria (CFU/m^3)
Primary Findings	The recall period of 7 days provided the most reliable data for health effect assessment. Both personal exposure and concentrations of pollutants at home were more frequently associated with health symptoms than work exposures.

Ho et al. (2004, 056804)

Study Design	Human exposure assessment
Period	25 Sept. 2002 to 8 March 2003
Location	Hong Kong
Population	Occupied buildings located near major roadways
Age Groups	NR
Indoor Source	Yes. Regression of indoor versus outdoor concentrations of OC and EC revealed an indoor source of OC not present for EC, presumably due to such activities of cooking, smoking, and cleaning.
Personal Method	Co-located mini-volume samplers (flow rate 5 L/min) and Partisol model 2000 sampler with 2.5 μm inlet. All samples on 47 mm Whatman quartz microfiber filters, weighed on an electronic microbalance. Analyzed for OC and EC using DRI Model 2001 Thermal/Optical Carbon Analyzer.
Personal Size	$PM_{2.5}$
Microenvironment Size	NR
Ambient Size	$PM_{2.5}$
Component(s)	OC, EC, OM, TC
Primary Findings	The major source of indoor EC, OC, and $PM_{2.5}$ appears to be penetration of outdoor air, with a much greater attenuation in mechanically ventilated buildings.

Hoek et al. (2008, 156554)

Study Design	Exposure assessment, characterizing indoor/outdoor particle relationships
Period	October 2002-March 2004
Location	4 European cities Amsterdam, Athens, Birmingham, Helsinki
Population	Urban populations
Age Groups	NR
Indoor Source	Smoking, candle burning, cooking/frying
Personal Method	No personal exposure assessment was conducted
Personal Size	NR
Microenvironment Size	PM_{10}, $PM_{2.5}$, $PM_{10-2.5}$, Ultrafine (UFP)
Ambient Size	PM_{10}, $PM_{2.5}$, $PM_{10-2.5}$, UFP
Component(s)	soot, sulfate
Primary Findings	Correlation between 24-h average central site and indoor concentrations was lower for UFP than for $PM_{2.5}$, soot, or SO_4^{2-}, probably related to greater losses during infiltration due to smaller particle size. Infiltration factors for UFP and $PM_{2.5}$ were low.

Hopke et al. (2003, 095544)

Study Design	Exposure assessment
Period	26 July to 22 August 1998
Location	Retirement facility in Towson, MD
Population	Elderly residents
Age Groups	Mean age of 84
Indoor Source	Ammonium sulfate and ammonium nitrate, secondary sulfate, OC, and motor vehicle exhaust
Personal Method	Inertial impactor PEM in the breathing zone of the subjects
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$
Ambient Size	$PM_{2.5}$
Component(s)	SO_4^{2-}
Primary Findings	Personal exposures were influenced by a combination of indoor and outdoor factors. Indoor factors included gypsum, personal grooming products, and an unknown indoor source. Outdoor factor included SO_4^{2-}, soil, and an unknown factor. Outdoor factors accounted for 63% of personal exposure, and SO42- was the largest ambient contributor to personal exposure (48%).

Jacquemin et al. (2007, 156600)

Study Design	Assessment of relationship between outdoor and personal concentrations of $PM_{2.5}$ absorbance and sulfur among post-myocardial infarction patients
Period	January 2004-June 2004
Location	Barcelona, Spain
Population	Survivors of a myocardial infarction exposed to ETS
Age Groups	n = 38, including 32 and 15 over age 64.
Indoor Source	ETS
Personal Method	Personal samplers (BGI GK2.05 cyclones and battery operated BGI AFC400S pumps)
Personal Size	$PM_{2.5}$
Microenvironment Size	NA
Ambient Size	$PM_{2.5}$
Component(s)	S
Primary Findings	Ambient measurements of light extinction and S can be used as surrogates to personal $PM_{2.5}$ exposure, especially for those exposed to ETS.

Janssen et al. (2005, 088692)

Study Design	Panel Study
Period	Amsterdam 11/2/1998-6/18/1999; Helsinki 11/1/1998-4/30/1999
Location	Amsterdam, The Netherlands; Helsinki, Finland
Population	Elderly Cardiovascular Patients
Age Groups	50-84 yr
Indoor Source	No
Personal Method	Personal $PM_{2.5}$ GK2.05; cyclones; indoor & outdoor Harvard Impactors; Reflectance EEL 43 reflectometers; Elemental Composition Tracor Spectrace 5000 ED-XRF system
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$
Ambient Size	$PM_{2.5}$
Component(s)	Estimated EC, elemental composition of a subset of personal, indoor and outdoor samples
Primary Findings	For most elements, personal and indoor; concentrations were lower than and highly correlated with outdoor concentrations. The highest correlations (median r = 0.9) were found for sulfur and particle absorbance (EC), which both represent fine; mode particles from outdoor origin. Low correlations were observed for elements that represent the coarser part of the $PM_{2.5}$ particles (Ca, Cu, Si, Cl^-).

Jedrychowski et al. (2006, 156606)

Study Design	Prospective cohort
Period	11/2000-3/2003
Location	Krakow, Poland
Population	Non-smoking pregnant women
Age Groups	Yes
Personal Method	Personal Exposure Monitor Sampler (PEMS, Harvard; School of Public Health)
Personal Size	$PM_{2.5}$
Microenvironment Size	NR
Ambient Size	PM_{10}
Component(s)	NR
Primary Findings	The contribution of the background ambient PM_{10} level was a very strong determinant of the total personal exposure to $PM_{2.5}$, and it explained about 31% of variance between the subjects.

Johannesson et al. (2007, 156614)

Study Design	Cohort
Period	Spring and fall seasons of 2002 and 2003
Location	Gothenburg, Sweden
Population	General adult population
Age Groups	23-51 yr
Indoor Source	NR
Personal Method	Fine particles were measured for 24 h using both personal and stationary monitoring equipment. Personal monitoring of $_{PM2.5}$ and PM_1 was carried out simultaneously with parallel measurements of $PM_{2.5}$ and PM_1 indoors in living rooms and outside the house on a balcony, porch, etc. In addition, urban background $PM_{2.5}$ levels were measured. Personal monitoring was performed in two ways. The 20 randomly selected subjects carried personal monitoring equipment for $PM_{2.5}$ only, while the 10 staff members carried two pieces of personal monitoring equipment at the same time. On the first measuring occasion, the staff members carried one $PM_{2.5}$ cyclone and one PM_1 cyclone. On the second occasion, duplicate monitors for $PM_{2.5}$ were used. For personal and residential monitoring, the BGI Personal Sampling Pump was used together with the GK2.05 cyclone for $PM_{2.5}$ sampling and the Triplex cyclone SCC1.062 for PM_1sampling. The personal sampling pump was placed in a small

	shoulder bag and the cyclone attached to the shoulder strap near the subject's breathing zone. The personal monitoring equipment was carried by the subject during awake time. During the night, it was placed in the living room. For indoor monitoring in living rooms, cyclones ($PM_{2.5}$ and PM_1) were placed at about 1.5 m above the floor. The same setup was used for residential outdoor monitoring. The urban background monitor was placed on top of a roof somewhat south of the city center but not near any major highway.
Personal Size	$PM_{2.5}$; PM_1
Microenvironment Size	$PM_{2.5}$; PM_1
Ambient Size	$PM_{2.5}$; PM_1
Component(s)	BS
Primary Findings	Personal exposure of $PM_{2.5}$ correlated well with indoor levels, and the associations with residential outdoor and urban background concentrations were also acceptable. Statistically significantly higher personal exposure compared with residential outdoor levels of $PM_{2.5}$ was found for nonsmokers. PM_1 made up a considerable proportion (about 70–80%) of $PM_{2.5}$. For BS, significantly higher levels were found outdoors compared with indoors, and levels were higher outdoors during the fall than during spring. There were relatively low correlations between particle mass and BS. The urban background station provided a good estimate of the residential outdoor concentrations of both $PM_{2.5}$ and BS2.5 within the city. The air mass origin affected the outdoor levels of both $PM_{2.5}$ and BS2.5; however, no effect was seen on personal exposure or indoor levels.

Kaur et al. (2005, 086504)

Study Design	Exposure assessment, evaluation of exposures between modes of transport, routes, timing
Period	April 28-May 23, 2003
Location	Street canyon intersection in Central London, UK
Population	Users of an urban street canyon intersection
Age Groups	NR
Indoor Source	NR
Personal Method	$PM_{2.5}$ measured usnig high-flow gravimetric personal samplers ($PM_{2.5}$) operating at a flow rate of 16 l/min carried in a backpack with sampling head positioned in personal breathing zone. UFP measured using TSI P-TRAK particle counters in which isopropyl alcohol condenses to form droplets that can be easily counted by a photodetector as they pass through a laser beam.
Personal Size	$PM_{2.5}$, UFP (0.02-1.0um)
Microenvironment Size	$PM_{2.5}$, UFP (0.02-1.0um)
Ambient Size	$PM_{2.5}$
Component(s)	NR
Primary Findings	Personal exposures to $PM_{2.5}$ while walking were significantly lower then while riding in a car or taxi, likely a function of greater distance to roadside. No significant differences in $PM_{2.5}$ were observed between exposures on the high traffic road compared with the backroad. Personal exposure levels were lowest during midday measurements for $PM_{2.5}$ and highest in the early evening. Personal exposures to ultrafine particles were lowest while walking and highest while riding the bus. Exposures to ultrafine particles were also significantly higher on the high traffic road and during morning measurements. Exposure to ultrafine particles were highest in the morning, likely the result of peak traffic density in the morning. Exposure assessment also revealed that the background and curbside monitoring stations were not representative of the personal exposure of individuals to $PM_{2.5}$ and CO at and around a street canyon intersection.

Kaur et al. (2005, 088175)

Study Design	Personal exposure assessment of pedestrians walking along high-traffic urban road
Period	April 19, 2004-June 11, 2004
Location	Central London, UK
Population	Pedestrians
Age Groups	NR
Indoor Source	NR
Personal Method	$PM_{2.5}$ gravimetric filter measurement, UFP (0.02-1 µm) P-TRAK device, reflectance reflectometer measurement of $PM_{2.5}$ filter
Personal Size	$PM_{2.5}$, UFP (0.02-1 µm)
Microenvironment Size	NR
Ambient Size	$PM_{2.5}$, UFP (0.02-1 µm)
Component(s)	Absorbance of $PM_{2.5}$ filter
Primary Findings	$PM_{2.5}$ pedestrian exposure was well correlated with and above background fixed-site monitoring levels. PM pedestrian exposure was influenced by proximity to curbside and the side of the road walked on.

Kim et al. (2005, 156640)

Study Design	Panel study
Period	8/1999-11/2001
Location	Toronto, Canada
Population	Cardiac-compromised patients
Age Groups	Mean age 64 yr
Indoor Source	Gas range (68%); indoor grill (11%); outdoor barbeque (30%); Gas heating fuel (68%); Oil heating fuel (7%)
Personal Method	Rupprecht and Patashnick ChemPass Personal Sampling System
Personal Size	$PM_{2.5}$
Microenvironment Size	NR
Ambient Size	$PM_{2.5}$
Component(s)	NR
Primary Findings	Personal $PM_{2.5}$ exposures were higher than outdoor ambient levels. Personal $PM_{2.5}$ exposures levels were correlated with ambient levels, mean r = 0.58

Koistinen et al. (2004, 156655)

Study Design	Representative Population-based study
Period	Oct 1996-Dec 1997
Location	Helsinki, Finland
Population	Non-smoking adults not exposed to environmental tobacco smoke.
Age Groups	Adults 25-55 yr
Indoor Source	Soil from outdoors, cooking, smoking, aerosol cleaners, sea salt, combustion sources
Personal Method	Integrated 24-h filter sample
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$
Ambient Size	$PM_{2.5}$
Component(s)	BS
Primary Findings	Population exposure assessment of $PM_{2.5}$, based on outdoor fixed-site monitoring, overestimates exposures to outdoor sources like traffic and long-range transport and does not account for the contribution of significant indoor sources.

Kousa et al. (2001, 025270)

Study Design	Population based exposure assessment
Period	October 1996 to June 1998
Location	Helsinki, Finland; Basel, Switzerland; Prague, Czech Republic; Athens, Greece
Population	Adult urban populations
Age Groups	25-55 yr
Indoor Source	Sometimes ETS
Personal Method	Integrated 48-h filter sample
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$
Ambient Size	$PM_{2.5}$, PM_{10}
Component(s)	NR
Primary Findings	Throughout the study, the highest correlations were those between personal exposures and indoor concentrations, which suggests that indoor sources were important. Correlations were generally lower between ambient concentrations and personal exposures.

Koutrakis et al. (2005, 095800)

Study Design	Panel study
Period	Baltimore 6/28/98-8/22/98 (summer), 2/1/99-3/16/99 (winter); Boston 6/13/99-7/23/99 (summer), 2/1/00-3/12/00 (winter)
Location	Baltimore, MD Boston, MA
Population	Healthy older adults, children, adults with COPD
Age Groups	Children 9-13 y/o; Seniors 65+ y/o
Indoor Source	NR
Personal Method	Personal exposure samples of $PM_{2.5}$; were collected using a specially designed multipollutant sampler (Demokritou et al. 2001). $PM_{2.5}$ was collected using personal environmental monitors (PEMs) and 37-mm; Teflon filters (Teflo, Gelman Sciences, Ann Arbor MI).
Personal Size	$PM_{2.5}$
Microenvironment Size	NR
Ambient Size	$PM_{2.5}$
Component(s)	EC, SO_4^{2-}
Primary Findings	Ambient $PM_{2.5}$ and SO_4^{2-} are strong predictors of respective personal exposures. Ambient SO_4^{2-} is a strong predictor of personal exposure to $PM_{2.5}$. Because $PM_{2.5}$ has substantial indoor sources and SO_4^{2-} does not, the investigators; concluded that personal exposure to SO_4^{2-} accurately reflects exposure to ambient $PM_{2.5}$ and therefore the ambient component of personal exposure to $PM_{2.5}$ as well.

Lai et al. (2004, 056811)

Study Design	Personal exposure study
Period	December 1998-February 2000
Location	Oxford, UK
Population	Adults
Age Groups	25-55 yr (avg = 41)
Indoor Source	Cooking, active smoking, passive smoking heating by gas heater
Personal Method	Integrated 48-h filter samples
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$
Ambient Size	$PM_{2.5}$
Component(s)	Ag, Cr, Mn, Si, Al, Cu, Na, Sm, As, Fe, Ni, Sn, Ba, Ga, P, Sr, Br, Ge, Pb, Ti, Ca, Hg, Rb, Tl, Cd, I, S, Tm, Cl, K, Sb, V, Co, Mg, Se, Zn, Zr
Primary Findings	Personal exposures were influenced by both indoor and ambient sources, and indoor levels exceeded ambient levels for $PM_{2.5}$ as well as for VOCs and eight other compounds. Correlation between personal and indoor $PM_{2.5}$ was 0.60 ($p < 0.001$).

Larson et al. (2004, 098145)

Study Design	Time-series epidemiologic study
Period	Sep 26, 2000-May 25, 2001
Location	Seattle, Washington
Population	"Susceptible Populations"
Age Groups	Time-activity diary
Personal Method	Harvard Personal Environmental Monitor
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$ outside subject's residence, and inside residence
Ambient Size	$PM_{2.5}$ at Central outdoor site (downtown Seattle)
Component(s)	Light absorbing carbon (LAC) and trace elements
Primary Findings	Five sources of $PM_{2.5}$ identified vegetative burning, mobile emissions, secondary sulfate, a source rich in chlorine, and crustal-derived material. The burning of vegetation (in homes) contributed more $PM_{2.5}$ mass on average than any other sources in all microenvironments.

Li et al. (2003, 047845)

Study Design	Concurrent 10-min avg indoor and outdoor concentrations of PM_{10} and $PM_{2.5}$ were recorded for 2 days each in 10 homes with swamp coolers
Period	Summer 2001
Location	El Paso, Texas
Population	Cooking, cleaning, walking
Age Groups	NR
Indoor Source	NR
Personal Method	$PM_{2.5}$ and PM_{10}; indoor and outdoor; tapered element oscillating microbalance (TEOM) instruments. 2 days were monitored for $PM_{2.5}$, and 2 for PM_{10}.
Personal Size	NR
Microenvironment Size	NR
Primary Findings	Evaporative coolers were found to act as PM filters, creating indoor concentrations approximately 40% of outdoor PM_{10} and 35% of outdoor $PM_{2.5}$, regardless of cooler type.

Liu et al. (2003, 073841)

Study Design	Comprehensive exposure assessment
Period	1999-2001
Location	Seattle, WA
Population	High-risk sub populations
Age Groups	Children 6-13 yr, elderly 65-90 yr (one person was below 65, but his/her age was not specified)
Personal Method	Harvard Personal Environmental Monitor for $PM_{2.5}$ ($HPEM_{2.5}$)
Personal Size	$PM_{2.5}$, PM_{10}
Microenvironment Size	$PM_{2.5}$, PM_{10}
Ambient Size	$PM_{2.5}$, PM_{10}
Primary Findings	Average personal $PM_{2.5}$ exposure was similar to ambient $PM_{2.5}$ concentrations but much higher than average indoor concentrations. Personal, indoor, and outdoor $PM_{2.5}$ and PM_{10}, as well as the ratio PM2.5/PM10, were all significantly higher during the winter. Personal $PM_{2.5}$ and PM_{10} exposures were highest for the children in the study.

Lung et al. (2007, 156719)

Period	Weekdays between Nov 1998 and Feb 1999
Location	6 communities in Taiwan, China 2 in Taipei, 2 in Taichung, and 2 in Kaohsiung. Sites are industrial, commercial, residential and mixed.
Age Groups	18 to >70
Indoor Source	Being in kitchen, park, major boulevard, stadium, incense burning, household work, factory, environmental tobacco smoke, traffic, ventilation conditions
Personal Method	Personal Environmental Monitor with a SKC personal pump at 2 L/min, 37 mm Teflon filters
Personal Size	PM_{10}
Microenvironment Size	PM_{10}
Ambient Size	PM_{10}
Component(s)	None
Primary Findings	Outdoor rather than indoor levels contributed significantly to personal exposure. Important factors include time spend outdoors and on transportation, riding a motorcycle, passing by factories, cooking or being in the kitchen, incense burning at home.

Meng et al. . (2005, 081194)

Study Design	Evaluation of the use of central-site PM, rather than actual exposure, in PM epidemiology
Period	Summer 1999-spring 2001
Location	3 cities: Houston (TX), Los Angeles County (CA), and Elizabeth (NJ)
Population	NR
Age Groups	NR
Indoor Source	NR
Personal Method	MSP monitors on the front strap of the sampling bag near the breathing zone. Pump, battery, and motion sensor were on the hip or back.
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$
Ambient Size	$PM_{2.5}$
Component(s)	EC, OC, S, Si
Primary Findings	Use of central-site $PM_{2.5}$ as an exposure surrogate underestimates the bandwidth of the distribution of exposures to PM of ambient origin.

Meng et al. (2005, 058595)

Study Design	RIOPA study matched indoor home & outdoor exposure assessment
Period	May-October (hot); November-April (cool); (1999-2001)
Location	Los Angeles County, CA; Elizabeth, NJ; Houston, TX
Population	Non-smoking homes
Indoor Source	Combustion (primary); atmospheric (secondary); sulfate, organics, nitrates; mechanically (abrasion) generated.
Personal Method	Filter (not specified)
Personal Size	NR
Microenvironment Size	Indoor home.; $PM_{2.5}$
Ambient Size	$PM_{2.5}$, outdoor home
Component(s)	Organic and elemental carbon; 24 elements (metals).
Primary Findings	The median contribution of ambient sources to indoor $PM_{2.5}$ using the mass balance approach was 56% for all study homes, 63% for California, 52% for New Jersey, and 33% for Texas.

Molnár et al. (2005, 156772)

Study Design	Indoor/outdoor exposure assessment related to domestic wood burning
Period	10 February to 12 March 2003
Location	Hagfors, Sweden
Population	Adult residents of Hagfors
Age Groups	NR
Indoor Source	NR
Personal Method	Integrated filter samples with a dichotomous virtual impactor to separate $PM_{10\text{-}2.5}$ from $PM_{2.5}$
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{10\text{-}2.5}$, $PM_{2.5}$
Ambient Size	$PM_{10\text{-}2.5}$, $PM_{2.5}$
Component(s)	BS, S, Cl, K, Ca, Mn, Fe, Cu, Zn, Br, Rb, Pb
Primary Findings	Wood burning made statistically significant contributions to personal exposure to K, Ca, and Zn. Cl, Mn, Cu, Rb, Pb, and BS were found to be potential personal exposures from wood smoke, but their association was not always statistically significant. S had no significant association with personal exposure to wood smoke.

Molnár et al. (2006, 156773)

Study Design	Cross-sectional
Period	Autumn and spring in 2002 and 2003
Location	Goteborg, Sweden,
Population	Persons living in urban settings
Age Groups	20 subjects 20-50 yr randomly selected from the population and 10 from departmental colleagues.
Indoor Source	NR
Personal Method	Integrated filter samples with cyclones for $PM_{2.5}$ and PM_1 cut points
Personal Size	$PM_{2.5}$ and PM_1
Microenvironment Size	NR
Ambient Size	NR
Component(s)	S, Cl, K, Ca, Ti, V, Mn, Fe, Ni, Cu, Zn, Br, Pb
Primary Findings	Personal exposure to Cl, K, Ca, Ti, Fe, and Cu in PM2.5 were significantly higher than outdoor and central site ambient concentrations, and personal exposure to Cl, Ca, Ti, Fe, and Br were also significantly higher than indoor levels. In most cases, indoor concentrations were not higher than outdoor concentrations.

Na and Cocker (2005, 156790)

Study Design	Human exposure assessment
Period	Sept. 2001-January 2002
Location	Mira Loma, CA
Population	Residential homes and a high school
Age Groups	NR
Indoor Source	Indoor EC (elemental carbon) concentrations primarily of outside origin; Indoor $PM_{2.5}$ significantly influenced by indoor OC (organic carbon) sources, including indoor smoking.
Personal Method	Integrated filter samples for $PM_{2.5}$
Personal Size	$PM_{2.5}$
Microenvironment Size	NR
Ambient Size	$PM_{2.5}$
Component(s)	EC, OC
Primary Findings	Indoor $PM_{2.5}$ was significant influenced by indoor OC sources. Indoor EC sources were predominantly of outdoor origin.

Naumova et al. (2003, 089213)

Study Design	RIOPA Study-PAH partitioning indoor and outdoor pollutants to evaluate the hypothesis that outdoor air pollution contributed strongly to indoor air pollution.
Period	July 1999-June 2000
Location	Los Angeles, CA, Houston, TX, Elizabeth, NJ
Population	Houses
Age Groups	NR
Indoor Source	NR
Personal Method	Modified MSP Samplers, 37 mm quartz filter
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$
Ambient Size	$PM_{2.5}$
Component(s)	OC, EC
Primary Findings	Both EC and OC were associated with gas/particle partitioning of PAHs, with EC being a better predictor. High correlation between EC and OC suggests that PAHs adsorb onto PM containing EC during combustion.

Nerriere et al. (2005, 089481)

Study Design	Exposure assessment with stratified sampling of children and adults in 3 environments: high traffic emissions, local industrial sources, and urban background.
Period	"Hot" season May-June and "cold" season Feb-Mar. Grenoble in 2001, Paris in 2002, Rouen in 2002-2003, Strasbourg 2003.
Location	Grenoble, Paris, Rouen, and Strasbourg, France
Population	Persons living, working, or going to school in 3 urban areas one highly exposed to traffic emissions, one influenced by local industrial sources, and a background urban environment. Industrial sources of pollution were present in each city.
Age Groups	6-13 yr and 20-71 yr. All non-smokers and not exposed to environmental tobacco smoke or industrial air pollution.
Indoor Source	NR
Personal Method	Rucksack with Harvard ChemPass
Personal Size	$PM_{2.5}$, PM_{10}
Microenvironment Size	NR
Ambient Size	$PM_{2.5}$, PM_{10}
Copollutant(s)	NO_2
Primary Findings	The difference between ambient air concentrations and average total exposure is pollutant specific. $PM_{2.5}$ and PM_{10} concentrations underestimate population exposures across almost all cities, season, and age groups, but the opposite is true for NO_2.

Noullett et al (2006, 155999)

Study Design	Cohort
Period	5 February to 16 March 2001
Location	Prince George, British Columbia
Population	Children
Age Groups	10-12 yr
Indoor Source	NR
Personal Method	$PM_{2.5}$ Harvard Personal Environment Monitors ($HPEM_{2.5}$)
Personal Size	$PM_{2.5}$
Microenvironment Size	NR
Ambient Size	$PM_{2.5}$
Component(s)	SO_4^{2-}, ABS (light absorbing carbon)
Primary Findings	Thermal inversions were associated with personal exposures as well as ambient $PM_{2.5}$ concentrations and likely caused observed spatial variability. However, ambient sampling locations were correlated in time. Similar observations were made for SO_4^{2-} and ABS.

Rojas-Bracho et al. (2004, 054772)

Study Design	Cohort study with repeated measures.
Period	Winter or summer of 1996-1997
Location	Boston, Massachusetts
Population	COPD patients
Age Groups	Adult
Indoor Source	Housecleaning, cooking, transport in motor vehicles, low-effort home activities, moderate-effort home activities, activities in public places, and resting or sleeping.
Personal Method	PEM
Personal Size	$PM_{2.5}$, PM_{10}, and $PM_{10-2.5}$
Microenvironment Size	$PM_{2.5}$, PM_{10}, & $PM10\text{-}2.5$
Ambient Size	NR
Component(s)	NR
Primary Findings	During both seasons, personal exposures were higher than indoor or outdoor means, except during the winter when indoor concentrations were higher than the personal or outdoor.

Rotko et al. (2002, 037240)

Study Design	European multi-city air pollution study
Period	Athens, Greece:26 January 1997–4 June 1998 Basel, Switzerland 3 February 1997–23 January 1998 Milan, Italy 10 March 1997–23 May 1998 Oxford, UK November 1998–7 October 1999 Prague, Czech Republic 3 June 1997–4 June 1998 Helsinki, Finland 26 September 1996–10 December 1997
Location	Athens, Greece; Basel, Switzerland; Milan, Italy; Oxford, UK; Prague, Czech Republic; Helsinki, Finland
Population	Adults
Age Groups	25-55 yr
Indoor Source	NR
Personal Method	Integrated 48-h $PM_{2.5}$ filter samples
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$
Ambient Size	$PM_{2.5}$
Copollutant(s)	NO_2
Primary Findings	Personal $PM_{2.5}$ and NO_2 levels were associated with subjects' level of annoyance. Highest annoyance levels occurred while in traffic.

Sanderson and Farant (2004, 156942)

Study Design	Indoor and outdoor air monitoring of PAH. Investigate the relationship between indoor and outdoor PAH.
Period	NR
Location	Canada
Population	Residential homes in neighborhoods around aluminum smelting plant
Age Groups	NR
Indoor Source	NR
Personal Method	Indoor quartz filter sample
Personal Size	$PM_{2.5}$
Microenvironment Size	NR
Ambient Size	NR
Component(s)	4-6 ring PAHs on indoor particle
Primary Findings	Indoor concentration of 4-6-ring PAH were linked to outdoor industrial sources in residences without any major indoor source, but with industrial facility as the main outdoor source. This study suggests that simultaneous measurements of indoor and outdoor concentrations of PAH >4 rings predominantly associated with fine PM could provide useful estimates of particle infiltration efficiency.

Sarnat et al. (2006, 089166)

Study Design	Outdoor-indoor pollutant infiltration, occupied residences
Period	July 28, 2001-February 25, 2002
Location	Los Angeles, CA
Population	NR
Indoor Source	Yes; cleaning, cooking, home ventilation (open windows/doors), kitchen fans, air conditioner/heating usage, number of occupants, nearby roadways
Personal Method	NR
Personal Size	NR
Microenvironment Size	$PM_{2.5}$, Particle number
Ambient Size	$PM_{2.5}$
Component(s)	BC (nonvolatile component); NO_3 (volatile component)
Primary Findings	Infiltration rate for $PM_{2.5}$ was intermediate, while BC was highest and NO_3 lowest. Infiltration rate varied with particle size, air exchange rate, outdoor NO_3. $PM_{2.5}$ infiltration was lowest for volatile components. Outdoor volatile $PM_{2.5}$ components may be less representative of indoor exposure to volatile $PM_{2.5}$ of ambient origin. Outdoor nonvolatile $PM_{2.5}$ components may be more representative of indoor exposure to nonvolatile $PM_{2.5}$ of ambient origin.

Sarnat et al. (2006, 090489)

Study Design	Personal and ambient exposure assessment
Period	June 14-August 18 (summer); Sep 24-Dec 15 (fall), 2000
Location	Steubenville, OH
Population	Non-smoking, older adults
Age Groups	NR
Personal Method	Integrated filter gravimetric measurement
Personal Size	$PM_{2.5}$
Microenvironment Size	NR
Ambient Size	$PM_{2.5}$
Component(s)	SO_4^{2-}; EC
Primary Findings	24-h ambient measurements are more representative of personal particle exposure than gases, and ventilation is an important exposure modifier.

Sarnat et al. (2005, 087531)

Study Design	Time-series epidemiologic study
Period	Summer 1999 and winter 2000
Location	Boston, MA. Comparisons to a previous study in Baltimore are also made.
Population	School children and seniors
Age Groups	NR
Indoor Source	$PM_{2.5}$
Personal Method	NR
Personal Size	$PM_{2.5}$
Microenvironment Size	NR
Ambient Size	$PM_{2.5}$
Component(s)	SO_4,
Copollutant(s)	O_3, NO_2, SO_2
Primary Findings	Substantial correlations between ambient $PM_{2.5}$ concentrations and corresponding personal exposures. Summertime gaseous pollutant concentrations may be better surrogates of personal $PM_{2.5}$ exposures (especially personal exposures to $PM_{2.5}$ of ambient origin) than they are surrogates of personal exposures to the gases themselves.

Shalat et al. (2007, 156971)

Study Design	Indoor home exposure assessment; sampling technology demonstration
Period	Winter heating season
Location	Residential home
Population	Children
Age Groups	Pre-toddler (6- to 12-month-old) children
Indoor Source	NR
Personal Method	Integrated filter and real-time nephelometer at floor height and at a height of 110 cm
Personal Size	TSP, inhalable PM
Microenvironment Size	NR
Ambient Size	NR
Copollutant(s)	NR
Primary Findings	The study results suggest that young children are exposed to more inhalable PM and TSP because PM becomes resuspended from the floor with motion.

Shao et al. (2007, 156973)

Study Design	Exposure assessment
Period	July and Winter 2003
Location	Beijing, China
Population	General population
Age Groups	NR
Indoor Source	NR
Personal Method	PM_{10} measured with integrated filter samples
Personal Size	PM_{10}
Microenvironment Size	PM_{10}
Ambient Size	PM_{10}
Component(s)	NR
Primary Findings	Plasmid scission assay, coupled with the image analysis, can be used to evaluate the relationship between particle physico-chemistry and toxicity.

Shilton et al. (2002, 049602)

Study Design	Respirable particulates inside and outside of a building were collected and compared
Period	24-h sampling from 12:45 pm Mondays to Fridays between 9/19/00 to 5/01/01
Location	Wolverhampton city center, University of Wolverhampton, UK
Population	NR
Indoor Source	Mn,Al, NO_3, Cl^- (wind-blown dust), Cu and Zn^-
Personal Method	Active sampling using Casella sampler (filter)-
Personal Size	Respirable PM
Microenvironment Size	Respirable PM
Ambient Size	Respirable PM
Component(s)	NO_3^-, metals (Zn, Cu, Mn, Al), SO_4^{2-}, Cl^-
Primary Findings	The indoor particulate concentration was driven by ambient concentration, and meteorological-induced changes in ambient PM were detected indoors.

Strand et al. (2007, 157018)

Study Design	Cohort
Period	Winter of 1999-2000 and winter of 2000-2001
Location	Denver, Colorado
Population	Asthmatic children
Indoor Source	NR
Personal Method	Modeling/extrapolation from fixed-site ambient monitoring (multiple methods)
Personal Size	NR
Microenvironment Size	NR
Ambient Size	$PM_{2.5}$
Component(s)	NR
Primary Findings	Using modeled or extrapolated personal ambient PM exposure results in a deattenuation of decrements in FEV_1 associated with PM exposure, relative to use of fixed-site ambient monitoring PM levels. Associations between FEV1 decrements and the various estimation procedures (modeling and extrapolation) were similar to each other.

Tang et al. (2007, 091269)

Study Design	Cohort Study
Period	12/2003-2/2005
Location	Sin-Chung City, Taiwan
Population	Asthmatic children
Age Groups	6-12 yr
Indoor Source	No
Personal Method	Portable particle monitor; DUSTcheck Portable Dust Monitor, model 1.108, GRIMM Labortechnik Ltd., Germany
Personal Size	PM_{10}, $PM_{2.5}$, PM_1, $PM_{10\text{-}2.5}$, $PM_{2.5\text{-}1}$
Microenvironment Size	NR
Ambient Size	PM_{10}, $PM_{2.5}$, $PM_{10\text{-}2.5\text{-}}$
Component(s)	NR
Primary Findings	Results of linear mixed-effect model analysis suggested that personal PM data was more suitable for the assessment of change in children's PEFR than ambient monitoring data.

Thornburg et al. (2004, 157052)

Study Design	PM exposure studies
Period	RTP: Summer 2000-spring 2001 Tampa: October-November 2002
Location	Research Triangle Park (RTP), NC and Tampa, FL
Population	Residential home occupants
Age Groups	NR
Indoor Source	Resuspension of PM_{10} from a carpet and cooking
Personal Method	Harvard impactors and PEMs, MIE pdr1000 nepholometer
Personal Size	$PM_{2.5}$, PM_{10}
Microenvironment Size	NR
Ambient Size	$PM_{2.5}$, PM_{10}
Component(s)	NR
Primary Findings	The association of duty cycle with indoor-outdoor (I/O) ratio was confounded by the short time span of ventilation system operation and the presence of strong indoor sources.

Toivola et al. (2002, 026571)

Study Design	Random sample of teachers
Period	Nov 1998-Mar 1999 and Nov-Dec 1999
Location	2 cities in eastern Finland
Age Groups	Adult
Indoor Source	Fungi, bacteria
Population	Elementary school teachers
Personal Method	Button inhalable aerosol sampler
Personal Size	Particle Mass; BS
Microenvironment Size	Particle Mass; BS
Ambient Size	NR
Component(s)	Total fungi, total bacteria, viable fungi, viable bacteria
Primary Findings	Personal BS exposure correlated with both home and work BS exposures. BS concentrations explained best the variation of particle mass in personal and home concentrations.

Trenga et al. (2006, 155209)

Study Design	Panel study with repeated measures
Period	3 sampling periods Oct 1999-Aug 2000, Oct 2000-May 2001, Oct 2001-Feb 2002
Location	Seattle, Washington
Population	Adults with and without COPD and children with asthma
Age Groups	adults ages 56-89 and children ages 6-13
Indoor Source	NR
Personal Method	Carrying personal monitor (Harvard Personal Environmental Monitor for $PM_{2.5}$)
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$
Ambient Size	$PM_{10-2.5}$, $PM_{2.5}$ for residential outdoor, $PM_{2.5}$ for central site
Component(s)	NR
Primary Findings	FEV_1 decrements associated with 1-day lagged central site $PM_{2.5}$ in adult subjects with COPD. Associations between PM and lung function decrements were significant only in asthmatic children not receiving anti-inflammatory medication.

Turpin et al. (2007, 157062)

Study Design	RIOPA Study 24-h integrated indoor, outdoor, and personal samples collected in 3 cites.
Period	Summer 1991-spring 2001
Location	Elizabeth, NJ, Houston, TX, and Los Angeles County, CA
Population	309 adults and 118 children (89-18)
Indoor Source	NR
Personal Method	PEM on the front strap of a harness near the breathing zone. The bag on the hip contained the pump, battery pack, and motion sensor
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$, in the main living area (not kitchen)
Ambient Size	$PM_{2.5}$, in the front or back yard
Component(s)	18 volatile organics, 17 carbonyl, $PM_{2.5}$ mass and >23 $PM_{2.5}$ species, organic carbon, elemental carbon, and PAHs
Primary Findings	The best estimate of the mean contribution of outdoor to indoor $PM_{2.5}$ was 73% and the outdoor contribution to personal was 26%.

Vallejo et al. (2006, 157081)

Study Design	Panel study
Period	4/2002-8/2002
Location	Mexico City, Mexico
Population	Health young, non-smoking adults
Age Groups	Mean age 27 yr
Indoor Source	NR
Personal Method	pDR nephelometric method
Personal Size	$PM_{2.5}$
Microenvironment Size	NR
Ambient Size	NR
Component(s)	NR
Primary Findings	The descriptive analysis showed that overall outdoor median concentration of $PM_{2.5}$ was higher than the indoor concentration. In the indoor microenvironment, the highest concentrations occurred in the subway followed by the school, and the lowest was at home. The outdoor microenvironment with the highest concentrations was the public transportation (bus), while the automobile had the lowest. It was found that $PM_{2.5}$ concentration levels had a circadian-like behavior probably related to an increase in the population daily activities during the morning hours, which decrease in the evening, especially at indoor microenvironments. The Center city area was found to have the highest concentrations of $PM_{2.5}$.; Multivariate analysis corroborated that $PM_{2.5}$ concentrations are mainly determined by geographical locations and hour of the day, but not by the type of microenvironment.

van Roosbroeck et al. (2006, 090773)

Study Design	Personal exposure assessment, effect of traffic-related pollutants
Period	March-June 2003
Location	Amsterdam, The Netherlands
Population	Schoolchildren
Age Groups	9-12 yr
Indoor Source	ETS, cooking
Personal Method	Integrated filter gravimetric measurement. Light absorbance.
Personal Size	$PM_{2.5}$
Microenvironment Size	NR
Ambient Size	$PM_{2.5}$
Component(s)	Absorbance
Primary Findings	Children living near busy roads had 35% higher personal exposure to ‘soot’ than children living in urban background locations.

Vinzents et al. (2005, 087482)

Study Design	Panel study
Period	3/2003-6/2003
Location	Copenhagen, Denmark
Population	Healthy young adults
Age Groups	Mean age = 25 yr
Indoor Source	No
Personal Method	Condensation particle counters
Personal Size	UFP (10-100 nm)
Microenvironment Size	UFP (10–100 nm)
Ambient Size	PM_{10}
Primary Findings	UFP exposure predicted oxidative DNA damage.

Wallace and Williams (2005, 057485)

Study Design	Cohort
Period	2000-2001
Location	Raleigh, North Carolina
Population	African-American persons with elevated risk from exposure to particles.
Age Groups	NR
Indoor Source	NR
Personal Method	PEM $PM_{2.5}$ monitor
Personal Size	$PM_{2.5}$
Microenvironment Size	Indoors $PM_{2.5}$
Ambient Size	Outdoors near residence $PM_{2.5}$ $PM_{2.5}$
Component(s)	S
Primary Findings	Using outdoor particles to determine the effect on health is not accurate. The infiltration factor is a good estimator for personal exposure. Indoor and outdoor measurements of sulfur could be used in the absence of personal exposure measurement to estimate the contribution of outdoor fine particles to personal exposures.

Wallace et al. (2006, 088211)

Study Design	Time series continuous monitoring of subjects with controlled hypertension or implanted defibrillators were monitored for 7 consecutive days in 4 seasons.
Period	2000-2001
Location	North Carolina
Population	Health-compromised adults, non-smokers
Age Groups	Adults
Indoor Source	Cooking, cleaning, personal care, smoking
Personal Method	PEM
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$; Indoor and outdoor
Ambient Size	NR
Component(s)	NR
Primary Findings	Use of continuous particle measuring instruments allowed more precise identification of sources, frequency and magnitude of short-term peaks, and more accurate calculation of individual personal clouds.

Wang et al. (2006, 157108)

Study Design	Exposure assessment, identification of sources of outdoor and indoor PM and trace elements
Period	Aug 4 -Sep 10, 2004
Location	Guangzhou, China
Population	4 hospitals
Age Groups	NR
Indoor Source	NR
Personal Method	No personal exposure assessment was conducted.
Personal Size	NR
Microenvironment Size	PM_{10}, $PM_{2.5}$
Ambient Size	PM_{10}, $PM_{2.5}$
Component(s)	Na, Al, Ca, Fe, Mg, Mn, Ti, K, V, Cr, Ni, Cu, Zn, Cd, Sn, Pb, As, Se
Primary Findings	High correlation between $PM_{2.5}$ and PM_{10} suggest that they came from similar emission sources. Outdoor infiltration could lead to direct transportation of PM indoors. Human activities and ventilation types could also influence indoor PM. levels.

Ward et al. (2007, 157112)

Study Design	Indoor air sampling to determine size fractionated concentrations of PM, OC, EC, and total carbon
Period	Jan-Mar 2005
Location	Libby, Montana
Population	Children exposed to wood-burning stoves in elementary and middle schools
Indoor Source	Burning wood in stoves for heating
Personal Method	NR
Personal Size	NR
Microenvironment Size	PM >2.5, 1.0-2.5, 0.5-1.0, 0.25-0.5, and < 0.25 µm
Ambient Size	PM >2.5, 1.0-2.5, 0.5-1.0, 0.25-0.5, and < 0.25 µm
Component(s)	OC and EC
Primary Findings	Total measured PM mass concentrations were much higher inside the elementary schools, with particle size fraction (>2.5, 0.5-1.0, 0.25-0.5, and < 0.25 mm) concentrations between 2 and 5 times higher when compared to the middle school. The 1.0-2.5 mm fraction had the largest difference between the two sites, with elementary school concentrations nearly 10 times higher than the; middle school values.

Weisel et al. (2005, 157131)

Study Design	Matched indoor, outdoor, and personal concentrations in proximity to pollution sources.
Period	May 1999-Feb 2001
Location	Elizabeth, NJ, Houston, TX, and Los Angeles County, CA
Population	urban children and adults
Age Groups	Children and adults (6-89 yr)
Indoor Source	Age of house, recent renovations (< 1 yr), type of home (single, multiple family), attached garage, carpet indoors, local pollution sources.
Personal Method	PEM on a harness with inlet near breathing zone.
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$
Ambient Size	$PM_{2.5}$
Component(s)	NR
Primary Findings	Personal $PM_{2.5}$ was significantly higher than indoor and outdoor $PM_{2.5}$ concentrations.

Wichmann et al. (2005, 086240)

Study Design	Exposure assessment
Period	November 29, 1993-March 30, 1994; October 17, 1994-December 22, 1994
Location	Amsterdam, The Netherlands
Population	Adults and schoolchildren living near high-traffic or low-traffic roads
Age Groups	Adults (50-70 yr), schoolchildren (10-12 yr)
Indoor Source	NR
Personal Method	Personal impactor
Personal Size	PM_{10}
Microenvironment Size	PM_{10}
Ambient Size	PM_{10}
Component(s)	Absorbance coefficient measurements
Primary Findings	Found tentative support for using type of road as a proxy for indoor and personal exposure to traffic-related absorbance PM.

Williams et al. (2003, 053338)

Study Design	Cohort study, longitudinal
Period	Summer 2000, fall 2000, winter 2001, and spring 2001
Location	Raleigh and Chapel Hill, North Carolina
Population	Elderly persons
Age Groups	> 50 yr
Indoor Source	Occasional ETS
Personal Method	Integrated filter samples
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$; PM_{10}; $PM_{10-2.5}$
Ambient Size	$PM_{2.5}$; PM_{10}; $PM_{10-2.5}$
Component(s)	NR
Primary Findings	When comparing cohorts, there was no statistically significant difference between $PM_{2.5}$ exposure. Little spatial variability was observed regarding $PM_{2.5}$ concentrations; this was observed to a lesser extent for PM_{10} as well.

Wilson and Brauer (2006, 088933)

Study Design	Exposure assessment
Period	April-September 1998
Location	Vancouver, Canada
Population	Subjects with physician-diagnosed COPD
Age Groups	54-86-years-old
Indoor Source	No
Personal Method	Personal integrated filter gravimetric measurement; TEOM outdoor ambient
Personal Size	$PM_{2.5}$
Microenvironment Size	NR
Ambient Size	NR
Component(s)	SO_4^{2-}
Primary Findings	It was observed that ambient $PM_{2.5}$ exposure, estimated with the SO_4^{2-} method, accounted for 71% of measured ambient concentration and 44% of measured total personal exposure. No correlation between nonambient exposure and ambient concentration was observed.

Wu et al. (2006, 179950)

Study Design	Panel study
Period	9/3/2002-11/1/2002
Location	Pullman, WA
Population	Asthmatic adults
Age Groups	18-52 yr
Indoor Source	No
Personal Method	Co-located Harvard Personal Environmental Monitors (HPEM2.5; Harvard School of Public Health, Boston, MA)\
Personal Size	PM2.5
Microenvironment Size	PM2.5
Ambient Size	PM2.5
Component(s)	Levoglucosan (LG); Elemental Carbon (EC); Organic Carbon (OC)
Primary Findings	The authors observed significant variability between subjects for burning and nonburning episodes. The authors postulated that activity patterns contribute to this variability and that central-site measurements of LG might not be a good surrogate for biomass combustion smoke exposurefor this reason.

Wu et al. (2005, 086397)

Study Design	Panel study
Period	1999-2000
Location	Alpine, CA
Population	Asthmatic children
Age Groups	9-17 yr
Indoor Source	NR
Personal Method	pDR
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$
Ambient Size	$PM_{2.5}$
Component(s)	NR
Primary Findings	Personal exposure was higher than those at fixed sites. Subjects received only 45.0% of their exposure indoors at, although they spent more than 60% of their time there. In contrast, 29.2% of their exposure was received at school where they spent only 16.4% of their time. Thus, exposures in microenvironments with high PM levels where less time is spent can make significant contributions to the total exposure.

Yeh and Small (2002, 040077)

Study Design	Comparative assessment of AME and IES models
Period	1997 (364 days) spring March-May, summer June-August, Fall September-November, winter December-February
Location	Los Angeles County, CA
Population	General population; ETS and non-ETS Homes
Age Groups	NR
Indoor Source	Indoor Cooking, ETS, Other sources and unexplained particulates that maybe generated with engaging in various activities
Personal Method	NR
Personal Size	PM_{10} $PM_{2.5}$
Microenvironment Size	NR
Ambient Size	PM_{10} $PM_{2.5}$
Component(s)	NR
Primary Findings	Adjusting from outdoor concentrations to personal exposures and correcting dose-response bias produce nearly equal results. Roughly the same premature mortalities associated with short-term exposure to both ambient $PM_{2.5}$ and PM_{10} are predicted by both models

Yip et al. (2004, 157166)

Study Design	A panel study with repeated measures with personal & home monitoring for 8 2-week Periods. Children were stratified into smoking and non-smoking households.
Period	2000-2001
Location	Detroit, Michigan
Population	School-age children with asthma
Age Groups	7-11 yr
Personal Method	PEM in a backpack
Personal Size	PM_{10}
Microenvironment Size	PM_{10}; indoor at home & indoor at school
Ambient Size	PM_{10}
Component(s)	NR
Primary Findings	Personal PM concentrations were significantly correlated with home environment (r = 0.38 to 0.70), with the strongest relationships in home with non-smokers.

Zhao et al. (2006, 156181)

Study Design	Aerosol source apportionment under four environments (personal, residential indoor, residential outdoor and ambient) to evaluate the relationship between different environments through exposure analysis, and to demonstrate the utility of the combined receptor model on air quality studies of various environments.
Period	June 2000 to May 2001
Location	Raleigh and Chapel Hill, NC
Population	NR. People with respiratory ailments most likely.
Age Groups	NR
Indoor Source	4 main sources to residential indoor PM Cu-factor mixed with indoor soil, secondary sulfate, Personal care and activity, ETS and its mixture
Personal Method	PEM and HI
Personal Size	NR
Microenvironment Size	NR
Ambient Size	NR
Component(s)	SO_4^{2-} , OC, EC, and trace elements
Primary Findings	Secondary SO_4^{2-} and vehicle emissions were significant contributors of personal PM exposure and residential indoor PM concentrations.

Zhao et al. (2007, 156182)

Study Design	Comprehensive analysis of the sources of PM_{15} exposure on children with moderate to severe asthma in urban-poor settings.
Period	Two winter periods (October 2002-March 2003 and October 2003-March 2004)
Location	Elementary school for children with significant asthma, Denver, CO
Population	Schoolchildren in urban-poor settings suffering from moderate to severe asthma
Age Groups	6-13 yr (60% in the range 10-13 yr, rest in the range 6-9 yr)
Indoor Source	Yes, House cleaning compounds, and smoking were identified as primary internal sources.
Personal Method	PEM
Personal Size	$PM_{2.5}$
Microenvironment Size	$PM_{2.5}$
Ambient Size	$PM_{2.5}$
Component(s)	EC, Cl, Si, NO_3
Primary Findings	Four external sources and three internal sources were resolved in this study. Secondary nitrate and motor vehicle were two major outdoor $PM_{2.5}$ sources. Cooking was the largest contributor to the personal and indoor samples. Indoor environmental tobacco smoking also has an important impact on the composition of the personal exposure samples.

Zhu et al. (2005, 157191)

Study Design	4 apartments near the freeway were monitored at 2 times for 6 consecutive days, 24 h per day. Subjects did not enter the bedrooms where the samplers were, no cooking, cleaning, children, or pets.
Period	Oct. 2003-Dec. 2003 and Dec. 2003-Jan. 2004
Location	Los Angles, CA
Population	Urban Populations near major freeways.
Age Groups	NR
Indoor Source	NR
Personal Method	NR
Personal Size	Indoor and Outdoor ultrafine particles (6-220 nm)
Microenvironment Size	NR
Component(s)	CO
Primary Findings	The size distributions of indoor aerosols showed less variability than the adjacent outdoor aerosols. Indoor to outdoor ratios for ultrafine particle concentrations depended strongly on particle size. I/O ratios were dependent on the indoor ventilation mechanisms applied. Size-dependent particle penetration factors and deposition rates were predicted from data by fitting a dynamic mass balance model.

Zöllner et al. (2007, 157192)

Study Design	Exposure assessment
Period	Winter Period of 2005 and 2006
Location	Baden-Wuerttemberg, Germany
Population	School children
Age Groups	NR
Personal Method	NR
Personal Size	NR
Microenvironment Size	They only reported concentrations for $PM_{2.5}$. PM ranging in size from 0.02 to >20 μm were collected and analyzed but only $PM_{2.5}$ concentration were reported.
Ambient Size	They only reported concentrations for $PM_{2.5}$. PM ranging in size from 0.02 to >20 μm were collected and analyzed but only $PM_{2.5}$ concentration were reported.
Primary Findings	The impaction of PM was strongly influenced by specific weather conditions. Time resolution of measurements in classrooms showed variation in particle concentration depending on the type of building and indoor activities. E'[Concentrations of very small particles indoors and in ambient air measured by condensation particle counter were influenced by traffic emissions.

Table A-59. Examples of studies showing developments with UFP sampling methods since the 2004 PM AQCD.

Reference	PM Size Ranges	PM Constituents	Instruments	Study Description
Biswas et al. (2005, 150694)			CPC (water)	Water-based CPC performance evaluation.
Feldpausch et al. (2006, 155773)	20-100 nm	Carbonaceous aerosols	DS with CPC, compared with DMA	The DS with CPC compared fairly well with the DMA for particle sizes up to 40 nm with 20-40% underestimation depending on discharge frequency settings. The DS sampling period is 3-5 s in comparison with the 1 min scanning time of the DMA.
Hering et al. (2005, 155838)			CPC (water)	Water-based CPC performance evaluation.
Hermann et al. (2007, 155840)	3-40 nm	Ag, NaCl	CPC (water and butanol)	Roughly 95% collection efficiency for d >5 nm for TSI models 3776 and 3786, 95% efficiency for d >20 nm for model 3775, near 90% efficiency for d>20 nm for model 3785, near 90% efficiency for d >25 nm for model 3772.
Kinsey et al. (2006, 130654)	10 nm-5 μm	DE	TEOM, SMPS, CPC, DustTrak, E-BAM, ELPI, integrated filter samples	TEOM compared best with gravimetric filter among mass concentration analyzers, ELPI and SMPS comparable for differential number distribution but ELPI not useful for gravimetric analysis because mass is not significant at small end of distribution.
Kulmala et al. (2007, 097838)			CPC	Changing temperature difference between saturator and condenser within CPC allowed for differences in cut-off diameters.
Kulmala et al. (2007, 155911)	2-20 nm	Atmospheric aerosol, Ag	Battery of CPCs (water, butanol, n-butanol)	Used the battery to discriminate between water-soluble, water-insoluble, butanol-soluble, and butanol-insoluble nucleation-mode particles.
Ntziachristos and Samaras (2006, 116722)	7 nm-1 μm	Automobile exhaust	5 instruments used simultaneously to reduce uncertainty: Teflon-coated filter downstream of constant volume sampling, ELPI with thermodenuder, CPC, SMPS, diffusion charger	Use of four reduced variables combining output from all instruments (ratio of particle number concentration from CPC and ELPI, estimated mean geometric mobility diameter from signal of diffusion charger and number concentration from CPC, ratio of signal of diffusion charger to constant volume sampler mass, ratio of constant volume sampler mass to volume collected by ELPI) resulted in identification of clear outliers and factors related to driving and fuel properties rather than measurement errors.
Olfert et al. (2008, 156004)	30-100 nm	NaCl, ambient	FIMS (compared with SMPS)	Particle number concentrations reported by the FIMS were 8-23% higher than the SMPS using an inversion technique designed to correct for particle residence time in the FIMS, which operates at 0.1 s resolution.
Petäjä et al. (2006, 156021)			CPC (water)	Water-based CPC performance evaluation.
Winkler et al. (2008, 156160)	1.5-4 nm	Tungsten oxide	CPC (n-Propanol)	Authors remove excess charge on particles with ion trap to detect particles down to ~ 1 nm (by eliminating electrostatic attraction to agglomerate).

Table A-60. Summary of in-vehicle studies of exposure assessment.

Reference	Study Design	Mode of Transport	Exposures	Primary Findings
Briggs et al. (2008, 156294)	UFP (P-Trak), PM_{10}, $PM_{2.5}$, and PM_1 (OSIRIS light scatter) were operated in a car while driving or walking on one of 48 routes in London. Trips ranged 1.5-15 min by car and were repeated up to 5 times to improve statistics. Study Period: Weekdays in May and June 2005.	Car Walking	Units: PM_1-PM_{10} (µg/m^3), UFP (p cm^{-3}) Avg Car Exposure: PM_{10} 5.87 (3.09) $PM_{2.5}$ 3.01 (1.10) PM_1 1.82 (1.10) UFP 21639 (14379) Avg Walking Exposure: PM_{10} 27.56 (13.16) $PM_{2.5}$ 6.59 (3.12) PM_1 3.37 (3.40) UFP 30334 (17245)	In-car concentrations of $PM_{2.5}$, PM_1, and UFP correlated well with walking concentrations (R = 0.806, 0.800, 0.799 respectively). Avg walking concentrations were 1.4-4.7 times higher than average in-car concentrations. Cumulative walking exposures (not shown here) were 4.4-15.2 times higher than those in cars, likely resulting from longer transit times for walking.
Diapouli et al. (2007, 156397)	UFP (CPC) concentrations were measured at school, residential, and in-vehicle environments in Athens, Greece. Study Period: school hours, Nov 2003-Feb 2004 and Oct-Dec 2004	Car	15-min median (1000p/cm^3): School indoor 13.6 School outdoor 16.6 Residence indoor 11.2 Residence outdoor 24.0 In-vehicle 78.0	In-vehicle UFP concentrations were roughly 3.5-7 times higher than school or residence concentrations. Indoor concentration diel patterns were also shown to follow outdoor levels, which suggests that indoor levels are of outdoor origin.
Fruin et al. (2008, 097183); Westerdahl et al. (2005, 086502) [Note: same data presented.]	On-road zero emissions vehicle driven on 33-mi arterial road and 75-mi freeway measured UFP (CPCs, SMPS, EAD), BC (aethalometer), NOX (chemiluminescence), PM-bound PAHs (UV-photoionization), and CO (Q-Trak). DVD analysis of traffic density and car speed. Study Period: Feb-Apr 2003 for 2- to 4-h periods.	Car	Arterial range of medians: UFP (1000p/cm^3) 13-43 $PM_{2.5}$ (µg/m^3) 7.9-45 BC (µg/m^3) 0.74-3.3 Freeway range of medians: UFP (1000p/cm^3) 47-190 $PM_{2.5}$ (µg/m^3) 25-110 BC (µg/m^3) 2.4-13	Measurements of freeway UFP, BC, PM-bound PAH, and NO_x concentrations were roughly one order of magnitude higher than ambient measurements. Multiple regression analysis suggests these concentrations were a function of truck density and total truck count. (Only PM measurements reported here).
Gomez-Perales et al. (2004, 054418)	$PM_{2.5}$ (personal filter pump), CO (T15 electrochemical cell), and benzene (canister) were measured on transit routes, and $PM_{2.5}$ filters were analyzed for mass, OC/EC, SO_4^{2-}, NO_3-, and trace metals. Study period: 3-h morning and evening rush hour May-June 2002	Bus Minibus Metro	$PM_{2.5}$ (µg/m^3): Bus 68 Minibus 71 Metro 61	Generally, $PM_{2.5}$ concentration was higher in the morning than evening rush hour, but variability was higher for minibuses than other modes of transport. Wind speed was found to be associated with $PM_{2.5}$ concentration on minibuses.

Reference	Study Design	Mode of Transport	Exposures	Primary Findings
Gomez-Perales et al. (2007, 138816)	$PM_{2.5}$ (personal filter pump), CO (T15 electrochemical cell), and benzene (canister) were measured on transit routes, and $PM_{2.5}$ filters were analyzed for mass, OC/EC, SO_4^{2-}, NO_3^-, and trace metals. Study period: 3-h morning and evening rush hour Jan-March 2003	Bus Minibus Metro	Units: $PM_{2.5}$ mass ($\mu g/m^3$), components (% of mass) Bus: $PM_{2.5}$ 20-58 $(NH_4O_3$ 5-8 $(NH_4)_2SO_4$ 10-18 OC 17-39 EC 8-20 Crustal 15-18 Non-crustal 2-3 Unknown 6-24 Minibus: $PM_{2.5}$ 25-55 $(NH_4O_3$ 4-13 $(NH_4)_2SO_4$ 7-22 OC 22-37 EC 9-19 Crustal 12-13 Non-crustal 3-3 Unknown 4-26 Metro: $PM_{2.5}$ 24-41 $(NH4O_3$ 5-8 $(NH4)2SO_4$ 10-21 OC 35-42 EC 9-13 Crustal 10-16 Non-crustal 2-4 Unknown 5-20	Buses and minibuses had similar concentration levels for $PM_{2.5}$ mass, and metro exposures were lower. CO and benzene concentrations were higher on minibuses than buses. OC was the largest PM constituent for all modes of transport. Measured concentrations were higher in the morning than in the evening rush hour periods. Maximum historical wind speeds (1995-2003) appeared to be inversely associated with measured concentration.
Gulliver and Briggs (2004, 053238)	PM_{10}, $PM_{2.5}$, and PM_1 sampled (OSIRIS light-scatter devices) in a car while driving or walking on northern corridor of Northhampton UK. Study Period: 1-h interval of morning and evening rush hour during Winter 1999-2000.	Car Walk	Walking concentrations, Units: $\mu g/m^3$ Walk, Car, Background PM_{10} 38.2,43.2, 26.6 $PM_{2.5}$ 15.1, 15.5 PM_1 7.1, 7.0	In-car PM_{10} concentrations were elevated compared with walking and background. $PM_{2.5}$ and PM_1 concentrations were comparable for walking and background. Periods of elevated $PM_{2.5}$ compared with PM_{10} generally corresponded to times when SO_4^{2-} levels were also high.
Gulliver and Briggs (2007, 155814)	TSP, PM_{10}, $PM_{2.5}$, and PM_1 sampled (OSIRIS light-scatter devices) in a car while driving or walking on one of 48 routes in London. Trips ranged 1.5-15 min by car and were repeated up to 4 times to improve statistics. Study Period: Jan-Mar 2005.	Car Walk	Mean concentrations, Units: $\mu g/m^3$ Walk, Car, Background TSP-PM_{10} 19.1 (19.8) 18.2 (18.0) 4.9 (5.1) $PM_{10-2.5}$ 22.1 (22.8) 15.1 (14.2) 10.0 (9.0) $PM_{2.5}$ -1 10.9 (10.4) 8.3 (8.4) 7.6 (7.1) PM_1 4.8 (3.4) 2.9 (2.6) 4.2 (2.4)	Walking exposures larger than car and background, and car exposures were generally larger than background except for PM_1. Peak exposures during walking were significantly higher than peak in-car exposures.
Rossner et al. (2008, 156927)	Measured $PM_{2.5}$ exposure of 50 city bus drivers and 50 controls in Prague, Czech Republic using personal samplers (type not specified) and VOCs using passive samplers. $PM_{2.5}$ filters analyzed for c-PAHs. Focus of study is oxidative stress biomarkers in drivers. Study period: winter 2005, summer 2006, winter 2006.	Bus	Units: ng/m^3 Winter 2005: Bus Control c-PAH 7.1 (3.7) 9.4 (5.5) B[a]P 1.3 (0.7) 1.8 (1.0) Smmer 2006: Bus Control c-PAH 1.8 (0.5) 2.0 (0.8) B[a]P 0.2 (0.1) 0.3 (0.2) Wnter 2006: Bus Control c-PAH 5.4 (3.5) 4.1 (1.7) B[a]P 1.0 (0.5) 0.8 (0.4)	c-PAH and B[a]P exposure to bus drivers was significantly higher in Winter 2006, but control exposure was significantly higher in Winter 2005 for c-PAH and B[a]P and in summer 2006 for c-PAH. No significant difference in VOC exposure between bus drivers and controls was observed. Oxidative stress markers were significantly higher in bus drivers than controls for all seasons.

Reference	Study Design	Mode of Transport	Exposures	Primary Findings
Sabin et al. (2005, 088300)	BC (aethalometer), particle-bound PAH (UV-photoionization), and NO (luminol reaction) were measured on 3 diesel school buses, 1 diesel school bus with a particle trap, and one compressed gas bus during before- and after-school commutes. Study Period: May-June 2002.	School bus (diesel, diesel with particle trap (TO), compressed gas (CNG))	In-bus mean concentration Units: BC ($\mu g/m^3$) PAH (ng/m^3) Windows closed: BC PAH Ambient: 2.5,27 CNG:2.3, 57 TO: 7.1, 190 Diesel:11, 290 Windows open: BC PAH Ambient: 1.9,26 CNG:1.5, 43 TO: 2.3, 42 Diesel: 3.9, 58	Mean concentrations on diesel buses without newer emissions control technologies were 2-4.4 times higher than background. On buses with particle traps, concentrations were 1.2-2.5 times higher than background, while concentrations on compressed gas-fueled school buses were actually lower than background.

Table A-61. Summary of personal PM exposure studies with no indoor source during 2002-2008.

Reference / Location	Personal	Micro	Ambient
SOUTHWEST			
Delfino et al. (2004, 056897) Alpine, California	Method: pDR, Units = $\mu g/m^3$ Last 2-h $PM_{2.5}$ 34.4 (33.7) Diurnal $PM_{2.5}$ 55.7 (31.6) Nocturnal $PM_{2.5}$ 22.3 (13.6) 1-h max $PM_{2.5}$ 151.0 (120.3) 4-h max $PM_{2.5}$ 87.5 (55.3) 8-h max $PM_{2.5}$ 67.6 (39.0) 24-h $PM_{2.5}$ 37.9 (19.9)	Method: HI, Units = $\mu g/m^3$ Indoor 24-h PM_{10}30.3 (11.9) Indoor 24-h $PM_{2.5}$ 12.1 (5.4) Outdoor 24-h PM_{10} 25.9 (10.4) Outdoor 24-h $PM_{2.5}$ 11.0 (5.4)	Method: TEOM, Units = $\mu g/m^3$ Diurnal PM_{10}35.1 (11.3) Nocturnal PM_{10} 23.3 (8.4) 1-h max PM_{10} 54.4 (13.8) 4-h max PM_{10} 44.5 (12.4) 8-h max PM_{10} 39.8 (11.2) 24-h PM_{10} 23.6 (9.1) 24-h $PM_{2.5}$ 10.3 (5.6)
Delfino et al. (2006, 090745) Riverside and Whittier, California	Method: PEM, Units = $\mu g/m^3$ Riverside: n13 24-h $PM_{2.5}$ 32.78 (21.84) 1-h max $PM_{2.5}$ 97.94 (70.29) 8-h max $PM_{2.5}$ 47.21 (30.0) Whittier: n32 24-h $PM_{2.5}$ 36.2 (21.84) 1-h max $PM_{2.5}$ 93.63 (75.19) 8-h max $PM_{2.5}$ 51.75 (36.88)		Method: FRM, Units = $\mu g/m^3$ Riverside: 24-h $PM_{2.5}$ 36.63 (23.46) 24-h PM_{10} 70.82 (29.36) Whittier: 24-h $PM_{2.5}$ 18.0 (12.14) 24-h PM_{10} 35.73 (16.6)
Turpin et al. (2007, 157062) Los Angeles County, CA (and Elizabeth, NJ, Houston, TX)	Method: PEM, Units = $\mu g/m^3$ Avg of 48-h $PM_{2.5}$ Child 40.2 Adult 29.2	Method: HI, Units = $\mu g/m^3$ Avg of 48-h $PM_{2.5}$: 16.2	Method: HI, Units = $\mu g/m^3$ Avg of 48-h $PM_{2.5}$: 19.2
Wu et al. (2005, 157155) Alpine, CA	Method: pDR, Units = $\mu g/m^3$ n11 Avg of 24-h $PM_{2.5}$ 11.4 (7.8)	Method: pDR, Units = $\mu g/m^3$ n14 Avg of 24-h $PM_{2.5}$ 5.6 (2.9) Method: HI n14 Avg of 24-h $PM_{2.5}$ 9.8 (2.5)	Method: pDR, Units = $\mu g/m^3$ n8 Avg of 24-h $PM_{2.5}$ 14.0 (11.4) Method: HI n8 Avg of 24-h $PM_{2.5}$ 14.3 (7.8)

Reference / Location	Personal	Micro	Ambient
NORTHWEST			
Jansen et al. (2005, 082236) Seattle, Washington, USA	NR	Method: HI, Units = μg/m^3 Indoor home: PM_{10} 11.93 $PM_{2.5}$ 7.29 Outdoor home: PM_{10} 13.47 $PM_{2.5}$ 10.47	Method: HI, Units = μg/m^3 PM_{10} 18.0 $PM_{2.5}$ 14.0
Koenig et al. (2003, 156653) Seattle, WA	13.4 ± 3.2 μg/m^3	Inside homes = 11.1 ± 4.9	Outside homes = 13.3 ± 1.4 3 Central-sites = 10.1 ± 5.7
Liu S et al. (2003, 073841) Seattle, WA	Summary of PM concentrations (μg/m^3) between October 1999 and May 2001 by study group. Group Mean ± SD Personal $PM_{2.5}$ COPD 10.5 ± 7.2 Healthy 9.3 ± 8.4 Asthmatic 13.3 ± 8.2 CHD 10.8 ± 8.4	Summary of PM concentrations (μg/m^3) between October 1999 and May 2001 by study group. Group Mean ± SD Indoor $PM_{2.5}$ COPD 8.5 ± 5.1 Healthy 7.4 ± 4.8 Asthmatic 9.2 ± 6.0 CHD 9.5 ± 6.8 PM_{10} COPD 14.1 ± 6.6 Healthy 12.7 ± 7.8 Asthmatic 19.4 ± 11.1 CHD 16.2 ± 11.3	Summary of PM concentrations (μg/m^3) between October 1999 and May 2001 by study group. Location Pollutant Group Mean ± SD Outdoor $PM_{2.5}$ COPD 9.2 ± 5.1 Healthy 9.0 ± 4.6 Asthmatic 11.3 ± 6.4 CHD 12.7 ± 7.9 PM_{10} COPD 14.3 ± 6.8 Healthy 14.5 ± 7.0 Asthmatic 16.4 ± 7.4 CHD 18.0 ± 9.0
Mar et al. (2005, 087566) Seattle, WA USA	Method: HI, Units = μg/m^3 $PM_{2.5}$: Healthy: 9.3 (8.4) CVD: 10.8 (8.4) COPD: 10.5 (7.2)	Method: HI, Units = μg/m^3 $PM_{2.5}$: Healthy: 7.4 (4.8) CVD: 9.5 (6.8) COPD: 8.5 (5.1) PM_{10}: Healthy: 12.7 (7.8) CVD: 16.2 (11.3) COPD: 14.1 (6.6)	Method: HI, Units = μg/m^3 $PM_{2.5}$: Healthy: 9.0 (4.6) CVD: 12.7 (7.9) COPD: 9.2 (5.1) PM_{10}: Healthy: 14.5 (7.0) CVD: 18.0 (9.0) COPD: 14.3 (6.8)
Trenga et al. (2006, 155209) Seattle, Washington	Method: PEM, Units = μg/m^3 Median $PM_{2.5}$ Child 11.3 Adult 8.5	Method: HI, Units = μg/m^3 Median $PM_{2.5}$ Child 7.5 Adult 7.6	Method: HI, Units = μg/m^3 Residential Outdoor Median $PM_{2.5}$ Child 9.6 Adult 8.6 Residential Outdoor Median PMcoarse Child 4.7 Adult 5.0 Residential Outdoor Median $PM_{2.5}$ central site Child 11.2 Adult 10.3
Wu et al. (2006, 179950) Pullman, WA	During non-burning times: 13.8 (11.1) During burning episodes: 19.0 (11.8)		
SOUTHCENTRAL			
Turpin et al. (2007, 157062) Houston (and Elizabeth, NJ, and Los Angeles County, CA)	Houston, Units = μg/m^3 (48-hr avg) Child: 36.6 Adult: 37.2	Houston: 17.1	Houston: 14.7

Reference / Location	Personal	Micro	Ambient
MIDWEST			
Adgate et al. (2002, 030676) Battle Creek, East St. Paul, and Phillips, Minnesota, constituting the Minneapolis-St. Paul metropolitan area.	$PM_{2.5}$, Units = $\mu g/m^3$ Battle Creek All Seasons: 118, 22.7, (25.7), 16.2 (2.2) Spring: 41, 26.3 (25.7), 19.4 (2.1) summer: 31, 28.5 (36.1), 20.3 (2.1) Fall 46, 15.5 (13.4), 11.9 (2.1) E. St. Paul All Seasons: 107, 30.5 (38.7), 20.6 (2.3) Spring: 44, 33.9 (34.4), 23.9 (2.3) summer: 25, 20.5 (15.0), 17.2 (1.8) Fall: 38, 33.1(51.9), 19.5 (2.5) Phillips All Seasons: 107, 26.5 (24.3), 20.9 (2.0) Spring: 28, 37.5 (37.6), 30.0 (1.8) summer: 40, 22.7 (15.3), 19.2 (1.7) Fall: 39, 22.7 (16.7), 17.6 (2.1)	$PM_{2.5}$, Units = $\mu g/m^3$ Battle Creek All Seasons: 108, 10.6 (6.6), 9.0 (1.8) Spring: 25, 12.7 (7.7), 11.0 (1.7) summer: 36, 8.9 (3.8), 8.1 (1.5) Fall: 47, 10.9 (7.4), 8.8 (2.0) E. St. Paul All Seasons: 97, 17.4 (20.3), 12.2 (2.2) Spring: 30, 20.7 (26.4), 13.6 (2.4) summer: 26, 15.8 (11.4), 13.7 (1.6) Fall 41 16.0 19.6 10.4 2.4 Phillips All Seasons: 89, 14.2 (13.0), 11.3 (1.9) Spring: 15, 16.9 (14.2), 13.0 (2.1) summer: 36, 13.2 (6.4), 11.4 (1.7) Fall: 38,14.4 (16.7), 10.6 (2.0)	$PM_{2.5}$, Units = $\mu g/m^3$ Battle Creek All Seasons: 88 9.4 (6.2), 7.8 (1.8) Spring: 36, 10.5 (7.1), 8.5 (2.0) summer: 22, 8.7 (4.4), 7.8 (1.6) Fall: 30, 8.4 (6.2), 7.1 (1.7) E. St. Paul All Seasons: 95, 10.8 (6.6), 9.3 (1.8) Spring: 36, 12.0 (7.3), 10.1 (1.9) summer: 25, 8.5 (3.2), 7.8 (1.6) Fall: 34, 11.3 (7.5), 9.6 (1.8) Phillips All Seasons: 88, 10.0 (5.8), 8.7, (1.7) Spring: 30 (12.1), 7.2 (10.5) summer: 30, 8.6 (3.8), 7.8 (1.6) Fall: 28, 9.3 (5.5), 8.1 (1.7)
Crist et al. (2008, 156372) Ohio River Valley near Columbus	$PM_{2.5}$, Units = $\mu g/m^3$ Athens (rural): 17.61 (17.81) Koebel (urban): 14.59 (13.05) New Albany (suburb): 13.93 (12.25)	$PM_{2.5}$, Units = $\mu g/m^3$ Indoor Athens (rural): 17.20 (13.56) Koebel (urban): 14.98 (12.30) New Albany (suburb): 16.52 (13.53)	$PM_{2.5}$, Units = $\mu g/m^3$ Athens (rural): 13.66 (8.91) Koebel (urban): 13.89 (9.29) New Albany (suburb): 12.72 (8.86)
Sarnat et al. (2006, 089784) Steubenville, OH	Mean (SD): $PM_{2.5}$, Units = $\mu g/m^3$ Summer n = 169 mean (SD) = 19.9 (9.4) Fall mean (SD) = 20.1 (11.6)		Mean (SD): $PM_{2.5}$, Units = $\mu g/m^3$ Summer n = 65 mean (SD) = 20.1 (9.3) Fall mean (SD) = 19.3 (12.2)
SOUTHEAST			
Wallace and Williams (2005, 057485) Raleigh, North Carolina	Units = $\mu g/m^3$ $PM_{2.5}$ pers = 23.0 (16.4) $PM_{2.5}$ pers/$PM_{2.5}$ out = 1.31 (0.99)	Units = $\mu g/m^3$ $PM_{2.5}$ in = 19.4 (16.5) $PM_{2.5}$ in/$PM_{2.5}$ out = 1.08 (1.05)	Units = $\mu g/m^3$ $PM_{2.5}$ out = 19.5 (8.6) 18.1 (8.1)
Williams et al. (2003, 053338) SE Raleigh, North Carolina Chapel Hill, North Carolina	Pooled PM mass concentrations ($\mu g/m^3$) across all subjects, residences, seasons, and cohorts Variable N Geo mean Mean RSD(a) Personal $PM_{2.5}$ (b) 712 19.2 23.0 70.1 (a) Relative standard deviation of the presented arithmetic mean. (b) measured using PEMs.	Pooled PM mass concentrations ($\mu g/m^3$) across all subjects, residences, seasons, and cohorts Variable N Geo mean Mean RSD(a) Indoor $PM_{2.5}$ (c) 761, 15.3, 19.1, 80.1 Outdoor $PM_{2.5}$ (c) 761, 17.5, 19.3, 43.7 Indoor PM_{10} (b) 761, 23.2, 27.7, 70.6 Outdoor PM_{10} (b) 761, 27.5, 30.4, 46.4 Indoor $PM_{10-2.5}$ (d) 761, 6.3, 8.6, 111.8 Outdoor $PM_{10-2.5}$ (d) 761, 8.5, 11.1, 86.9 (a) Relative standard deviation of the presented arithmetic mean. (b) measured using PEMs. (c) measured using HI samplers. (d) measured by difference in PEM PM_{10} monitor and co-located HI $PM_{2.5}$ mass concentrations.	Pooled PM mass concentrations ($\mu g/m^3$) across all subjects, residences, seasons, and cohorts Variable N Geo mean Mean RSD(a) Ambient $PM_{2.5}$ (c) 746, 17.3, 19.2, 44.9 Ambient PM_{10} (b) 752, 27.9, 31.4, 51.5 Ambient $PM_{10-2.5}$ (d) 210, 8.6, 10.0, 62.3 (a) Relative standard deviation of the presented arithmetic mean. (b) measured using PEMs. (c) measured using HI samplers. (d) measured by difference in PEM PM_{10} monitor and co-located HI $PM_{2.5}$ mass concentrations.

Reference / Location	Personal	Micro	Ambient
NORTHEAST			
Koutrakis et al. (2005, 095800) Baltimore, MD Boston, MA	$PM_{2.5}$, Units = $\mu g/m^3$: (Baltimore, Boston) Winter: Seniors: 15.1 (14.6), 14.1 (6.0) Children: 24.0 (21.8), 18.5 (12.8) COPD: 16.4 (12.7), NR Summer: Seniors: 22.1 (10.1), 18.8 (9.7) Children: 18.6 (8.1), 30.3 (14.2) COPD: NR, NREC: (Baltimore, Boston) Winter: Seniors: NR, 1.4 (0.9) Children: 2.8 (1.8), 1.6 (1.6) COPD: 2.0 (1.2), NR Summer: Seniors: NR, NR Children: NR, NR COPD: NR, $NRSO_4$: (Baltimore, Boston) Winter: Seniors: 1.9 (1.1), 1.9 (1.2) Children: NR, 2.3 (1.7) COPD: 1.5 (0.8), NR Summer: Seniors: 5.7 (3.5), 2.9 (1.9) Children: NR, NR COPD: NR, NR	NR	$PM_{2.5}$, Units = $\mu g/m^3$: (Baltimore, Boston) Winter: All: 20.1 (9.4), 11.6 (6.8) summer: Seniors: 25.2 (11.5), 12.7 (5.4) Children: 23.2 (14.0), 17.0 (11.5) COPD: NR, NREC: (Baltimore, Boston) Winter: All: 1.2 (0.6) summer: NR, $NRSO_4$: (Baltimore, Boston) Winter: All: 4.0 (1.7), 3.1 (1.8) summer: Seniors: 10.5 (7.1), 3.1 (1.8) Children: NR, 6.5 (6.0)
Sarnat et al. (2005, 087531) Boston, Massachusetts. Comparisons to a previous study in Baltimore are made.	Units = $\mu g/m^3$: Winter-Children: $PM_{2.5}$: 17.4-25.8 SO_4: 1.6-3.3 Winter-Seniors: $PM_{2.5}$: 10.8-16.2 SO_4: 1.6-2.6 Summer-Children $PM_{2.5}$: 25.4-32.8 SO_4: 2.7-3.3 Summer-Seniors $PM_{2.5}$: 17.8-20.5 SO_4: 2.7-3.3	NR	Units = $\mu g/m^3$: Winter: $PM_{2.5}$: 6.5-15.5 SO_4: 1.7-4.2 Summer: $PM_{2.5}$: 11.9-21.4 SO_4: 3.6-9.0
Turpin et al. (2007, 157062) Elizabeth, NJ, (and Houston, TX, and Los Angeles County, CA+	48-h avg $PM_{2.5}$, Units = $\mu g/m^3$: Elizabeth Child: 54.0 Adult: 44.8	Elizabeth: 20.1	Elizabeth: 20.4

Table A-62. Summary of PM species exposure studies.

Reference	Particle Sizes Measured	Component	Results	Primary Findings
Adgate et al. (2007, 156196)	Personal, Micro, and Ambient: $PM_{2.5}$ - broken down into TE	Ag, Al, Ca, Cd, Co, Cr, Cs, Cu, Fe, K, La, Mg, Mn, Na, Ni, Pb, S, Sb, Sc, Ti, Tl, V, Zn	Median, units: ng/m^3: Outdoor, Indoor, Personal S 334.4,272.1,351.6 Ca 232.2,85.0,174.1 Al 96.3,23.3, 58.6 Na 33.1, 20.6, 31.9; Fe 12.6, 43.1, 78.6 Mg 10.9, 16.3, 27.5 K 3.2, 38.4, 47.5 Ti 3.0, 0.8, 1.4 Zn 2.7, 6.5, 9.6 Cu 2.4, 1.5, 4.9 NiNA -0.1, 1.8 Pb 1.5, 2.4, 3.2 Mn 0.6, 1.5, 2.3 Sb 0.08,0.21, 0.30 Cd 0.05, 0.12, 0.14 V 0.05, 0.12, 0.16 La 0.02, 0.05, 0.11 Cs 0.00, 0.00,0.00 Th 0.00, 0.00, 0.00 Sc 0.00, 0.00, 0.01 Ag 0.00, 0.07, 0.08 Co NA 0.02, 0.07 Cr -0.09, 1.2, 2.6	The relationships among P, I, and O concentrations varied across TEs. Unadjusted mixed-model results demonstrated that ambient monitors are more likely to underestimate than overestimate exposure to many of the TEs that are suspected to play a role in the causation of air pollution related health effects. These data also support the conclusion that TE exposures are more likely to be underestimated in the lower income and centrally located PHI community than in the comparitively higher income BC K community. Within the limits of statistical power for this sample size, the adjusted models indicated clear seasonal and community related effects that should be incorporated in long-term exposure estimates for this population.
Brunekreef et al. (2005, 090486)	Personal, Micro & Ambient: $PM_{2.5}$	NO_3^-	Mean (SD), units = ng/m^3: Amsterdam: Personal 1389(1965) Indoor 1348(1843) outdoor 4063(4435) Helsinki: Personal 161(202) Indoor 267(215) Outdoor 1276(1181)	In both cities, personal and indoor $PM_{2.5}$ were lower than highly correlated with outdoor concentrations. For most elements, personal and indoor concentrations were also highly correlated with outdoor concentrations.
Brunekreef et al. (2005, 090486)	Personal, Micro, and Ambient: $PM_{2.5}$	SO_4^{2-}, NO_3^-	Mean, units = $\mu g/m^3$: SO_4^{2-}: P, I, O Amsterdam 4.6 4.7 5.9 Helsinki 2.7 3.0 5.0 NO_3^-: P, I, O Amsterdam 1.4 1.4 4.0 Helsinki 0.2 0.3 1.3	In both cities personal and indoor $PM_{2.5}$ were lower than highly correlated with outdoor concentrations. For most elements, personal and indoor concentrations were also highly correlated with outdoor concentrations.
Chillrud et al. (2004, 054799)	Personal: $PM_{2.5}$ Micro: $PM_{2.5}$ Home indoor and home outdoor Ambient: Urban fixed-site and upwind fixed site operated for three consecutive 48-h periods each week.	Elemental iron, manganese, and chromium are reported in this study out of 28 elements sampled.	Mean of duplicate samples: $PM_{2.5}$: 62 $\mu g/m^3$ Fe: 26 $\mu g/m^3$ Mn: 240 ng/m^3 Cr: 84 ng/m^3 Variability: 1-15%	Personal samples had significantly higher concentration of iron, manganese, and chromium than home indoor and ambient samples. The ratios of Fe (ng/ µg of $PM_{2.5}$) vs Mn (pg/ µg $PM_{2.5}$) showed personal samples to be twice the ratio for crustal material. Similarly for the Cr/Mn ratio. The ratios and strong correlations between pairs of elements suggested steel dust as the source. Time-activity data suggested subways as a source of the elevated personal metal levels.

Reference	Particle Sizes Measured	Component	Results	Primary Findings
Ebelt et al. (2005, 056907)	Personal: $PM_{2.5}$ Micro: "ambient exposure": $PM_{2.5}$, PM_{10}, $PM_{2.5-10}$; "non-ambient exposure:" $PM_{2.5}$ Ambient: $PM_{2.5}$, PM_{10}, $PM_{2.5-10}$	Ambient SO_4^{2-}, Ambient non-sulfate, Personal sulfate, personal ambient non-sulfate	Mean (SD),Units µg/m^3 Ambient sulfate: 2.0 (1.1), Ambient non-sulfate: 9.3 (3.7), Personal sulfate: 1.5 (0.9), personal ambient non-sulfate: 6.5 (3.0)	Ambient exposures and (to a lesser extent) ambient concentrations were associated with health outcomes; total and nonambient particle exposures were not.
Farmer et al. (2003, 089017)	Personal: PM_{10} Micro: NR Ambient: PM_{10} Extractable organic material (EOM) B[a]P cPAHs	Benzo[a]pyrene (B[a]P) Carcinogenic polycyclic aromatic hydrocarbons (cPAHs)	Units: ng/m^3 Exposed, controls: Prague: cPAHs = 12.04(11.10), 6.17 (3.48) B[a]P = 1.79 (1.67), 0.84 (0.60) Kosice: cPAHs = 21.72 (3.12), 6.39 (1.56) B[a]P = 2.94 (1.44), 1.07 (0.66) Sofia: cPAHs = 93.84 (55.0) police, 94.74 (120.34) bus drivers, 41.65 (33.36) B[a]P = 4.31 (2.6) police, 5.4 (3.18) bus drivers, 1.96 (1.53)	Personal exposure to B[a]P and to total carcinogenic PAHs in Prague was two fold higher in the exposed group compared to controls, in Kosice three fold higher, and in Sofia 2.5 fold higher.
Farmer et al. (2003, 089017)	Personal: PM_{10} Micro: NR Ambient: PM_{10} $PM_{2.5}$ (not reported)	PM_{10} EOM EOM2 B[a]P c-PAHsb	Prague-SMWinter Summer EOM (µg/m^3) 14.93 4.96 EOM2 (%)23.9 13.4 B[a]P (µg/m^3)3.5 0.28 c-PAHsb (µg/m^3) 24.69 2.29 Prague-LB Winter Summer EOM (µg/m^3) 10.86 3.72 EOM2 (%)27.9 14.1 B[a]P (µg/m^3)2.9 0.17 c-PAHsb (µg/m^3) 20.36 1.32 Košice Winter Summer EOM (µg/m^3) 15.3 1.67 EOM2 (%)26.4 6.9 B[a]P (µg/m^3)1.37 0.15 c-PAHsb (µg/m^3) 11.87 1.2 Sofia Winter Summer EOM (µg/m^3) 24.6 3.95 EOM2 (%)27.37 13.3 B[a]P (µg/m^3)4.84 0.36 c-PAHsb (µg/m^3) 36.44 2.43	Extractable organic matter (EOM) per PM_{10} was at least 2-fold higher in winter than in summer, and c-PAHs over 10-fold higher in winter than in summer. Personal exposure to B[a]P and to total c-PAHs in Prague ca. was 2-fold higher in the exposed group compared to the control group, in Košice ca. 3-fold higher, and in Sofia ca. 2.5-fold higher.
Gadkari et al. (2007, 156459)	Personal: Respirable PM (RPM) Micro: NR Ambient: RPM	Fe, Ca, Mg, Na K, Cd, Hg, Ni, Cr, Zn, As, Pb, Mn and Li	Source contributions varied widely among 12 sites. Indoor: 0-95% Ambient: 0-26% Road: 0-94% Soil: 0-75%	Authors conclude that personal exposure to ambient RPM is related to local traffic and soil resuspension. They felt that indoor activities or ventilation determined indoor levels of RPM.

Reference	Particle Sizes Measured	Component	Results	Primary Findings
Geyh et al. (2005, 186949)	Personal: TD, PM_{10}, $PM_{2.5}$ Micro: NR Ambient: TD, PM_{10}, $PM_{2.5}$	EC OC VOC also assessed	Mean (SD), units = $\mu g/m^3$: Summary Statistics by Area Location October 2001: Albany and West EC 5.9 (NA) OC 36 (NA) Liberty and Greenwich EC 5.3 (59) OC 30 (56) Park Place and Greenwich EC 14.5 (5.4) OC 72 (26) Church and Dey EC 7.9 (3.3) OC 48 (15) April 2002: Liberty and West EC 4.2 (2.1) OC 26 (13) Barclay and Greenwich EC 4.0 (2.6) OC 18 (14) Church and Dey EC 4.5 (1.9) OC 27 (15) Middle of the Pile EC 6.7 (1.0) OC 40 (25)	Comparison of recorded EC and OC values from October 2001 and April 2002 with previous studies suggests that the primary source of exposure to EC for the WTC truck drivers was emissions from their own vehicles.
Hanninen et al. (2004, 056812)	Personal: $PM_{2.5}$ Micro: NR Ambient: $PM_{2.5}$	$PM_{2.5}$ -bound S	Indoor Outdoor Athens 5.3 (2.0) 7.6 (5.1) Basel 2.6 (1.6) 3.3 (1.6) Helsinki 1.6 (1.3) 2.2 (1.5) Prague 3.1 (1.3) 4.0 (1.5)	Associated with indoor concentration: wooden building material, city, building age, floor of residence (i.e. ground, 1st, etc.), and use of stove other than electric.
Ho et al. (2004, 056804)	Personal: $PM_{2.5}$ Micro: NR Ambient: $PM_{2.5}$	OC EC OM TCA	Mean, Unit = $\mu g/m^3$ Indoors: OM = 18.1; TCA = 22.9 Outdoors: OM = 20.1; TCA = 26.5	The major source of indoor EC, OC, and $PM_{2.5}$ appears to be penetration of outdoor air, with a much greater attenuation in mechanically ventilated buildings.
Jacquemin et al. (2007, 192372)	Personal: $PM_{2.5}$ Micro: NA Ambient: $PM_{2.5}$	S	Mean, units = $\mu g/m^3$: Personal: 1.3 outdoor: 1.2	Authors suggest that "outdoor measurements of absorbance and sulphur can be used to estimate both the daily variation and levels of personal exposures also in Southern European countries, especially when exposure to ETS has been taken into account. For $PM_{2.5}$, indoor sources need to be carefully considered."
Jansen et al. (2005, 082236)	Personal, Micro, and Ambient: $PM_{2.5}$	Estimated Elemental Carbon (Abs) Elemental composition of a subset of personal, indoor and outdoor samples	Mean (SD), units = $\mu g/m^3$: Amsterdam, Helsinki P,O,P,O $PM_{2.5}$ 14.5, 15.7, 9.4, 11.4 Abs 1.4, 1.6, 1.3, 1.9 S 912.3, 1299.9, 605.3, 1435.7 Zn 13.2, 18.3, 11.7, 18.6 Fe 57.0, 71.3, 41.6, 79.2 K 87.4, 70.3, 103.1, 93.9 Ca 72.9, 40.2, 68.5, 36.4 Cu 5.4, 2.5, 4.3, 1.8 Si 29.7, 13.7, 79.5, 93.9 Cl 40.8, 72.7, 9.8, 44.2	For most elements, personal and indoor concentrations were lower than and highly correlated with outdoor concentrations. The highest correlations (median r.0.9) were found for sulfur and particle absorbance (EC), which both represent fine mode particles from outdoor origin. Low correlations were observed for elements that represent the coarser part of the $PM_{2.5}$ particles (Ca, Cu, Si, Cl).

Reference	Particle Sizes Measured	Component	Results	Primary Findings
Johannesson et al. (2007, 156614)	Personal, Micro, and Ambient: $PM_{2.5}$, PM_1	BS	$BS_{2.5}$ Mean SD Personal 0.65 0.47 Exclusively smokers 0.62 0.47 Residential indoor 0.56 0.47 Exclusively smokers 0.52 0.46 Residential outdoor 0.68 0.51 Exclusively smokers 0.71 0.54 Urban background 0.63 0.37 All measurements 0.68 0.40 PM_1/BS1 Personal 0.55 0.20 Residential indoor 0.54 0.45 Exclusively smokers 0.49 0.43 Residential outdoor 0.66 0.51 Exclusively smokers 0.68	Personal exposure of $PM_{2.5}$ correlated well with indoor levels, and the associations with residential outdoor and urban background concentrations were also acceptable. Statistically significantly higher personal exposure compared with residential outdoor levels of $PM_{2.5}$ was found for nonsmokers. PM_1 made up a considerable proportion (about 70–80%) of $PM_{2.5}$. For BS, significantly higher levels were found outdoors compared with indoors, and levels were higher outdoors during the fall than during spring. There were relatively low correlations between particle mass and BS. The urban background station provided a good estimate of the residential outdoor concentrations of both $PM_{2.5}$ and $BS_{2.5}$ within the city. The air mass origin affected the outdoor levels of both $PM_{2.5}$ and $BS_{2.5}$; however, no effect was seen on personal exposure or indoor levels.
Kim et al. (2005, 156640)	Personal: $PM_{2.5}$ Micro: NR Ambient: $PM_{2.5}$	SO_4^{2-}, EC, Ca^{2+}, Mn^{2+}, K, Na^+	Mean (SD), Units = $\mu g/m^3$: SO_4^{2-}: 2.7 (3.2) Ca^{2+}: 0.12 (0.12) Mg^{2+}: 0.02 (0.01) K: 0.07 (0.08) Na^+: 0.09 (0.20) EC: 0.60 (0.54)	Traffic-related combustion, regional, and local crustal materials were found to contribute 19% ± 17%, 52% ± 22%, and 10% ± 7%, respectively. Among participants that spent considerable time indoors, exposure to outdoor $PM_{2.5}$ includes a greater relative contribution from combustion sources, compared with outdoor (ambient) $PM_{2.5}$ measurements.
Koistinen et al. (2004, 156655)	Personal, Micro, and Ambient: $PM_{2.5}$	Black smoke, SO_4^{2-}, NO_3^-, NH_4^+, Al, Ca, Cl, Cu, K, Mg, P, S, Si, Zn	% contribution to $PM_{2.5}$ Outdoor - Indoor - Work - Personal CoPM * 35, 28, 32, 33 Secondary** 46, 36, 37, 31 Soil 16, 27, 27, 27 Detergents 0, 6, 2, 6 Sea Salt 3, 2, 1, 2 * CoPM is the difference between total mass and other identified components; i.e., primary combustion particles, nonvolatile primary and secondary organic particles, and particles from tire wear, water, etc. ** Secondary particles are the sum of sulfate, nitrate, and ammonium. 4 factors were identified for each exposure type (residential indoor, residential outdoor, workplace indoor, and personal). The factors contained the elements Al, Ca, Cl, Cu, K, Mg, P, S, Si, Zn, and black smoke. (insert in cell to left after consolidating PM size)	Population exposure assessment of $PM_{2.5}$, based on outdoor fixed-site monitoring, overestimates exposures to outdoor sources like traffic and long-range transport and does not account for the contribution of significant indoor sources.

Reference	Particle Sizes Measured	Component	Results	Primary Findings
Koutrakis et al. (2005, 095800)	Personal: $PM_{2.5}$ Micro: NR Ambient: $PM_{2.5}$	Elemental Carbon (EC), SO_4^{2-}	Mean (SD) data are provided for Baltimore and Boston, Units = $\mu g/m^3$: EC: (Baltimore, Boston) Winter: Seniors: NR, 1.4 (0.9) Children: 2.8 (1.8), 1.6 (1.6) COPD: 2.0 (1.2), NR SO_4^{2-}: (Baltimore, Boston) Winter: Seniors: 1.9 (1.1), 1.9 (1.2) Children: NR, 2.3 (1.7) COPD: 1.5 (0.8), NR Summer: Seniors: 5.7 (3.5), 2.9 (1.9)	Ambient $PM_{2.5}$ and SO_4^{2-} are strong predictors of respective personal exposures. Ambient SO_4^{2-} is a strong predictor of personal exposure to $PM_{2.5}$. Because $PM_{2.5}$ has substantial indoor sources and SO_4^{2-} does not, the investigators concluded that personal exposure to SO_4^{2-} accurately reflects exposure to ambient $PM_{2.5}$ and therefore the ambient component of personal exposure to $PM_{2.5}$ as well.
Kulkarni and Patil (2003, 156664)	Personal: PM_5 Micro: NR Ambient: PM_5	Pb Ni Cd Cu Cr Fe Mn	Personal samples, Units = $\mu g/m^3$: Mean ± SD Type Pb Occupational 4.384 ± 7.766 $\mu g/m^3$ Residential 4.093 ± 5.925 $\mu g/m^3$ 24-h integrated 4.205 ± 1.523 $\mu g/m^3$ Cd Occupational 0.201 ± 0.158 $\mu g/m^3$ Residential 0.111 ± 0.165 $\mu g/m^3$ 24-h integrated 0.134 ± 0.140 $\mu g/m^3$ Mn Occupational 1.979 ± 7.842 $\mu g/m^3$ Residential 0.180 ± 0.261 $\mu g/m^3$ 24-h integrated 1.983 ± 6.824 $\mu g/m^3$ K Occupational 3.473 ± 4.691 $\mu g/m^3$ Residential 4.589 ± 4.619 $\mu g/m^3$ 24-h integrated Check	All listed metals were detected in the ambient air where as only Lead, Cadmium, Manganese, and Potassium were detected in personal exposures. Mean daily exposure to lead exceeds the Indian NAAQS by a factor of 4.2. However, ambient concentration of lead conforms to this standard. There is a rising trend in the personal exposures and ambient levels of cadmium. However, they are low and do not pose any major health risk as yet. Personal exposures to toxic metals exceed the corresponding ambient levels by a large factor ranging from 6.1 to 13.2. Thus, ambient concentrations may underestimate health risk due to personal exposure of toxic metals. Outdoor exposure to toxic metals is greater than the indoor (ratios ranging from 2.3 to 1.1) except for potassium (ratio 0.77). However, there is no significant correlation between these two.

Reference	Particle Sizes Measured	Component	Results	Primary Findings
Lai et al. (2004, 056811)	Personal, Micro, and Ambient: $PM_{2.5}$	Ag Cr Mn Si Al Cu Na Sm As Fe Ni Sn Ba Ga P Sr Br Ge Pb Ti Ca Hg Rb Tl Cd I S Tm Cl K Sb V Co Mg Se Zn Zr	GM (GSD), Units: ng/m^3 P, RI, RO, WI, I/O Al 280 (7.0), 67 (7.2), 22 (2.9), 110 (7.5), 1.4 As 4.7 (1.6), 3.7 (1.8), 2.6 (2.7), 6 (—), 1.4 Br 4.7 (2.2), 3.9 (2.0), 2.4 (2.5), 6.2 (2.5), 1.6 Ca 260 (2.0), 120 (2.1), 30 (1.6), 280 (2.9), 3.3 Cd 23 (1.4), 19 (1.8), 7 (—), 43 (2.2), — Cl 400 (3.0), 270 (3.9), 220 (5.2), 380 (3.9), 1.0 Cu 120 (1.3), 88 (1.7), 2.3 (2.8), 230 (2.1), 37.1 Fe 59 (2.3),30 (3.8), 19 (3.5), 85 (2.9), 1.6 Ga 0.9 (2.1), 0.6 (2.2), 0.2 (2.2), 2.0 (3.4), 2.4 K 250 (2.4), 180 (2.7), 93 (2.0), 130 (4.0), 1.7 Mg 260 (2.1), 130 (3.1), 140 (2.9), 120 (2.8), 0.7 Mn 2.1 (2.6), 1.8 (2.4), 2.2 (1.5), 3.5 (3.0), 0.8 Na 2100 (1.6) ,1800 (1.7), 1100 (3.2), 2700 (1.9), 1.6 Ni 11 (2.2), 8.6 (2.5), 18 (—), 23 (2.9),— P 110 (2.1), 70 (2.2), 27 (1.8), 86 (2.4), 2.5 Pb 26 (1.7), 19 (1.8), 9.4 (2.8), 32 (2.0), 1.9 S 1200 (1.9), 1200 (2.0), 890 (4.8), 1.2 Se 8.4 (1.5), 6.8 (1.7), 2.3 (1.8), 16 (2.2), 2.8 Si 740 (3.4), 360 (2.9), 95 (2.2), 570 (3.8), 2.6 Sn 35 (1.5), 27 (1.8), 0 (—), 68 (2.6), — Ti 6.2 (1.7), 2.8 (2.2), 1.1 (2.0), 6.1 (3.2), 2.3 V 1.8 (1.5), 1.4 (1.9), 4 (—), — Zn 18 (2.4), 15 (2.2), 13 (2.5), 23 (2.4), 0.9	Both the indoor and outdoor environments have sources that elevated the indoor concentrations in a different extent, in turn led to higher personal exposures to various pollutants. Geometric mean (GM) of personal and home indoor levels of $PM_{2.5}$, 14 elements, total VOC (TVOC) and 8 individual compounds were over 20% higher than their GM outdoor levels. Those of NO_2, 5 aromatic VOCs, and 5 other elements were close to their GM outdoor levels. For $PM_{2.5}$ and TVOC, personal exposures and residential indoor levels (in GM) were about 2 times higher among the tobacco-smoke exposed group compared to the non-smoke exposed group, suggesting that smoking is an important determinant ofthese exposures. Determinants for CO were visualised by real-time monitoring, and the authors showed that the peak levels of personal exposure to CO were associated with smoking, cooking and transportation activities. Moderate to good correlations were only found between the personal exposures and residential indoor levels for both $PM_{2.5}$ ($r = 0: 60$; $p < 0: 001$) and NO_2 ($r = 0: 47$; $p = 0: 003$).

Reference	Particle Sizes Measured	Component	Results	Primary Findings
Larson et al. (2004, 098145)	Personal: $PM_{2.5}$ Micro: $PM_{2.5}$ outside subject's residence, and inside residence Ambient: $PM_{2.5}$ at Central outdoor site (downtown Seattle)	Light absorbing carbon (LAC) and Al, As, Br, Ca, Cl, Cr, Cu, Fe, K, Mn, Ni, Pb, Si, S, Ti, V	Personal, RI, RO, Central Mass 10,500 10,250 12,693 11,970 Al 32, 19, 21, 31 As 1, 1, 2, 2 LAC * 1439, 1105, 1830, 1741 Br 3, 2, 3, 3 Ca 72, 46, 36, 50 Cl 248,173, 75, 78 Cr 2, 2, 1, 2 Cu 3, 4, 2, 3 Fe 63, 35, 61, 95 K 57, 54, 78, 67 Mn 2, 2, 3, 6 Ni 0 ,0, 1, 1 Pb 2, 2, 5, 5 Si 109, 65, 66, 62 S 289, 289, 468, 492 Ti 4, 3, 3, 6 V 0, 1, 2, 3	Five sources of $PM_{2.5}$ identified: vegetative burning, mobile emissions, secondary sulfate, a source rich in chlorine, and crustal-derived material. The burning of vegetation (in homes) contributed more $PM_{2.5}$ mass on avg than any other sources in all microenvironments.
Maitre et al. (2002, 156726)	Personal: PM_4 Micro: NR Ambient: PM_4	PAH, benxene-toluene-xylenes (BTX), aldehydes, BaP PAHc, formaldehyde, acetaldehyde	Median Personal Ambient Resp µg/m^3 124, 124 (mean) BaP ng/m^3 0.28,0.14 PAHc ng/m^3 1.19,1.56 PAH ng/m^3 13.14,12.26 Benzene µg/m^3 23.5, 17 Toluene µg/m^3 94.5, 52 Xylene µg/m^3 74, 39 BTX µg/m^3 192, 108 Formaldehyde µg/m^3 21, 17.5 Acetaldehyde µg/m^3 17, 10.5 Aldehyde µg/m^3 38, 28	The occupational exposure of policemen does not exceed any currently applicable occupational or medical exposure limits. Individual particulate levels should preferably be monitored in Grenoble in winter to avoid underestimations.
Meng et al. (2005, 081194)	Personal: $PM_{2.5}$ Micro: NA Ambient: NR	EC, OC, S, Si	Mean (SD), units = ng/m^3: Indoor: EC: 1165.9 (2081.0) OC: 7725.5 (9359.3) S: 902.3 (602.2) Si: 124.0 (79.0) Outdoor: EC: 1144.1 (968.1) OC: 3777.7 (2520.1) S: 1232.3 (633.2) Si: 141.1 (171.3)	Use of central-site $PM_{2.5}$ as an exposure surrogate underestimates the bandwidth of the distribution of exposures to PM of ambient origin.

Reference	Particle Sizes Measured	Component	Results	Primary Findings
Molnár et al. (2005, 156772)	Personal: $PM_{2.5}$ Micro and Ambient: $PM_{10-2.5}$ and $PM_{2.5}$	BS S Cl K Ca Mn Fe Cu Zn Br Rb Pb	Median, unit = ng/m^3 Wood burners Ref 1-sided p-value BS 0.97, 0.74, 0.053 S 880, 650, 0.500 Cl 200, 160, 0.036 K 240, 140, 0.024 Ca 76, 43, 0.033 Mn 4.8, 3.5, 0.250 Fe 64, 49, 0.139 Cu 8.9, 2.4, 0.016 Zn 38, 22, 0.033	Statistically significant contributions of wood burning to personal exposure and indoor concentrations have been shown for K, Ca, and Zn. Increases of 66–80% were found for these elements, which seem to be good wood-smoke markers. In addition, Cl, Mn, Cu, Rb, Pb, and BS were found to be possible wood-smoke markers, though not always to a statistically significant degree for personal exposure and indoor concentrations. For some of these elements, subgroups of wood burners had clearly higher levels which could not be explained by the information available. Sulfur, one of the more typical elements mentioned as a wood-smoke marker, showed no relation to wood smoke in this study due to the large variations in outdoor concentrations from LDT air pollution. This was also the case for $PM_{2.5}$ mass. Personal exposures and indoor levels correlated well among the subjects for all investigated species, and personal exposures were generally higher than indoor levels.
Molnar et al. (2006, 156773)	Personal: $PM_{2.5}$ and PM_1 Micro and Ambient: NR	S Cl K Ca Ti V Mn Fe Ni Cu Zn Br Pb	Urban background $PM_{2.5}$ Mean, median, range (ng/m^3) S 620, 320, 95-1900 Cl 97, 54, 25-460 K 55, 50, 32-130 Ca 21, 17, 6.6-6.2 Ti 2.1, 1.9, 1.3-3.8 V 3.4, 2.4, 1.0-13 Mn 1.6, 1.4, 0.67- 3.8 Fe 36, 33, 7.1-100 Ni 1.6, 1.2, 0.33- 5.7 Cu 2.1, 1.4, 0.33-11 Zn 14, 11, 2.8-38 Br 1.7, 1.4, 0.47-44.3 Pb 3.3, 2.1, 0.94-11 Personal $PM_{2.5}$ Mean, median, range ($\mu g/m^3$) S –, < 470, 270-1400 Cl 270, 170, 60-920 K 140, 96, 39-690 Ca 110, 80, 27-670 Ti 11, 9.5, 3.7-27 V 4.7, 4.0, 2.7-9.4 Mn - - - Fe 68, 69, 23-150 Ni 4.2, 2.6, 0.89-46 Cu 10, 6.6, 1.1-81 Zn 21, 16, 6.6-70 Br 2.0, 1.3, 0.91-14 Pb 2.9, 2.6, 0.92-8.3 Personal PM_1 Mean, median, range ($\mu g/m^3$) S –, < 470, 240-1200 Cl –, < 110, 54-160 K 80, 82, 50-130 Ca 32, 23, 8.4-87 Ti 6.5, 6.3, 3.7-11 V –, < 4.2, 2.8-8.9	$PM_{2.5}$ personal exposures were significantly higher than both outdoor and urban background for the elements Cl, K, Ca, Ti, Fe, and Cu. Personal exposure was also higher than indoor levels of Cl, Ca, Ti, Fe, and Br, but lower than outdoor Pb. Residential outdoor levels were significantly higher than the corresponding indoor levels for Br and Pb, but lower for Ti and Cu. The residential levels were also significantly higher than the urban background for most elements.

Reference	Particle Sizes Measured	Component	Results	Primary Findings
			Mn - - - Fe 28, 25, 7.6-68 Ni 8.2, 1.2, 0.83-58 Cu 5.0, 4.4, 1.6-14 Zn 15, 14, 7.6-37 Br 1.6, 1.5, 0.83-4.4 Pb 3.6, 2.8, 1.1-11 Residential Outdoor $PM_{2.5}$ Mean, median, range S 640, 460, 190-1800 Cl 6.3, 140, 57-840 K 200, 78, 32-200 Ca 82, 28, 4.6-85 Ti 34, 5.2, 3.3-21 V 6.3, 3.9, 2.1-14 Mn --- Fe 5.5, 31, 8.8-200 Ni 45, < 1.6, 0.65-5.5 Cu 2.6, 1.3, 0.65-17 Zn 22, 15, 5.5-85 Br 2.0, >450, 0.91-51 Pb 4.6, 2.6, 0.90-20 Residential Outdoor PM_{1} S –, 1.3, 24-2000 Cl –, < 110, 44-170 K 76, 68, 34-170 Ca –, < 12, 5.1-78 Ti –, < 5.0, 2.2-9.5 V 5.6, 4.47, 2.2-14 Mn --- Fe 23, 14, 3.7-140 Ni 3.3, 1.4, 0.73-28 Cu –, < 1.1, 0.73-12 Zn 15, 14, 5.2-30 Br 1.5, 1.4, 0.78-4.3 Pb 4.1, 1.5, 1.0-17	
Na and Cocker (2005, 156790)	Personal: $PM_{2.5}$ Micro: NR Ambient: $PM_{2.5}$	EC, OC	Mean (SD), units = µg/m^3 Residential homes: EC 2.0 (NR) OC 14.8 (NR) High school (EC): Weekday samples 1.1 (0.9) Weekend samples 1.0 (0.5) High school (OC): Weekday samples 8.8 (4.7) Weekend samples 7.4 (2.4)	Indoor $PM_{2.5}$ was significant influenced by indoor OC sources. Indoor EC sources were predominantly of outdoor origin.
Noulett et al. (2006, 155999)	Personal: $PM_{2.5}$ Micro: NR Ambient: $PM_{2.5}$	SO_4^{2-} ABS (light absorbing carbon)	Measurement Mean s.d. Ambient $_{SO4}^{2-}$ 2.72* 3.11 Ambient ABS 1.4** 1.0 Personal SO_4^{2-} 1.33* 1.47 Personal ABS 1.0** 1.7 * Mean SO_4^{2-} values reported in µg/m^3 ** Mean ABS values reported in 10-5/m^{-1}	SO_4^{2-} and light absorbing carbon concentrations had higher personal-ambient correlations and less variability. This indicates that SO_4^{2-} and ABS were of outdoor origin, while $PM_{2.5}$ mass was of varied indoor and outdoor origin.

Reference	Particle Sizes Measured	Component	Results	Primary Findings
Salma et al. (2007, 113852)	Personal: $PM_{10-2.0}$ and $PM_{2.0}$ Micro: NA Ambient: NR	30 elements (Na, Mg, Al, Si, P, S, Cl, K, Ca, Ti, V, Cr, Mn, Fe, Ni, Cu, Zn, Ga, Ge, As, Se, Br, Rb, Sr, Y, Zr, Nb, Mo, Ba, and Pb)	Units: ng/m^3: $PM_{10-2.0}$; $PM_{2.0}$ Mg 296 130 Al 531 93 Si 2.09 442 S 978 828 Cl 305 104 K 318 127 Ca 2.57 413 Ti 47 25 Cr 35 15 Mn 310 148 Fe 33.5 15.5 Ni 29 8 Cu 496 190 Zn 118 50 Br 13 DL Ba 145 DL Pb 47 21 PM 83.6 33.0	The concentrations observed in the Astoria underground station were clearly lower (by several orders of magnitude) than the corresponding workplace limits.
Sarnat et al. (2005 RMID 9171) (2005, 087531)	Personal: $PM_{2.5}$ Micro: N/A Ambient: $PM_{2.5}$	SO_4, O_3, NO_2, SO_2	Correlations between personal $PM_{2.5}$ and ambient gas O_3 correlated in summer. Spearman's R≈0.4, Anti-correlated in winter, R≈0.3-0.1. NOX somewhat correlated in summer. R≈0.3 Winter, R≈0.2-0.4 SO_2 not well correlated in summer or winter. R≈0-0.1. CO somewhat correlated in summer. R≈0.1-0.3. Correlated in winter R≈0.2-0.3. No results were significant.	Substantial correlations between ambient $PM_{2.5}$ concentrations and corresponding personal exposures. Summertime gaseous pollutant concentrations may be better surrogates of personal $PM_{2.5}$ exposures (especially personal exposures to $PM_{2.5}$ of ambient origin) than they are surrogates of personal exposures to the gases themselves.
Sarnat et al. (2006, 089784)	Personal: $PM_{2.5}$ Micro: NR Ambient: $PM_{2.5}$	SO_4^{2-} EC	Mean (SD), units = $\mu g/m^3$: Personal Ambient SO_4^{2-} Summer 5.9 (4.2) 7.7 (4.8) Fall 4.4 (3.3) 6.2 (4.7) EC Summer 1.1 (0.6) 1.1 (0.5) Fall 1.2 (0.7) 1.1 (0.7)	High association between personal and ambient SO_4^{2-} and EC, especially for SO_4^{2-} for which there is no significant indoor source.
Shilton et al. (2002, 049602)	Personal, Micro, and Ambient: Respirable PM	Respirable PM, metals (Zn, Cu, Mn, Al), SO_4^{2-}, NO_3^-, and Cl^-	IndoorOutdoor Zn (ng/m^3) 241.1, 179.5 Cu (ng/m^3) 43.3, 24.99 Mn (ng/m^3) 15.6, 4.18 Al (ng/m^3) 305.2, 52.90 SO_4^{2-} (ng/m^3) 4.72, 3.47 Cl (ng/m^3) 1.08, 0.15 NO_3^- (ng/m^3).35, 1.08	The indoor particulate conc was driven by ambient conc; meteorological-induced changes in ambient PM were detected indoors;

Reference	Particle Sizes Measured	Component	Results	Primary Findings
Smith et al. (2006, 156990)	Personal: $PM_{2.5}$ Micro: $PM_{2.5}$ Area samplers in the offices, freight dock, or shop. Ambient: $PM_{2.5}$ Samplers were located in the yard upwind of the terminal.	EC OC	Work Area EC, OC, EC/TC Office 0.31 (3.72), 11.29 (1.63) Dock 0.53 (3.24), 5.01 (1.76), 3% (3.10) Yard 0.73 (2.89), 7.77 (1.65), 9% (2.49) Shop 1.54 (3.52), 10.37 (2.00), 8% (2.21) Non-smokers on-site: 12% (2.13) Clerk 0.09 (9.98), 15.97 (1.31) Dock worker 0.76 (2.13), 13.89 (1.45),1% (10.19) Mechanic 2.00 (3.82), 16.89 (1.64), 5% (1.96) Hostler 0.88 (3.04), 14.89 (1.86), 10% (2.71) Non-smokers off-site 5% (2.09) Pickup/deliver driver 1.09 (2.46), 12.40 (1.54) Long haul driver 1.12 (1.91), 19.26 (2.30),8% (2.13) Smokers On-Site 7% (1.82) Clerk 1.19 (1.70), 32.25 (1.70), NR Dock worker 0.98 (1.93), 24.02 (1.87) Mechanic 2.41 (2.27), 24.35 (1.78) Hostler 1.74 (2.21), 43.92 (2.03) Smokers off-site Pickup & Delivery drivers 1.33 (3.84), 24.24 (2.14) Long haul drivers 1.37 (2.40),32.81 (3.23)	

Reference	Particle Sizes Measured	Component	Results	Primary Findings
Sørensen et al. (2003, 157000)	Personal: $PM_{2.5}$ Micro: NR Ambient: $PM_{2.5}$	BS	Units: 10^{-6}/m n Median Q25-Q75 All 177 6.8 (5.0-13.2) Autumn 42 7.1 (6.5-17.2) Winter 46 8.2 (5.1-13.3) Spring 46 12.6 (5.4-10.4) Summer 47 8.1 (3.4-9.0)	Personal $PM_{2.5}$ exposure was found to be a predictor of 8-oxodG in lymphocyte DNA. No other associations between exposure markers and biomarkers could be distinguished. ETS was not a predictor of any biomarker in the present study. The current study suggests that exposure to $PM_{2.5}$ at modest levels can induce oxidative DNA damage and that the association to oxidative DNA damage was confined to the personal exposure, whereas the ambient background concentrations showed no significant association. For most of the biomarkers and external exposure markers, significant differences between the seasons were found. Similarly, season was a significant predictor of SBs and PAH adducts, with avg outdoor temperature as an additional significant predictor.
Sorenson et al. (2005, 089428)	Personal: $PM_{2.5}$ and BS Micro: $PM_{2.5}$ and BS Ambient: Street monitoring station and roof of a campus building $PM_{2.5}$ and BS	BS	Mean, IQR, Units = $\mu g/m^3$: Personal: Cold Season: 10.2 (5.6-14.8) Warm Season: 7.1 (5.5-11.4) Micro: Cold Season Home Indoor: 6.2 (5.5-11.4) Home front door: 10.8 (7.4-16.3) Warm Season Home Indoor: 6.1 (3.7-7.6) Home front door: 8.8 (5.6-11.54) Ambient: Cold Season: Street Station: 31.6 (27.5-34.0) Urban Background: 7.7 (5.9-11.0) Warm Season: Street Station: 30.6 (24.7-36.0) Urban Background: 6.8 (4.6-8.6)	Indoor sources of PM and BS were shown to be greatly influenced by indoor sources.
Sram et al. (2007, 192084)	Personal: PM_{10}, $PM_{2.5}$ Micro: NR Ambient: PM_{10}, $PM_{2.5}$	c-PAHs, B[a]P	B[a]P: Exposed 1.6 ng/m^3 Control 0.8 ng/m^3 c-PAHs: Exposed 9.7 ng/m^3 Control 5.8 ng/m^3	Ambient air exposure to c-PAHs increased fluorescent in situ hybridization (FISH) cytogenetic parameters in non-smoking policemen exposed to ambient PM

Reference	Particle Sizes Measured	Component	Results	Primary Findings
Turpin et al. (2007, 157062)	Personal: $PM_{2.5}$ Micro: $PM_{2.5}$, in the main living area (not kitchen) Ambient: $PM_{2.5}$, in the front or back yard	18 volatile organics, 17 carbonyl, $PM_{2.5}$ mass and >23 $PM_{2.5}$ species, organic carbon, elemental carbon, and PAHs	For Los Angeles Carbon (µgC/m^3) EC 1.4 OC 4.1 Elements (ng/m^3) Ag 0.5 Al 24.7 As 0.5 Ba 22.9 Br 5.3 Ca 80.9 Cd 0.4 Cl 62.0 Co ND Cr 0.6 Cu 5.5 Fe 162.9 Ga 0.1 Ge 0.1 Hg 0.1 In 0.3 K 74.1 La 2.3 Mn 2.9 Mo 0.4 Ni 2.0 Pb 4.7 Pd 0.3 P 0.1 Rb 0.1 S 1022.9 Sb 2.1 Se 1.4 Si 128.9 Sn 7.9 Sr 1.8 Ti 10.4 V 5.3 Y 0.1 Zn 16.4 Zr 0.5	The best estimate of the mean contribution of outdoor to indoor $PM_{2.5}$ was 73% and the outdoor contribution to personal was 26%.
Wallace and Williams (2005, 057485)	Personal: $PM_{2.5}$ Indoor Micro: $PM_{2.5}$ Outdoor Micro: $PM_{2.5}$	S	Mean (SD), units = ng/m^3: Personal: 1046 (633) Indoor: 1098 (652) Outdoor: 1951 (1137)	Generally, F_{inf} provides a reliable estimate of personal exposure. S can be used in lieu of personal exposure to PM because it is generally derived from outdoors.
Wu et al. (2006, 179950)	Personal: $PM_{2.5}$ Micro: $PM_{2.5}$ Ambient: $PM_{2.5}$	LG EC OC	Mean personal exposure (µg/m^3): LG: 0.018 (0.024) EC: 0.4 (0.5) OC: 8.5 (2.7). Ambient: check component During non-burning times: 0.026 (0.030) During burning episodes: 0.010 (0.012)	Authors “found a significant between-subject variation between episodes and non-episodes in both the Exposure during agricultural burning estimates and subjects’ activity patterns. This suggests that the LG measurements at the central site may not always represent individual exposures to agricultural burning smoke “Evidence of “Hawthorne Effect”: During declared episodes (i.e. real and sham), subjects spent less time indoors at home and more time in transit or indoors away from home than during non-declared episode periods. The differences remained even when limited to weekdays only.

Reference	Particle Sizes Measured	Component	Results	Primary Findings
Zhao et al. (2007, 156182)	Personal, Micro, and Ambient: $PM_{2.5}$	EC, Cl, Si, NO_3	Units = $\mu g/m^3$: Personal: EC: 1.64 NO_3: 0.135 Si: 0.176 Cl: 0.116 Indoor: EC: 1.819 NO_3: 0.013 Si: 0.051 Cl: 0.024 Outdoor: EC: 1.876 NO_3: 0.292 Si: 0.115 Cl: 0.013	Four external sources and three internal sources were resolved in this study. Secondary NO_3^- and motor vehicle exhaust were two major outdoor $PM_{2.5}$ sources. Cooking was the largest contributor to the personal and indoor samples. Indoor environmental tobacco smoking also has an important impact on the composition of the personal exposure samples.

Table A-63. Summary of personal PM exposure source apportionment studies.

Reference	Study Design	Results	Primary Findings
Hopke et al. (2003, 095544)	Source apportionment of personal and indoor central and apartment and outdoor $_{PM2.5}$. Baltimore retirement home with 10 elderly subjects. July-Aug 1998.	% control P,I, C, O External Secondary SO_4^{2-} 46.3, 64.0, 79.0, 64.0 Unknown 13.6, 14.5, 17.4, 14.5 Soil 2.8, 3.1, 3.6, 3.1 Internal Gypsum 0.7, 0.4, 0.0, 0.0 Activity 36.2, 17.8, 0.0, 0.0 Personal care 0.4, 0.3, 0.0, 0.0	63% of personal exposure could be attributed to outdoor sources (with 46% from SO_4^{2-}), and resuspension of indoor PM during vacuuming, cleaning, or other activities contributed 36% of personal exposure.
Larson et al. (2004, 098145)	Source apportionment of personal and residences and central outdoor $PM_{2.5}$ around Seattle with 10 elderly subjects and 10 asthmatic children. The purpose of the article was to compare PMF2 and PMF3 methods. Seattle Sep 2000 and May 2001	PMF2: % control P,I,O Veg burn 28.8, 47.6, 56.7 Mobile 0.0, 3.6, 7.5 Fuel oil 0.0, 0.0, 6.7 S, Mn, Fe 8.1, 0.0, 0.0 Secondary 0.0, 34.5, 20.9 Cl-rich 9.9, 3.6, 3.7 Crustal 25.2, 10.7, 4.5 Crustal 2 27.9, 0.0, 0.0 PMF3: % control P,I, O Veg burn 41.0, 57.4, 71.3 Mobile 7.2, 4.3, 8.2 Secondary 19.3, 13.8, 18.0 Crustal 32.5, 24.,5 2.5	Results showed that vegetative burning was the largest contributor to personal exposure and that was related to outdoor combustion. Crustal exposures were related to indoor activities.
Zhao et al. (2006, 156181)	Source apportionment of personal and residential indoor and residential outdoor and central outdoor $PM_{2.5}$, Raleigh and Chapel Hill NC with 38 subjects. Summer 2000 and Spring 2001.	% control P, I, R,O Motor vehicle 10.0, 9.4, 17.2, 19.4 Soil 3.5, 3.7, 9.3, 8.5 Secondary SO_4^{2-} 15.9, 22.5, 59.3, 61.9 Secondary NO_3^- 4.4, 4.7, 7.6, 7.8 ETS 7.0, 10.0, 0.0, 0.0 Personal care and activity 8.0, 19.1, 0.0, 0.0 CU-factor mix with indoor soil 0.4, 1.2, 0.0, 0.0 Cooking 52.5, 53.6, 0.0, 0.0	Secondary sulfate was the largest ambient source and the largest ambient contribution to personal exposure. Cooking produced the largest contribution to personal and indoor concentrations. Note that sums over 100% because multiple sources obscured PMF resolution.

Reference	Study Design	Results	Primary Findings
Meng et al. (2007, 194618)	Source apportioned infiltration for personal and residential indoor and residential outdoor and central outdoor $_{PM2.5}$. Los Angeles, Houston, and Elizabeth, NJ with 100 non-smoking residences and residents in each city. In each season between summer 1999 and spring 2001 (RIOPA).	% contr Outdoor Indoor (Outdoor Origin) Mechanically generated 2, 17 Primary Combustion 43, 43 Secondary Formation* 55, 40 *excludes nitrates	Differential infiltration of the $PM_{2.5}$ resulted in a reduction of secondary formation products relative to outdoors.
Reff et al. (2007, 156045)	Functional group distinction for personal and residential indoor and residential outdoor and central outdoor $PM_{2.5}$, $PM_{2.5}$ samples from 219 homes were used for this analysis. Los Angeles, Houston, and Elizabeth, NJ with 100 non-smoking residences and residents in each city. In each season between summer 1999 and spring 2001 (RIOPA).	SO_4^{2-}: R, O, I, P O 1.0 I 0.54-0.76 1.0 P 0.54-0.73 0.84-0.90 1.0 C = O: R, O, I, P O 1.0 I 0.12-0.61 1.0 P -0.13-0.69 0.07-0.77 1.0 CH: R, O, I, P O 1.0 I -0.08-0.35 1.0 P -0.07-0.19 0.41-0.85 1.0	The main finding was that indoor and personal levels of CH in organic carbons were found to be substantially higher than outdoors. This reduced the polarity of indoor and personal organic carbons
Zhao et al. (2007, 156182)	Source apportionment of personal and indoor school and outdoor school $PM_{2.5}$. Denver with 56 asthmatic children. Oct 2002-March 2003 and Oct 2003-March 2004.	% contr P IO Secondary SO_4^{2-} 4.3 8.9 9.6 Soil 6.6 4.2 12.4 Secondary NO_3^- 9.4 2.8 40.8 Motor vehicle 13.3 26.5 26.5 Cl-based cleaning 2.8 0.4 0.0 Cooking 54.8 30.2 0.0 ETS 9.2 2.1 0.0	The largest personal exposure was from cooking (54.8%), but motor vehicle emissions were the largest outdoor contributor (13.3%) to personal exposure. Secondary nitrate comprised the largest outdoor source but accounted for only 9.4% of personal exposure.
Strand et al. (2006, 089203)	Using positive matrix factorization and an extrapolation method to estimate $PM_{2.5}$ based on SO_4^{2-}Fe components. Denver. Winter 1999-2000 and 2000-2001.	Estimation method, Mean (SD, range): PMF: 7.42 (1.93, 3.43-12.89) Extrapolation Method: Using SO_4^{2-}: 6.38 (1.60, 3.20-10.97) Using SO_4^{2-} and Fe: 6.50 (1.36, 3.54-10.12) Using SO_4^{2-} and Fe, temperature adjusted: 7.02 (1.48, 3.79-11.02) Using SO_4^{2-} (no gamma): 8.23 (2.06, 4.12-14.14)	Similar results were found with each technique.

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Table A-64. Summary of PM infiltration studies.

Reference	Study Design	F_{inf}	I/O
Allen et al. (2003, 053578)	Objective: Enhance knowledge of the outdoor contribution to total indoor and personal PM exposures. Methods: Continuous light scattering monitoring. Subjects: Elderly and children spending most of their time indoors. Healthy individuals, elderly with COPD or CHD and children with asthma. 44 residences measured for 55 10-day sessions. Seattle, WA.	$PM_{2.5}$ avg- 0.65 ± 0.21 Non-heating season- 0.79 ± 0.18 Heating season- 0.53 ± 0.16 Open windows (mean)- 0.69 Closed windows (mean)- 0.58 All days (mean)- 0.65	Light scattering (whole peak): 0.75 ± 0.25 Light scattering (uncensored data): 0.77 ± 0.24 Sulfur concentration (slope): 0.65 ± 0.01
Arhami et al. (2009, 190096)	Objective: To examine associations between size-segregated PM, their particle components, and gaseous copollutants. Methods: Data analyzed with linear mixed-effect models. Subjects: Four different retirement communities in San Gabriel Valley, CA and Riverside, CA. 2005-2007.	$PM_{2.5}$: 0.38-0.57 EC: 0.64-0.82 OC: 0.60-0.98	N/A
Balasubramanian et al. (2007, 156248)	Objective: PM monitoring and assessment based on analysis of chemical and physical characteristics of indoor and outdoor particles. Methods: Particle number and mass concentrations measured using real-time particle counter and low-volume particulate sampler. Subjects: 3 residential indoor and 1 residential outdoor environments in Choa Chu Kang, Singapore. May 12-May 23, 2004.	N/A	$PM_{2.5}$: 0.93-1.90 Chemical Species: Cl^-: 0.35-0.45 NO_2^-: 2.50-4.13 NO_3^-: 1.41-5.41 SO_4^{2-}: 1.21-1.70 Na^+: 0.43-0.74 NH_4^+: 1.43-2.39 EC: 0.75-0.96 OC: 1.04-1.92 Al: 1.04-1.92 Co: 0.86-1.32 Cr: 1.35-2.90 Cu: 0.50-0.69 Fe: 0.30-0.42 Mn: 0.23-0.42 Pb: 0.40-2.47 Zn: 0.59-0.81 Cd: 0.74-1.75 Ni: 0.71-1.32 Ti: 0.73-0.78 V: 1.01-1.05
Barn et al. (2008, 156252)	Objective: Measure infiltration factor from $PM_{2.5}$ from forest fires and determine effectiveness of HEPA filter. Methods: pDR for ambient air sampling. Subjects: Homes affected by forest fire or residential wood smoke. British Columbia, Canada. 38 homes sampled (valid samples: 19 winter, 13 summer).	$PM_{2.5}$ (mean) Summer: HEPA: 0.19 ± 0.20 Unfiltered: 0.61 ± 0.27 Winter: HEPA: 0.10 ± 0.08 Unfiltered: 0.28 ± 0.18 Both: HEPA: 0.13 ± 0.14 Unfiltered: 0.42 ± 0.27	Mean: Summer: HEPA: 0.43 Unfiltered: 0.77 Winter: HEPA: 0.21 Unfiltered: 0.36 Both: HEPA: 0.25 Unfiltered: 0.47

Reference	Study Design	F_{inf}	I/O
Baxter et al. (2007, 092726)	Objective: To develop predictive models of residential indoor air pollutant concentrations for lower SES, urban households. Part of ACCESS cohort study of asthma etiology. Methods: Regression analysis; mass balance model; F_{inf} from slope in univariate regression analyses. Subjects: Lower SES populations. 43 homes, 23 homes monitored in both seasons, 15 in the non-heating season (May-Oct) only, 5 in heating season (Dec-Mar) only; 2003-2005.	$PM_{2.5}$: 0.91±0.23 EC: 0.72 ± 0.49 Ca: 0.56 ± 0.30 Fe: 0.38 ± 0.26 K: 0.83 ± 0.52 Si: 0.02 ± 0.00 Na: 0.46 ± 0.43 Cl: 0.40 ± 0.12 Zn: 0.85 ± 0.28 S: 0.95 ± 0.78 V: 0.60 ± 0.77	$PM_{2.5}$ (mean, coefficient of variation (CV)): 1.14 (0.71) EC: 0.89 (0.64) Ca: 1.16 (1.90) Fe: 0.69 (1.40) K: 1.10 (0.95) Si: 1.04 (1.31) Na: 1.05 (1.84) Cl: 3.18 (3.79) Zn: 0.83 ± (1.13) S: 0.76 ± (0.32) V: 0.76 ± (0.46)
Baxter et al. (2007, 092725)	Objective: To predict residential indoor concentrations of traffic-related air pollutants in lower SES urban households. Part of ACCESS cohort study of asthma etiology. Methods: Regression modeling, Bayesian variable selection I/O is slope from multivariate model Subjects: Lower statuses, urban households in Boston, MA. 43 sites among 39 households, 66 sampling sessions, nonheating (May-Oct) and heating (Dec-Mar) 2003-2005	N/A	$PM_{2.5}$: Open Windows: 0.98 Closed Windows: 0.64 EC: 0.38
Brown et al. (2008, 190894)	Objective: To examine if ambient, home outdoor, and home indoor particle concentrations can be used as proxies of corresponding personal exposure. Methods: Associations characterized using univariate mixed effects models that included a random subject term. Subjects: 15 participants in Boston, MA in winter (Nov. 1999-Jan. 2000) and summer (June-July 2000).	N/A	$PM_{2.5}$: Winter: Median: 1.2, Range: 0.8-1.8 Summer: Median: 0.9, Range: 0.6-1.2 EC: Winter: Median: 1.1, Range: 0.7-4.5 Summer: Median- 1.0, Range: 0.9-1.3 SO_4^{2-}: Winter: Median: 0.5, Range: 0.3-0.8 Summer: Median: 0.8, Range: 0.4-1.0
Cao et al. (2005, 156321)	Objective: To determine relationships and distributions of indoor and outdoor $PM_{2.5}$, OC, and EC. To determine indoor/outdoor sources of indoor carbonaceous aerosol. Methods: Gravimetric analysis to determine $PM_{2.5}$ concentrations. OC and EC determined by TOR following IMPROVE protocol. Subjects: 6 residences in Hong Kong (2 roadside, 2 urban, 2 rural). March 6-April 18, 2004.	N/A	20min $_{PM2.5}$: Roadside: 0.7-4.0 Urban: 0.9-6.7 Rural: 0.5-1.7 24h $PM_{2.5}$: Roadside: 0.8-1.4 Urban: 1.2-2.0 Rural: 1.0-1.8 OC (average and range): Roadside: 1.9 (1.1-2.3) Urban: 2.3 (1.5-4.0) Rural: 1.3 (1.2-2.2) EC (average and range): Roadside: 1.0 (0.9-1.1) Urban: 1.1 (0.8-1.3) Rural: 1.1 (0.9-1.8)

Reference	Study Design	F_{inf}	I/O
Cortez-Lugo et al. (2008, 156368)	Objective: To determine personal $PM_{2.5}$ and its relationship with outdoor and indoor $PM_{2.5}$ and PM_{10}. Methods: Linear regression model used to compare personal and indoor $PM_{2.5}$. I/O variation studied using analysis of variance and predictors determined by generalized estimating equation models. I/O $PM_{2.5}$ ratio transformed into natural logarithm. Subjects: 38 nonsmoking long-time Mexico residents with COPD. Mexico City, Mexico. Feb-Nov 2000.	N/A	$PM_{2.5}$: Average: 1.2 Range: 0.05-6.1
Diapouli et al. (2008, 190893)	Objective: To characterize the PM_{10f} $PM_{2.5}$, UFP concentrations at primary schools. To examine the relationship between indoor and outdoor concentrations. Methods: Chemical analysis of collected filters. Regressions to examine correlations between indoor and outdoor concentrations. Subjects: 7 primary schools with different characterizations of urbanization and traffic density in Athens, Greece. No ventilation system. Nov. 2003-Feb. 2004 and Oct.-Dec. 2004.	N/A	PM_{10}: 0.54-2.46 $PM_{2.5}$- 0.67-2.77 UFP- 0.33-0.74
Dimitroulopoulou et al. (2006, 090302)	Objective: To develop a probabilistic indoor air model (INDAIR). Methods: INDAIR predicts frequency distributions of concentrations of up to 4 pollutants simultaneously (NO_2, CO, PM_{10}, $PM_{2.5}$). 3 scenarios: no source, gas cooking, smoking. Subjects: 5 UK sites- Harwell (rural), Birmingham East (urban background), Bradford (urban center), Bloomsbury (urban center), Marylebone Road (roadside). Winter (October 1-March 31), summer (April 1-September 30), 1997-1999.	N/A	No source: PM_{10}: 0.5-0.65; $PM_{2.5}$: 0.6-0.7 Gas cooking: PM_{10}: 0.6-0.9 (bedroom), 1.0-2.0 (lounge), 1.6-4.3 (kitchen); $PM_{2.5}$: 0.74-0.9 (bedroom), 0.9-1.6 (lounge), 1.6-2.9 (kitchen) Smoking: PM_{10}: 0.7-1.1 (bedroom), 1.1-2.7 (lounge), 1.1-2.5 (kitchen); $PM_{2.5}$: 0.8-1.3 (bedroom), 1.3-2.8 (lounge), 1.4-2.6 (kitchen)
Fromme et al. (2008, 155147)	Objective: To characterize the chemical and morphological properties of PM in classrooms and in corresponding outdoor air. Methods: PM F_{inf} derived from sulfate Finf and a correction factor that results from division of BPM (increase of indoor PM per outdoor PM, linear relationship) by B^{sulf} (increase of indoor sulfate per outdoor sulfate, linear relationship). If no indoor source, the sulfate F_{inf} is equal to the sulfate I/O. Subjects: Primary school in northern Munich. Densely populated residential area 160m away from a very busy street. Classrooms had 21-23 students. Sampling during teaching hours. Oct.-Nov. 2005.	N/A	PM_{10}: SO_4^{2-}: 0.3, NO_3^-: 0.1, Cl^-: 0.6, Na^{2+}: 0.9, NH_4^+: 0.1, Mg: 0.6, Ca^{2+}: 1.4, EC: 0.7, OC: 1.1 $PM_{2.5}$: SO_4^{2-}: 0.4, NO_3^-: 0.2, Cl^-: 0.5, Na^{2+}: 0.6, NH_4^+: 0.3, Mg: 0.5, Ca^{2+}: 1.6

Reference	Study Design	F_{inf}	I/O
Guo et al. (2004, 156506)1	Objective: To investigate pollutant concentrations at air-conditioned and non-air-conditioned markets. To compare indoor air quality with the Hong Kong standard. Methods: PM_{10} concentrations measured by Hi-Vol sampler correlated with corresponding levels measured by Dust-Trak monitor. Subjects: 3 non-air-conditioned and 2 air-conditioned markets in Hong Kong. Sept. 2001-Jan. 2002.	N/A	PM_{10}: Non-air-conditioned: ~0.7, Air-conditioned: ~0.98
Hänninen et al. (2004, 056812)2	Objective: To assess indoor $PM_{2.5}$ by origin and potential determinants. Methods: Part of EXPOLIS study. Pump and filter with gravimetric analysis. Univariate single and stepwise-multiple regression analyses. Subjects: Residential homes in Athens, Greece; Basle, Switzerland; Helsinki, Finland; Prague, Czech Republic. Homes by city: Athens 50, Basle 50, Helsinki 189, Prague 49.	$PM_{2.5}$ (mean): Athens- 0.70 ± 0.12 Basle- 0.63 ± 0.15 Helsinki- 0.59 ± 0.17 Prague- 0.61 ± 0.14 S (mean): Athens- 0.82 ± 0.14 Basle- 0.80 ± 0.19 Helsinki- 0.70 ± 0.20 Prague- 0.72 ± 0.16	$PM_{2.5}$: Athens: ~0.84 Basle: ~1.37 Helsinki: ~1.30 Prague: ~1.33 S: Athens:~0.70 Basle: ~0.80 Helsinki: ~0.74 Prague: ~0.77
Ho et al. (2004, 056804)3	Objective: $PM_{2.5}$, OC, and EC exposure assessment of occupied buildings located near major roadways under natural ventilation (NV) and mechanical ventilation (MV). Methods: Co-located mini-volume samplers and Partisol model 2000 sampler with 2.5 micron inlet. IMPROVE TOR carbon analysis. Subjects: Occupants of MV (1 classroom and office) and NV (3 residences) buildings located within 10m of major roadway; Hong Kong, China. Sep. 2002-Feb. 2003.	$PM_{2.5}$: 0.42 EC: MV: 0.42, NV: 0.76 OC: MV: 0.66, NV: 0.71	$PM_{2.5}$ (average): 0.2-1.6 MV (average): <0.7 NV (average): 0.6-1.6 EC: Range: 0.5±0.1-1.1±0.4 OC: Range: 0.6±0.2-1.5±1.0
Hoek et al. (2008, 156554)	Objective: Exposure assessmentof indoor/outdoor particle relationships.RUPIOH study. Methods: Sampling by condensation particle counters and Harvard impactors. Gravimetric analysis and reflectance. Calculations performed for 24h avg concentrations. F_{inf} estimated by linear regression analysis. Subjects: 4 European cities (Helsinki, Finland; Athens, Greece; Amsterdam, The Netherlands; Birmingham, England). Urban populations. >35yrs. Asthma or COPD. Non-smoking households. Work <16h/wk outside home. 153 homes sampled Oct. 2002-Mar. 2004.	Regression slope for indoor vs. central site outdoor: $PM_{2.5}$: 0.30-0.51 PM_{10}: 0.17-0.41 $PM_{10-2.5}$: 0.01-0.17 SO_4^{2-}: 0.59-0.78 Soot: 0.43-0.87 Regression slope for indoor vs. residential outdoor: $PM_{2.5}$: 0.34-0.48 PM_{10}: 0.26-0.44 $PM_{10-2.5}$: 0.11-0.16 Soot: 0.63-0.84	N/A

Reference	Study Design	F_{inf}	I/O
Hopke et al. (2003, 095544)	Objective: To use advanced factor analysis models to identify and quantify PM sources. 1998 BPMEES data. Methods: PEM, outdoor and indoor sampling of unoccupied apartment in retirement facility. PMF used to derive source contributions. Multilinear Engine used to derive joint factors. Subjects: 10 non-smoking elderly subjects of mean age 84 who did not cook.Towson, MD. July 26-Aug. 22, 1998.	NO_3^-- SO_4^{2-}: 0.03 SO_4^{2-}: 0.38 OC: 0.77 MV Exhaust: 0.32	N/A
Hystad et al. (2008, 190890)	Objective: To explore the feasibility of modeling residential $PM_{2.5}$ F_{inf} for occupied residences using data readily available for most of North America. Methods: F_{inf} calculated by recursive mass balance model where F_{inf} is a function of penetration efficiency, particle removal rate, and air exchange. Subjects: 46 residences in Seattle, WA 1999-2003. 38 nonsmoking residences in Victoria, British Columbia, Canada 2006. Heating (Oct.-Feb.) and nonheating (March-Sept.).	Seattle: Mean (all): 0.59 ± 0.21 Mean (detached residences): 0.60 ± 0.20 Victoria: Mean (all): 0.62 ± 0.22 Mean (detached residences): 0.59 ± 0.22	N/A
Klinmalee et al. (2008, 190888)	Objective: To monitor indoor and outdoor pollution in an university campus and shopping center. Methods: PM measured by PEM and quartz filters. Analyzed for mass, water soluble ions by ion chromatography, and black carbon by a smokestain reflectometer. I/O calculated for each sample pair then average taken. Subjects: University campus and shopping center in northern suburb of Bangkok, Thailand. Dec. 2005-Feb. 2006.	N/A	$PM_{2.5}$: University: Weekdays: 0.6, Weekends: 0.5 Shopping center: Weekdays: 1.5, Weekends: 2.0 BC in $PM_{2.5}$: University: 0.9 Shopping center: 0.67

Reference	Study Design	F_{inf}	I/O
Koistinen et al. (2004, 156655)	Objective: To identify $PM_{2.5}$ sources in personal exposures with principal component analysis of the elemental compositions in residential outdoor, indoor, and workplace indoor microenvironments. Part of EXPOLIS study. Methods: Principal component analysis to identify sources of microenvironmental and personal $PM_{2.5}$ exposure. Specific mass contributions of sources calculated by source reconstruction. Subjects: Non-smoking, 25-55yrs. Helsinki, Finland. Oct. 1996-Dec. 1997.	N/A	Median seasonal: $PM_{2.5}$: Winter: 0.77, Spring: 1.03, Summer: 0.95, Fall: 0.92, Total: 0.92 Pb: Winter: 0.67, Spring: 0.56, Summer: 0.86, Fall: 0.69, Total: 0.67 S: Winter: 0.60, Spring: 0.63, Summer: 0.90, Fall: 0.75, Total: 0.69 Br: Winter: 0.57, Spring: 0.72, Summer: 0.98, Fall: 0.89, Total: 0.77 BS: Winter: 0.65, Spring: 0.67, Summer: 0.91, Fall: 0.88, Total: 0.79 Zn: Winter: 0.58, Spring: 0.75, Summer: 0.66, Fall: 0.75, Total: 0.68 Fe: Winter: 0.52, Spring: 0.96, Summer: 0.90, Fall: 0.95, Total: 0.83 K: Winter: 0.95, Spring: 1.05, Summer: 1.01, Fall: 1.08, Total: 1.05 Cl: Winter: 1.01, Spring: 1.24, Summer: 1.37, Fall: 1.74, Total: 1.24 Al: Winter: 1.19, Spring: 1.08, Summer: 1.41, Fall: 2.20, Total: 1.27
Li et al. (2003, 047845)	Objective: To establish effects of evaporative coolers on indoor PM concentrations. Methods: Concurrent 10min avg indoor and outdoor concentrations recorded for 2 days.I/O determined by equation based on mass conversation principles. Subjects: 10 homes with evaporative coolers. El Paso, TX. June 22-Aug. 23, 2001.	N/A	PM_{10}: All: 0.60 Cooler On: 0.57 Cooler Off: 0.66 $PM_{2.5}$: All: 0.65 Cooler On: 0.63 Cooler Off: 0.73
Lunden et al. (2008, 155949)	Objective: To investigate the physiochemical processes that influence the transport and fate of outdoor particles to the indoor environment. Methods: I/O calculated from measurements of aerosols collected on quartz filters. Subjects: 3-bedroom single-story unoccupied house in Clovis, CA. 3 periods: Oct. 9-23, 2000; Dec. 1-19, 2000; Jan. 12-23, 2001.	N/A	$PM_{2.5}$: Oct.: 0.46 ± 0.2, Dec.: 0.39 ± 0.2, Jan.: 0.38 ± 0.3, All periods: 0.41 ± 0.2 Carbon: Oct.: 0.50 ± 0.1, Dec.: 0.46 ± 0.1, Jan.: 0.52 ± 0.2, All periods: 0.50 ± 0.2 OC: Oct.: 0.48 ± 0.1, Dec.: 0.44 ± 0.1, Jan.: 0.50 ± 0.2, All periods: 0.47 ± 0.2 Black carbon: Oct.: 0.60 ± 0.2, Dec.: 0.60 ± 0.2, Jan.: 0.65 ± 0.2, All periods: 0.61 ± 0.2
MacIntosh et al. (2009, 190887)	Objective: To estimate the potential for residential air cleaning systems to mitigate exposure to fine particles of ambient origin. Methods: Multi-zone indoor air quality model to examine annual, 24h avg and diurnal concentrations of outdoor $PM_{2.5}$ in residential indoor air. Subjects: Homes in Cincinnati, Cleveland, and Columbus, OH that have natural ventilation, forced air heating and cooling with conventional in-duct filtration, or forces air heating and cooling with high-efficiency in-duct air cleaning. 2005.	N/A	$PM_{2.5}$ (range): Natural ventilation: 0.23-0.97 Forced air – conventional filtration: 0.13-0.94 Forced air – high-efficiency electrostatic: 0.02-0.80

Reference	Study Design	F_{inf}	I/O
Martuzevicius et al. (2008, 190886)	Objective: To determine the contribution of traffic-related PM to the indoor aerosols. Methods: Receptor modeling based on a PARAFAC model. Subjects: 6 houses 30-300m from a highway, with conventional windows, central HVAC, and with smoking and cooking allowed. Spring: Mar. 30-May 14, 2004. Fall: Sept. 13-Oct. 22, 2004. Cincinnati, OH.	N/A	Range- $PM_{2.5}$: Spring: 0.5 ± 0.2-2.9 ± 1.2; Fall: 0.7 ± 0.1-4.7 ± 6.9 EC: Spring: 0.3 ± 0.1-2.2 ± 1.7; Winter: 0.6 ± 0.1-1.3 ± 0.7 OC: Spring: 1.0 ± 0.7-6.9 ± 3.9; Winter: 1.2 ± 0.1-7.6 ± 10 Si: Spring: 0.4 ± 0.1-5.1 ± 3.9; Winter: 0.5 ± 0.1-5.3 ± 4.5 S: Spring: 0.4 ± 0.1-0.7 ± 0.1; Winter: 0.5 ± 0.1-0.9 ± 0.4 Mn: Spring: 0.3 ± 0.2-0.8 ± 0.6; Winter: 0.3 ± 0.2-1.0 ± 0.2 Fe: Spring: 0.3 ± 0.0-1.3 ± 0.8; Winter: 0.4 ± 0.1-0.9 ± 0.6 Zn: Spring: 0.3 ± 0.1-0.7 ± 0.6; Winter: 0.6 ± 0.1-1.1 ± 0.8 Br: Spring: 0.3 ± 0.1-1.0 ± 0.5; Winter: 0.2 ± 0.1-0.9 ± 0.6 Pb: Spring: 0.3 ± 0.3-0.9 ± 0.6; Winter: 0.2 ± 0.2-1.9 ± 2.3
Meng et al. (2005, 058595)	Objective: Analyses of RIOPA data, which investigated relationships between indoor, outdoor, and personal exposure for several air pollutants. Methods: PM measured on Teflon filters collected by PEMs for 48h. The mass balance model and RCS statistical model used to estimate indoor and and personal PM concentrations. Subjects: 212 nonsmoking homes sampled. Houston, TX; Los Angeles County, CA; Elizabeth, NJ. Summer 1999-spring 2001, all 4 seasons.	$PM_{2.5}$- 0.46	Los Angeles: $PM_{2.5}$: Mean: 0.84, Median: 0.90; EC: Mean: 0.93, Median: 0.92; OC: Mean: 1.32, Median: 1.31 Elizabeth: $PM_{2.5}$: Mean: 0.99, Median: 0.86; EC: Mean: 1.0, Median: 0.85; OC: Mean: 2.4, Median: 1.8 Houston: $PM_{2.5}$: Mean: 1.16, Median: 1.02; EC: Mean: 1.0, Median: 0.71; OC: Mean: 2.25, Median: 2.35
Molnár et al. (2007, 156774)	Objective: To characterize and compare indoor and outdoor $PM_{2.5}$ trace element concentrations in difference microenvironments related to children. Methods: Elemental concentrations analyzed using X-ray fluorescence spectroscopy. Subjects: 40 sampling sites (10 classrooms in 5 schools, 10 preschools, 20 non-smoking homes). 3 communities in Stockholm, Sweden. Sampled once during spring and once during winter. Dec. 1, 2003-July 1, 2004.	$PM_{2.5}$ (containing S or Pb): 0.4-0.9	S (median): Both seasons: 0.61 (homes), 0.53 (schools), 0.69 (preschools); Winter: 0.47 (homes), 0.36 (schools), 0.63 (preschools); Spring: 0.63 (homes), 0.55 (schools), 0.90 (preschools) Pb (median): Both seasons: 0.70 (homes), 0.59 (schools), 0.70 (preschools); Winter: 0.62 (homes), 0.43 (schools), 0.63 (preschools); Spring: 0.70 (homes), 0.64 (schools), 0.75 (preschools)

Reference	Study Design	F_{inf}	I/O
Ng et al. (2005, 155996)	Objective: To estimate PM exposures following the September 11, 2001 attack in NYC. Methods: Outdoor $PM_{2.5}$ interpolated and used in a deterministic micro-environmental model (INTAIR) to simulate analytically concentrations in indoor micro-environments. Linear regression equations used. Subjects: Lower Manhattan residents divided into representative individuals – home-maker, office/shop-worker, student/child. Estimates Sept. 14-31.	N/A	Mean I/O in home simulated with INTAIR: No Source: 0.6 Smoking: 1.9 Cooking: 1.3 Smoking and Cooking: 2.3 I/O of micro-environments simulated by analytical and empirical methods (no indoor source) : Office/Shop: 0.4 Classroom: 0.9: Transport Area: 1.9 Store: 1.2
Paschold et al. (2003, 156847)	Objective: To identify PM sources inside homes with evaporative coolers. Methods: PM element composition analysis by ICP-MS. Subjects: 10 residences. El Paso, TX. Summer 2001.	N/A	PM_{10}: Na: 0.33, Mg: 0.43, Al: 0.50, K: 0.48, Ca: 0.40, Ti: 0.52, Mn: 0.48, Fe: 0.46, Cu: 0.74, Zn: 0.52, Ba: 0.54, Pb: 0.76 $PM_{2.5}$: Na: 0.20, Mg: 0.29, Al: 0.34, K:0.30, Ca: 0.52, Ti: 0.40, Mn: 0.35, Fe: 0.30, Cu: 0.67, Zn: 0.34, Ba: 0.47, Pb: 0.51
Polidori et al. (2007, 156877)	Objective: To investigate the relationships of indoor and outdoor $PM_{2.5}$, its components, seasonal variations, and gaseous copollutants. Methods: F_{inf} estimated by analysis of I/O's and a recursive model technique. Subjects: 2 retirement facilities in Los Angeles, CA. July 6-Aug. 20, 2005. Aug. 24-Oct. 15, 2005. Oct. 19-Dec. 10, 2005. Jan. 4-Feb. 18, 2006.	$PM_{2.5}$: July 6-Aug. 20: 0.71 ± 0.10; Aug. 24-Oct. 15: 0.60 ± 0.05; Oct. 19-Dec. 10: 0.59 ± 0.07; Jan. 4-Feb. 18: 0.45 ± 0.06 OC: July 6-Aug. 20: 0.86 ± 0.05; Aug. 24-Oct. 15: 0.77 ± 0.09; Oct. 19-Dec. 10: 0.82 ± 0.07; Jan. 4-Feb. 18: 0.64 ± 0.10 EC: July 6-Aug. 20: 0.73 ± 0.07; Aug. 24-Oct. 15: 0.71 ± 0.05; Oct. 19-Dec. 10: 0.77 ± 0.06; Jan. 4-Feb. 18: 0.64 ± 0.10	Only I/O's ≤1considered
Ramachandran et al. (2003, 195017)	Objective: To examine variability in measurements of 24h avg and 15min avg $PM_{2.5}$ concentrations. Methods: Linear regression of gravimetric measurements. Subjects: 3 urban residential neighborhoods in Minneaopolis-St. Paul, MN. 9-10 nonsmoking residences. Spring (April 26-June 2), summer (June 20-Aug. 10), fall (Sept. 23-Nov. 20) of 1999.	N/A	24h avg: Mean: 1.7, Median: 1.3, Standard deviation: 1.6 15min avg: Mean: 2.7, Median: 1.2, Standard deviation: 8.7
Rojas-Bracho et al. (2004, 054772)	Objective: To examine determinants of personal exposure to $PM_{2.5}$, PM_{10}, $PM_{2.5-10}$. Methods: 2 sets of mixed models. Personal exposures modeled as dependent variables. Subject variability modeled using random effects. Explanatory variables and season modeled as fixed effects. Subjects: 18 COPD subjects in nonsmoking households. Boston, MA. Winters of 1996 and 1997, summer of 1996.	N/A	$PM_{2.5}$: Winter: Mean: 1.58, Median: 2.11; Summer: Mean: 1.08, Median: 0.88 PM_{10}: Winter: Mean: 2.02, Median: 3.77; Summer: Mean: 1.14, Median: 1.05 $PM_{2.5-10}$: Winter: Mean: 2.65, Median: 3.59; Summer: Mean: 1.26, Median: 1.39

Reference	Study Design	F_{inf}	I/O
Sarnat et al. (2006, 089166)	Objective: To assess the ability of outdoor $PM_{2.5}$ its volatile and nonvolatile components and particle sizes to infiltrate indoors. Methods: $PM_{2.5}$ mass contributions estimated by the mean concentration ratio between each component and $PM_{2.5}$. Indoor and outdoor particle concentrations relationships examined by Spearman correlation coefficient. I/O concentration ratios used during overnight (nonsource) period to estimate fraction of ambient particles remaining airborne indoors (F_{inf}). Subjects: 17 occupied, nonsmoking Los Angeles, CA residences. July 28, 2001-Feb. 25, 2002.	$PM_{2.5}$: Median: 0.48, Interquartile range: 0.39-0.57 BC: Median: 0.84, Interquartile range: 0.70-0.96 UFP (0.02-0.03 µm): Median: 0.50, Interquartile range: 0.39-0.60 UFP (0.08-0.3 µm): Median: ~0.75 Coarse particles (5-10 µm): Median: <0.17	$PM_{2.5}$: Overnight: 0.40-0.57, Morning: 0.43-0.74, Afternoon: 0.45-0.90, Evening: 0.42-0.82 BC: Overnight: 0.70-0.97, Morning: 0.67-0.98, Afternoon: 0.77-1.04, Evening: 0.70-1.01
Stranger et al. (2008, 190884)	Objective: To assess indoor air quality by determining indoor and outdoor $PM_{2.5}$ mass concentrations, elemental composition, and gaseous compounds. Methods: PM mass concentrations determined gravimetrically. Subjects: 27 primary schools in city center and suburbs of Antwerp, Belgium. Dec. 2002 and June 2003.	N/A	$PM_{2.5}$: Urban: Range: 0.3-6.9, Average: 1.3; Suburban: Range: 0.2-8.8, Average: 2.3 V, Ni, Zn, Pb, Br, Mn: <1 Cl, Ca, Al, Si, K, Ti, Fe: >1 BS: Urban: Average: Dec.- 0.7 ± 0.1, June- 1.1 ± 0.3; Suburban: Dec.- 0.8 ± 0.2, June-1.0 ± 0.4
Stranger et al. (2009, 190883)	Objective: To assess indoor air quality in residences by quantifying various gaseous pollutants, and PM mass concentrations, elemental composition, and water-soluble ionic content. Methods: PM mass concentrations gravimetrically determined. Elemental bulk analysis on filters. Subjects: 19 residential homes in Antwerp, Belgium that were a subset of participants in the ECRHS II study.	N/A	PM_1: Houses 1-15: Average: 2.0, Range: 0.3-9.6; Smokers: Average: 3.9, Range: 1.2-9.7; Non-smokers: Average: 0.8, Range: 0.3-14 $PM_{2.5}$: Houses 1-15: Average: 1.5, Range: 0.4-5.4, Smokers average: 2.5, Smokers range: 1.2-5.4, Non-smokers average: 0.8, Non-smokers range: 0.4-1.3; Houses 16-19: Average: 2.6, Range: 0.3-3.9 PM_{10}: Houses 1-15: Average: 1.3, Range: 0.4-4.1, Smokers average: 2.1, Smokers range: 1.1-4.1, Non-smokers average: 0.8, Non-smokers range: 0.4-1.2 Ca, Ti, V, Cr, Mn, Fe, Ni, Zn, Pb, Si, S, Cl: <1 K, Cu, Br, Al: >1
Turpin et al. (2007, 157062)	Objective: To characterize and compare outdoor, indoor, personal $PM_{2.5}$ exposure. Identify indoor and personal $PM_{2.5}$ sources. Estimate outdoor $PM_{2.5}$ effect on indoor and personal $PM_{2.5}$. RIOPA study. Methods: F_{inf} calculated in three ways: RCS model used to obtain constant F_{inf}. Mass balance model shows F_{inf} varying with AER. Robust regression uses major $PM_{2.5}$ species for home-specific F_{inf}. Subjects: 309 nonsmoking adults and 118 children with no preexisting conditions. 219 homes sampled. Elizabeth NJ, Houston TX, and Los Angeles County CA.	$PM_{2.5}$: RCS model: 0.46 Least-Trimmed Squared Regression: Mean: 0.69, Median: 0.70, SD: 0.23 Mass Balance Model: ~0.08-~0.85	Los Angeles: $PM_{2.5}$: Mean: 0.84, Median: 0.90 EC: Mean: 0.93, Median: 0.92 OC: Mean: 1.32, Median: 1.31 Elizabeth: $PM_{2.5}$: Mean: 0.99, Median: 0.86 EC: Mean: 1.0, Median: 0.85 OC: Mean: 2.4, Median: 1.8 Houston: $PM_{2.5}$: Mean: 1.16, Median: 1.02 EC: Mean: 1.0, Median: 0.71 OC: Mean: 2.25, Median: 2.35

Reference	Study Design	F_{inf}	I/O
Wallace and Williams (2005, 057485)	Objective: To estimate the contribution of outdoor $PM_{2.5}$ to personal exposure in high-risk subpopulations. Methods: Longitudinal regressions of estimated indoor and outdoor $PM_{2.5}$ for F_{inf}. Subjects: 29 African-Americans with hypertension and 8 with implanted cardiac defibrillators. Measured 7d/season, 4 seasons in 2000-2001. Raleigh, NC.	Range: 0.35-0.87	$PM_{2.5}$: Mean: 1.08 ± 1.05, Median: 0.75, Range: 0.24-9.48 S: Mean: 0.59 ± 0.16, Median: 0.58, Range: 0.17-1.06
Williams et al. (2003, 053338)	Objective: To estimate ambient $PM_{2.5}$ contributions to personal and indoor residential PM mass concentrations. Methods: F_{inf} estimated from least squares, regression analysis, and mixed model slope. Subjects: Nonsmoking, ambulatory, ≥ 50yrs. 2 cohorts: mostly Caucasian with implanted cardiac defibrillators in Chapel, NC; 30 African-Americans with controlled hypertension in low-to-moderate SES neighborhoods in Raleigh, NC. 7d/season, 4 seasons in 2000-2001.	Least squares estimate of indoor filtration factors: Mean: 0.42 ± 0.38, Range: -0.55 to 1.62 Regression analysis: 0.43 ± 0.06 Mixed model slope: Mean- 0.45 ± 0.21, Range- 0.05-0.94	N/A
Williams et al. (2008, 191201)	Objective: To examine the spatial variability of $PM_{2.5}$ and $PM_{10-2.5}$ and their components to determine the suitability of conducting health outcome studies using a central site monitor in a metropolitan area having multiple source impacts. Methods: Gravimetric analysis of PM mass concentrations. ED-XRF analysis of PM elements. Subjects: Non-smoking, ambulatory, and living in detached homes and non-smoking households. Detroit, MI.	$PM_{2.5}$: Range: 0.16-6.45, Mean: 0.7 ± 0.33, Median: 0.70 (indicate indoor sulfur source when F_{inf}>1)	N/A
Wilson and Brauer (2006, 088933)	Objective: To provide additional insight into factors affecting exposure to airborne PM and the resultant health effects. Methods: F_{inf} estimated by mass balance equation. Subjects: 16 nonsmoking subjects with COPD. 54-86yrs. Vancouver, British Columbia. April-Sept. 1998.	SO_4^{2-}: 0.72	N/A
Wu et al. (2006, 179950)	Objective: To assess personal $PM_{2.5}$ exposures from ambient sources and agriculture burning smoke. Methods: F_{inf} estimated by RCS model. Application of Robust regression algorithm. Subjects: 33 adult asthmatics. 18-52yrs. Pullman, WA. Sept. 3, 2002-Nov. 1, 2002.	Range: 0.25-0.94	N/A

Reference	Study Design	F_{inf}	I/O
Yang et al. (2009, 190885)	Objective: To characterize the concentrations of different indoor air pollutants. Methods: PM_{10} collected on pall flex membrane filer using MiniVol portable air samplers. Arithmetic and geometric means calculated for indoor concentrations. Differences in concentrations measured by Kruskal-Wallis test. Subjects: 55 schools in 6 metropolitan areas in Korea. Samples from a classroom, laboratory, and computer classroom. 3 seasons, July-Dec. 2004.	N/A	PM_{10}: Classroom: Summer: 1.98, Autumn: 2.25, Winter: 2.07, Total: 2.06 Laboratory: Summer: 1.33, Autumn: 1.32, Winter: 1.72, Total: 1.46 Computer classroom: Summer- 0.77, Autumn: 1.43, Winter: 2.08, Total: 1.43
Zhu et al. (2005, 190081)	Objective: To determine penetration behavior of outdoor ultrafine particles into indoor environments in areas close to freeways. Methods: Dynamic mass balance model. Subjects: 4 2-bedroom apartments within 60m from the center of the 405 Freeway in Los Angeles, CA. Non-smoking tenants. 2 sampling periods (non-cooking, non-cleaning): Oct.-Dec. 2003 and Dec. 2003-Jan. 2004.	N/A	Highest (largest ultrafine particles-70-100nm): 0.6-0.9 Lowest (smallest ultrafine particles-10-20nm): 0.1-0.4

1. I/O estimated from Figure 8 in study.
2. I/O calculated from indoor and outdoor concentrations in Table 1 in study.
3. F_{inf} measured by coefficient of determination, R^2.
4. RIOPA calculated I/O's.
5. I/O calculated from mean and median indoor and outdoor concentrations listed in Table 1 of study.
6. I/O's estimated from Figure 3 in study.
7. Mean and median I/O concentrations calculated from all residences in study.
8. F_{inf} estimated from Figure 2 in study.
9. F_{inf} presented in box plot (Figure 8), however data is difficult to deduce. No numeric values reported.

Table A-65. Summary of PM – copollutant exposure studies.

<table>
<tr><th>Reference</th><th>PM metric</th><th>Copollutant metric</th><th>Association between PM and copollutant</th><th>Primary findings</th></tr>
<tr><td>Fruin et al. (2008, 097183)</td><td>In-vehicle UFP, BC, PM-bound PAH</td><td>In-vehicle NO_X, CO</td><td>
<table>
<tr><th>R</th><th>UFP</th><th>$PM_{2.5}$</th><th>NO</th><th>BC</th><th>CO</th><th>CO_2</th></tr>
<tr><td>UFP</td><td>1</td><td>0.71</td><td>0.97</td><td>0.95</td><td>0.63</td><td>0.72</td></tr>
<tr><td>$PM_{2.5}$</td><td></td><td>1</td><td>0.69</td><td>0.89</td><td>0.66</td><td>0.68</td></tr>
<tr><td>NO</td><td></td><td></td><td>1</td><td>0.91</td><td>0.78</td><td>0.85</td></tr>
<tr><td>BC</td><td></td><td></td><td></td><td>1</td><td>0.65</td><td>0.74</td></tr>
<tr><td>CO</td><td></td><td></td><td></td><td></td><td>1</td><td>0.94</td></tr>
<tr><td>CO_2</td><td></td><td></td><td></td><td></td><td></td><td>1</td></tr>
</table>
Note that these correlations are computed from data presented by Fruin et al. (2008, 097183) for mean concentrations at different loc ations.
</td><td>Measurements of freeway UFP, BC, PM-bound PAH, and NO concentrations were roughly one order of magnitude higher than ambient measurements. Multiple regression analysis suggests these concentrations were a function of truck density and total truck count.</td></tr>
<tr><td>Schwartz et al. (2007, 090220)</td><td>Ambient and personal $PM_{2.5}$ data from the Baltimore panel study</td><td>Ambient and personal O_3 and NO_2 data from the Baltimore panel study.</td><td>Median β for regressions:
<table>
<tr><th></th><th>Ambient $PM_{2.5}$</th><th>Ambient O_3</th><th>Ambient NO_2</th></tr>
<tr><td>Personal $PM_{2.5}$</td><td>0.0143</td><td>-0.0016</td><td>0.0115</td></tr>
<tr><td>Personal $PM_{2.5}$ of ambient origin</td><td>0.0183</td><td>-0.0037</td><td>0.0124</td></tr>
<tr><td>Personal SO_4^{2-}</td><td>0.0051</td><td>0.0035</td><td>0.0006</td></tr>
<tr><td>Personal O_3</td><td>0.0014</td><td>0.0010</td><td>0.0009</td></tr>
<tr><td>Personal NO2</td><td>0.0015</td><td>0.0009</td><td>0.0010</td></tr>
</table>
</td><td>Results suggest that ambient O_3 exposure may be related to personal SO_4^{2-} exposure but not to personal $PM_{2.5}$ exposure on the whole. Ambient NO_2 exposure was associated with personal $PM_{2.5}$ exposure, possibly because both have traffic sources.</td></tr>
<tr><td>Tolbert et al. (2007, 090316)</td><td>Ambient PM_{10}, $PM_{10-2.5}$, $PM_{2.5}$, EC, OC, TC, SO_4^{2-}, water-soluble metals, oxygenated hydrocarbons</td><td>Ambient O_3, NO_2, CO, SO_2</td><td>
<table>
<tr><th></th><th>PM_{10}</th><th>O_3</th><th>NO_2</th><th>CO</th><th>SO_2</th><th>PMc</th><th>$PM_{2.5}$</th></tr>
<tr><td>PM_{10}</td><td>1.0</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>O_3</td><td>0.6</td><td>1.0</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>NO_2</td><td>0.5</td><td>0.4</td><td>1.0</td><td></td><td></td><td></td><td></td></tr>
<tr><td>CO</td><td>0.5</td><td>0.3</td><td>0.7</td><td>1.0</td><td></td><td></td><td></td></tr>
<tr><td>SO_2</td><td>0.2</td><td>0.2</td><td>0.4</td><td>0.3</td><td>1.0</td><td></td><td></td></tr>
<tr><td>PMc</td><td>0.7</td><td>0.4</td><td>0.5</td><td>0.4</td><td>0.2</td><td>1.0</td><td></td></tr>
<tr><td>$PM_{2.5}$</td><td>0.8</td><td>0.6</td><td>0.6</td><td>0.4</td><td>0.2</td><td>0.5</td><td>1.0</td></tr>
<tr><td>SO_4^{2-}</td><td>0.7</td><td>0.6</td><td>0.1</td><td>0.1</td><td>0.1</td><td>0.3</td><td>0.8</td></tr>
<tr><td>EC</td><td>0.6</td><td>0.4</td><td>0.6</td><td>0.7</td><td>0.2</td><td>0.5</td><td>0.7</td></tr>
<tr><td>OC</td><td>0.7</td><td>0.5</td><td>0.6</td><td>0.6</td><td>0.2</td><td>0.5</td><td>0.7</td></tr>
<tr><td>TC</td><td>0.7</td><td>0.5</td><td>0.7</td><td>0.6</td><td>0.2</td><td>0.5</td><td>0.7</td></tr>
<tr><td>Metals</td><td>0.7</td><td>0.4</td><td>0.3</td><td>0.4</td><td>0.1</td><td>0.5</td><td>0.7</td></tr>
<tr><td>OHC</td><td>0.5</td><td>0.4</td><td>0.2</td><td>0.3</td><td>0.1</td><td>0.4</td><td>0.5</td></tr>
<tr><td>SO_4^{2-}</td><td>EC</td><td>OC</td><td>TC</td><td>Metals</td><td>OHC</td><td></td><td></td></tr>
<tr><td>SO_4^{2-}</td><td>1.0</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>EC</td><td>0.3</td><td>1.0</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>OC</td><td>0.3</td><td>0.8</td><td>1.0</td><td></td><td></td><td></td><td></td></tr>
<tr><td>TC</td><td>0.3</td><td>0.9</td><td>1.0</td><td>1.0</td><td></td><td></td><td></td></tr>
<tr><td>Metals</td><td>0.7</td><td>0.5</td><td>0.5</td><td>0.5</td><td>1.0</td><td></td><td></td></tr>
<tr><td>OHC</td><td>0.5</td><td>0.4</td><td>0.4</td><td>0.4</td><td>0.5</td><td>1.0</td><td></td></tr>
</table>
</td><td>Low correlations were seen between SO_2 and PM constituents. Components were used in a multi-pollutant model to predict emergency department visits in Atlanta. CO was found to be the most significant predictor of cardiovascular disease visits in one-, two-, and three-pollutant models, and O_3 was the most significant predictor of respiratory disease visits in one-, two-, and three-pollutant models.</td></tr>
<tr><td>Brook et al. (2007, 091153)</td><td>Anbient PM_{10}, $PM_{10-2.5}$, $PM_{2.5}$, SO_4^{2-}, and trace metals in 10 Canadian cities.</td><td>Ambient NO_2, NO</td><td>R with NO_2 (min, Max)
NO_2 1.00 (1.00, 1.00)
NO 0.67 (0.51, 0.77)
$PM_{2.5}$ 0.54 (0.45, 0.71)
$PM_{10-2.5}$ 0.31 (0.04, 0.50)
PM_{10} 0.50 (0.23, 0.70)
SO_4^{2-} 0.33 (0.10, 0.48)
Fe 0.44 (0.29, 0.56)
Zn 0.39 (0.28, 0.52)
Ni 0.20 (0.06, 0.40)
Mn 0.51 (0.37, 0.62)
As 0.21 (0.07, 0.39)
Al 0.07 (-0.17, 0.18)
Cu 0.03 (-0.07, 0.15)
Pb 0.28 (0.16, 0.39)
Si 0.19 (0.00, 0.32)
Se 0.14 (-0.04, 0.35)</td><td>NO_2 showed the strongest association with mortality, but it is unclear if this association is due to health effects of NO_2 or health effects of copollutant PM.</td></tr>
</table>

Reference	PM metric	Copollutant metric	Association between PM and copollutant	Primary findings
Ito et al. (2007, 156594)	Ambient $PM_{2.5}$	Ambient O_3, NO_2, SO_2, CO	Shown in figure format only.	Authors tested relationship between meteorological variables and copollutants to determine if multi-pollutant models are impacted by spatial or temporal variation or by meteorological conditions. Multicollinearity varied by pollutant and season.
Kaur et al. (2005, 086504)	Fixed-site and personal $PM_{2.5}$, personal UFP	Fixed site and personal CO	Personal R: $PM_{2.5}$ UFPCO $PM_{2.5}$ 1 0.5 0.2 UFP 0.5 1 0.7 CO 0.2 0.7 1	Fairly low correlation was observed between $PM_{2.5}$ and CO and between $PM_{2.5}$ and UFP, stronger correlations between UFP and CO.
Kaur et al. (2005, 088175)	Fixed-site and personal $PM_{2.5}$ analyzed post-sample for light absorbance (as indicator for carbonaceous aerosol), personal UFP	Fixed site and personal CO	Personal R: R $PM_{2.5}$ Abs CO UFP $PM_{2.5}$ 1 0.3 -0.1 0.0 Abs 0.3 1 0.2 0.7 CO -0.1 0.2 1 0.1 UFP 0.0 0.7 0.1 1	Strongest correlation observed between UFP and absorption, which is reasonable given that much absorptive carbonaceous aerosol is in the ultrafine range.
Sørenson et al. (2005, 089428)	Personal, indoor residential, and outdoor residential $PM_{2.5}$ and BC	Personal, indoor residential, and outdoor residential NO_2	Personal exposure regression coefficients to: | | $PM_{2.5}$ | BC | NO_2 | | --- | --- | --- | --- | | Bedroom | 0.72 | 0.47 | 0.70 | | Front door | 0.46 | 0.61 | 0.60 | | Background | 0.29 | 0.03 | 0.56 |	Personal NO_2 concentration is more strongly influenced by background than $PM_{2.5}$ or BC.
Sabin et al. (2005, 087728)	BC, particle-bound PAH on a school bus.	NO_2 on a school bus.	| | BC | PB-PAH | NO_2 | | --- | --- | --- | --- | | BC | 1 | 0.94 | 0.49 | | PB-PAH | | 1 | 0.37 | | NO_2 | | | 1 | Note that these correlations are computed from data presented by Sabin et al. for mean concentrations when the test bus travelled behind different vehicles.	Less correlation was observed between NO_2 and PM species. This study was aimed more at fuel choices and control technologies for children's exposures on school buses.
Lai et al. (2004, 056811)	Microenvironmental and personal $PM_{2.5}$ and trace elements for personal exposure (P), residential indoor (RI), residential outdoor (RO), and workplace (WI) measurements.	Microenvironmental and personal VOCs, NO_2, and CO.	| R ($PM_{2.5}$) | P | RI | RO | WI | | --- | --- | --- | --- | --- | | TVOC | 0.21 | 0.21 | 0.41 | -0.32 | | NO_2 | -0.1 | -0.02 | -0.16 | 0.09 | | CO | -0.07 | NR | NR | NR |	The EXPOLIS Oxford study was more focused on the indoor-outdoor exposure relationship, but the correlation results showed no important relationships between the pollutants shown.
Gomez-Perales et al. (2004, 054418; 2007, 138816)	Microenvironmental $PM_{2.5}$ with SO_4^{2-}, NO_3-, EC, OC.	Microenvironmental CO.	Ratio of Conc $PM_{2.5}$ CO Benzene Minibus/Bus 1.04 1.54 2.01 1.20 1.40 1.33 Minibus/Metro 1.70 2.02 3.20 1.43 3.03 3.10	Morning and evening measurements of $PM_{2.5}$ were on avg higher and more variable than for benzene and CO (in order). Benzene and CO had higher and more variable concentrations for minibuses than for buses and metros, respectively, while $PM_{2.5}$ concentrations were not substantially different for buses and minibuses.

Reference	PM metric	Copollutant metric	Association between PM and copollutant	Primary findings
Sarnat et al. (2001, 019401)	Fixed site and personal $PM_{2.5}$ monitors.	Ambient O_3, NO_2, SO_2, and CO	R: $PM_{2.5}$ 1; O_3 0.67; NO_2 0.37; SO_2 ---; CO 0.15 $PM_{2.5}$: O_3 -0.72; NO_2 0.75; SO_2 -0.17; CO 0.69 O_3: NO_2 -0.71; SO_2 0.41; CO -0.67 NO_2: SO_2 -0.17; CO 0.76 SO_2: CO -0.12 CO: 1	Strong association between ambient NO_2 and personal $PM_{2.5}$ suggests that ambient gas may be a suitable surrogate for personal exposure.

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Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISA) and the Integrated Risk Information System (IRIS)

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Annex B. Dosimetry

B.1. Ultrafine Disposition

Table B-1. Ultrafine disposition in humans.

Reference	Study Group	Aerosol	Study Protocol	Observations
Mills et al.(2006, 088770)	Healthy nonsmokers (5 M, 5 F; 21-24 yr)	Carbon - 99mTc 108 nm CMD (σg = 2.2) Technegas Generator	Lung activity in the lung was measured at 0, 1, and 6 h post aerosol inhalation.	On avg, lung activity decreased 3.2 ± 0.7% during the first h and 1.2 ± 1.7% over the next 5 h. With 95.6% of the particles in the lungs at 6 h post inhalation and no accumulation of radioactivity detected over the liver or spleen, findings did not support rapid translocation from the lungs into systemic circulation.
Möller et al. (2008)	Healthy nonsmokers (n = 9; 50 ± 11 yr) Smokers (n = 10; 51 ± 10 yr) COPD patients (n = 7; 69 ± 10 yr)	Carbon - 99mTc ~100 nm CMD Technegas Generator	On two separate occasions, subjects inhaled 100 mL aerosol boli to target front depths of 150 and 800 mL into the lungs to target the airways and alveoli, respectively. Retention measured at 10 min, 1.5, 5.5, 24 and 48 h post inhalation. Isotope (99mTc) leaching from particles assessed via filters in saline, blood, and urine. 81mKr utilized to assess ventilation.	Shallow airways boli-Total deposition in airways (shallow boli) similar between groups. Pattern of deposition was significantly more central in the healthy subjects which was thought due to non-uniform ventilation distribution in smokers and COPD patients as visualized by gamma-camera scans. Airway retention after 1.5 h was significantly lower in healthy subjects (89 ± 6%) than smokers (97 ± 3%) or COPD patients (96 ± 6%). At 24 and 48 h, retention significantly remained higher in COPD patients (86 ± 6% and 82 ± 6%) than healthy subjects (75 ± 10% and 70 ± 9%). Deep alveolar boli - Total deposition in alveoli (deep boli) significantly greater in smokers (64 ± 11%) and COPD patients (62 ± 5%) than healthy subjects (50 ± 8%). Alveolar retention of particles similar at all times between groups. For example, at 48 h, 97 ± 3% in healthy subject, 96 ± 3% in smokers, and 96 ± 2% in COPD patients. Retention at 24 and 48 correlated with isotope leaching, suggesting that the small amount of clearance primarily reflected the disassociation of 99mTc from the particles with little transport of particles from the lungs.
Wiebert et al. (2006, 156154)	Subjects having varied health status (9M, 6F; 46-74 yr) 6 healthy 5 asthmatic 4 smokers	Carbon - 99mTc 87 nm CMD (σg = 1.7) Technegas Generator	Technegas system was modified to reduce leaching of 99mTc radiolabel from particles. The avg tidal volume during aerosol inhalation was 1.8 L (range 0.8-3.3). Activity in chest region measured at 0, 2, 24, 46, and 70 h after inhalation. Leaching assessed in vitro and via urine collection.	Lung function not significantly different between healthy and affected lungs. The aerosol deposition fraction was 41 ± 10%. Lung retention was 99 ± 3%, 99 ± 5%, and 99 ± 10% at 24, 46, and 70 h post inhalation. Cumulative in vitro leaching by 70 h was 2.6 ± 0.96%. Except for radiotracer leaching from particles (1.0 ± 0.6% of initially deposited activity in urine by 24 h), there was not significant clearance from the lungs by 70 h. Individual leaching was not correlated with individual retention.
Wiebert et al. (2006, 157146)	Healthy subjects (4M, 5F; 56 ± 9 yr) Asthmatics (2M, 3F; 59 ± 6 yr) Control (1M; 50 yr)	Carbon - 99mTc 34 nm CMD (σg = 1.5) Technegas Generator	Slow deep aerosol inhalations with 10 s breath hold. Mean inhalation time of 6 min. Control subject inhaled aerosol with loosely bound radiolabel. Retention scans at 10 min, 60 min, 100 min, and 24 h post inhalation. Leaching assessed in vitro and via collection of blood and urine.	Avg deposition fraction of 60 ± 17% which was correlated with tidal volume during aerosol inhalation (p = 0.01). Activity excreted in urine over 24-h post inhalation was 51% in the control subject (high 99mTc disassociation) and 3.6 ± 0.9% of deposited activity. In the blood of the control subject, activity was 30%, 31%, and 5% of the deposited activity at 20 min, 80 min, and 24-h (respectively), whereas it was only 0.9 ± 0.6%, 1.1 ± 0.4%, and 1.5 ± 0.5% the other 13 subjects at these times. Lung retention in the control subject was 30% at 1-h and 18% at 24 h. In the remainder of subjects, lung retention was approximately 100% through 24 h.

Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISA) and the Integrated Risk Information System (IRIS).

Table B- 2. Ultrafine disposition in animals.

Reference	Study Group	Aerosol	Study Protocol	Observations
Bermudez et al.(2004, 056707)	Fischer 344 rats, females (6 wk) B3C3F1 mice, females (6 wk) Hamsters, females (6 wk)	TiO_2: 1.29-1.44 µm MMAD (σg = 2.46-3.65), 21 nm primary particles	Animals exposed 6 h/day, 5 day/wk, for 13 wk to 0.5, 2 and 10 mg/m^3. Control animals exposed to filtered air. Animals sacrificed at 0, 4, 13, 26, and 56 (49 for hamsters) post-exposure. Groups of 25 animals per species and time point.	TiO_2 pulmonary retention half-times for the low-, mid-, and high-exposure groups, respectively: 63, 132, and 365 days in rats; 48, 40, and 319 days in mice; and 33, 37, and 39 days in hamsters. Burden of TiO_2 in lymph nodes increase with time postexposure in mid- and high-dosed rats; in high-dosed mice; but was unaffected in hamsters at any time or dosage group. In high-exposure groups of mice, epithelial permeability remained elevated (~2× control groups) out to 52 wk without signs of recovery. Epithelial permeability was 3-4× control in high exposed rats through 4 wk post exposure, but approached control by 13 wk . Epithelial permeability was unaffected in all groups of hamsters.
Chen et al. (2006, 087947)	Sprague-Dawley male rats (220 ± 20 g)	Polystyrene 125I radiolabel Ultrafine: 56.4 nm Fine: 202 nm	Intratracheal instillation of particles in healthy rats or those pretreated with LPS (12 h before particle instillation). Healthy rats sacrificed between 0.5-2 h and at 24 or 48 h post-instillation. LPS treated rats were sacrificed 0.5-2 h post-instillation.	In healthy rats, there were no marked differences in lung retention or systemic distribution between the ultrafine and fine particles. Results for healthy animals focused on ultrafine particles which were primarily retained in lungs (72 ± 10% at 0.5-2 h; 65 ± 1% at 1 day; 62 ± 5% at 5 days). Initially, there was rapid particle movement into the blood (2 ± 1% at 0.5-2 h; 0.1 ± 0.1% at 5 days) and liver (3 ± 2% at 0.5-2 h; 1 ± 0.1% at 5 days). At 1 day post-instillation, about 13% of the particles where in the urine or feces. Following LPS treatment, ultrafine accessed the blood (5 vs. 2%) and liver (11 vs. 4%) to a significantly greater extent than fine particles.
Geiser et al. (2005, 087362) Also included in in vitro studies	Wistar rats 20 adult males (250 ± 10 g)	TiO_2 (22 nm CMD, 1.7 σg) Spark generated 0.11 mg/m^3 7.3 × 106 particles/cm^3	Rats exposed 1-h via endotracheal tube while anesthetized and ventilated at constant rate. Lungs fixed at 1 or 24-h postexposure.	Distributions of particles among lung compartments followed the volume distribution of compartments and did not differ significantly between 1 and 24-h post-inhalation. On avg, 79.3 ± 7.6% of particles were on the luminal side of the airway surfaces, 4.6 ± 2.6% in epithelial or endothelial cells, 4.8 ± 4.5% in connective tissues, and 11.3 ± 3.9% within capillaries. Particles within cells were not membrane-bound.
Kapp et al. (2004, 156624)	Charles River rats 5 young adult male (250 ± 10 g)	TiO_2 (22 nm CMD, 1.7 σg) Spark generated	Rats exposed 1-h via endotracheal tube while anesthetized and ventilated at constant rate. Lungs fixed immediately postexposure.	Of particles in tissues, 72% were aggregates of 2 or more particles; 93% of aggregates were in round or oval shape aggregates, 7% were needle-like. The size distribution of particles in lung tissues (29 nm CMD, 1.7 σg) was remarkably similar to the aerosol; the small discrepancy may have been due to differences sizing techniques. A large 350 nm aggregate was found in a type II pneumocyte, a 37 nm particle in a capillary close to the endothelial cells, and a 106 nm particle within the surface-lining layer close to the alveolar epithelium.

Table B- 3. In vitro studies of ultrafine disposition.

Reference	Animal	Particles	Study Protocol	Observations
Edetsberger et al. (2005, 155759)	Human cervix carcinoma cells (HeLa cells)	Polystyrene spheres (0.020 µm)	Cells incubated with polystyrene particles having negative surface charges. Cell cultures were naïve or treated with Genistein or Cytochalasin B (CytB) prior to particle application. Genistein inhibits endocytotic processes, expecially caveolae internalization. CytB inhibits actin polymerization and phagocytosis.	Particles translocated into cells by first measurement (~1 min after particle application) independent of treatment group. In naïve cells, agglomerates of 88-117 nm were seen by 15-20 min and of 253-675 nm by 50-60 min after particle application. Intracellular aggregates thought to be result from particle incorporation into endosomes or similar structures. In treated cells, only a small number of agglomerates (161-308 nm) were found and only by 50-60 min. At 50-60 min, 90% and 98% of particles were in the 20-40 nm range in naïve and treated cells, respectively. Particles did not translocate into dead cells, rather they attached to outside of the cell membrane.
Geiser et al. (2005, 087362) Also included inhalation study	Porcine lung macrophages (106 cell/mLuman red blood cells (RBC; 8 × 106 cells/mL)	Fluorescent polystyrene spheres (0.078, 0.2, and 1 µm) Gold shheres (0.025 µm)	Cells cultured for 4 h with each sized polystyrene spheres. RBC were employed as a model of nonphagocytic cells. Some macrophages cultures were treated with cytochalasin D (cytD) to inhibit phagocytosis. In addition, RBC were also cultured with gold particles.	Of the non-cytD treated macrophages, 77 ± 15%, 21 ± 11%, and 56 ± 30% contained 0.078, 0.2, and 1 µm particles, respectively. CytD treatment of macrophages effectively blocked the phagocytosis of 1 µm particles, but did not alter the uptake of the 0.078 and 0.2 µm particles. Human RBC were found to contain 0.078 and 0.2 µm polystyrene spheres as well as the 0.025 µm gold particles, which were not membrane bound. In contrast, the RBC did not contain the larger 1 µm polystyrene spheres. Results suggest that ultrafine and fine (0.078 and 0.2 µm diameter) particles cross cellular membranes by a non-endocytic (i.e. not involving vesicle formation) mechanisms such as adhesive interactions and diffusion.
Geys et al. (2006, 155789)	Human alveolar (A549) and bronchial (Calu-3) epithelial cellsRat primary type II pneumocytes	Amine- and carboxyl-modified fluorescent polystyrene (46 nm)	Cells cultured in clear polyester transwells with 0.4 or 3 µm pores. Monolayer considered "tight" when <1% sodium fluorescein moved from apical to basolateral compartment. Particle translocation assessed in transwells with and without cells. Cells incubated with particles for 14-16 h to assess translocation from apical to basolateral compartment.	Without cells, 13.5% of carboxyl-modified particles passed through the 0.4 µm pores (n = 7) and 67.5% through 3 µm pores (n = 3). Movement of the amine-modified particles was 4.2% through 0.4 µm pores (n = 7) and 52.7% through 3 µm pores (n = 3). The integrity of the monolayer was insufficient for translocation studies using the A549 cells (0.4 and 4 µm pore size) and rat pneumocytes (0.3 µm pore). Using 0.4 µm pores, there was no detectable translocation through either Calu-3 or rat pneumocyte monolayers. Using 3 µm pores, ~6% of both particle types passed through the Calu-3 monolayer; however, results were highly variable with no translocation in 2 (of 5) and 3 (of 6) trials with carboxyl- or amine-modified particles, respectively.

B.2. Olfactory Translocation

Table B-4. Olfactory particle translocation.

Reference	Study Group	Aerosol	Study Protocol	Observations
DeLorenzo (1970, 156391)	Squirrel monkeys Young males (1 kg)	Silver-coated colloidal gold (50 nm)	Intranasal instillation of 1 mL particle suspension. Animals sacrificed at 0.25, 0.5, 1, and 24-h after instillation.	Rapid movement (30-60 min) into olfactory bulbs. Within 30 min of being placed on nasal mucosa, particle aggregates were seen in axoplasm of the fila olfactoria Within 1 h, particles were in olfactory glomerulus. Particles in the olfactory bulb were located preferentially in mitochondria and not free in the cytoplasm.
Dorman et al. (2001, 055433)	Crl: CD rats Males (6 wk old)	Soluble and insoluble Mn particle types; MMAD = 1.3-2.1 µm; GSD<2	Whole body exposure (6 h/day, 14 consecutive days) to 0, 0.03, 0.3, and 3 mg Mn/m^3. Tissues analyzed in six animals per concentration exposed to soluble ($MnSO_4$) or insoluble (Mn_3O_4) aerosols.	Increased Mn levels in olfactory bulb observed following $MnSO_4$ of ≥ 0.3 mg Mn/m^3 and following Mn_3O_4 of 3 mg Mn/m^3. At 3 mg Mn/m^3, Mn levels were significantly greater in olfactory bulb (1.4-fold) and striatum (2.7-fold) following soluble MnO_4 than insoluble Mn_3O_4. Mn levels in the cerebellum were unaffected following all exposures.

Reference	Study Group	Aerosol	Study Protocol	Observations
Dorman et al. (2004, 155752)	Crl: CD rats Males (6 wk old)	Soluble and insoluble Mn particle types; MMAD = 1.5-2 µm; GSD = 1.4-1.6	Whole body exposure (6 h/day, 5 days/wk, 13 wk) to $MnSO_4$ at 0, 0.01, 0.1, and 0.5 mg Mn/m^3. Compared to Mn phosphate (as hureaulite) exposure of 0.1 mg Mn/m^3. Brain Mn levels assessed immediately following 90 days of exposure or 45 days postexposure.	Relative to air, the insoluble hureaulite was significantly increased at 90 days of exposure in the olfactory bulb, but not striatum or cerebellum. The soluble Mn phosphate showed a dose dependent increase in olfactory bulb Mn levels at 90 days. At 0.1 mg Mn/m^3, Mn levels following Mn phosphate were significantly increased in the olfactory bulb and striatum relative to hureaulite and air exposures. At 45 days postexposure, relative to air, olfactory bulb Mn levels only remained increased Mn phosphate group at 0.5 mg Mn/m^3.
Elder et al. (2006, 089253)	Fisher 344 rats Males (200-250 g)	Mn oxide (~30 nm equivalent sphere with 3-8 nm primary particles) Spark generated 0.5 mg/m^3 18 × 106 particles/cm^3	Whole body inhalation exposure to either filtered air or Mn oxide for 12 days (6 h/day, 5 days/wk) with both nares open or Mn oxide for 2 days (6 h/day) with right nostril blocked. Intranasal instillation in left nostril of Mn oxide particles or soluble MnCl2 suspended in 30 µL saline. Analyzed Mn in the lung, liver, olfactory bulb, and other brain regions.	After 12 day exposure via both nostrils, Mn in the olfactory bulb increased 3.5-fold, whereas in the lung Mn concentrations doubled; there were also increases in the striatum, frontal cortex, and cerebellum. After the 2 days exposure with the right nostril blocked, Mn accumulated in the mainly in the left olfactory bulb (~2.4-fold increase) in to a lesser extent in the right olfactory bulb (1.2-fold increase). At 24-h post instillation, the left olfactory bulb contained similar amounts of the poorly soluble Mn oxide (8.2 ± 0.7%) and soluble MnCl2 (8.2 ± 3.6%) as a percent of the amount instilled.
Oberdörster et al. (2004, 055639)	Fisher 344 rats Males (14 wk; 284 ± 9 g)	13C (36 nm CMD, 1.7 σg) Spark generated	Rats (n = 12, 3 per time point) exposed to 160 $µg/m^3$ for 6 h in whole-body chamber and sacrificed at 1, 3, 5, and 7 day postexposure. Lung, olfactory bulb, cerebrum, and cerebellum removed for 13C analysis. Tissue 13C-levels were determined by isotope ratio mass spectroscopy and background corrected for 13C levels in unexposed controls (n = 3).	At 1 day postexposure, the lungs of rats exposed to ultrafine 13C particles contained 1.34 ± 0.22 µg of 13C (1.39 µg/g-lung) following background corrected. By 7 days postexposure, the 13C concentration had decreased to 0.59 µg/g-lung. There was a significant and persistent increase in 13C in the olfactory bulb of 0.35 µg/g on day 1, which increased to 0.43 µg/g by day 7. Day 1 concentrations of 13C in the cerebrum and cerebellum were also significantly increased but the increase was inconsistent, possibly reflecting translocation of particles from the blood across the blood-brain barrier into brain regions.
Persson et al. (2003, 051846)	Sprague-Dawley male rats (150 g) Freshwater Pike female (3 kg)	65ZnCl2 dissolved in 0.1 M HCl	Rats: intransal (0.03 µg Zn in 10 µL) or intraperitoneally (0.03 µg Zn in 100 µL); autoradiography and γ spec at 1 day or 1, 3, or 6 wk postexposure. Pike: instilled (0.12 µg Zn in 10 µL) in right or both olfactory chambers, assayed 2 wk postexposure	Zn uptake in olfactory epithelium and transport along olfactory neurons to olfactory bulb. Zn continued into interior of olfactory bulb and in rat went into anterior olfactory cortex. Zn found bound to both cellular constituents and cytosolic components. Some Zn bound to metallothionein in olfactory mucosa and olfactory bulb.
Wang et al. (2007, 156147)	CD-1 (ICR) mice	Rutile TiO_2 21 and 80 nm Anatase TiO_2 155 nm	Twenty mice (n = 5 per group) exposed 0 or 0.01 g-TiO_2 per mL DI. Instilled 25 µL each day for 5 days, then inhaled 10 µL every other day. Mice sacrificed after 1 mo.	Rutile particles were observed to be column/fiber shaped, whereas anatase was octahedral. TiO_2 particles taken up by olfactory bulb via the olfactory nerve layer, olfactory ventricle, and granular cell layer of the olfactory bulb. Fine TiO_2 showed greater entry into the olfactory bulb presumably due to aggregation of smaller rutile particles that was not seen for the fine anatase particles.
Yu et al. (2003, 156171)	Sprague-Dawley male rats, 6 wk old (218 ± 10 g)	Stainless steel welding-fume <0.5 µm	Whole body exposure 2 h/day for 1, 15, 30, or 60 days Low: 64 ± 4 mg/m^3 (1.6 mg/m^3 Mn) High: 107 ± 6 mg/m^3 (3.5 mg/m^3 Mn)	Significant increases in cerebellum Mn at 15-30 days of exposure. Slight increases in Mn in substantia nigra, basal ganglia, temporal cortex, and frontal cortex after 60 days. Significant increase at 30 days in basal ganglia at low dose. Authors suggested that pharmacokinetics and distribution of welding fume Mn differs from pure Mn.

B.3. Clearance and Age

Table B-5. Studies of respiratory tract mucosal and macrophage clearance as a function of age.

Reference	Animal	Particles	Study Protocol	Observed Effect(s)
NASAL AND TRACHEAL CLEARANCE				
Ho et al. (2001, 156549)	Human, males and females	Not applicable	Ninety subjects (47 M, 43 F; 52 ± 23 yr) between 11 and 90 yr of age were recruited to measure nasal saccharine clearance and ciliary beat frequency.	Ciliary beat frequency (n = 90; r = -0.48, p <0.0001) and nasal mucociliary clearance time (n = 43; r = 0.64, p <0.001) were correlated with subject age. Nasal clearance times were significantly (p <0.001) faster in individuals under 40 yr of age (9.3 ± 5.2 min) versus older subjects (15.4 ± 5.0 min). Results similar between males and females.
Goodman et al. (1978, 071130)	Humans, males and females	Radiolabed Teflon disks (1 mm diameter, 0.8 mm thick)	Tracheal mucus velocity following delivery via bronchoscope to the tracheal mucosa. Ten young (2 M, 8 F; 23 ± 3 yr) and ten elderly (2 M, 5 F; 63 ± 5 yr) nonsmokers served as control subjects. Measurements were also made in young smokers, ex-smokers, and individuals with chronic bronchitis.	Young nonsmokers had a tracheal mucus velocity of 10.1 ± 3.5 mm/min which was significantly faster than the velocity of 5.8 ± 2.6 observed in the elderly nonsmokers.
Whaley et al. (1987, 156153)	Beagle dogs, males and females	Macroaggregated albumin99mTc labelled	Intratracheal instillation of 10- µl droplet of labelled albumin in saline. Tracheal clearance followed 25 min. Longitudinal measure measurements in 5 males and 3 females when young adults (2.8-3 yr), middle-aged (6.7-6.9 yr), and mature (9.6-9.8 yr). Additional 5 females and 3 males comprised immature group (9-10 mo) and 4 males and 4 females used as aged group (13-16 yr).	Tracheal mucus velocity significantly (p <0.05) greater in young (9.7 ± 0.6 [SE] mm/min) and middle-aged (6.9 ± 0.5) groups than in immature (3.6 ± 0.4), mature (3.5 ± 0.8), and aged (2.9 ± 0.5) dogs.
Yeates et al. (1981, 095391)	Humans, males and females	Radioaerosols 99mTc labelled	Tracheal mucus velocities compiled for 74 healthy non-smoking subjects (60 M, 14 F; 10-65 yr, mean 30 yr) from prior studies. Forty-two (32 M, 10 F) inhaled albumin in saline droplets (6.2-6.5 µm MMAD), Yeates et al. (1975); twenty-two (21 M, 1 F) inhaled iron oxide (4.2 µm MMAD), Yeates et al. (1981b); and ten (7 M, 3 F) inhaled monodisperse iron oxide aerosol (7.5 µm MMAD), Leikauf et al. (1981). Inhalations were via a mouthpiece with an inspiratory flow of ~1 liter/sec.	A lognormal distribution of tracheal mucus velocities was reported. Age did not appear to affect velocities, e.g., 4.7 ± 2.5 mm/min in 18-24 yr olds vs. 4.6 ± 3.2 mm/min in individuals >30 yr of age. However, it should be noted that only 2 subjects were greater than 45 yr of age and that the data was complied from three studies using differing experimental techniques. Rather similar tracheal mucus velocities in males (4.7 ± 3.0 mm/min) and females (4.9 ± 2.4 mm/min).
BRONCHI AND BRONCHIOLES CLEARANCE				
Puchelle et al. (1979, 006863)	Human, males	7.4 µm MMAD99mTc labelled resin	Mucociliary clearance measured for 1 h post aerosol inhalation in 19 healthy non-smoking males (21-69 yr of age). Clearance measure on two occasions in 16 individuals.	Negative correlation (r = -0.472, p <0.05) between mucociliary clearance and age. Younger subjects (n = 9; 21-37 yr) had 1-h clearance of 34 ± 14% which was significantly greater than the 22 ± 8% found in the older subjects (n = 5; >54 yr). Separated by 5.4 wk (on avg), there was a good correlation between repeated clearance measurements (r = 0.65, p <0.001)
Svartengren et al. (2005, 157034)	Humans, males and females	6 µm MMAD111In labelled Teflon	Small airway clearance measured in five age groups (≤ 24 yr, n = 13; 25-29 yr, n = 8; 30-49 yr, n = 7; 50-64, n = 9; >65 yr, n = 9) of healthy subjects. Aerosol inhaled via mouthpiece at extremely slow rate of 0.05 L/s. Activity in lungs measured at 1 day, 2 days, and 1, 2, and 3 wk post-exposure. Under the presumption that most large airway clearance was complete by 24 h, retention at 24 h was normalized to 100%.	Large and small airway clearance slowed with increasing age. Clearance correlated with age at all times (r = -0.46 to -0.50, -0.55, -0.66, and -0.70 at 1 day, 2 days, 1 wk, 2 wk, and 3 wk, respectively). Based on linear regression, the clearance from 1 to 21 days post-exposure was 47% in a 20 yr-old versus 23% in an 80 yr-old. Lung function was not a significant predictor of clearance when age considered.

Reference	Animal	Particles	Study Protocol	Observed Effect(s)
Vastag et al. (1985, 157088)	Humans, males and females	Monodisperseerythrocytes99mTc labelled	Clearance measured for 1-h post-inhalation in eighty healthy (59 M, 21 F; 43 ± 17 yr) subjects who had never smoked. Smokers and ex-smokers also studied. Aerosol inhalation not described.	Clearance significantly associated with age. Based on linear regression, total mucociliary clearance at 1-h post-exposure was 46% in a 20 yr old versus 23% in an 80 yr old. Similar results for males and females.
ALVEOLAR CLEARANCE				
Muhle et al. (1990, 006853)	Fischer 344 rats	3.5 µm MMAD 85Sr labelled polystyrene latex	Control animals compared across several studies. Aerosol inhaled by short-term nose only exposure. Alveolar clearance determined by exponential fit to thoracic activity measured over 75-100 days excluding the first 15 days post-exposure.	Typical alveolar clearance half-time of 45 days in 5-mo-old rats compared to 74 days in 23-mo-old rats. Statistical significance of findings not proved.

Annex B References

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Annex C.
Controlled Human Exposure Studies

Table C-1. Cardiovascular effects.

Study	Pollutant	Exposure	Findings
Reference: Barregard et al. (2006, 091381) **Subjects:** 13 healthy adults **Gender:** 6 M/7 F **Age:** 20-56 yr	Wood smoke **Particle Size:** Session 1: GMD 42 nm; Session 2: GMD 112 nm **Particle Number/Count:** Session 1: 180,000/cm^3; Session 2: 95,000/cm^3 **Concentration:** Session 1: median: 279 µg/m^3; Session 2: median 243 µg/m^3	Subjects exposed in two groups for 4 h to filtered air, followed a wk later by a 4-h exposure to wood smoke. Exposures conducted with two 25-min periods of light exercise. Other measured combustion products: Session 1: NO_2 (0.08 ppm), CO (13 ppm), formaldehyde (114 µg/m^3), acetaldehyde (75 µg/m^3), benzene (30 µg/m^3), 1,3-butadiene (6.3 µg/m^3); Session 2: NO_2 (0.09 ppm), CO (9.1 ppm), formaldehyde (64 µg/m^3), acetaldehyde (40 µg/m^3), benzene (20 µg/m^3), 1,3-butadiene (3.9 µg/m^3). **Time to analysis**: Immediately following exposure as well as 3 and 20 h post-exposure.	Statistically significant increase in plasma factor VIII 20 h post wood smoke exposure relative to filtered air. The factor VIII/von Willebrand ratio in plasma was increased with wood smoke relative to filtered air at 0, 3, and 20 h post-exposure. Wood smoke exposure increased the urinary excretion of free 8-iso-prostaglandin2α relative to clean air 20 h post-exposure (n = 9). These findings were more pronounced in session 1 than session 2 (similar mass concentration but higher number concentration in Session 1).
Reference: Beckett et al. (2005, 156261) **Subjects:** 12 healthy adults **Gender:** 6 M/6 F **Age:** 23-52 yr	Ultrafine and fine zinc oxide **Particle Size:** UF: <0.1 µm; Fine: 0.1-1.0 µm **Particle Number/Count:** UF: 4.6×10^7/cm^3; Fine: 1.9×10^5/cm^3 **Concentration:** 500 µg/m^3	Subjects exposed via mouthpiece for 2 h during rest to filtered air, ultrafine, and fine zinc oxide in a randomized crossover study design. Exposures were separated by at least 3 wk. **Time to analysis:** Immediately following exposure and 3, 6, 11, 23, and 24 h after exposure.	Exposure to ultrafine and fine zinc oxide did not affect HRV (time and frequency domain parameters) relative to clean air immediately following exposure, or at 3, 6, 11, and 23 h post-exposure. Exposure did not affect blood pressure through 24 h post-exposure. No effects of exposure to either fine or ultrafine zinc oxide observed on factor VII, von Willebrand factor (vWf), tissue plasminogen activator (t-PA), or fibrinogen. No effect of exposure observed on peripheral blood cell counts or levels of pro-inflammatory cytokines.
Reference: Blomberg et al. (2005, 191991) **Subjects:** 15 older adults (former smokers) with COPD **Age:** 56-72 yr	DE **Concentration:** 300 µg/m^3	Subjects exposed for 1 h with intermittent exercise to DE and filtered air in a randomized crossover study design. **Time to analysis:** 6 and 24 h post-exposure.	DE was not observed to affect blood levels of C-reactive protein, fibrinogen, D-Dimer, prothrombin factor 1-2, or von Willebrand factor activity at 6 and 24 h post-exposure.
Reference: Brauner et al. (2007, 091152) **Subjects:** 29 healthy adults **Gender:** 20 M/9 F **Age:** 20-40 yr	Urban traffic particles **Particle Number/Count:** 6–700nm: 10,067/cm^3 **Concentration:** $PM_{2.5}$: 9.7 µg/m^3; $PM_{10\text{-}2.5}$: 12.6 µg/m^3	Subjects exposed to urban traffic particles and filtered air for 24 h with and without two 90-min periods of light exercise in a randomized crossover study design. Concentrations of NO_X and NO were low and did not differ between filtered and unfiltered exposures. CO concentrations were higher with filtered air (0.35 and 0.41 ppm), while O_3 concentrations were lower with filtered air (12.08 and 4.29 ppb). **Time to analysis:** 6 and 24 h after the start of exposure.	An increase in DNA strand breaks and formamidopyrimidine-DNA glycosylase sites in peripheral blood mononuclear cells were observed after 6 and 24 h of exposure to urban particulates. The particle concentration at the 57nm mode was shown to be the major contributor to these effects.

Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISA) and the Integrated Risk Information System (IRIS).

Study	Pollutant	Exposure	Findings
Reference: Brauner et al. (2008, 156293) **Subjects:** 42 healthy older adults (21 couples) **Age:** 60-75 yr	Indoor air particles **Particle Number/Count:** 10-700 nm: 10,016/cm^3 **Concentration:** Coarse: 9.4 µg/m^3; Fine: 12.6 µg/m^3	Exposures consisted of two 48 h periods in the home of each subject with or without the use of a HEPA filter (randomized crossover design). HEPA filters reduced coarse concentration from 9.4 to 4.6 µg/m^3,, and fine concentration from 12.6 to 4.7 µg/m^3. Concentrations of NO_2 did not differ between the 2 sessions (20 ppb). **Time to analysis:** After the completion of each 48 h session.	The use of HEPA filters significantly improved microvascular function (p = 0.04) after 48 h (reactive hyperemia-peripheral arterial tonometry). Microvascular function was assessed using a scoring system representing the extent of reactive hyperemia. The reduction in PM concentration through the use of HEPA filters did not significantly affect blood pressure following the 48-h exposures. Lowering PM concentration did not significantly affect inflammatory response markers in peripheral venous blood (IL-6, TNF-α, C-reactive protein, plasma amyloid A).
Reference: Brauner et al. (2008, 191966) **Subjects:** 29 healthy adults **Gender:** 20 M, 9 F **Age:** M avg 27 yr, F avg 26 yr	Urban traffic particles **Particle Number/Count:** 11,600/cm^3 **Concentration:** $PM_{2.5}$: 10.5 µg/m^3; $PM_{10-2.5}$: 13.8 µg/m^3	Subjects exposed to urban traffic particles and filtered air for 24 h with and without two 90-min periods of light exercise in a randomized crossover study design. Concentrations of NO_X and NO were low and did not differ between filtered and unfiltered exposures. CO concentrations were higher with filtered air, while O_3 concentrations were lower with filtered air. **Time to analysis:** 6 and 24 h after the start of exposure.	Exposure to urban traffic particles was not observed to affect microvascular function (digital peripheral artery tone) at 6 or 24 h after the start of exposure. No difference in various blood markers of coagulation, inflammation, or protein oxidation (e.g., fibrinogen, platelet count, CRP, IL-6, TNF- α) were demonstrated between particle and filtered air exposure.
Reference: Carlsten et al. (2007, 155714) **Subjects:** 13 healthy adults **Gender:** 11 M/2 F **Age:** 20-42 yr	DE 2002 Cummins B-series diesel engine (6BT5.9G6, 5.9 L) operating at load **Concentration:** Fine PM: 100, 200 µg/m^3	Subjects exposed for 2 h at rest to filtered air and each of the two DEPs concentrations in a randomized crossover study design. Exposures were separated by at least 2 wk. Other diesel emissions measured: NO_2 (10-35 ppb), CO (0.7-1.8 ppm). **Time to analysis:** 3, 6, and 22 h after the start of exposure.	No statistically significant changes in plasminogen activator inhibitor-1 (PAI-1), vWf, D-dimer, or platelet count observed 3, 6, or 22 h following exposure to DE relative to filtered air. Non-statistically significant increases in D-dimer, vWf, and platelet count were observed at 6 h following the start of exposure (4 h post-exposure). No diesel-induced increase in C-reactive protein observed relative to filtered air in peripheral venous blood at 1 or 20 h post-exposure.
Reference: Carlsten et al. (2008, 156323) **Subjects:** 16 adults with metabolic syndrome **Gender:** 10 M/6 F **Age:** 25-48 yr	DE 2002 Cummins B-series diesel engine (6BT5.9G6, 5.9 L) **Concentration:** Fine PM: 100, 200 µg/m^3	Subjects exposed for 2 h at rest to filtered air and each of the two DE particle concentrations in a randomized crossover study design. Exposures were separated by at least 2 wk. Other diesel emissions measured: NO_2 (30 ppb), NO (1.69 ppm), CO (0.65 ppm). **Time to analysis:** 3, 7, and 22 h after the start of exposure.	At 5 h after the end of diesel exposure (fine particulate concentration 200 µg/m^3), the authors observed a significant decrease in vWf in peripheral venous blood. No other changes in thrombotic markers (vWf, D-dimer, PAI-1) were observed at either concentration between 1 and 20 h post-exposure.
Reference: Danielsen et al. (2008, 156382) **Subjects:** 13 healthy adults **Gender:** 6 M/7 F **Age:** 20-56 yr	Wood smoke **Particle Size:** Session 1: GMD 42 nm; Session 2: GMD 112 nm **Particle Number/Count:** Session 1: 180,000/cm^3; Session 2: 95,000/cm^3 **Concentration:** Session 1: median: 279 µg/m^3; Session 2: median 243 µg/m^3	Subjects exposed in two groups for 4 h to filtered air, followed a wk later by a 4-h exposure to wood smoke. Exposures conducted with two 25-min periods of light exercise. Other measured combustion products: Session 1: NO_2 (0.08 ppm), CO (13 ppm), formaldehyde (114 µg/m^3), acetaldehyde (75 µg/m^3), benzene (30 µg/m^3), 1,3-butadiene (6.3 µg/m^3); Session 2: NO_2 (0.09 ppm), CO (9.1 ppm), formaldehyde (64 µg/m^3), acetaldehyde (40 µg/m^3), benzene (20 µg/m^3), 1,3-butadiene (3.9 µg/m^3). **Time to analysis:** 3 and 20 h post-exposure.	Exposure to wood smoke increased the mRNA levels of hOGG1 in PBMCs relative to filtered air 20 h after exposure. DNA strand breaks were shown to decrease in PBMCs 20 h after wood smoke exposure.
Reference: Devlin et al. (2003, 087348) **Subjects:** 10 healthy older adults **Gender:** 7 M/3 F **Age:** Avg 66.9 yr	Fine CAPs (Chapel Hill, NC) **Concentration:** Mean: 40.5 µg/m^3, Range: 21.2-80.3 µg/m^3	Exposures conducted for 2 h at rest to filtered air and CAPs in a randomized crossover study design. **Time to analysis:** Immediately following exposure and 24 h post-exposure.	CAPs exposure resulted in statistically significant reductions (p <0.05) in time domain (PNN50) and frequency domain (HF power) parameters relative to clean air immediately following exposure. These relative decreases were still apparent 24 h after exposure (p <0.08).

Study	Pollutant	Exposure	Findings
Reference: Fakhri et al. (2009, 191914) **Subjects:** 50 adults (40 healthy, 10 asthmatic) **Gender:** 24 M/26 F **Age:** 19-48 yr	Fine CAPs (Toronto) **Concentration:** 127 ± 62 µg/m^3 with and without co-exposure to O_3 (114 ± ppb)	Exposures conducted through a facemask which covered the subject's nose and mouth. Subjects were exposed to CAPs, O_3, CAPs + O_3 and filtered air for 2 h at rest in a randomized crossover study design. **Time to analysis:** Every 30 min during exposure, with the final measurement made immediately prior to the end of the exposure.	Exposure to CAPs or O_3, alone or in combination, resulted in no significant changes in HRV or blood pressure relative to filtered air. However, a negative concentration response relationship was reported between CAPs concentration with co-exposure to O_3 and SDNN, rMSSD, HF power and LF power (statistically significant for LF power). Diastolic blood pressure was observed to increase with exposure to CAPs + O_3, but not with either pollutant alone. There was no difference in response between asthmatics and healthy subjects.
Reference: Frampton et al. (2006, 088665) **Subjects:** 16 asthmatic adults, 40 healthy adults **Gender:** Asthmatics: 8 M/8 F, Healthy: 20 M/20 F **Age:** 18-40 yr	Ultrafine EC **Particle Size:** CMD ~25 nm **Particle Number/Count:** 10 µg/m^3: ~2.0 × 10^6/cm^3; 25 µg/m^3: ~7.0 × 10^6/cm^3; 50 µg/m^3: ~10.8 × 10^6/cm^3 **Concentration:** 10, 25, and 50 µg/m^3	Study conducted using a randomized crossover design with 2-h exposures. Asthmatics (n = 16) exposed to filtered air and 10 µg/m^3. 12 healthy adults exposed to filtered air and 10 µg/m^3 at rest; 12 healthy adults exposed to filtered air, 10 and 25 µg/m^3 with intermittent exercise; 16 healthy adults exposed to filtered air and 50 µg/m^3 with intermittent exercise. Exposures were conducted via mouthpiece. **Time to analysis:** Immediately following exposure as well as 3.5, 21, and 45 h post-exposure.	No effect of ultrafine particle exposure on leukocyte counts or leukocyte expression of adhesion molecules observed in healthy subjects exposed at rest to 10 µg/m^3. Among healthy adults exposed to ultrafine carbon during exercise, monocyte expression of adhesion molecules CD54 and CD18 decreased relative to filtered air immediately following exposure. An ultrafine particle-induced decrease in PMN expression of CD18 was also observed 0-21 h post-exposure. Expression of CD11b on monocytes and eosinophils was reduced following exposure to ultrafine particles in exercising asthmatics 0-21 h post-exposure. A decrease in total leukocyte count was observed following ultrafine particle exposure in exercising healthy and asthmatic subjects.
Reference: Gong et al. (2004, 087964) **Subjects:** 13 older adults with COPD, 6 healthy older adults **Gender:** COPD: 5 M/8 F, Healthy: 2 M/4 F **Age:** COPD: avg 68 yr, Healthy: avg 73 yr	Fine CAPs (Los Angeles) **Particle Size:** 85% of mass between 0.1 and 2.5 µm **Concentration:** Mean: 194 µg/m^3, Range: 135-229 µg/m^3	Exposures to CAPs and filtered air (randomized crossover) for 2 h with intermittent light exercise (four 15-min periods). Exposures were separated by at least 2 wk. **Time to analysis:** Immediately following exposure as well as 4 and 22 h post-exposure.	SDNN shown to decrease following CAPs exposure relative to filtered air in healthy older adults (4-22 h post-exposure). No CAPs-induced changes in HRV were observed in older adults with COPD. Ectopic heart beats were observed to increase slightly with CAPs relative to filtered air among healthy subjects, but decreased among subjects with COPD. Exposure to CAPs did not affect platelet or white blood cell count, or levels of fibrinogen, vWF, or factor VII.
Reference: Gong et al. (2004, 055628) **Subjects:** 12 adult asthmatics, 4 healthy adults **Gender:** Asthmatics: 4 M/8 F, Healthy: 2 M/2 F **Age:** Asthmatics: avg 38 yr, Healthy: avg 32 yr	Coarse CAPs (Los Angeles) **Particle Size:** 80% of mass between 2.5 and 10 µm, 20% of mass <2.5 µm **Concentration:** Mean: 157 µg/m^3, Range: 56-218 µg/m^3	Exposures to CAPs and filtered air (randomized crossover) for 2 h with intermittent light exercise (four 15-min periods). Exposures were separated by at least 2 wk. **Time to analysis:** Immediately following exposure as well as 4 and 22 h post-exposure.	SDNN shown to decrease following CAPs exposure relative to filtered air in healthy adults (4-22 h post-exposure). Decrease in PNN50 also observed in healthy adults at 4 h post-exposure. No CAPs-induced decreases in HRV demonstrated in asthmatics.
Reference: Gong et al. (2008, 156483) **Subjects:** 14 adult asthmatics, 17 healthy adults **Gender:** Asthmatics: 9 M/5 F, Healthy: 5 M/12 F **Age:** Asthmatics: 34 ± 12 yr, Healthy: 24 ± 8 yr	Ultrafine CAPs (Los Angeles) **Particle Number/Count:** 145,000/cm^3, Range 39,000-312,000/cm^3 **Concentration:** Mean-100 µg/m^3, Range-13-277 µg/m^3	Subjects exposed for 2 h during intermittent exercise (15-min periods) to both CAPs and filtered air in random order. The first 7 subjects underwent whole body exposure, while the remaining subjects were exposed through a facemask. Facemask exposures had higher particle counts but lower particle mass than whole body exposures. Exposures were separated by at least 2 wk. **Time to analysis:** Immediately following exposure as well as 4 and 22 h post-exposure.	Relative to filtered air, exposure to ultrafine CAPs resulted in a transient decrease in LF power 4 h post-exposure. This effect of CAPs on HRV was not influenced by health status. CAPs exposure was not observed to affect any other measures of HRV, blood pressure, or blood markers of inflammation or coagulation. There were no differences in response observed between facemask and whole body exposures.

Study	Pollutant	Exposure	Findings
Reference: Graff et al. (2009, 191981) **Subjects:** 14 healthy adults **Gender:** 8 M/6 F **Age:** 20-34 yr	Coarse CAPs (Chapel Hill, NC) **Concentration:** 89 ± 49.5 µg/m^3 (estimated inhaled dose ≈ 67% of measured particle mass)	Subjects exposed for 2 h with intermittent exercise (15-min periods) to coarse CAPs and filtered air in a randomized crossover design. Exposures were separated by at least 2 mos. **Time to analysis:** 0-1 and 20 h post-exposure.	At 20 h post-exposure, tPA was observed to decrease by 32.9% from baseline (pre-exposure) per 10 µg/m^3 increase in CAPs concentration (p = 0.01). D-dimer concentration decreased 11.3% per 10 µg/m^3, a change of marginal statistical significance (p = 0.07). No other coarse CAPs-induced changes in blood biomarkers of coagulation (e.g., vWF, factor VII, plasminogen, fibrinogen, or PAI-1) or inflammation (e.g., CRP) were observed. At 20 h post-exposure, overall HRV (SDNN) was shown to decrease by 14.4% relative to pre-exposure measurements per 10 µg/m^3 increase in CAPs concentration. No other changes in HRV were observed following exposure to coarse CAPs.
Reference: Huang et al. (2003, 087377) **Subjects:** 38 healthy adults **Gender:** 36 M/2 F **Age:** Avg 26.2 ± 0.7 yr	Fine CAPs (Chapel Hill, NC) **Concentration:** 23.1-311.1 µg/m^3	Subjects exposed to CAPs (n = 30) or filtered air (n = 8) for 2 h with intermittent exercise (subjects did not serve as their own controls). Component data of CAPs was available for 37 of the 38 subjects. **Time to analysis:** 18 h after exposure.	The increase in blood fibrinogen following exposure to fine CAPs reported by Ghio et al. (2000, 012140) was shown to be associated with copper, zinc, and vanadium content in the CAPs.
Reference: Larsson et al. (2007, 091375) **Subjects:** 16 healthy adults **Gender:** 10 M/6 F **Age:** 19-59 yr	Traffic particles (road tunnel) **Particle Size:** $PM_{2.5}$, PM_{10}; $PM_{2.5}$ mass constituted ~36% of PM_{10} mass **Particle Number/Count:** 20-1,000 nm: 1.1 × 10^5/cm^3, < 100 nm: 0.85 × 10^5/cm^3 **Concentration:** $PM_{2.5}$-46-81 µg/m^3; PM_{10}-130-206 µg/m^3	Exposures were conducted for 2 h with intermittent exercise in a room adjacent to a busy road tunnel. Study used a randomized crossover design with each subject also exposed to normal air (control). Exposures were separated by 3-10 wk. No exposures to filtered air were conducted. Other traffic emissions measured: NO (874 µg/m^3), NO_2 (230 µg/m^3), CO (5.8 µg/m^3 reported, likely 5.8 mg/m^3). **Time to analysis:** 14 h post-exposure.	No change in plasma levels of fibrinogen or PAI-1 observed 14 h post-exposure.
Reference: Lucking et al. (2008, 191993) **Subjects:** 20 healthy adults **Gender:** M **Age:** 21-44 yr	DE Protocol 1 (n=8): idling Deutz diesel engine (F3M2011, 2.2 L, 500 rpm) using gas oil Protocol 2 (n=12): idling Volvo diesel engine (TD45, 4.5 L, 4 cylinders, 680 rpm) using Gasoil E10 **Particle Number/Count:** Protocol 1: 1.2 × 10^6/cm^3; Protocol 2: 1.26 × 10^6/cm^3 **Concentration:** Protocol 1: 348 µg/m^3, Protocol 2: 330 µg/m^3	In both protocols, exposures were conducted with intermittent exercise (15-min periods) to DE and filtered air in a randomized crossover design with exposures separated by at least one wk. Protocol 1 (n=8): Exposures conducted for 2 h. Other diesel emissions measured: NO_X (0.58 ppm), NO_2 (0.23 ppm), NO (0.36 ppm), CO (3.54 ppm), total hydrocarbon (2.8 µg/m^3). **Time to analysis:** 6 h post-exposure. Protocol 2 (n=12): Exposures conducted for 1h. Other diesel emissions measured: NO_X (2.78 ppm), NO_2 (0.62 ppm), NO (2.15 ppm), CO (3.08 ppm), total hydrocarbon (1.58 µg/m^3). **Time to analysis:** 2 and 6 h post-exposure.	Thrombus formation was observed to increase with diesel 2 and 6 h post-exposure using an ex vivo perfusion chamber. Both platelet-neutrophil and platelet-monocyte aggregates increased relative to filtered air 2 h following exposure to diesel (only evaluated in Protocol 2). Plasma concentrations of soluble CD40L were also observed to increase with diesel. Exposure to diesel was not shown to affect total leukocyte, monocyte, or platelet counts.
Reference: Lund et al. (2009, 180257) **Subjects:** 10 healthy adults **Gender:** 4 M/6 F **Age:** 18-40 yr	DE Idling Cummins diesel engine (5.9 L) using commercial No. 2 fuel **Particle Size:** MMAD 0.10 µm **Concentration:** 100 µg/m^3	Subjects exposed for 2 h with intermittent exercise (15-min periods) to DE and filtered air in a randomized crossover study design. Other diesel emissions measured: NO_X (4.7 ppm), NO_2 (0.8 ppm), CO (2.8 ppm), total hydrocarbons (2.4 ppm). **Time to analysis:** 30 min and 24 h post-exposure.	Exposure to diesel resulted in an increase in MMP-9 plasma concentration and activity as well as an increase in endothelin-1 plasma concentration at both 30 min and 24 h post-exposure.

Study	Pollutant	Exposure	Findings
Reference: Lundback et al. (2009, 191967) **Subjects:** 12 healthy adults **Gender:** M **Age:** 21-30 yr	DE Idling Volvo diesel engine (TD45, 4.5 L, 4 cylinders, 680 rpm) using Gasoil E10 **Particle Number/Count:** $1.26 \times 10^6/cm^3$ **Concentration:** 330 $\mu g/m^3$	Subjects exposed for 1 h with intermittent exercise (15-min periods) to DE and filtered air in a randomized crossover study design. Exposures were separated by at least one wk. Other diesel emissions measured: NO_X (2.78 ppm), NO_2 (0.62 ppm), NO (2.15 ppm), CO (3.08 ppm), total hydrocarbon (1.58 $\mu g/m^3$). **Time to analysis:** 10, 20, 30, and 40 min post-exposure.	Diesel-induced increase in arterial stiffness (increases in augmentation pressure and augmentation index, as well as decrease in time to wave reflection) observed at 10 and 20 min post-exposure using radial artery pulse wave analysis. No effect of diesel observed on carotid-femoral pulse wave velocity which was assessed 40 min post-exposure, but not at earlier time points. No effect of diesel observed on blood pressure 10-30 min post-exposure.
Reference: Mills et al. (2005, 095757) **Subjects:** 30 healthy adults **Gender:** M **Age:** 20-38 yr	DE Idling 1991 Volvo diesel engine (TD45, 4.5 L, 4 cylinders, 680 rpm) **Particle Number/Count:** $1.2 \times 10^6/cm^3$ **Concentration:** 300 $\mu g/m^3$	Subjects exposed for 1 h with intermittent exercise (15-min periods) to DE and filtered air in a randomized crossover study design. Exposures were separated by two wk. Other diesel emissions measured: NO_2 (1.6 ppm), NO (4.5 ppm), CO (7.5 ppm), total hydrocarbon (4.3 ppm), formaldehyde (0.26 $\mu g/m^3$). **Time to analysis:** 2-4 h post-exposure for 15 subject; 6-8 h post-exposure for the other 15 subjects.	Forearm blood flow increase (induced by bradykinin, acetylcholine, and sodium nitroprusside) was attenuated by DE 2 and 6 h post-exposure. A 6 mmHg increase in diastolic blood pressure ($p = 0.08$) 2 h following exposure to DE was observed relative to filtered air control. Bradykinin-induced release of t-PA was attenuated by diesel exposure 6 h post-exposure. DE did not affect the release of t-PA 2 h post-exposure. No diesel-induced changes in serum IL-6 or TNF-α observed 6 h post-exposure.
Reference: Mills et al. (2007, 091206) **Subjects:** 20 older adults with prior myocardial infarction **Gender:** M **Age:** 60 ± 1 yr	DE Idling 1991 Volvo diesel engine (TD45, 4.5 L, 4 cylinders, 680 rpm) using low sulfur gas-oil E10 **Particle Size:** Median particle diameter 54 nm, Range 20-120 nm **Particle Number/Count:** $1.26 \times 10^6/cm^3$ **Concentration:** 300 $\mu g/m^3$	Subjects exposed for 1 h with intermittent exercise (15-min periods) to DE and filtered air in a randomized crossover study design. Exposures were separated by at least two wk. Other diesel emissions measured: NO_X (4.45 ppm), NO_2 (1.01 ppm), NO (3.45 ppm), CO (2.9 ppm), total hydrocarbon (2.8 ppm). **Time to analysis:** During exposure and 6-8 h post-exposure.	A greater increase in exercise induced ST-segment depression and ischemic burden was observed during exposure to DE than clean air. No diesel-induced effects on vasomotor dysfunction observed 6 h post-exposure. Bradykinin-induced release of t-PA was attenuated by diesel exposure relative to filtered air 6 h post-exposure. Effect of diesel on t-PA release was not evaluated at earlier times post-exposure. No diesel-induced changes in blood leukocyte counts or serum C-reactive protein 6 h post-exposure.
Reference: Mills et al. (2008, 156766) **Subjects:** 12 adults with coronary heart disease, 12 healthy adults **Gender:** M **Age:** CHD: 59 ± 2 yr, Healthy: 54 ± 2 yr	Fine CAPs (Edinburgh, Scotland, UK) **Particle Size:** Mean 1.23 µm **Particle Number/Count:** $99{,}400/cm^3$ **Concentration:** 190 ± 37 $\mu g/m^3$	Exposures conducted for 2 h with intermittent exercise. Subjects exposed to CAPs and filtered air using a randomized crossover design with exposures separated by at least 2 wk. **Time to analysis:** 2, 6-8, and 24 h post-exposure.	CAPs exposure had no significant effect on vascular function in healthy adults or adults with coronary heart disease 6-8 h post-exposure (i.e., no change in forearm blood flow as assessed using venous occlusion plethysmography). The authors attributed this lack of response to a low concentration of combustion-derived particles. Small increase in blood platelet and monocyte concentration observed following CAPs exposure. Exposure to CAPs did not affect serum CRP concentration or total leukocyte or neutrophil count.
Reference: Peretz et al. (2007, 156853) **Subjects:** 5 healthy adults **Gender:** M **Age:** 20-31 yr	DE 2002 Cummins B-series diesel engine (6BT5.9G6, 5.9 L); operating at 75% of rated capacity **Concentration:** Fine PM 50, 100, 200 $\mu g/m^3$	Subjects exposed for 2 h at rest to filtered air and each of the three DE particle concentrations in a randomized crossover study design. Exposures were separated by at least 2 wk. Other diesel emissions measured, 200 $\mu g/m^3$ exposure: NO_2 (23 ppb), NO (1.75 ppm), CO (1.58 ppm). **Time to analysis:** 6 and 22 h after the start of exposure.	PBMC expression of 10 genes involved in the inflammatory response were observed to be significantly affected by exposure to DE at the highest concentration tested (8 upregulated, 2 downregulated) 6 h after the start of exposure. The expression of 4 genes (1 upregulated, 3 downregulated) associated with the inflammatory response showed significant changes 22 h after diesel exposure. PBMC expression of 5 genes involved in the oxidative stress pathways showed significant changes at 6 h after the start of diesel exposure at the highest concentration tested (4 upregulated, 1 downregulated). 7 genes involved in the oxidative stress pathways showed significant changes at 22 h following exposure (4 upregulated, 3 downregulated).

Study	Pollutant	Exposure	Findings
Reference: Peretz et al. (2008, 156854) **Subjects:** 17 adults with metabolic syndrome, 10 healthy adults **Gender:** Metabolic syndrome: 11 M/6 F, Healthy: 8 M/2 F **Age:** Metabolic syndrome: 20-48 yr, Healthy: 20-42 yr	DE 2002 Cummins B-series diesel engine (6BT5.9G6, 5.9 L) using No. 2 undyed on-highway fuel; operating at 75% of rated capacity **Particle Size:** Median particle diameter 1.04 µm **Concentration:** Fine PM 100, 200 µg/m^3	Subjects exposed for 2 h at rest to both concentrations of DE as well as filtered air in a randomized crossover design. Exposures were separated by at least 2 wk. Other diesel emissions measured, 100 µg/m^3 exposure: NO_2 (16.5 ppb), NO (0.96 ppm), CO (0.51 ppm); 200 µg/m^3 exposure: NO_2 (24.7 ppb), NO (1.54 ppm), CO (0.89 ppm). **Time to analysis:** Immediately following exposure (within 30 min post-exposure) and 3 h from the start of exposure.	Exposure to 200 µg/m^3 elicited a statistically significant decrease in brachial artery diameter relative to filtered air immediately following exposure. A smaller decrease in brachial artery diameter was also observed following exposure to DE at 100 µg/m^3. Plasma levels of endothelin-1 were observed to increase following DE exposure (200 µg/m^3). The observed effects were more pronounced in healthy subjects than in subjects with metabolic syndrome. DE did not affect endothelium-dependent flow-mediated dilatation. No effect of DE on blood pressure was demonstrated immediately following exposure.
Reference: Peretz et al. (2008, 156855) **Subjects:** 13 adults with metabolic syndrome, 3 healthy adults **Gender:** Metabolic syndrome: 8 M/5 F, Healthy: 3 M/0 F **Age: M**etabolic syndrome: 31-48 yr, Healthy: 24-39 yr	DE 2002 Cummins B-series diesel engine (6BT5.9G6, 5.9 L) using No. 2 undyed on-highway fuel; operating at 75% of rated capacity **Concentration:** Fine PM 100, 200 µg/m^3	Subjects exposed for 2 h at rest to both concentrations of DE as well as filtered air in a randomized crossover design. Exposures were separated by at least 2 wk. Other diesel emissions measured, 100 µg/m^3 exposure: NO_2 (20.6 ppb), NO (0.95 ppm), CO (0.47 ppm); 200 µg/m^3 exposure: NO_2 (28.3 ppb), NO (1.63 ppm), CO (0.74 ppm). **Time to analysis:** 1, 3, 6, and 22 h from the start of exposure.	Exposure to 200 µg/m^3 increased HF power and decreased the LF/HF ratio 1h post-exposure; however, this effect was not consistent across subjects. No effect of DE was observed at later time points. Subjects with metabolic syndrome did not experience greater changes in HRV than healthy subjects.
Reference: Power et al. (2008, 191982) **Subjects:** 5 adults with mild-to-moderate allergic asthma **Gender:** 1 M/4 F **Age:** 28-51 yr	Carbon and ammonium nitrate particles **Concentration:** With co-exposure to 0.2ppm O_3: 255 µg/m^3, Without co-exposure to 0.2ppm O_3: 313 µg/m^3	Subjects exposed for 4 h with intermittent exercise (30-min periods) to filtered air, particles, and particles + O_3 in a crossover study design. Exposures were separated by at least 3 wk. **Time to analysis:** 3 h 40 min from the start of exposure.	Time and frequency domain HRV parameters were not affected by particle exposure relative to filtered air. However, exposure to particles with O_3 resulted in a significant decrease in SDNN as well as changes to both high and low frequency power normalized to the difference between total and very low frequency power.
Reference: Routledge et al. (2006, 088674) **Subjects:** 20 older adults with coronary artery disease, 20 healthy older adults **Gender:** CAD: 17 M/3 F, Healthy: 10 M/10 F **Age:** CAD: 52-74 yr, Healthy: 56-75 yr	Ultrafine carbon **Particle Size:** <10-300 nm; mode at 20-30 nm **Concentration:** Ultrafine carbon: 50 µg/m^3; SO_2: 200 ppb	Exposures conducted (head dome system) to filtered air, ultrafine carbon, SO_2, and ultrafine carbon + SO_2 for 1 h at rest using a randomized crossover study design. **Time to analysis:** Immediately following exposure as well as 3 and 23 h post-exposure.	No PM-induced changes in HRV observed among subjects with coronary artery disease. Among healthy subjects, small increase in HRV (RR, SDNN, rMSSD, and LF power) demonstrated immediately post-carbon exposure. Relative to filtered air control, exposure to ultrafine carbon did not significantly affect blood pressure in healthy adults or adults with coronary artery disease 0-3 h post-exposure. Exposure to ultrafine carbon, either alone or with SO_2, did not affect plasma levels of fibrinogen or D-dimer at 3 or 23 h post-exposure. Exposure to ultrafine carbon did not affect peripheral blood leukocyte count or C-reactive protein levels 3 or 23 h post-exposure.
Reference: Rundell and Caviston (2008, 191986) **Subjects:** 15 healthy college athletes **Gender:** M **Age:** Avg 19.5 yr	Gasoline emissions 2.5 hp gasoline engine running 10 s each min during exposure and in the min prior to exposure **Particle Size:** PM1.0 **Particle Number/Count:** Trial 1: 336,730 ± 149,206/cm^3; Trial 2: 396,200 ± 82,564/cm^3	Subjects were exposed twice to both clean air and dilute gasoline exhaust during 6-min periods of maximal exercise on a cycle ergometer. Clean air exposures occurred first and were separated by 3 days. Gasoline exhaust exposures were also separated by 3 days, with the first occurring 7 days after the second clean air exposure. Other emissions measured: CO (6.3 ± 3.4 ppm). **Time to analysis:** 6 min	There was no difference in total work done (kJ) between the clean air exposures or between the clean air exposures and the first exposure to gasoline exhaust. However, the second gasoline exhaust exposure was demonstrated to significantly decrease work accumulated over the 6min exercise period compared with either of the other exposure conditions ($p < 0.01$).

Study	Pollutant	Exposure	Findings
Reference: Samet et al. (2007, 156940) **Subjects:** Ultrafine CAPs: 20 healthy adults, Coarse CAPs: 14 healthy adults **Gender:** Ultrafine CAPs: 11 M/9 F, Coarse CAPs: 8 M/6 F **Age:** Ultrafine CAPs: 18-35 yr, Coarse CAPs: 18-35 yr	CAPs (Chapel Hill, NC) **Particle Size:** Ultrafine 0.049 ± 0.009 µm; Coarse 3.59 ± 0.58 µm **Concentration:** Ultrafine 47.0 ± 20.2 µg/m^3; Coarse 89.0 ± 49.5 µg/m^3	Preliminary report comparing effects of controlled exposures to coarse, fine, and ultrafine CAPs among healthy adults (3 separate studies). A randomized crossover design was used in evaluating effects of coarse CAPs (n=14) and ultrafine CAPs (n=20) relative to filtered air following 2-h exposures with intermittent exercise. Results compared with previous study of controlled exposure to fine CAPs (Chapel Hill, NC) where subjects did not serve as their own controls (Ghio et al., 2000, 012140). **Time to analysis:** 0-20 h post-exposure.	Statistically significant decrease in SDNN observed 20 h following exposure to coarse CAPs relative to filtered air. Subjects in the high ultrafine CAPs group experienced a decrease in SDNN based on an analysis of 24 h ambulatory Holter monitoring relative to filtered air. Fine CAPs did not significantly affect HRV. Increased levels of D-dimer observed 18 h following exposure to ultrafine CAPs. No CAPs-induced changes in plasma factor VII, plasminogen, fibrinogen, PAI-1, vWf, or t-PA. No CAPs-induced changes in C-reactive protein levels were observed.
Reference: Samet et al. (2009, 191913) **Subjects:** 19 healthy adults **Gender:** 10 M/9 F **Age:** 18-35 yr	Ultrafine CAPs (Chapel Hill, NC) **Particle Size:** < 0.16 µm **Particle Number/Count:** 120,662 ± 48,232 particles/cm^3 **Concentration:** 49.8 ± 20 µg/m^3	Subjects exposed for 2 h with intermittent 15 periods of exercise to UF CAPs and filtered air using a randomized crossover study design. **Time to analysis:** Immediately following exposure and 1 and 18 h post-exposure.	UF CAPs exposure resulted in an increase in plasma concentrations of D-dimer both immediately following exposure (20.6% increase per 10^5 particles/cm^3) as well as 18 h post-exposure (18.2% increase per 10^5 particles/cm^3). Plasma concentration of PAI1 also increased with UF CAPs, although this increase was not statistically significant (24% increase, p = 0.1). No UF CAPs-induced changes observed in plasma concentrations of tPA, vWF, CRP, fibrinogen, plasminogen, or Factor VII. HF and LF power were both observed to increase with UF CAPs exposure relative to filtered air at 18 h post-exposure (41.8% and 36%, respectively, per 10^5 particles/cm^3 increase in UF CAPs). UF CAPs expressed as mass concentration was not observed have a statistically significant effect in HF total power. UF CAPs was not observed to affect time domain measures of HRV over 24 h. The QT interval was shown to decrease both immediately following and at 18 h post exposure (not statistically significant immediately following exposure).
Reference: Shah et al. (2008, 156970) **Subjects:** 16 healthy adults **Age:** 26.9 ± 6.9 yr	Ultrafine EC **Particle Number/Count:** 10.8 ± 1.7 × 10^5 /cm^3 **Concentration:** 50 µg/m^3	Exposures conducted via mouthpiece for 2 h with intermittent exercise to filtered air and ultrafine carbon in a randomized crossover study design. **Time to analysis:** Immediately following exposure as well as 3.5, 21, and 45 h post-exposure.	Exposure to ultrafine carbon attenuated peak forearm blood flow after ischemia relative to filtered air 3.5 h post-exposure. Venous nitrate levels were significantly lower at 21 h following exposure to UF carbon compared with filtered air exposure. PM exposure was not observed to affect blood pressure relative to filtered air at times 0-45 h post-exposure.
Reference: Tornqvist et al. (2007, 091279) **Subjects:** 15 healthy adults **Gender:** M **Age:** 18-38 yr	DE Idling 1991 Volvo diesel engine (TD45, 4.5 L, 4 cylinders, 680 rpm) **Concentration:** 300 µg/m^3	Subjects exposed for 1h with intermittent exercise (15-min periods) to DE and filtered air in a randomized crossover study design. Exposures were separated by at least two wk. Other diesel emissions measured: NO_X (4.44 ppm), NO_2 (0.82 ppm), NO (3.62 ppm), total hydrocarbon (2.21 ppm). **Time to analysis:** 24 h post-exposure.	DE was observed to significantly attenuate endothelium-dependent vasodilation 24 h post-exposure. Endothelium-independent vasodilation was not affected by diesel exposure. Exposure to DE did not affect blood pressure relative to filtered air 24 h after exposure. DE significantly increased plasma levels of IL-6 and TNF-α 24 h following exposure. Exposure to diesel resulted in an increase in total antioxidant capacity of plasma relative to filtered air 24 h post-exposure.
Reference: Urch et al. (2004, 055629) **Subjects:** 24 healthy adults **Gender:** 14 M/10 F **Age:** 35 ± 10 yr	Fine CAPs (Toronto) **Concentration:** 150 µg/m^3 (range 101-257 µg/m^3) with 120 ppb O_3	Exposures conducted through a facemask which covered the subject's nose and mouth. Subjects were exposed to CAPs + O_3 and filtered air for 2 h at rest in a randomized crossover study design. Exposures were separated by at least 2 days. **Time to analysis:** Immediately following exposure.	CAPs + O_3 exposure resulted in a significant decrease in brachial artery diameter immediately post-exposure (Brook et al., 2002, 024987), which was demonstrated to be associated with both the organic and EC fractions of the CAPs.

Study	Pollutant	Exposure	Findings
Reference: Urch et al. (2005, 081080) **Subjects:** 23 healthy adults **Gender:** 13 M/10 F **Age:** 32 ± 10 yr	Fine CAPs (Toronto); **Concentration:** 150 µg/m^3 (range 102-214 µg/m^3) with 120 ppb O_3	Exposures conducted through a facemask which covered the subject's nose and mouth. Subjects were exposed to CAPs + O_3 and filtered air for 2 h at rest in a randomized crossover study design. **Time to analysis:** Every 30 min during exposure, with the final measurement made immediately prior to the end of the exposure.	An increase in diastolic blood pressure of 6 mmHg was observed at the end of CAPs + O_3 exposure, which was statistically different from the change in blood pressure experienced during exposure to filtered air (1 mmHg). This effect was associated with the organic fraction of $PM_{2.5}$.
Reference: Zareba et al. **(2009, 190101)** **Subjects:** 24 healthy adults **Gender:** 12 M/12 F **Age:** 18-40 yr	Ultrafine EC **Particle Size:** Count median diameter 25 nm **Particle Number/Count:** 2×10^6/cm^3 (10 µg/m^3), 7×10^6/cm^3 (25 µg/m^3) **Concentration:** 10 µg/m^3; 25 µg/m^3	Protocol 1 (n=12, 6 M/6 F): Subjects exposed to 10 µg/m^3 UF carbon and filtered air for 2 h at rest in a randomized crossover design. Exposures were separated by at least 2 wk. Protocol 2 (n=12, 6 M/6 F): Subjects exposed to 10 µg/m^3, 25 µg/m^3, and filtered air for 2 h with intermittent exercise (15-min periods) in a restricted randomized crossover design (all subjects exposed to 10 µg/m3 before 25 µg/m3). Exposures were separated by at least 2 wk. **Time to analysis (both protocols):** Immediately following exposure and 3.5 and 21 h post-exposure.	Exposure to 10 µg/m^3 at rest resulted in no change in HRV frequency domain parameters relative to filtered air exposure. Time domain parameters were observed to increase slightly with UF carbon exposure (10 µg/m^3 at rest), however, only the increase in rMSSD was statistically significant (p = 0.032). Some trends toward less shortening of QT interval, increase in ST segment, and increase in variability of repolarization (variability of T wave complexity) were observed with exposure to 10 µg/m^3 at rest, none of which were statistically significant. In Protocol 2, exposure to 10 µg/m^3 UF carbon was observed to slightly increase HRV time domain parameters as was demonstrated in Protocol 1. However, this was not observed at the higher concentration (25 µg/m^3). As with exposure at rest, exposure to UF carbon during exercise was observed to affect repolarization (reduction in QT duration and increase in T-wave amplitude), although this effect was not statistically significant.

Table C-2. Respiratory effects.

Reference	Pollutant	Exposure	Findings
Reference: Alexis et al. (2006, 154323) **Subjects:** 9 healthy adults **Gender:** 3 M/6 F **Age:** 18-35 yr	Coarse fraction particles (Chapel Hill, NC) Heat-treated (biologically inactive) and non-heated particles **Particle Size:** MMAD 5 µm **Concentration:** 0.65 mg per subject	Subjects were administered heat-treated $PM_{10-2.5}$, non-heated $PM_{10-2.5}$, and 0.9% saline (control) via nebulization in a randomized crossover study design. Exposures were separated by at least 1 wk. **Time to analysis:** 2-3 h post-inhalation.	Both heat-treated and non-heated coarse PM were observed to increase neutrophil counts in induced sputum 2-3 h post-inhalation. Biologically active PM (non-heated) induced an increase expression of macrophage TNF-α mRNA, eotaxin, and immune surface phenotypes on macrophages (mCD14, CD11b/CR3, and HLA-DR).
Reference: Barregard et al. (2008, 155675) **Subjects:** 13 healthy adults **Gender:** 6 M/7 F **Age:** 20-56 yr	Wood smoke **Particle Size:** Session 1: geometric mean diameter 42 nm, Session 2: geometric mean diameter 112 nm **Particle Number/Count:** Session 1: 180,000/cm^3; Session 2: 95,000/cm^3 **Concentration:** Session 1: median 279 µg/m^3; Session 2: median 243 µg/m^3	Subjects exposed in two groups for 4 h to filtered air, followed a wk later by a 4-h exposure to wood smoke. Exposures conducted with two 25-min periods of light exercise. Other measured combustion products: Session 1: NO_2 (0.08 ppm), CO (13 ppm), formaldehyde (114 µg/m^3), acetaldehyde (75 µg/m^3), benzene (30 µg/m^3), 1,3-butadiene (6.3 µg/m^3); Session 2: NO_2 (0.09 ppm), CO (9.1 ppm), formaldehyde (64 µg/m^3), acetaldehyde (40 µg/m^3), benzene (20 µg/m^3), 1,3-butadiene (3.9 µg/m^3). **Time to analysis:** Immediately following exposure as well as 3 and 20 h post-exposure.	Relative to filtered air, exposure to wood smoke was observed to increase levels of eNO 3 h post-exposure. Serum Clara cell protein increased 20 h after wood smoke exposure. Wood smoke was observed to increase levels of malondialdehyde in breath condensate immediately after as well as 20 h post-exposure. Effects of wood smoke on eNO and malondialdehyde levels were similar between the two sessions of wood smoke exposure. However, serum Clara cell protein was significantly increased with wood smoke in session 1 (higher particle count) but not in session 2.
Reference: Bastain et al. (2003, 098690) **Subjects:** 18 nonsmoking adults with positive allergy skin test to short ragweed **Gender:** 7 M/11 F **Age:** 18-38 yr	DEP Isuzu diesel engine, 4 cylinder, 4JB1 **Concentration:** 0.3 mg in 200 µl saline	Subjects underwent nasal provocation challenge (intranasal spray) with allergen and either DEP or placebo (saline) in a randomized crossover study design. Challenges were separated by 30 days. This protocol was then repeated 30 days after the last exposure. **Time to analysis:** 24 h post-exposure and 4 and 8 days after exposure.	DEP significantly increased allergic responses to short ragweed. Relative to allergen + placebo, allergen + DEP increased allergen specific IgE 4days following exposure, and increased IL-4 1 day post-exposure. The enhancement of allergic response with DEP was observed to be reproducible within subjects.
Reference: Beckett et al. (2005, 156261) **Subjects:** 12 healthy adults **Gender:** 6 M/6 F **Age:** 23-52 yr	Ultrafine and fine zinc oxide **Particle Size:** UF: <0.1 µm; Fine: 0.1-1.0 µm **Particle Number/Count:** UF: $4.6 \times 10^7/cm^3$; Fine: $1.9 \times 10^5/cm^3$ **Concentration:** 500 µg/m^3	Subjects exposed via mouthpiece for 2 h during rest to filtered air, ultrafine, and fine zinc oxide in a randomized crossover study design. Exposures were separated by at least 3 wk. **Time to analysis:** 11 and 24 h after exposure.	No changes observed in neutrophil count in induced sputum. No PM (zinc oxide)-induced changes in respiratory symptoms observed 0-24 h post-exposure.
Reference: Behndig et al. (2006, 088286) **Subjects:** 15 healthy adults **Gender:** 8 M/7 F **Age:** 21-27 yr	DE Idling 1991 Volvo diesel engine (TD45, 4.5 L, 4 cylinders, 680 rpm) **Particle Size:** PM_{10}; majority of PM mass made up of particles < 1 µm in diameter **Concentration:** 100 µg/m^3	Exposures conducted for 2 h with intermittent exercise to both DE and filtered air in a randomized crossover design. Exposures were separated by at least 3 wk. Other diesel emissions measured: NO_X (1.8 ppm), NO_2 (0.4 ppm), NO (1.3 ppm), CO (10.4 ppm), total hydrocarbons (1.3 ppm). **Time to analysis:** 18 h post-exposure.	Exposure to DE increased neutrophil and mast cell numbers in bronchial mucosa at 18 h post-exposure. Neutrophils, IL-8, and myeloperoxidase observed to increase in bronchial lavage fluid following exposure relative to filtered air. No inflammatory response observed in the alveolar compartment. Exposure to DE increased urate and reduced glutathione bronchoalveolar lavage at 18 h post-exposure.
Reference: Blomberg et al. (2005, 191991) **Subjects:** 15 older adults (former smokers) with COPD **Age:** 56-72 yr	DE **Concentration:** 300 µg/m^3	Subjects exposed for 1 h with intermittent exercise to DE and filtered air in a randomized crossover study design. **Time to analysis:** 6 and 24 h post-exposure.	DE was not observed to affect levels of Clara cell protein in peripheral blood at 6 and 24 h post-exposure.

Reference	Pollutant	Exposure	Findings
Reference: Bosson et al. (2007, 156286) **Subjects:** 16 healthy adults **Gender:** 7 M/9 F **Age:** 20-28 yr	DE Idling Volvo diesel engine **Concentration:** PM 300 µg/m^3 followed by exposure to filtered air or 0.2 ppm O_3	Subjects exposed to DE for 1 h followed 5 h later by a 2-h exposure to either filtered air or O_3 (0.2 ppm) using a randomized crossover study design. All exposures were conducted with subjects engaged in intermittent exercise. **Time to analysis:** 18 h after second exposure (filtered air or O_3).	The percentage of neutrophils and concentration of myeloperoxidase in induced sputum (18 h post-O_3/air exposure) was significantly higher following diesel + O_3 than diesel + air.
Reference: Bosson et al. (2008, 196659) **Subjects:** 14 healthy adults **Gender:** 9 M/5 F **Age:** 21-29 yr	DE Idling 1991 Volvo diesel engine (TD45, 4.5 L, 4 cylinders) **Concentration:** PM 300 µg/m^3 or filtered air followed by exposure to 0.2 ppm O_3	Subjects exposed to DE or filtered air for 1h followed 5 h later by a 2-h exposure to O_3 (0.2 ppm) using a randomized crossover study design. All exposures were conducted with subjects engaged in intermittent exercise. Other diesel emissions measured: NO_2 (0.51 ppm), NO (1.65 ppm), total hydrocarbons (1.18 ppm). **Time to analysis:** 24 h after the start of the initial exposure.	Neutrophil and macrophage numbers in bronchial wash were significantly increased 16 h following O_3 exposure when preceded by exposure to diesel, compared to O_3 exposure preceded by exposure to filtered air.
Reference: Brauner et al. (2009, 190244) **Subjects:** 29 healthy adults **Gender:** 20 M, 9 F **Age: M** avg 27 yr, F avg 26 yr	Urban traffic particles **Particle Size:** $PM_{2.5}$, $PM_{10-2.5}$ **Particle Number/Count:** 6-700 nm: 10,067/cm^3 **Concentration:** $PM_{2.5}$: 9.7 µg/m^3, $PM_{10-2.5}$: 12.6 µg/m^3	Subjects exposed to urban traffic particles and filtered air for 24 h with and without two 90-min periods of light exercise in a randomized crossover study design. Concentrations of NO_X and NO were low and did not differ between filtered and unfiltered exposures. CO concentrations were higher with filtered air (0.35 and 0.41 ppm), while O_3 concentrations were lower with filtered air (12.08 and 4.29 ppb). **Time to analysis:** 2.5, 6, and 24 h after the start of exposure.	Epithelial membrane integrity and blood-gas barrier permeability, assessed using pulmonary clearance of 99mTc-labeled diethylenetriamine pentaacetic acid (DTPA), was observed to increase with exercise, but was not affected by exposure to urban particles (2.5 h of exposure). Exposure to urban particles was not shown to affect plasma or urine concentration of Clara cell 16 protein at 6 and 24 h after the start of exposure. No relationship between exposure and pulmonary function was observed at 2.5 h.
Reference: Gilliland et al. (2004, 156471) **Subjects:** 19 adults with allergic rhinitis and positive skin test to ragweed, GSTM1 (14 null, 5 present); GSTT1 (9 null, 10 present); GSTP1 codon 105 variants (13 I/I, 6 I/V, 0 V/V) **Gender:** 7 M/12 F **Age:** 20-34 yr	DEP Isuzu diesel engine, 4 cylinder, 4JB1 **Concentration:** 0.3 mg DEP in 300 µL saline	Subjects were challenged intranasally with allergen and placebo (saline) as well as allergen plus DEP in saline in a randomized crossover design. Challenges were separated by at least 6 wk. **Time to analysis:** 10 min, 24 h, and 72 h post-challenge.	Subjects who were GSTM1 null or homozygous for GSTP1 I105 wild-type allele experienced significantly greater increase in nasal IgE and histamine with diesel plus allergen compared to subjects with functional GSTM1 or who were heterozygous for GSTP1 I/V(105).
Reference: Gong et al. (2004, 087964) **Subjects:** 13 older adults with COPD, 6 healthy older adults **Gender:** COPD: 5 M/8 F, Healthy: 2 M/4 F **Age:** COPD: avg 68 yr, Healthy: avg 73 yr	Fine CAPs (Los Angeles) **Particle Size:** 85% of mass between 0.1 and 2.5 µm **Concentration:** Mean: 194 µg/m^3, Range: 135-229 µg/m^3	Exposures to CAPs and filtered air (randomized crossover) for 2 h with intermittent light exercise (four 15-min periods). Exposures were separated by at least 2 wk. **Time to analysis:** Immediately following exposure as well as 4 and 22 h post-exposure.	No CAPs-induced respiratory symptoms observed in healthy older adults or older adults with COPD at 0, 4, or 22 h post-exposure. Exposure to CAPs did not significantly affect FVC or FEV_1. CAPs exposure caused a decrease in arterial oxygen saturation immediately following exposure which was more pronounced in healthy older adults than in older adults with COPD. Exposure to CAPs was not observed to affect the levels of white blood cells, columnar epithelial cells, IL-6, or IL-8 in induced sputum.
Reference: Gong et al. (2004, 055628) **Subjects:** 12 adult asthmatics, 4 healthy adults **Gender:** Asthmatic: 4 M/8 F, Healthy: 2 M/2 F **Age:** Asthmatic: avg 38 yr, Healthy: avg 32 yr	Coarse CAPs (Los Angeles) **Particle Size:** 80% of mass between 2.5 and 10 µm, 20% of mass <2.5 µm **Concentration:** Mean: 157 µg/m^3; Range: 56-218 µg/m^3	Exposures to CAPs and filtered air (randomized crossover) for 2 h with intermittent light exercise (four 15-min periods). Exposures were separated by at least 2 wk. **Time to analysis:** Immediately following exposure as well as 4 and 22 h post-exposure.	No effect of CAPs exposure on spirometry or arterial oxygen saturation was observed 0, 4, or 22 h post-exposure. No respiratory symptoms reported 0-22 h post-exposure in either healthy or asthmatic adults. Sputum cell counts at 22 h post-exposure did not differ between CAPs and filtered air.

Reference	Pollutant	Exposure	Findings
Reference: Gong et al. (2005, 087921) **Subjects:** 18 older adults with COPD, 6 healthy older adults **Gender:** COPD: 9 M/9 F, Healthy: 2 M/4 F **Age:** COPD: avg 72 yr, Healthy: avg 68 yr	Fine CAPs (Los Angeles) **Concentration:** CAPs: 200 µg/m^3; NO_2: 0.4 ppm	Each subject was exposed to CAPs, NO_2, CAPs + NO_2, and filtered air for 2 h with intermittent exercise. Exposure order was not fully counterbalanced as NO_2 exposures were conducted after the majority of the CAPs and filtered air exposures had been completed. Exposures were separated by at least 2 wk. **Time to analysis:** Immediately following exposure as well as 4 and 22 h post-exposure.	Exposure to CAPs was observed to decrease maximal mid-expiratory flow and arterial oxygen saturation relative to filtered air 4-22 h post-exposure. This response was more pronounced in healthy older adults than in older adults with COPD. Concomitant exposure to NO_2 did not enhance the response. No other respiratory responses (symptoms, spirometry, sputum cell counts) were affected by exposure to CAPs.
Reference: Gong et al. (2008, 156483) **Subjects:** 14 adult asthmatics, 17 healthy adults **Gender:** Asthmatics: 9 M/5 F, Healthy: 5 M/12 F **Age:** Asthmatics: 34 ± 12 yr, Healthy:24 ± 8 yr	Ultrafine CAPs (Los Angeles) **Particle Number/Count:** 145,000/cm^3, Range 39,000-312,000/cm^3 **Concentration:** Mean: 100 µg/m^3, Range: 13-277 µg/m^3	Subjects exposed for 2 h during intermittent exercise (15-min periods) to both CAPs and filtered air in random order. The first 7 subjects underwent whole body exposure, while the remaining subjects were exposed through a facemask. Facemask exposures had higher particle counts but lower particle mass than whole body exposures. Exposures were separated by at least 2 wk. **Time to analysis:** Immediately following exposure as well as 4 and 22 h post-exposure.	No significant differences in respiratory symptoms observed between filtered air and ultrafine CAPs exposures. Individuals exposed to higher particle counts tended to experience greater symptoms with CAPs than with filtered air. An ultrafine CAPs-induced decrease in arterial oxygen saturation (0.5%) was observed at 0, 4, and 22 h post-exposure. A decrease in FEV_1 (2%) was also observed 22 h post-exposure relative to filtered air. Responses were not significantly different between healthy and asthmatic adults. CAPs exposure was not observed to affect total sputum cell counts or cytokine levels. There were no differences in response observed between facemask and whole body exposures.
Reference: Graff et al. (2009, 191981) **Subjects:** 14 healthy adults **Gender:** 8 M/6 F **Age:** 20-34 yr	Coarse CAPs (Chapel Hill, NC) **Concentration:** 89 ± 49.5 µg/m^3 (estimated inhaled dose ≈ 67% of measured particle mass)	Subjects exposed for 2 h with intermittent exercise (15-min periods) to coarse CAPs and filtered air in a randomized crossover design. Exposures were separated by at least 2 mos. **Time to analysis:** 0-1 and 20 h post-exposure.	Pulmonary function (FVC, FEV_1, and carbon monoxide diffusing capacity) was not affected by exposure to coarse CAPs either immediately following exposure or 20 h post-exposure. A significant increase in percent PMNs (10.7% increase per 10 µg/m^3 coarse CAPs) was observed in BAL fluid 20 h post-exposure. Percent monocytes in BL fluid were slightly decreased at 20 h post-exposure (2.0% decrease per 10 µg/m^3 CAPs; p = 0.05). Total protein in BAL fluid was also observed to decrease following CAPs exposure (1.8% decrease per 10 µg/m^3 CAPs). Markers of inflammation in BAL and BL fluids including IL-6, IL-8, and PGE2 were not affected by exposure to coarse CAPs.
Reference: Huang et al. (2003, 087377) **Subjects:** 38 healthy adults **Gender:** 36 M/2 F **Age:** Avg 26.2 ± 0.7 yr	Fine CAPs (Chapel Hill, NC) **Concentration:** 23.1-311.1 µg/m^3	Subjects exposed to CAPs (n = 30) or filtered air (n = 8) for 2 h with intermittent exercise (subjects did not serve as their own controls). Component data of CAPs was available for 37 of the 38 subjects. **Time to analysis:** 18 h after exposure.	The increase in bronchoalveolar lavage fluid neutrophils observed by Ghio et al. (2000, 012140) following exposure to fine CAPs was shown to be associated with iron, selenium, and sulfate content of the CAPs.
Reference: Kongerud et al. (2006, 156656) **Subjects:** 17 asthmatic adults, 46 healthy adults **Gender:** Asthmatics- 6 M/11 F, Healthy- 24 M/22 F **Age:** Asthmatics: avg 23 yr, Healthy: avg 26 yr	DEP NIST 1650, heavy duty diesel engine **Concentration:** Untreated and treated with 0.1 ppm O_3 (48 h); 300 µg per nostril	DEP (with and without O_3 pre-treatment) were intranasally instilled, using the saline vehicle as control. Subjects did not serve as their own controls (not a crossover design). **Time to analysis:** 4 and 96 h post-instillation.	Exposure to DEP was not observed to alter markers of inflammation in nasal lavage fluid (e.g., cell counts, IL-8, IL-6) at 4 or 96 h post-instillation.
Reference: Larsson et al. (2007, 091375) **Subjects:** 16 healthy adults **Gender:** 10 M/6 F **Age:** 19-59 yr	Traffic particles (road tunnel) **Particle Size:** $PM_{2.5}$, PM_{10}; $PM_{2.5}$ mass constituted ~36% of PM_{10} mass **Particle Number/Count:** 20-1,000 nm: 1.1 × 10^5/cm^3, < 100 nm: 0.85 × 10^5/cm^3 **Concentration:** $PM_{2.5}$-46-81 µg/m^3; PM_{10}-130-206 µg/m^3	Exposures were conducted for 2 h with intermittent exercise in a room adjacent to a busy road tunnel. Study used a randomized crossover design with each subject also exposed to normal air (control). Exposures were separated by 3-10wks. No exposures to filtered air were conducted. Other traffic emissions measured: NO (874 µg/m^3), NO_2 (230 µg/m^3), CO (5.8 µg/m^3 reported, likely 5.8 mg/m^3). **Time to analysis:** 14 h post-exposure.	An increase in bronchoalveolar lavage fluid cell number, lymphocytes, and alveolar macrophages were observed 14 h after road tunnel exposure relative to control. Traffic particulate exposure was not shown to effect cytokine or adhesion molecule expression in bronchial tissues. Respiratory symptoms were reported to increase during exposure to road tunnel air relative to pre-exposure symptom ratings. Exposure to road tunnel air was not shown to affect lung function.

Reference	Pollutant	Exposure	Findings
Reference: Mudway et al. (2004, 180208) **Subjects:** 25 healthy adults **Gender:** 16 M/9 F **Age:** 19-42 yr	DE Idling 1991 Volvo diesel engine (TD45, 4.5 L, 4 cylinders, 680 rpm) **Concentration:** PM_{10} 100 µg/m^3	Subjects exposed to DE and filtered air for 2 h with intermittent exercise (15-min periods) in a randomized crossover design. Exposures were separated by at least 3 wk. Other diesel emissions measured: NO_2 (0.2 ppm), NO (0.6 ppm), CO (1.7 ppm), total hydrocarbons (1.4 ppm), formaldehyde (43.5 µg/m^3). **Time to analysis:** 1 h after the start of exposure, immediately following exposure, and 6 h post-exposure.	DE caused mild throat irritation in some subjects and a significant increase in airways resistance (Raw) during or immediately following exposure. No changes in FEV_1 or FVC were observed following exposure to diesel. Neutrophil numbers in the bronchial airways tended to increase following exposure to DE; however, this increase was highly variable between subjects and did not reach statistical significance. Exposure to DE did not affect levels of SOD or malondialdehyde in the airways. An increase in levels of ascorbate and GSH in nasal lavage fluid was observed 6 h following exposure to DE.
Reference: Pietropaoli et al. (2004, 156025) **Subjects:** 16 asthmatic adults, 40 healthy adults **Gender:** Asthmatic: 8 M/8 F, Healthy: 20 M/20 F **Age:** 18-40 yr	Ultrafine EC **Particle Size:** CMD ~25 nm **Particle Number/Count:** 10 µg/m^3: ~2.0 × 10^6/cm^3; 25 µg/m^3: ~7.0 × 10^6/cm^3; 50 µg/m^3: ~10.8 × 10^6/cm^3 **Concentration:** 10, 25, and 50 µg/m^3	Study conducted using a randomized crossover design with 2-h exposures. Asthmatics (n = 16) exposed to filtered air and 10 µg/m^3. 12 healthy adults exposed to filtered air and 10 µg/m^3 at rest; 12 healthy adults exposed to filtered air, 10 and 25 µg/m^3 with intermittent exercise; 16 healthy adults exposed to filtered air and 50 µg/m^3 with intermittent exercise. Exposures were conducted via mouthpiece. **Time to analysis:** Immediately following exposure as well as 3.5, 21, and 45 h post-exposure.	No PM-induced changes in eNO or cell counts, IL-6, or IL-8 in induced sputum were observed in any of the protocols 21 h following exposure. Ultrafine carbon was not observed to increase respiratory symptoms in any of the study protocols. Healthy adults experienced an ultrafine PM-induced reduction in maximal mid-expiratory flow and CO diffusing capacity relative to filtered air 21 h following exposure.
Reference: Pourazar et al. (2005, 088305) **Subjects:** 15 healthy adults **Gender:** 11 M/4 F **Age:** 21-28 yr	DE Idling Volvo diesel engine **Particle Number/Count:** 4.3 × 10^6/cm^3 **Concentration:** PM_{10} 300 µg/m^3	Subjects exposed to DE and filtered air for 1 h with intermittent exercise (randomized crossover study design). Other diesel emissions measured: NO_2 (1.6 ppm), NO (4.5 ppm), CO (7.5 ppm), total hydrocarbons (4.3 ppm), formaldehyde (0.26 mg/m^3). **Time to analysis:** 6 h post-exposure.	Exposure to DE significantly increased nuclear translocation of NF-κB, AP-1, phosphorylated p38, and phosphorylated JNK in bronchial epithelium 6 h post-exposure.
Reference: Pourazar et al. (2008, 156884) **Subjects:** 15 healthy adults **Gender:** 11 M/4 F **Age:** 21-28 yr	DE Idling Volvo diesel engine **Particle Number/Count:** 4.3 × 10^6/cm^3 **Concentration:** PM_{10} 300 µg/m^3	Subjects exposed to DE and filtered air for 1 h with intermittent exercise (randomized crossover study design). Other diesel emissions measured: NO_2 (1.6 ppm), NO (4.5 ppm), CO (7.5 ppm), total hydrocarbons (4.3 ppm), formaldehyde (0.26 mg/m^3). **Time to analysis:** 6 h post-exposure.	Exposure to DE observed to enhance epidermal growth factor receptor (EGFR) expression in bronchial epithelium 6 h post-exposure.
Reference: Riechelmann et al. (2004, 180120) **Subjects:** 30 healthy adults **Gender:** 11 M/19 F **Age:** 22-32 yr	Urban dust NIST SRM 1649a **Concentration:** 150, 500 µg/m^3	Subjects exposed to both concentrations of urban dust (nose only exposure system) as well as filtered air for 3h at rest in a randomized crossover design. Exposures were separated by at least 1 wk. **Time to analysis:** 30 min, 8 h, and 24 h post-exposure.	An increase in nasal secretion (nasal cytology) of IL-6 and IL-8 were observed 24 h after exposure to 500 µg/m^3 urban dust.
Reference: Samet et al. (2007, 156940) **Subjects:** Ultrafine CAPs: 20 healthy adults, Coarse CAPs: 14 healthy adults **Gender:** Ultrafine CAPs: 11 M/9 F, Coarse CAPs: 8 M/6 F **Age:** 18-35 yr	CAPs (Chapel Hill, NC) **Particle Size:** Ultrafine: 0.049 ± 0.009 µm, Coarse: 3.59 ± 0.58 µm **Concentration:** Ultrafine: 47.0 ± 20.2 µg/m^3, Coarse: 89.0 ± 49.5 µg/m^3	Preliminary report comparing effects of controlled exposures to coarse, fine, and ultrafine CAPs among healthy adults (3 separate studies). A randomized crossover design was used in evaluating effects of coarse CAPs (n=14) and ultrafine CAPs (n=20) relative to filtered air following of 2-h exposures with intermittent exercise. Results compared with previous study of controlled exposure to fine CAPs (Chapel Hill, NC) where subjects did not serve as their own controls (Ghio et al., 2000, 012140) **Time to analysis:** 0-20 h post-exposure.	As was shown with fine CAPs, exposure to coarse CAPs increased the percentage of neutrophils in bronchoalveolar lavage fluid 20 h following exposure. Unlike fine CAPs, coarse CAPs did not increase the percent of monocytes in bronchoalveolar lavage fluid. Ultrafine CAPs were not shown to affect any markers of pulmonary inflammation in bronchoalveolar lavage fluid 18 h after exposure. No CAPs-induced changes in lung function were observed.
Reference: Samet et al. (2009, 191913) **Subjects:** 19 healthy adults **Gender:** 10 M/9 F **Age:** 18-35 yr	Ultrafine CAPs (Chapel Hill, NC) **Particle Size:** < 0.16 µm **Particle Number/Count:** 120,662 ± 48,232 particles/cm^3 **Concentration:** 49.8 ± 20 µg/m^3	Subjects exposed for 2 h with intermittent 15 periods of exercise to UF CAPs and filtered air using a randomized crossover study design. **Time to analysis:** Immediately following exposure and 1 and 18 h post-exposure.	No effect of UF CAPs observed on pulmonary function immediately following exposure or 18 h post-exposure. IL-8 in BAL fluid was observed to increase with UF CAPs 18 h post-exposure. UF CAPs was not shown to alter any other inflammatory markers in BAL fluid.

Reference	Pollutant	Exposure	Findings
Reference: Schaumann et al. (2004, 087966) **Subjects:** 12 healthy adults **Gender:** 4 M/8 F **Age:** Avg 27 ± 2.5 yr	Fine PM Collected (filter) from industrialized and non-industrialized areas in Germany **Concentration:** 100 µg per subject	Bronchoscopic instillation of particles collected from both areas was conducted in contralateral lung segments for each subject. **Time to analysis:** 24 h post-instillation.	Particles collected from the industrialized area (transition metal-rich) increased the percentage of monocytes and oxidant radical generation in bronchoalveolar lavage fluid 24 h after exposure compared with PM containing less metal.
Reference: Stenfors et al. (2004, 157009) **Subjects:** 15 asthmatic adults, 25 healthy adults **Gender:** Asthmatic: 10 M/5 F, Healthy: 16 M/9 F **Age:** Asthmatic: 22-52 yr, Healthy:19-42 yr	DE Volvo diesel engine **Concentration:** PM_{10} 108 µg/m^3	Subjects were exposed for 2 h with intermittent exercise to DE and filtered air using a randomized crossover study design. Other diesel emissions measured: NO_2 (0.7 ppm). **Time to analysis:** 1 h after the start of exposure, immediately following exposure, and 6 h post-exposure.	DE was observed to increase neutrophilia and IL-8 in bronchial lavage fluid among healthy subjects 6 h after exposure. Among asthmatic subjects, exposure to DE did not cause an increase in inflammatory markers. No diesel-induced change in pulmonary function was observed during or immediately following exposure.
Reference: Tunnicliffe et al. (2003, 088744) **Subjects:** 12 asthmatic adults, 12 healthy adults **Gender:** Asthmatics: 7 M/5 F, Healthy: 5 M/7 F **Age:** Asthmatics: avg 35.7 yr, Healthy: avg 34.5 yr	Aerosols of ammonium bisulfate and sulfuric acid **Particle Size:** MMD 0.3 µm **Concentration:** 200, 2,000 µg/m^3	Subjects were exposed for 1 h at rest to ammonium bisulfate (low and high concentrations), sulfuric acid (low and high concentrations) and filtered air in a randomized crossover design. Exposures were separated by at least 2 wk and were conducted using a head dome exposure system. **Time to analysis:** Immediately following exposure as well as 5.5-6 h post-exposure.	Neither ammonium bisulfate nor aerosolized sulfuric acid were observed to affect lung function or respiratory systems following exposures to 200 or 2,000 µg/m^3 among healthy or asthmatic adults. Exposures to ammonium bisulfate at both concentrations resulted in a significant increase in eNO in the asthmatic subjects.

Table C- 3. Central nervous system effects.

Reference	Pollutant	Exposure	Findings
Reference: Cruts et al. (2008, 156374) **Subjects:** 10 healthy adults **Gender:** M **Age:** 18-39 yr	DE Idling Volvo diesel engine (TD45, 4.5 L, 4 cylinders, 680 rpm) **Particle Number/Count:** 1.2 × 10^6/cm^3 **Concentration:** 300 µg/m^3	Subjects were exposed to DE and filtered air for 1 h at rest in a randomized crossover study design. Exposures were separated by 2-4 days. Other diesel emissions measured: NO_2 (1.6 ppm), NO (4.5 ppm), CO (7.5 ppm), total hydrocarbons (4.3 ppm). **Time to analysis:** From onset of exposure until 1 h post-exposure.	Exposure to DE was observed to significantly increase the median power frequency (MPF) in the frontal cortex during exposure, as well as in the hour following the completion of the exposure.

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Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISA) and the Integrated Risk Information System (IRIS).

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Annex D. Toxicological Studies

Table D-1. Cardiovascular effects.

Study	Pollutant	Exposure	Effects
Reference: Anselme et al. (2007, 097084) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** Adult **Weight**: 200-225g	**DE:** monocylinder Diesel engine using Euro 4 ELF 85A reference gasoline **Particle Size:** DE: 10-650 nm (85 nm mean mobility diameter)	**Route:** Whole-body Inhalation **Dose/Concentration:** DE: 0.5 mg/m^3; Other emissions measured: non-methane hydrocarbons (7.7 ppm), NO_2 (1.1 ppm), CO (4.3 ppm) **Time to Analysis:** Experiments started 3 mo after L coronary artery ligation. ECG started at t0 and the DE exposure at t30 min for a 3-h period; ventricular premature beats (VPBs) and RMSSD calculated every 30 min during clean room air exhaust and PE periods. Early (t210-300 min) and late (t480-540 min) PE were analyzed.	Immediate decrease in RMSSD was observed in both healthy and CHF rats PE. Immediate increase in VPBs observed in CHF rats only; which lasted 4-5 h after exposure ceased. Whereas HRV progressively returned to baseline values within 2.5 h post-exposure (PE), the proarrhythmic effect persisted as late as 5 h PE termination in CHF rats
Reference: Bagate et al. (2004, 055638) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 13-15 wk	**LPS and EHC-93 (PM):** Urban Air collected at the Health Effects Institute Ottawa, Canada **Particle Size:** EHC-93: 0.8-0.4 µm (mean) (range: <3 µm)	**Route:** IT Instillation **Dose/Concentration:** PM: 10 mg/kg; LPS- 350 EU/animal **Time to Analysis:** Sacrificed 4 or 24 h post-instillation	PM and LPS elicited a significant increase in receptor-dependent vasorelaxation of the aorta compared to saline-instilled rats.
Reference: Bagate et al. (2004, 055638) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 13-15 wk	EHC-93 (PM), CB-V or CB-Fe, LPS **Particle Size:** EHC-93: 0.8-0.4 µm (mean) (range: <3 µm)	**Route:** Aortic Suspension Fluid **Dose/Concentration:** Cumulative concentrations of EHC-93, CB-V and CB-Fe (10, 25, 50, 75, 100 µg/mL) CB 1.5-2.0 nm (mean) (range <5 µm) **Time to Analysis:** Immediately post-exposure of aortic rings to cumulative concentrations of EHC-93, CB-V, CB-Fe and LPS.	CB-V particles induced more relaxation than CB-Fe particles or EHC-93 in a dose-dependent manner. PM and LPS had an acute transient effect on the receptor dependent vasorelaxation. PM and LPS attenuated ACh-elicited vasocontraction in denuded aortic rings (DARs).

Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISA) and the Integrated Risk Information System (IRIS).

Study	Pollutant	Exposure	Effects
Reference: Bagate et al. (2004, 055638) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 13-15 wk	EHC-93 (PM): Urban Air collected at the Health Effects Institute Ottawa, Canada. EHC-93 filtrate (PMF) Zn^{2+} and Cu^{2+} particles (10,000 and 845 µg PM respectively) **Particle Size:** PM: 4.6 µm (GSD = 3.2)	**Route:** In Vitro **Dose/Concentration:** PM Suspensions: 10-100 µg/mL; $CuSO_4$/$ZnSO_4$ 1-100 µmol; Phe 2 µm; arbacol: 10 µm **Time to Analysis:** Measured immediately after maximum response for each cumulative dose was achieved.	**PM-Induced Contraction:** No effect of suspension or filtrate seen on resting tension of aorta and SMRA. **PM- and Metal-Induced Vasorelaxation:** Cumulative concentrations (10-100 µg/mL) of PM suspension and its water soluble components (PMF) elicited dose-dependent relaxation in aorta. Relaxation induced by particle suspension was higher than relaxation induced by free filtrate. The difference was significant at 100 µg/mL. In SMRA, vasorelaxation similar to aorta's was observed, and the activity of the particle suspension was stronger than the filtrate, with the difference being significant starting at 30 µg/mL. Both Zn^{2+} and Cu^{2+} in sulfate salts (10-100 µmol) induced relaxation in pre-contracted aortic rings, with Cu^{2+} having a greater effect than Zn^{2+} at the same concentration. Ions didn't affect ACh relaxation. **Effect of PM on α-Adrenergic Contraction:** Phenylephrine-induced dose-response contraction, starting at 1µM with max at 100 µmol. Pre-treatment of SMRA did not change the phenylephrine-induced contraction.
Reference: Bagate et al. (2006, 097608) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto and SH **Age:** 13-15 wk	EHC-93 (PM) EHC-93 (Filtrate) Cu^{2+} and Zn^{2+} solutions **Particle Size:** PM: 4.6 µm (GSD = 3.2)	**Route:** In Vitro **Dose/Concentration:** PM and PMF Suspensions: 10-100 µg/mL; $CuSO_4$ or $ZnSO_4$:10-100 µmol; Phenylephrine: 2 µm; Carbacol: 10 µm **Time to Analysis:** Responses evaluated at maximum of each dose-response.	PM and its soluble components elicited endothelium-independent vasodilation in rat aorta rings. This response is a result of the activation of sGC since its inhibition by NS2028 practically eliminated relaxation. PM suspensions stimulated cGMP production in purified isolated sGC. Neither receptor nor their signaling pathways played a significant role in the direct relaxation by PM or metals. Vasodilation responses were significantly higher in SH than WKY control rats.
Reference: Bagate et al. (2006, 096157) **Species:** Rat **Gender:** Male **Strain:** SH/NHsd **Age:** 11-12 wk **Weight:** 250-350 g	EHC-93 (PM): Urban Air collected at the Health Effects Institute Ottawa, Canada. EHC-93 (Filtrate), Zinc (in PM), LPS **Particle Size:** PM: 4.6 µm (GSD = 3.2)	**Route:** IT Instillation **Dose/Concentration:** PM: 10 mg/kg; LPS: 350 EU/animal (0.5 mL) **Time to Analysis:** 4 h post-exposure	**Effect of Pretreatment on Baseline Parameters of Isolated Perfused Heart:** After PM exposure a slight increase of baseline coronary flow (CF) and heart rate (HR) was noted. In contrast, a significant decrease of left developing ventricular pressure (LDVP) was observed in SH. LPS also elicited a non-significant decrease in LVDP. **Effect of Pretreatment and Ischemia on Cardiac Function:** When SH rats were pretreated with PM or LPS the isolated heart had a reduced ability to recover to baseline levels after occlusion, in comparison with saline treated rats. After occlusion was released CF went back to baseline values. Saline and LPS treated rats, showed a gradual decrease in CF noted during the reperfusion period. Isolated hearts from PM-exposed SH showed a complete restoration of CF and no gradual decrease. The increase of Zn2+ elicited a rapid decrease of LDVP and HR. The impairment of cardiac function measured by LDVP and HR started immediately upon Zn2+ infusion and remained the same during the perfusion period (no Zn2+ was present in the perfusate).
Reference: Bagate et al. (2006, 096157) **Species:** Rat **Strain:** H9c2 (EACC), cardiomyocyte cells	EHC-93 (PM) Filtrate: Urban Air collected at the Health Effects Institute Ottawa, Canada, $ZnSO_4$ **Particle Size:** PM: 4.6 µm (GSD = 3.2); Carbon Particles: 44 nm	**Route:** In Vitro **Dose/Concentration:** PM: 1, 50, 100 µg/mL; $ZnSO_4$: 50 µmol **Time to Analysis:** 30 min incubation	**Effect of EHC-93 filtrate on Ca^{2+} Uptake in Cardiomyocytes:** Both PMF and Zn^{2+} inhibited ATP or ionophore-stimulated Ca^{2+} influx in cardiomyocytes.

Study	Pollutant	Exposure	Effects
Reference: Bartoli et al. (2009, 156256) **Species:** Dog **Gender:** Female **Strain:** Mixed breed **Age:** 2-12 yr **Weight:** Average: 15.7 kg, Range: 13.6-18.2 kg	CAPs (Boston; Harvard Ambient Particle Concentrator) **Particle Size:** Diameter: 0.15-2.5 µm	**Route:** Permanent Tracheostomy **Dose/Concentration:** Concentration range and mean: CAPs: 94.1-1557(358.1 ± 306.7) µg/m^3, BC: 1.3-32(7.5 ± 6.1) µg/m^3, Particle count: 3000-69300(18230 ± 13.151) particles/cm^3 **Time to Analysis:** Preanesthetized. Tracheostomy. 5 h exposures separated by minimum 1wk. Prazosin administered in 8 of 13 dogs 30-60 min before exposure. 55 exposure days.	CAPs significantly increased SBP, DBP, mean arterial pressure, HR and rate-pressure product. Prazosin (α-adrenergic antagonist) decreased these CAPs-induced effects. CAPs mass, BC, particle number concentrations were positively and significantly associated with each of the cardiovascular parameters except for pulse pressure.
Reference: Bartoli et al. (2009, 179904) **Species:** Dog **Gender:** Female **Strain:** Mixed breed **Age:** Adult **Weight:** 14-18 kg	CAPs (Boston; Harvard Ambient Particle Concentration) **Particle Size:** Diameter: ≤2.5 µm	**Route:** Permanent Tracheostomy **Dose/Concentration:** Concentration range and mean: CAPs: 94.1-1556.8 (349 ± 282.6) µg/m^3, BC: 1.3-32 (7.5 ± 5.6) µg/m^3, Particle number: 3000-69300 (20381 ± 13075) particles/cm^3 **Time to Analysis:** Tracheostomy. Minimum 3 wk recovery. Acclimatized. Exposed 5 h. 2 5 min occlusions of LAD coronary artery separated by 20 min rest. Exposure days separated by 1wk minimum.	During coronary artery occlusion, CAPs exposure reduced myocardial blood flow and increased coronary vascular resistance, SBP and DBP. CAPs effects were greater in ischemic tissue than nonischemic. Increases in CAPs mass, particle number and BC concentrations were significantly associated with decreased myocardial blood flow and increased coronary vascular resistance.
Reference: Campen et al. (2005, 083977) **Species:** Mouse **Gender:** Male **Strain:** C57BL/6J and Apo E$^{-/-}$ **Age:** 10-12 wk	High Whole DE (HWDE); Low Whole DE (LWDE); High PM Filtered (HPMF); Low PM Filtered (LPMF) **Particle Size:** NR	**Route:** Whole-body Inhalation and Ex-vivo Exposures (isolated, pressurized septal coronary arteries) **Dose/Concentration:** HWDE: PM = 3.6 mg/m^3; NO_X = 102 ppm LWDE: PM = 0.512 mg/m^3; NO_X = 19 ppm; PM = 0.770 mg/m^3; NO_X = 105 ppm LPMF: PM = 0.006 mg/m^3; NO_X = 26 ppm **Time to Analysis:** Whole-body Exposures: DE or PFDE for 6 h/day for 3 days, euthanized at the end of last exposure. **Coronary Vessels Exposure:** PSS bubbled with DE to expose coronary vessels to the soluble contents of DE. Analysis occurred immediately post exposure.	**Whole-body Exposure on ApoE$^{-/-}$:** During DE exposure, ApoE$^{-/-}$ mice HR consistently decreased during high concentration exposures, compared to the C57BL/6J strain. **Coronary Vascular Effects on ApoE$^{-/-}$:** DE had no significant effects on the resting myogenic tone of isolated septal coronary arteries. Control coronary arteries showed constrictive responses to ET-1 and dilatory responses to SNP. DE exposed PSS vessels responses to ET-1 enhanced compared to control. SNP-induced dilation blunted in vessels resting in diesel-exposed saline.
Reference: Campen et al.(2003, 055626) **Species:** Rat **Gender:** Male and Female **Strain:** SH **Age:** 4 mo	DE: generated by either of two Cummins (2000 model) 5.9-L ISB turbo engines fueled by Number 2 Diesel Certification Fuel. **Particle Size:** 0.1-0.2 µm aerodynamic diameter	**Route:** Whole-body exposure **Dose/Concentration:** 0, 30, 100, 300, 1000 µg/m^3 **Time to Analysis:** 6 h/day for 7 days; ECG measurements taken 4 days post-exposure.	**HR:** Significantly higher in exposed animals and not concentration-dependent. More substantial results seen in male rats. **ECG:** The PQ interval was significantly prolonged among exposed animals in a concentration-dependent manner.
Reference: Campen et al. (2006, 096879) **Species:** Mouse **Gender:** Male **Strain:** ApoE$^{-/-}$ **Age:** 10 wk	Road dust from paved surfaces (Reno, NV) Gasoline engine emissions, containing PM, NOX, CO and HC **Particle Size:** Road dust: 1.6 µm (Standard Deviation 2.0) Gasoline engine emissions: Average particle diameter of 15 nm	**Route:** Whole-body inhalation **Dose/Concentration:** Road dust: 0.5 and 3.5 mg/m^3 Gasoline engine emissions: 5 to 60 µg/m^3 (at dilutions of 10:1, 15:1, and 90:1) Mean concentrations of PM: 61 µg/m^3; NO_X: 18.8 ppm; CO: 80 ppm. **Time to Analysis:** 6 h/days for 3 days. Sacrificed 18 h post-exposure.	**ET-1:** Gasoline exhaust significantly upregulated ET-1 in a dose-dependent manner. ET-1 increased levels in the PM filtered group and decreased in the low levels of road dust. **ECG:** HR consistently decreased from beginning to end of exposure in all groups. No significant HR effects on road dust or gasoline exposure was observed. No significant effects on P-wave, PQ-interval, QRS-interval, or QT-interval were observed in either treatment. **T-wave:** Mice exposed to whole gasoline exhaust displayed significant increases in T-wave morphology from the beginning of exposures; this effect was consistent on all exposure days.

Study	Pollutant	Exposure	Effects
Reference: Cascio et al. (1987, 007583) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6-10 wk	UFPM: Ultra fine PM, EPA Chapel Hill, NC **Particle Size:** <0.1 µm	**Route:** IT Instillation **Dose/Concentration:** 100 µg in 100 µl **Time to Analysis:** 24 h post-exposure (single exposure)	UFPM exposure double the size of myocardial infarction attendant to an episode of ischemia and reperfusion while increasing post ischemic oxidant stress. UFPM alters endothelium-dependent/independent regulation of systemic vascular tone; increases platelet number, plasma fibrinogen, and soluble P-selectin levels; reduces bleeding time.
Reference: Chang et al. (2007, 155720) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 60 days	UfCB: Ultra fine carbon black Ferric sulfate $Fe_2(SO_4)_3$ Nickel sulfate $NiSO_4$ **Particle Size:** UfCB	**Route:** IT Instillation **Dose/Concentration:** UfCB: 415 and 830 µg Ferric Sulfate: 105 and 210 µg Nickel Sulfate: 263 and 526 µg Combined UfCB and ferric sulfate: 830 µg UfCB + 105 µg ferric sulfate Combined UfCB with Nickel Sulfate: 830 µg UfCB + 263 µg Nickel Sulfate **Time to Analysis:** Single dose, radiotelemetry readings recorded for 72 h post- exposure.	Both high/low-dose UfCB decreased ANN (normal-to-normal intervals) slightly around the 30th h, concurrent increases of LnSDNN. LnRMSSD returned to baseline levels after small initial increases. Minor effects observed after low-dose Fe and Ni instillation; biphasic changes occurred after high-dose instillations. Combined exposures of UfCB and either Fe or Ni resulted in HRV trends different from values estimated from individual-component effects.
Reference: Chang et al. (2007, 155720) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 10 wk	CAPs: collected during a dust storm from Chung-Li, Taipei **Particle Size:** $PM_{2.5}$	**Route:** Nose-only Inhalation **Dose/Concentration:** 315.55 µg/m^3 **Time to Analysis:** 6 h	A linear mixed-effects model revealed sigmoid increases in HR and a sigmoid decrease of QAI during exposure, after an initial incubation period.
Reference: Chang et al. (2004, 055637) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 60 days	CAPs collected in Chung-Li, Taipei (spring and summer periods) **Particle Size:** $PM_{2.5}$	**Route:** Nose-only Inhalation **Dose/Concentration:** Spring exposure: 202.0 ± 68,8 µg/m^3; Mean number concentration: 2.30 × 10^5 particles/cm^3 (range: 7.12 ×10^3 - 8.26 ×10^5) Summer exposure: 141.0 ± 54.9 µg/m^3; Mean number concentration: 2.78 ×10^5 particles/cm^3 (range: 7.76 ×10^3 - 8.87 × 10^5) **Time to Analysis:** 4 days of spring exposure and days of summer exposure for 5 h each exposure. Parameters measured throughout duration of exposures.	During spring exposures, the maximum increase of heart rate (HR) and blood pressure (BP) were 51.6 bpm and 8.5 mmHg respectively. The maximum decrease of QAI (measures cardiac contractility) noted at the same time was 1.6 ms. Similar pattern was observed during summer exposure, however., the responses were less prominent.
Reference: Chang, et al. (2005, 097776) **Species:** Rat **Gender:** Male **Strain:** SH **Weight**: 200 g	CAPs collected in Chung-Li, Taipei **Particle Size:** $PM_{2.5}$ (0.1-2.5 µm)	**Route:** Nose-only Inhalation **Dose/Concentration:** 202.0 ± 68.8 µg/m^3 **Time to Analysis:** 5 h/days for 4 days	During the inhalation stage, crude effects of both LnSDNN and LnRMSSD for exposure and control groups decreased from the baseline values. Immediately after the experiments, both LnSDNN and LNRMSSD decreased due to stresses produced by release from the exposure system, then returned to the baseline values.
Reference: Chauhan et al. (2005, 155722) **Tumor Cell Line:** A549 derived from alveolar type II epithelial cells	SRM-1879 (SiO_2) and SRM-154b (TiO_2) from the NIST EHC-93 from Ontario, Canada (EHCsol, EHCinsol) **Particle Size:** EHC-93 median physical diameter: 0.4 µm; TiO_2 and SiO_2 particle size distribution: 0.3-0.6 µm	**Route:** Cell Culture **Dose/Concentration:** 0, 1, 4, and 8 mg EHC total equivalent per 5 mL **Time to Analysis:** Culture medium was removed from flasks and replaced w/ 5 mL of the particle suspension media. Plates were incubated for 24 h. After 24 h cell culture supernatants were collected and analyzed.	The decreased expression of preproET-1 in A549 cells suggests that epithelial cells may not be the source of higher pulmonary ET-1 spillover in the circulation measured in vivo in response to inhaled urban particles. However, higher levels ECE-1 in A549 post-exposure to particles suggests an increased ability to process bigET-1 into mature ET-1 peptide, while increased receptor expression implies responsiveness. The increased release of Il-8 and VEGF by epithelial cells in response to particles could possibly up regulate ET-1 production in the adjacent pulmonary capillary endothelial cells, with concomitant increased ET-1 spillover in the systemic circulation.

Study	Pollutant	Exposure	Effects
Reference: Chen et al. (2005, 087218) **Species:** Mouse **Strain:** C57 and ApoE$^{-/-}$	CAPs (NYU, NY) **Particle Size:** $PM_{2.5}$	**Route:** Whole-body Inhalation **Dose/Concentration:** 19.7 µg/m^3 average concentration over 5 mo (daily average exposure concentration was 110 µg/m^3) **Time to Analysis:** 6 h/days, 5 days/wk, for 5 mo. Parameters measured continuously throughout.	Significant decreasing patterns of HR, body temperature, and physical activity for ApoE$^{-/-}$ mice, with nonsignificant changes for C57 mice. SDNN and RMSSD in the late afternoon and overnight for ApoE$^{-/-}$ mice showed a gradual increase for the first 6 wk, a decline for about 12 more weeks, and a slight turn upward at the end of the study period. For C57 mice, there were no chronic effect changes in SDNN or RNSSD in the late afternoon, and a slight increase after 6 wk for the overnight period.
Reference: Chen and Nadziejkov(2005, 087219)**(Chen and Nadziejko, 2005, 087219)** **Species:** Mouse **Strain:** C57, ApoE$^{-/-}$ **Age:** 26-28 wk (C57), 39-41 wk (ApoE$^{-/-}$), and 18-20 wk (LDLr$^{-/-}$ [DK])	CAPs (NYU, NY) **Particle Size:** $PM_{2.5}$	**Route:** Whole-body Inhalation **Dose/Concentration:** Mean exposure concentration: 110 µg/m^3 **Time to Analysis:** 6 h/days, 5 days/wk for up to 5mo. Sacrificed 3-6 days after last exposure.	All DK mice developed extensive lesions in the aortic sinus regions. In male DK mice, the lesion areas appeared to be enhanced by CAPs exposure. Plaque cellularity was increased, but there were no CAPs-associated changes in the lipid content. ApoE$^{-/-}$ and DK mice showed prominent areas of severe atherosclerosis. Quantitative measurements showed that CAPs increased the percentage of aortic intimal surface covered by grossly discernible atherosclerotic lesion.
Reference: Corey LM et al. (2006, 156366) **(2006, 156366)**(Corey et al., 2006, 156366) **Species:** Mouse **Gender:** Male **Strain:** ApoE$^{-/-}$ **Age:** 11-12 mo **Weight**: 32.84 g (avg)	PM collected November - March between 1996-1999 (Seattle, WA) Silica (U.S. Silica Company, Berkeley Springs, WV) **Particle Size:** $PM_{2.5}$	**Route:** Nasal Instillation **Dose/Concentration:** PM: 1.5 mg/kg; Saline: 50 ul; Silica: Min-u-Sil 5 in 50 µl saline **Time to Analysis:** Mice monitored for 1 day baseline prior to and for 4 days following exposure.	After an initial increase in both HR and activity in all groups, there was delayed bradycardia with no change in activity of the animals in the PM and silica exposed groups. In addition, with PM and silica exposure, there was a decrease in HRV parameters.
Reference: Cozzi et al. (2006, 091380) **Species:** Mouse **Strain:** ICR **Age:** 6-10 wk	Ultrafine PM (collected continuously over 7-day periods in Oct 2002 in Chapel Hill, NC) **Particle Size:** <150 nm	**Route:** IT Instillation **Dose/Concentration:** 100 µg of PM in vehicle **Time to Analysis:** 24 h post-exposure	**Ischemia-Reperfusion:** PM exposure doubled the relative size of myocardial infarction compared with the vehicle control. No difference was observed in the percentage of the vehicle at the risk of ischemia. PM exposure increased the level of oxidative stress in the myocardium after I-R. The density of neutrophils in the reperfused myocardium was increased by PM exposure, but differences in the numbers of blood leukocytes, expression of adhesion molecules on circulating neutrophils, and activation state of circulating neutrophils, 24 h after PM exposure, could not be correlated to the increase I-R injury observed. **Isolated Aortas:** Aortas isolated from PM-exposed animals exhibited a reduced endothelium-dependent relaxation response to ACh.
Reference: Dvonch JT et al. (2004, 055741) **Species:** Rat **Gender:** Male **Strain:** Brown Norway	CAPs, Detroit, MI **Particle Size:** $PM_{2.5}$	**Route:** Whole-body Inhalation **Dose/Concentration:** Average concentration 354 µg/m^3 **Time to Analysis:** 8 h/days for 3 consecutive days; plasma samples collected 24 h post-exposure.	Plasma concentrations of asymmetric dimethylarginine (ADMA) were significantly elevated in rats exposed to CAPs versus filtered air.

Study	Pollutant	Exposure	Effects
Reference: Elder et al. (2004, 055642) **Species:** Rat **Gender:** Male **Strain:** Fischer 344 and SH **Age:** 23 mo (Fischer); 11-14 mo (SH) **Weight:** NR	UFP - Ultrafine carbon particles; LPS (Sigma) **Particle Size:** UFP: 36 nm (median size)	**Route:** Whole-body inhalation; intraperitoneal injection (ip) for saline and LPS **Dose/Concentration:** Particles: 150 µg/m^3; LPS: 2 mg/kg bw **Time to Analysis:** Single 6-h exposure to particles. Sacrificed 24 h after ip LPS exposure.	**BAL Fluid Cells:** Neither inhaled UFP nor ip LPS cause a significant increase in BAL fluid total cells or the percentage of neutrophils in either rat strain. No significant exposure-related alteration in total protein concentration or the activities of LDH and b-glucuronidase. **Peripheral Blood:** In both rat strains ip LPS induced significant increase in the number and percentage of circulating PMNs. When combined with inhaled UFP, PMNs decreased, significantly for F-344 rats. Plasma fibrinogen increased with ip LPS in both rat strains with the magnitude of change greater in SH rats. UFP alone decreased plasma fibrinogen in SH rats. Combined UFP and LPS response was blunted, but significantly higher than controls. Hematocrit was not altered in either rat strain by any treatment. **TAT Complexes:** With all exposure groups averaged, plasma TAT complexes in SH rats were 6.5 times higher than in F-344 rats. LPS caused an overall increase in TAT complexes for F-344 rats that was further augmented by inhaled UFP. UFP alone decreased response. In SH rats, UFP alone significant increased response and LPS decreased response. **ROS in BAL Cells:** In F-344 rats both UFP and LPS have independent and significant effects on DCFD oxidation. Effects were in opposite directions; particles decreased ROS, LPS increased ROS.
Reference: Finnerty et al. (2007, 156434) **Species:** Mouse **Gender:** Male **Strain:** C57BL/6 **Age:** 9 wk **Weight**: 22-2 7g	Coal Fly Ash (U.S. EPA), Analysis: ($PM_{2.5}$ samples) low unburned carbon (0.53 wt%), moderate levels of transition metals, including (in µg/g): Fe (30, 400), Mg (31, 200), Ti (6, 180), Mn (907), and V (108). **Particle Size:** 1.8 and 2.5 µm	**Route:** IT Instillation **Dose/Concentration:** PM: 200 µg; 200 µg PM+10 µg LPS; 200 µg PM+100 µg LPS **Time to Analysis:** 18 h after IT instillation	**Plasma:** TNF-α significantly increased in both PM+LPS10 and PM+LPS100 treatments. For plasma IL-6, all groups tended to rise with a significant increase in the PM+LPS100 group.
Reference: Floyd et al. (2009, 190350) **Species:** Mouse **Gender:** Male **Strain:** $ApoE^{-/-}$ **Age:** 20 wk	CAPs: $PM_{2.5}$ concentrated from Tuxedo, NY (April-Sept 2003) **Particle Size:** NR	**Route:** Whole-body Inhalation **Dose/Concentration:** Avg 120 µg/m^3 (n=6/group) **Time to Analysis:** 6 h/days × 5 days/wk × 5 mo	**Gene Expression:** Microarry gene expression identified 395 genes downregulated and 216 genes upregulated in the aortic plaques. Ontologic analysis identified a list of functional processes associated with gene expression and included: inflammation, tissue development, cellular movement, cellular growth and proliferation, hematological system development and function, lipid metabolism, cardiovascular system function, cellular assembly and organization, and cell death.
Reference: Folkmann et al. (2007, 097344) **Species:** Mouse **Gender:** Female **Strain:** Wild type and $ApoE^{-/-}$ **Age:** 11-13 wk **Weight**: 21 g (avg)	DEP: SRM2975 (particulate fraction of exhaust from a filtering system designed for diesel-powered forklifts). **Particle Size:** DEP: NR	**Route:** Intraperitoneal Iinjection **Dose/Concentration:** 0, 50, 500, 5,000 µg DEP/kg **Time to Analysis:** 6 or 24 h post-ip injection	The expression of inducible nitric oxide synthase (iNOS) mRNA was increased in the liver 6 h post-ip injection. The level of oxidized purine bases, determined by formamidopyrimidine DNA glycosylase sites increased significantly in the liver after 24 h in mice injected w/ 50µg/kg. There was no indication of systemic inflammation determined as the serum concentration of nitric oxide and iNOS expression, and DNA damage was not increased in the aorta.

Study	Pollutant	Exposure	Effects
Reference: Furuyama et al. (2006, 097056) **Species:** Rat **Cell Type:** Heart Micro vessel Endothelial (RHMVE) Cells	OE-DEP, OE-UFP (from Urawa, Saitama, Japan) OE = Organic Extracts **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 0, 5, 10, 25 µg/mL of OE-DEP or OE-UFP **Time to Analysis:** Exposed for 0, 6, 12, 24, or 36 h	The cell monolayer exposed to 10 µg/mL OE-UFP produced a larger amount of HO-1 than cells exposed to 10 µg/mL OE-UFP. OE-DEP and OE-UFP exposure reduced PAI-1 production by the cells but did not affect the production of thrombomodulin, tissue-type PA, or urokinase-type PA. Increased PAI-1 synthesis in response to treatment with 1 ng/mL TNF-α or 0.5ng/mL TGF-β1 was reduced by OE-DEP exposure. Suppression of PAI-1 production by OE-DEP exposure was mediated through oxidative stress and was independent of HO-1 activity.
Reference: Gerlofs-Nijland et al. (2009, 190353) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 12 wk **Weight:** 200-300 g	PM (Prague, Czech Republic; Duisburg, Germany; Barcelona, Spain) (Prague and Barcelona coarse PM organic extracts) **Particle Size:** Coarse: 2.5-10 µm, Fine: 0.2-2.5 µm	**Route:** IT Instillation **Dose/Concentration:** 7 mg /kg **Time to Analysis:** DTPA added to some PM samples preinstillation. Instilled with PM. Necropsy 24 h post-exposure.	Inflammation (LDH, protein, albumin), cytotoxicity (NAG, MPO, TNF-α), and fibrinogen were increased by PM, and were greatest in the coarse PM fraction. Metal-rich PM had greater inflammatory and cytotoxic effects, and increased fibrinogen and vWF and decreased ACE. PAH content influenced greater inflammation (including neutrophils), cytotoxicity, and fibrinogen. Generally, whole PM and coarse PM were more potent than organic extracts and fine PM, respectively.
Reference: Gerlofs-Nijland et al. (2007, 097840) **Species:** Rat **Gender:** Male **Strain:** SH/NHsd **Age:** 13 wk **Weight:** 250-350 g	PM samples collected from: 1. MOB high traffic density 2. HIA high traffic density 3. ROM high traffic density 4. DOR moderate traffic density 5 MGH low traffic density 6 LYC low traffic density **Particle Size:** Coarse: 2.5-10 µm; Fine: 0.1-2.5 µm	**Route:** IT Instillation **Dose/Concentration:** 3, 10 mg/kg **Time to Analysis:** 24 h	**Hematology:** Fibrinogen responses of SH rats increased significantly at the high dose of both fractions of all PM samples, except fine PM from DOR. **Location-Related Differences:** Coarse PM from LYC lowered fibrinogen values more than PM from location MOB, HIA, and MGH. Fine PM showed less differences among the various sites.
Reference: Gerlofs-Nijland et al. (2005, 088652) **Species:** Rat **Gender:** Male **Strain:** SH/NHsd **Age:** 11-12 wk **Weight:** 250-350 g	RTD: road tunnel dust (obtained from a Motorway tunnel in Hendrik-Ido-Ambacht, Netherlands) EHC-93 (Ottawa, Canada) **Particle Size:** Coarse: 2.5-10 µm; fine: 0.1-2.5 µm	**Route:** IT Instillation **Dose/Concentration:** 0.3, 1, 3, 10 mg/kg; EHC-93: 10 mg/kg **Time to Analysis:** 4, 24, 48 h	**Hematology:** No significant changes in plasma for bigET-1 or von Willebrand factor were observed. At the highest dose, fibrinogen levels significantly increased at 24 and 4 h for both PM types.
Reference: Ghelfi et al. (2008, 156468) **Species:** Rat **Strain:** SD **Age:** Adult	CAPs CPZ (Capsazepine) (Axxora LLC, San Diego, CA) **Particle Size:** $PM_{2.5}$	**Route:** CAPs: Whole-body Inhalation; CPZ: IP Injection or Aerosol **Dose/Concentration:** CAPs: mean mass concentration: 218 ± 23 µg/m^3; CPZ: 10 mg/kg (ip), 500 µmol (aerosol) **Time to Analysis:** Experiment 1: CPZ ip or 20 min aerosol pretreatment immediately prior to CAPs exposure. Single CAPs exposure for 5 h. Parameters measured immediately following exposure. Experiment 2: CPZ ip pretreatment prior to CAPs exposure. Exposed to CAPs for 5 h/day for 4 mo. Parameters measured throughout duration of experiment.	CPZ (ip or aerosol) decreased CAPs-induced chemiluminescence (CL), lipid thiobarbituric acid reactive substances (TBARS), and edema in the heart, indicating that blocking TRP receptors, systemically or locally, decreases heart CL. CAPs exposure led to significant decreases in HR and in the length of QT, RT, Pdur and Tpe intervals. These changes were observed immediately upon exposure, and were maintained throughout the 5-h period of CAPs inhalation. Changes in cardiac rhythm and ECG morphology were prevented by CPZ.

Study	Pollutant	Exposure	Effects
Reference: Gilmour et al. (2004, 054175) **Species:** Rat **Gender:** Male **Strain:** Wistar	ufCB (Printex 90 from Frankfurt, Germany) fCB (Huber 990 from UK) **Particle Size:** ufCB: 114 nm (MMAD); fCB: 268 nm (MMAD).	**Route:** Whole-body Inhalation **Dose/Concentration:** ufCB: 1.66 mg/m^3; fCB: 1.40 mg/m^3 **Time to Analysis:** Single exposure for 7 h. Sacrificed and samples taken at 0, 16, and 48 h post-exposure.	Exposure to ultrafine, but not fine, CB particles was also associated with significant increases in the total number of blood leukocytes. Plasma fibrinogen factor VIII and vWF were unaffected by particle treatments as was plasma Trolox equivalent antioxidant status.
Reference: Gilmour et al. (2005, 087410) **Species:** Human **Cell Types:** Primary Human Monocyte Derived Macrophages (MP); Human Umbilical Vein Endothelial Cells (HUVEC); A549 cells; 16HBE	PM_{10}: (Carbon Black from Degussa Ltd, Frankfurt, Germany) **Particle Size:** PM_{10}	**Route:** Cell Culture **Dose/Concentration:** PM_{10}: 50 and 100 µg/mL **Time to Analysis:** 6 and 20 h	The culture media from MPs and 16HBE cells but not A549 cells, exposed to PM_{10} had an enhanced ability to cause clotting. H_2O_2 also increased clotting activity. Apoptosis was significantly increased in MPs exposed to PM_{10} and LPS as shown by annexin V binding. TF gene expression was enhanced in MPs exposed to PM_{10} and HUVEC tissue factor. tPA gene and protein expression were inhibited.
Reference: Gilmour et al. (2006, 156472) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 12-14 wk **Weight:** 280-340 g	Zinc Sulfate ($ZnSO_4$ in saline solution) **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 131 µg/kg (2 µmol/kg) **Time to Analysis:** 1, 4, 24, 48 h	**Zinc levels in plasma and tissue:** At 1-24 h post-exposure, zinc plasma levels increased to nearly 20% above baseline. **mRNA expression:** Cardiac tissues demonstrated similar temporal increases in expressions of TF, PAI-1 and thrombomodulin mRNA, following pulmonary instillation of Zn. **Cardiac histopathology:** Mild and focal acute, myocardial lesions developed in a few Zn exposed rats. No changes in fibrin deposition or troponin disappearance were observed. At 24 and 48h PE to Zn, increases occurred in levels of systemic fibrinogen an the activated partial thromboplastin time.
Reference: Gong et al. (2007, 091155) **Species:** Mouse **Cell Type:** Human Microvascular Endothelial Cells (HMEC) **Strain:** C57BL/6J **Gender:** Male **Age:** 2 mo	Organic DEP extract: collected from exhaust in a 4JB1-type LD, 2.74 liter, 4-cylinder Isuzu diesel engine (provided by Masaru Sagai, Tsukuba, Japan) ox-PAPC: (provided by Judith Berliner, UCLA, CA) In vivo validation: Ultrafine (ufp) and fine (fp) particulate matter **Particle Size:** DEP <1 µm (diameter)	**Route:** Cell culture; In vivo validation via Whole-body inhalation **Dose/Concentration:** ox-PAPC: 10, 20, and 40 µg/mL; DEP: 5, 15, and 25 µg/mL; DEP (5 µg/mL)+ox-PAPC: 10 or 20 µg/mL In Vivo Validation: Ufp: 3.2 4×10^5/cm^3; fp: 2.7 $\times10^5$/cm^3 In vivo validation: Ufp: <0.18 µm; fp: <2.5 µm **Time to Analysis:** 4 h In vivo validation: Exposed to CAPs for 5 h/day, 3 days/wk for 8 wk. Sacrificed 24 h after last CAPs exposure.	Gene-expression profiling showed that both DEP extract and ox-PAPC co-regulated a large number of genes. Network analysis to identify co-expressed gene modules, led to the discovery of three modules that were highly enriched in genes that were differentially regulated by the stimuli. These modules were also enriched in synergistically co-regulated genes and pathways relevant to vascular inflammation. **In vivo validation:** Results were validated by demonstrating that hypercholesterolemic mice exposed to ambient ultrafine particles inhibited significant upregulation of the module genes in the liver.

Study	Pollutant	Exposure	Effects
Reference: Goto et al. (2004, 088100) **Species:** Rabbit **Gender:** Female **Strains:** New Zealand White **Age:** NR **Weight:** 2.3 kg	EHC-93 (Ottawa, ON,Canada) CC: Coilloidal Carbon (obtained from Hamburg, Germany) **Particle Size:** EHC-93: PM_{10}; CC: <1 µm	**Route:** Intrabronchial Instillation **Dose/Concentration:** AMs incubated with EHC-93 or CC: 0.6 ml/kg EHC-93 alone: 1 mL (500 µg/ mL) CC alone: 1mL (1% CC) **Time to Analysis:** WBC counts measured 4-168 h after BrdU injection. Sacrificed 7days post instillation.	**Lung Distribution of PM_{10}:** PM-containing AMs were distributed diffusely. PM-containing AMs were more prevalent in the PM exposed animals. There was no AM-containing particle difference between the CC-exposed and EHC-93-exposed groups. **Monocyte Release from Bone Marrow:** EHC exposure increased WBC and band cell counts from 12 h after instillation. Monocyte count was not affected. Labeled monocytes peaked more quickly after DEP exposure (12 vs 16 h for control). There was no observed change in BM monocyte pool. **Cytokine Release:** EHC stimulation increased the release of GM-CSF, IL-6, IL-1β, TNF-α, IL-8 and MCP-1. No effect on m-CSF and MIP-1β. CC particles induced increases in IL-6 and TNF-α; other cytokine levels did not differ from control. **Supernatant Instillation:** AM+EHC increased circulating WBC and band cell counts. Circulating monocyte counts were unaffected. AM+EHC showed a major increase in fraction and amount of monocyte released as well as faster clearance when compared to control. The BM monocyte pool was similar in all groups. **Monocyte Transit Time Through BM:** Exposure to EHC, CC only shortened the transit time of monocytes as compared to controls. AM+EHC also shortened monocyte transit time whereas AM+CC had a nonsignificant effect.
Reference: Gottipolu et al. (2009, 190360) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto, SH **Age:** 14-16 wk **Weight:** NR	DE (30-kW (40hp) 4-cylinder indirect injection Deutz diesel engine) (O_2- 20%, CO- 1.3-4.8 ppm, NO- <2.5-5.9 ppm, NO_2- <0.25-1.2ppm, SO_2 0.2-0.3 ppm, OC/EC- 0.3 ± 0.03) **Particle Size:** Number Median Diameter: Low- 83 ± 2 nm, High- 88. 2 nm; Volume Median Diameter: Low- 207 ± 2 nm, High- 225 ± 2 nm	**Route:** Inhalation **Dose/Concentration:** Low: 507 ± 4 µg/m^3; High: 2201 ± 14 µg/m^3 **Time to Analysis:** Exposed 4 h/days, 5 days/wk, 4 wk. Necropsied 1day post-exposure.	DE dose-dependently inhibited mitochondrial aconitase activity. DE caused 377 genes to be differentially expressed within WKY rats, most of which were downregulated, but none in SH rats. However, WKY rats had an expression pattern shift that mimicked baseline expression of SH rats without DE. These genes regulated compensatory response, matrix metabolism, mitochondrial function, and oxidative stress response.
Reference: Graff et al. (2005, 087956) **Species:** Rat **Cell Type:** Ventricular Myocytes	Zn; V **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 0, 6.25, 12.5, 25, or 50 µm **Time to Analysis:** Toxicity: 24 h post- exposure **Beat Rate:** 0.5, 1, 2, 4, and 24 h PE **PCR:** 6 and 24 h PE	**Beat Rate:** There were statistically significant reductions in spontaneous beat rate 4 and 24 h post-exposure (greater reductions were observed with Zn). **Inflammation:** Exposure to Zn or V (6.25-50 µm) for 6 h produced significant increases in IL-6, IL-α, heat shock protein 70, and connexin 43 (Cx43). **Impulse Conduction:** 24 h post-exposure, Zn induced significant changes in the gene expression of Kv4.2 and KvQLt, α-1 subunit of L-type Ca channel, Cx43, IL-6, and IL-1α. V produced a greater effect on Cx43 and affected only KvLQT1.
Reference: Gunnison and Chen (2005, 087956) **Species:** Mouse **Gender:** Male **Strain:** F2 generation DK ($ApoE^{-/-}$, $LDLr^{-/-}$) **Age:** 18-20 wk	CAPs (Tuxedo, NY) Copollutants measured: O_3 and NO_2. **Particle Size:** 389 ± 2 nm	**Route:** Whole-body Inhalation **Dose/Concentration:** CAPs: 131 ± 99 µg/m^3 (range 13-441 µg/m^3) O_3: 10 ppb NO_2: 4.4 ppb **Time to Analysis:** 6 h/days, 5 days/wk for approximately 4 mo. Tissue collection was performed 3-4 days after the last day of exposure.	**Gene Expression:** In CAPs-exposed heart tissue, the expression of Limd1 and Rex3 were the most consistently affected genes among the exposed mice. Limd1 was down regulated by 1.5-fold or greater from moderate baseline expression. Rex3 showed a relatively small increase in absolute expression.

Study	Pollutant	Exposure	Effects
Reference: Gurgueira et al. (2002, 036535) **Species:** Rat **Gender:** Male **Strain:** SD **Weight:** 250-300 g	CAPs; Carbon Black (CB from Fisher Scientific, Pittsburgh, PA): C (85.9 ± 0.2%); O (13 ± 0.2%); S (1.17 ± 0.02%) ROFA: obtained from an oil-fired power plant (Boston, MA) **Particle Size:** CAPs size range: 0.1-2.5 µm; CB and ROFA ($PM_{2.5}$)	**Route:** Whole-body Inhalation **Dose/Concentration:** CAPs: average mass concentration: 300 ± 60 µg/m^3; ROFA: 1.7 mg/m^3; CB: 170 µg/m^3 **Time to Analysis:** CAPs: 1, 3, and 5 h; ROFA: 30 min; CB: 5 h	**Oxidative Stress:** Rats breathing CAPs aerosols for 5 h showed significant oxidative stress, determined as in situ chemiluminescence (CL) in the lung, heart, but not in the liver. ROFA also triggered increases in oxidant levels but not particle-free air or CB. Increases in CL showed strong associations with the CAPs content of Fe, Al, Si and Ti in the heart. The oxidant stress imposed by 5 h exposure to CAPs was associated with slight, but significant increases in the lung and heart water content, with increased serum levels of lactate dehydrogenase, indicating mild damage to tissues. CAPs inhalation also led to tissue-specific increases in the activities of SOD and catalase.
Reference: Gursinsky et al. (1976, 015607) **Species:** Rat **Cell Type:** Fibroblasts isolated from adult male Wistar rats hearts	Fly ash (TAF98) **Particle Size:** NR	**Route:** In Vitro **Dose/Concentration:** TAF98: 0, 1, 2 3, 10, 25, 50, 100, 200 µg/mL **Time to Analysis:** 0, 5, 10, 30, 60, 120 min	Brief treatment of fibroblasts with fly ash triggered the immediate formation of ROS. Using phosphospecific antibodies the activation of p38 MAP kinase, p44/42 MAP kinase (ERK1/2) and p70S6 kinase. Prolonged incubation with fly ash increased the expression of collagen 1 and TGF-β1, but decreased mRNA levels of MMP9 and TNF-α. Cell proliferation was inhibited at high concentrations of fly ash. An increase in the level of advanced glycation end product modification of various cellular proteins was observed.
Reference: Hansen et al. (2007, 090703) **Species:** Mouse **Gender:** Female **Strain:** $ApoE^{-/-}$ and C57BL/6J $ApoE^{+/+}$ **Age:** 11-13 wk	DEP: SRM-2975 (NIST) **Particle Size:** DEP: 215 nm (geometric mean diameter)	**Route:** Intraperitoneal Injection **Dose/Concentration:** DEP: 0, 0.5 and 5 mg/kg; Aorta segments incubated with 0, 10 and 100 µg DEP/mL **Time to Analysis:** Sacrificed 1 h after ip injection.	Exposure to 0.5 mg/kg DEP caused a decrease in the endothelium-dependent Ach elicited vasorelaxation in $ApoE^{-/-}$ mice, whereas the response was enhanced in $ApoE^{+/+}$ mice. No significant changes were observed after administration of 5 mg/kg DEP. K^+ or phenylephrine induced constriction was not affected.
Reference: Hansen et al. (2007, 090703) **Species:** Mouse **Gender:** Female **Strain:** $ApoE^{-/-}$ and C57BL/6J $ApoE^{+/+}$ **Use:** Aorta rings used for in-vitro studies	DEP: SRM-2975 (NIST) **Particle Size:** DEP: 215 nm (geometric mean diameter)	**Route:** Cell Culture **Dose/Concentration:** 0, 10 and 100 µg DEP/mL **Time to Analysis:** Basal tone measured at 5 different points throughout experiment.	Exposure to 100 µg DEP/mL enhanced ACh-induced relaxation and attenuated phenylephrine-induced constriction. Vasodilatation induced by sodium nitroprusside was not affected by any DEP exposure.
Reference: Harder et al. (2005, 087371) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 12-15 wk	Carbon UFPs ((generated by Electric Spark Generator GFG 1000; Palas, Karlsruhe, Germany) **Particle Size:** 37.6 ± 0.7 nm (mean)	**Route:** Whole-body Inhalation **Dose/Concentration:** 180 µg/m^3 **Time to Analysis:** Days 1-3: baseline reading, Day 4: exposure to UFPs or filtered air for 4 or 24 h then sacrificed immediately following exposure period OR Sacrificed following 1-3 days recovery period.	**Cardiovascular Performance:** Mild but consistent increase in HR, which was associated with a significant decrease in HR variability during exposure (particle-induced alteration of cardiac autonomic balance, mediated by a pulmonary receptor activation). **Lung Inflammation and Acute-Phase Response:** BALF revealed significant but low-grade pulmonary inflammation. **Effects on Blood:** There was no evidence of an inflammation-mediated increase in blood coagulability; no changes in plasma fibrinogen or factor VIIa. **Pulmonary and Cardiac Histopathology:** Sporadic accumulation of particle-laden macrophages found in the alveolar region. No signs of cardiac inflammation or cardiomyopathy. **mRNA Expression Levels:** No significant changes in the lung or heart.

Study	Pollutant	Exposure	Effects
Reference: Hirano et al. (2003, 097345) **Species:** Rat **Cell Types:** Heart Microvessel Endothelial Cells (RHMVE)	Organic Extracts of DEP (DEP) and Organic Extracts of Ultra Fine Particles (UFP). (Urawa City, Saitama, Japan) **Particle Size:** DEP and UFP: <2.0 µm	**Route:** Cells Culture **Dose/Concentration:** NAC effects on viability: DEP: 25 µg/ml; UFP: 50 µg/ml mRNA levels for DEP and UFP: 0,1,3,10 µg/ml cell monolayer exposed to DEP and UFP: 1,10,100 µg/ml **Time to Analysis:** mRNA levels measured after 6 h incubation with DEP or UFP. Other parameters measured after 24 h.	**Cytotoxicity and Oxidative Stress:** LC50 values were 17 and 34 µg/mL for DEP and UFP respectively. The viability of DEP and UFP exposed cells was ameliorated by N-acetyl-L-cysteine (NAC). **mRNA Levels:** mRNA levels increased dose-dependently with DEP and HO-1 mRNA showed the most marked response to DEP. mRNA levels of antioxidant enzymes and heat shock protein 72 (HSP72) in DEP-exposed cells were higher than UFP exposed cells at the same concentration. The transcription levels of HO-1 and HSP72 in DEP and UFP-exposed cells were also reduced by NAC.
Reference: Hwang et al. (2005, 089454) **Species:** Mouse **Strain:** C57 and ApoE$^{-/-}$	CAPs (Tuxedo, NY) **Particle Size:** 389 ± 2 nm	**Route:** Whole-body Inhalation **Dose/Concentration:** CAPs Range: 5-627 µg/m^3. Mean CAPs Concentration: 133µg/m^3. Mean Concentrations of O_3 and NO_2 in CAPs: 10 and 4.4 ppb respectively. **Time to Analysis:** 6 h/day, 5 days/wk for 5 mo.	**Long-term Analysis:** Significant decreasing patterns of HR, body temperature, and physical activity in ApoE$^{-/-}$ mice. Nonsignificant changes for C57 mice. The chronic effect changes for ApoE$^{-/-}$ mice were maximal in the last three wk. **Short-term Analysis:** Dose-dependent relationship for HR variations in ApoE$^{-/-}$ mice. **Heart Rate Fluctuation:** HR fluctuations in ApoE$^{-/-}$ mice during the period of 3-6 h increased by 1.35 fold at the end of the exposure and during a 15 min period increases by 0.7 fold at the end of the exposure.
Reference: Inoue et al. (2006, 190142) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6- 7 wk	DEP (obtained from a 4Jb1-type light-duty, 4-cylinder, 2.74-L Isuzu diesel engine) Washed DEP (carbonaceous nuclei of DEP after extraction) and DEP-OC (organic chemicals in DEP extracted with CH_2Cl_2); Washed DEP+LPS and DEP-OC+LPS **Particle Size:** $PM_{2.5}$	**Route:** IT Instillation **Dose/Concentration:** Washed DEP: 4 mg/kg. DEP-OC: 4 mg/kg. LPS: 2.5 mg/kg. Washed DEP+LPS and DEP-OC+LPS: respective additions of LPS to each component prior-experimentation. **Time to Analysis:** Sacrificed 24 h post single dose instillation.	Both DEP components exacerbated vascular permeability. The increased fibrinogen and E-selectin levels induced by LPS. This exacerbation was more prominent with washed DEP than with DEP-OC. Washed DEP+LPS significantly decreased protein C and antithrombin-III and elevated circulatory levels of IL-6, KC and LPs without significance.
Reference: Inoue et al. (2006, 097815) **Species:** Mouse **Gender:** Male **Strains:** C3H/HeJ (TLR-4 point mutant) and C3H/HeN (Control) **Age:** 6 wk	DEP (derived from 4 cyl, 2.74l light duty diesel engine) **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 12 mg/kg **Time to Analysis:** 24 h	**Hematology:** DEP increased plasma fibrinogen in both strains but with a greater increase in the knockout mice than the wild type.
Reference: Ito et al. (2008, 096823) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto (Specific pathogen-free) **Age:** 13-14 wk	CAPs (f-PM), Yokohama City, Japan. **Particle Size:** 0.1-2.5 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** 0.6-1.5 mg/m^3 **Time to Analysis:** Three groups exposed to: (1) filtered air for 4 days, (2) filtered air for 3 days and CAPs for 1 day or (3) CAPs for 4 days. All groups exposed for a maximum of 4.5 h/days for 4 consecutive days.	**mRNA Expression and Cardiovascular Function:** In samples of heart tissue, the mRNA of cytochrome P450 (CYP) 1B1, heme oxygenase-1 (HO-1), and endothelin A (ETA) receptor were up-regulated by CAPs; their levels were significantly correlated with the cumulative weight of CAPs in the exposure chamber. The up-regulation of ETA receptor mRNA was significantly correlated with the increase in HO-1 mRNA and weakly with the increase in MBP.

Study	Pollutant	Exposure	Effects
Reference: Khandoga A et al. (2004, 087928) **Species:** Mouse **Gender:** Female **Strain:** C57B1/6 **Age:** 5-7 wk	UFPs: Ultra fine carbon black particles (Printex 90) **Particle Size:** 14 nm diameter (60% <100 nm)	**Route:** Aortic Infusion **Dose/Concentration:** 1×10^7 and 5×10^7 total particles infused 300 m^2/g surface area **Time to Analysis:** Single exposure, analysis 2 h post-exposure	**Platelet Effects:** Application of UFPs caused significantly enhanced platelet accumulation on endothelium of postsinusodal venules and sinusoids in healthy mice. UFP-induced platelet adhesion was not preceded by platelet rolling but was strongly associated with fibrin deposition and an increase in vWF expression on the endothelial surface. **Inflammatory Effects:** In contrast, inflammatory parameters such as the number of rolling/adherent leukocytes, P-selectin expression/translocation, and the number of apoptotic cells were not elevated. UFPs did not affect sinusoidal perfusion and Kupffer cell function.
Reference: Knuckles et al. (2007, 156652) **Species:** Rat **Gender:** Female (Pregnant, purchased at GD19) **Strain** SD **Age:** 60-90 days **Weight:** 300 g **Use:** RMCs were harvest from 1 day-old neonatal pups	ROFA-L: Leachate **Particle Size:** <0.2 µm	**Route:** Cell Culture **Dose/Concentration:** 3.5 µg/mL **Time to Analysis:** 1 h	**ROFA-L Induced Alterations to the RCM Transcriptosome:** 38 genes were suppressed and 44 genes were induced PE. Genomic alterations in pathways related to IGF-1, VEGF, IL-2, PI3/AKT, CVD, and free radical scavenging were detected. Global gene expression was altered in a manner consistent with cardiac myocyte electrophysiological remodeling, cellular oxidative stress and apoptosis. **ROFA-L Induced Alterations to the RCM Transcription Factor Proteome:** ROFA-L altered the transcription factor proteome by suppressing activity of 24 and activating 40 transcription factors out of 149.
Reference: Knuckles et al. (2008, 191987) **Species:** Mouse **Gender:** Male **Strain:** C57BL/6 **Age:** 8-10 wk **Weight:** NR	DE (single cylinder Yanmar diesel generator burning #2 certified diesel fuel (Chevron-Phillips, Borger, TX) under 100% load) **Particle Size:** $PM_{2.5}$	**Route:** Whole-body Inhalation. Ex Vivo. **Dose/Concentration:** In vivo: 350 µg/m^3; Ex vivo: $PM_{2.5}$ concentration 2-3 mg/m^3 flow rate 500 mL/min **Time to Analysis:** Exposed 4 h. Ex vivo assays.	**Veins:** DE increased vascular reactivity to ET-1. Ex vivo exposed vessels had greater vasoconstriction. L-NAME (an arginine blocker) did not promote constriction in DE-exposed rats but did so in controls. **Arteries:** DE did not significantly alter vascular reactivity. Carbonyls or alkanes alone or with DE did not alter vasoconstriction.
Reference: Kodavanti et al. (2008, 155907) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 12-14 wk	G1: saline (control); G2: Mount Saint Helen's ash (SH); G3: whole suspension of oil combustion PM at high concentration (PM-HD); G4: whole suspension of oil combustion PM at low concentration (PM-LD); G5: saline-leachable fraction of PM high-concentration suspension; G6: zinc sulfate **Particle Size:** $PM_{2.5}$	**Route:** IT Instillation **Dose/Concentration:** Doses (mg/kg/wk) are for 8 and 16 wk (PM-solid and soluble Zn) respectively. G1: 0.00-0.00 and 0.00-0.00; G2: 4.60-0.00 and 2.30-0.00; G3: 4.60-66.8 and 2.30-33.4; G4: 2.30-33.4 and 1.15-16.7; G5: 0.00-66.8 and 0.00-33.4; G6: 0.00-66.8 and 0.00-33.4 **Time to Analysis:** 1 x/wk for 8 or 16 wk; analyzed 48 h after last instillation.	**DNA Damage (left ventricular tissue):** All groups except MSH caused varying degrees of damage relative to control. Total cardiac aconitase activity was inhibited in rats receiving soluble Zn. Analysis of heart tissue revealed modest changes in mRNA for genes involved in signaling, ion channels function, oxidative stress, mitochondrial fatty acid metabolism, and cell cycle regulation in Zn, but not MSH-exposed rats.
Reference: Kooter et al. (2006, 097547) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 12-14 wk	CAP-F = fine (Site I) CAP-UF = fine + ultrafine (Site II) (Netherlands) Some measured components: Ammonium, nitrate, sulfate ions: 56 ± 16% CAP-F mass, 17 ± 6% CAP-UF mass **Particle Size:** 0.15<CAP-F<2.5 0.65-0.75 µm CAP-UF<2.5 0.58-1.41 µm	**Route:** Nose-only Inhalation **Dose/Concentration:** CAP-F 399- 3613 µg/m^3 CAP-UF 269-556 µg/m^3 **Time to Analysis:** 6 h/days for 2 days consecutive, 18 h	**Hematology:** WBC and lymphocytes decreased with both CAP-F and CAP-UF. MPV and MPC (mean platelet volume and component) increased with CAP-UF.

Study	Pollutant	Exposure	Effects
Reference: Kyoso et al. (2005, 186998) **Species:** Rat **Gender:** NR **Strain:** NR **Age:** 15 mo	DE PM and NO_X exposures **Particle Size:** NR	**Route:** Whole-body Inhalation **Dose/Concentration:** PM (mg/m^3): 0.01, 0.109, 0.54, 1.09, 0.01 (from 1.09 concentration w/o PM) NO_X (ppm): 0.19, 0.59, 2.60, 5.53, 5.47 (w/o PM) **Time to Analysis:** Exposed 16 h/days (from 5pm-9am) for 7 mo	All of the resting R-R intervals before exposure were lower at night than during the day, but few changes were found after exposure.
Reference: Lei et al. (2004, 087884) **Species:** Rat **Gender:** Male **Strain:** SD **Weight:** 300-350 g	CAPs from Asian dust storm (Taiwan) Measured Components: Si, Al, S, Ca, K, Mg, Fe, As, Ni, W, V, OC, EC, SO_2, NO_2, nitrate, sulfate **Particle Size:** 0.01- 2.5 µm	**Route:** Nose-only Inhalation **Dose/Concentration:** 315.6 $µg/m^3$ (Low) or 684.5 $µg/m^3$ (High) **Time to Analysis:** Low: Exposed for 6 h. Sacrificed 36 h post-exposure High: Exposed for 4.5 h. Sacrificed 36 h post-exposure Pulmonary hypertension induced 2 wk pre-exposure.	**Hematology:** PM induced a dose-dependent increase in WBCs. No change was seen in RBCs. Platelet results were highly variable.
Reference: Lei et al. (2005, 088660) **Species:** Rat **Gender:** Male **Strain:** SD **Weight:** 200-250 g **Use:** ip STZ (60 mg/kg) dissolved in citric acid buffer administered to 8 rats to induce diabetes; ip citric acid buffer administered to 8 non-diabetic rats	CAPs: Hsin-Chuang, Taipei **Particle Size:** PM: 0.01-2.5 µm	**Route:** IT Instillation **Dose/Concentration:** $PM_{2.5}$: 200 µg in 0.5 mL saline. Components ($µg/m^3$): (9.8-SD 2.4)), EC (3.6-SD 3.2), Sulfate (4.8-SD 1.2), Nitrate (6.3-SD 3.4) **Time to Analysis:** Single dose. Animals sacrificed 24 h post instillation.	**Effects of Diabetes:** Body weight (bw) of diabetic (D) rats (397.5 g) was lower than non-diabetic (ND) rats (483.1 g). Mean plasma glucose level was 163 mg/daysL in ND rats and 448.2 mg/daysL in D rats. D rats had significant greater levels of 8-OHdG in plasma compared to ND rats. D rats had significantly increased levels of plasma [nitrate+nitrite]. No observable changes in TNF-α for D and ND rats. **Effects of PM Exposure ND Rats:** Increase in plasma levels of 8-OHdG and plasma IL-6, TNF-α, and serum CRP. Significant reduction of plasma [nitrate+nitrite]. No significant effect on plasma ET-1. **Effects of PM Exposure STZ-D Rats**: Significant elevation of plasma ET-1. Decrease in plasma [nitrate+nitrite] Plasma 8-OHdG and TNF-α significantly increased. No significant alterations in IL-6 and CRP.
Reference: Lemos et al. (2006, 088594) **Species:** Mouse **Gender:** NR **Strain:** BALB/c **Age:** 1day (neonatal) **n:** 10 **Weight:** 4-6 g	PM_{10}, CO, NO_2, and SO_2 from Universidade de Sao Paulo, Brazil. **Particle Size:** PM_{10}	**Route:** Whole-body Inhalation **Dose/Concentration:** Mean (± SD) concentrations were: CO_2: 2.06 ± 0.08 ppm (8h mean); NO_2: 104.75 ± 42.62 $µg/m^3$ (24 h mean); SO_2: 11.07 ± 5.32 $µg/m^3$ (24 h mean); PM_{10}: 35.52 ± 12.84 $µg/m^3$ (24 h mean) **Time to Analysis:** 24 h/days, 7 days/wk for 4 mo	Morphometric measurements of the ratio between the lumen and the wall (L/W) areas were performed on transverse sections of renal, pulmonary and coronary arteries. A significant decrease of L/W with exposure to air pollution was detected in pulmonary and coronary arteries, whereas no effects of air pollution were observed in renal vessels.
Reference: Li et al. (2005, 088647) **Species:** Rat **Strain:** SD **Tissues/Cell Types:** Cultured HPAECs; Pulmonary Artery Rings (PARs)	Urban Particles (UPs SRM 1648) Major Constituents (mass fraction in %): Al (3.4), Fe (3.9), K (1.1). Minor Constituents (mass fraction in %): Na (0.43), Pb (0.66), Zn (0.48). Trace Constituents (ng/mg): As (115), Cd (75), Cr (403), Cu (609), Mn (786), Ni (82), Se (27), U (5.5), V (127). **Particle Size:** NR	**Route:** PARs: In vitro organ model HPAECs: grown to 80% confluence **Dose/Concentration:** PARs and HPAECs: 1 to 100 µg/mL; Losartan treatment: 0.2 µmol Captopril treatment: 100 µmol **Time to Analysis:** PARs were exposed to increasing doses of UPs from 1 to 100 µg/mL. Maximum tension was recorded within 5 min after each UPs dose. HPAECs: exposed to UPs from 1 to 100 µg/mL for up to 2 min	Effects of UPs on the constriction of isolated rat pulmonary PARs and the activation of extracellular signal-regulated kinases 1 and 2 (ERK1/2) and p38 mitogen-activated protein kinases (MAPKs) in HPAECs with or without Losartan at 1-100 µg/mL induced acute vasoconstriction. UPs also produced a time- and dose-dependent increase in phosphorylation of ERK1/2 and p38 MAPK. Losartan pre-treatment inhibited both vasoconstriction and activation of ERK1/2 and p38. The water soluble fraction of UPs was sufficient for inducing ERK1/2 and p38 phosphorylation, which was also inhibited by Losartan. Cu (CuSO4) and V (VOSO4), induced pulmonary vasoconstriction and phosphorylation of ERK1/2 and p38, but only phosphorylation of p38 was inhibited by Losartan. UPs induced activation of ERK1/2 and p38 was attenuated by Captopril.

Study	Pollutant	Exposure	Effects
Reference: Li et al. (2006, 156693) **Species:** Rat, Rabbit, and Human **Tissues/Cell Types:** Pulmonary Artery Rings (PARs) (rat); isolated buffer-infused lungs (rabbits) and cultured HPAECs **Strain:** SD Rats, New Zealand White Rabbits **Weight:** Rat: 200-350 g; Rabbit: 2.5-3.0 kg	Urban Particles (UPs SRM 1648). Major Constituents (mass fraction in %): Al (3.4), Fe (3.9), K (1.1). Minor Constituents (mass fraction in %): Na (0.43), Pb (0.66), Zn (0.48). Trace Constituents (ng/mg): As (115), Cd (76), Cr (403), Cu (609), Mg (786), Ni (82), Se (27), U (5.5), V (127). **Particle Size:** NR	**Route:** In Vitro **Dose/Concentration:** PARs and HPAECs: 1 to 100 µg/mL **Time to Analysis:** PARs: treatment given 15 min prior to exposure. Exposed to increasing doses of UPs from 1 to 100 µg/mL. Maximum tension was recorded within 5 min after each UPs dose. HPAECs: exposed to UPs from 1 to 100 µg/mL for 20 and 120 min.	**Effects of UP on H_20_2 Release:** Within minutes after UPs treatment, HPAEC increased H_2O_2 production that could be inhibited by DPI, APO, and NaN_3. The water soluble fraction of UPs as well as its two transition metal components Cu and V, also stimulated H_2O_2 production. NaN_3 inhibited H_2O_2 production stimulated by Cu and V, whereas DPI and APO inhibited only Cu-stimulated H_2O_2 production. Inhibitors of other H_2O_2-producing enzymes, including N-methyl-L-arginine, indomethacin, allopurinol, cimetidine, rotenone, and antimycin, had no effects. **Effects of UP-induced H_20_2 on MAPK Activation:** DPI but not NaN_3 attenuated UPs-induced pulmonary vasoconstriction and phosphorylation of ERK1/2 and p38 MAPKs. Knockdown of p47phox gene expression by small interfering RNA attenuated UPs-induced H_2O_2 production and phosphorylation of ERK1/2 and p38 MAPKs.
Reference: Lippmann et al. (2005, 087453) **Species:** Mouse **Strain:** C57 and ApoE$^{-/-}$	(March-September 2003). Chemical Composition: regional secondary sulfate (SS) characterized by high S, Si, and organic C; resuspended soil (RS) characterized by high concentrations of Ca, Fe, Al, and Si; RO-fired powered emissions of the Eastern U.S. identified by the presence of V, Ni, and Se; and motor vehicle (MV) traffic and other sources. Contributors to Average Mass: SS (56.1%), RS (11.7%), RO combustion (1.4%), MV traffic and other sources (30.9%) **Particle Size:** $PM_{2.5}$	**Route:** Whole-body Inhalation **Dose/Concentration:** $PM_{2.5}$ concentrated ten-fold, producing an average of 113 µg/m^3 **Time to Analysis:** 6 h/days, 5 days/wk for 5 mo. Parameters measured daily: during exposure, the afternoon after exposure, and late at night	**Associations Between Sources and Short-term Heart Rate Changes**: There were no significant associations between SS, RS, RO, and MV factors and HR in C57 mice at any of the three intervals. There were significant associations between $PM_{2.5}$ and the RS source factor and decreases in HR for the ApoE$^{-/-}$ mice during the daily CAPs exposures but no associations with the other factors. There was no residual association of HR with $PM_{2.5}$ or the RS factor later in the afternoon or late at night. In the afternoon, there was a significant association between decreases in HR and the SS factor for the ApoE$^{-/-}$ mice that had not been present during exposure and did not persist into the night time period. MV traffic and others were not significantly associated with HR during any of these three time periods. For the C57 mice, there were no significant associations of HR with $PM_{2.5}$ or any of its components during any of the three daily time periods. **Associations Between Sources and Short-term HRV Changes:** Signal noise during exposures did not permit reliable analyses of HRV changes during the hours of CAP exposure.
Reference: Lippmann et al. (2005, 087453) **Species:** Mouse **Gender:** NR **Strain:** ApoE$^{-/-}$, ApoE$^{-/-}$ LDLr$^{-/-}$, C57BL/6 **Age:** NR **Weight:** NR	CAPs (Sterling Forest, spring-summer 2003) **Particle Size:** $PM_{2.5}$	**Route:** Inhalation **Dose/Concentration:** $PM_{2.5}$ average concentration: 110 µg/m^3, Long-term average: 19.7 µg/m^3 **Time to Analysis:** Exposed 6 h/days, 5 days/wk, 5 or 6 mo. Semicontinuous EKG recordings.	HR increased in ApoE$^{-/-}$ mice but not C57 mice. HRF increased over the duration of the experiment. Atherosclerotic plaque deposits and coronary artery disease lesions occurred in both CAPs-exposed mice and controls, but invasive lesions were only present in CAPs-exposed mice. A gene affecting circadian rhythm was upregulated in double knockout mice. CAPs activated NF-κB. No inflammation occurred in the pulmonary system.
Reference: Lippman M et al. (2006, 091165) **Species:** Mouse **Gender:** Male **Strain:** ApoE$^{-/-}$ **Age:** 6 wk	CAPs from Tuxedo, NY. Component of interest: Ni. **Particle Size:** $PM_{2.5}$	**Route:** Whole-body Inhalation **Dose/Concentration:** Average daily CAPs: 85.6 µg/^{m3}; Average daily Ni: 43 ng/m^3 **Time to Analysis:** 6 h/day, 5 days/wk, for 6 mo (July 2004-January 2005). 10-s ECG, HR, activity, and body temperature data were sampled every 5 min for the duration of the experiment.	For the CAPs-exposed mice, on 14 days there were Ni peaks at approximately 175 ng/m^3 and usually low CAPs and V. For those days back-trajectory analysis identified a remote Ni point source. ECG measurements on CAPs-exposed and sham-exposed mice showed Ni to be significantly associated with acute changes in HR and HRV.

Study	Pollutant	Exposure	Effects
Reference: Lund et al. (2007, 125741) **Species:** Mouse **Gender:** Male **Strain:** ApoE$^{-/-}$ **Age:** 10 wk **Use:** Mice were placed on a high fat at the beginning of the exposure.	Varying dilutions of gasoline emissions: (generated using two 1996 model 4.3L General Motors V-6 engines, fueled with conventional, unleaded, non-oxygenated gasoline, equipped with stock exhaust systems). Composition for Hi, Med, and Lo dilutions: PM, NO_X, CO, and Total Hydrocarbons (THC) **Particle Size:** NR	**Route:** Whole-body Inhalation **Dose/Concentration:** FA: PM (2 µg/m^3), NO_X (0 ppm), CO (0.1 ppm), HC (0.1 ppm); Low (1: 90 dilution of exhaust): PM (8 µg/m^3), NO_X (2 ppm), CO (9 ppm), HC (0.9 ppm); Mid (1: 20): PM (39 µg/m^3), NO_X (12 ppm), CO (50 ppm), HC (8.4 ppm); High (1: 12): PM (61 µg/m^3), NO_X (19 ppm), CO (80 ppm), HC (12 ppm); High-filtered (1:12): PM (2 µg/m^3), NO_X (18 ppm), CO (80 ppm), HC (12.7 ppm). **Time to Analysis:** 6 h/day, 7 days/wk for 7 wk. Mice were sacrificed within 16 h PE. During the study period all animals concurrently exposed to the following: FA: 8 µg/m^3 and 40 µg/m^3; PM Whole Exhaust: 60 µg/m^3; or Filtered Exhaust w/ gases matching the 60 µg/m^3 concentration.	Inhalation exposure to gasoline engine emissions resulted in increased aortic mRNA expression of matrix metalloproteinase-3 (MMP-3), MMP-7, and MMP-9, tissue inhibitor of MMP-2, ET-1 and HO-1 in ApoE$^{-/-}$ mice; increased aortic MMP-9 protein levels were confirmed through immunochemistry. Elevated ROS were also observed in arteries from exposed animals, despite absence of plasma markers. Similar findings were also observed in the aortas ApoE$^{-/-}$ mice exposed to particle filtered atmosphere, implicating the gaseous components of the whole exhaust in mediating the expression of markers associated with vasculopathy.
Reference: Lund et al. (2007, 125741) **Species:** Mouse **Gender:** Male **Strain:** ApoE$^{-/-}$ **Age:** 10 wk **Weight:** NR	GEE (conventional unleaded, nonoxygenated, nonreformulated gasoline- ChevronPhillips Specialty Fuels Division) **Particle Size:** 0.150 µm (MMAD)	**Route:** Inhalation **Dose/Concentration:** PM: 60 µg/m^3, NO_2: 2 ppm, NO: 16 ppm, CO: 80 ppm, THC: 12.7 ppm **Time to Analysis:** Mice fed high-fat diet 30 days before exposure. Exposed 6 h/day, 1 or 7 days. Some groups dosed with Tempol or BQ-123. Killed within 18 h of last exposure.	Aorta gelatinase activity increased with GEE exposure time. MMP-2/9 activity spread throughout the vasculature by day 7. 7 day GEE exposure significantly increased the aorta protein expression of MMP-9, MMP-2, TIMP-2, and plasma MMP-9. Generally, in GEE-exposed mice, Tempol decreased TBARS and vascular ET-1, and BQ-123 decreased vascular ROS, ET-1, MMP-9, and gelatinase activity.
Reference: McQueen et al. (2007, 096266) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Weight:** 228-500 g	DEP: SRM 2975 (NIST) **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 0.5 mL/rat of 1 mg/mL; 1-2.2 mg/kg **Time to Analysis:** 6 h. Pre-exposure: Vagotomy (sectioning of vagus nerve) or atropine, 1mg/kg i.p. administered 30 min prior, 2 and 4 h post.	**Cardiovascular Response:** Blood pressure and heart rate were unaffected. Average arterial O_2 increased after DEP, but not when compared for each animal. CO_2 and pH were not affected
Reference: Medeiros et al. (2004, 096012) **Species:** Mouse **Gender:** Male **Strain:** BALB/c **Age:** 60 days **Weight:** 20-30 g	CP: Carbon particles PSA: ROFA (solid waste incinerator hospital Sao Paulo, Brazil) PSB: electric precipitator, steel plant, Brazil) PSA/PSB Characteristics: Generally, PSB had greater component concentrations than PSA: Br (100+x), Cr (3x), Fe (10+x), Mn (2x), Rb (60+x), Se (7x), Zn (4x). PMA>PMB: Ce (3x), Co (10+x), La (100x), Sb (15x), V (50x). **Particle Size:** CP: 1.7 ± 2.5 µm (78%<2.5 µm) PMA: 1.2 ± 2.2 µm(98 %<2.5 µm) PMB: 1.2 ± 2.2 µm (98%<2.5 µm)	**Reference:** Intranasal Instillation **Dose/Concentration:** CP: 10 µg/mouse; 0.5mg/kg PSA: 0.1, 1 or 10 µg/mouse; 0.005, 0.05, 0.5 mg/kg PSB: 0.1, 1 or 10 µg/mouse; 0.005, 0.05, 0.5 mg/kg **Time to Analysis:** Single, 24 h	**Hematology:** PSA and PSB decreased leukocyte count (all 3 doses) and platelet count (2 high doses). No effect on hemoglobin, erythrocytes and reticulocytes was observed. Fibrinogen levels increased for both PSB and PSA with PSB seeing a higher increase. None of the effects were dose-dependent. **Bone Marrow:** Erythroblasts increased for PSA at all dose levels and PSB at mid and high dose levels (high variability).

Study	Pollutant	Exposure	Effects
Reference: Montiel-Davalos et al.(2007, 156778) **Species:** Human **Cell Types:** HUVEC (from primary human endothelial cells) and U937 (human leukemia pro-monocytic) cell cultures.	$PM_{2.5}$ and PM_{10} from Mexico City **Particle Size:** $PM_{2.5}$, PM_{10}	**Route:** In Vitro **Dose/Concentration:** HUVEC TNF-α (10 ng/mL), and a PM range of 5, 10, 20, and 40 μg/cm^2 concentrations. **Time to Analysis:** 6 or 24 h (early and late adhesion molecules respectively)	Results showed that both $PM_{2.5}$ and PM_{10} induced the adhesion of U937 cells to HUVEC, and their maximal effect was observed at 20 μg/cm^2. This adhesion was associated with an increase in the expression of all adhesion molecules evaluated for PM_{10}, and E-selectin, P-selectin, and ICAM-1 for $PM_{2.5}$. In general the maximum expression of adhesion molecules induced by $PM_{2.5}$ and PM_{10} was obtained with 20 μg/cm^2; however PM_{10}-induced expression was observed from 5 μg/cm^2. E-selectin and ICAM-1 had the strongest expression in response to particles.
Reference: Moyer et al. (2002, 052222) **Species:** Mouse **Gender:** Male and Female **Strain:** B6C3F1	In phosphide (InP), Co sulfate heptahydrate ($CoSO_4 \cdot 7H_2O$), Vanadium pentoxide(V_2O_5) Gallium arsenide (GaAs), Ni oxide (NiO), Ni subsulfide (Ni_3S_2), Ni sulfate hexahydrate ($NiSO_4 \cdot 6H_2O$), talc, and Mo trioxide (MoO_3) **Particle Size:** MMAD particle size (μm): InP (1.1-1.3), $CoSO_4 \cdot 7H_2O$ (1.5-1.8), V_2O_5: (1.0), GaAs: (1.0)	**Route:** Inhalation **Dose/Concentration:** High-Dose Concentration in Chronic Studies, Male (μg/m^3): InP: 0.3, $CoSO_4 \cdot 7H_2O$: 3.0, V_2O_5: 4.0, GaAs: 1.0 High-Dose Concentration in Sub-Chronic Studies, Male or Female (μg/m^3): InP: 100, $CoSO_4 \cdot 7H_2O$: 30, V_2O_5: 16, GaAs: 75 **Time to Analysis:** Phase One: Evaluation of heart, kidney and lung tissues from all control and high dose male B6C3F1 mice exposed by inhalation to 9 particulate compounds for a 2yr period. Phase Two: evaluated heart, lung, kidney and mesentery tissues of control and high dose male and female B6C3F1 mice from the 90-day studies of the 4-compounds demonstrating arteritis after a 2-yr period.	**Phase One:** High-dose males developed significantly increased incidences of arteritis over controls in 2 of the 9 studies (InP and $CoSO_4 \cdot 7H_2O$), while marginal increases of arteritis were detected in 2 additional studies (V_2O_5 and GaAs). In contrast, arteritis of the muscular arteries of the lung was not observed. Morphological features of arteritis in these studies included an influx of mixed inflammatory cells including neutrophils, lymphocytes, and macrophages. Partial and complete effacement of the normal vascular wall architecture, often with the extension of the inflammatory process into the periarterial connective tissue, was observed. **Phase Two:** Results showed that arteritis did not develop in the 90-day studies, suggesting that long-term chronic exposure to lower-dose metallic PM may be necessary to induce or exacerbate arteritis.
Reference: Mutlu et al. (2007, 121441) **Species:** Mouse **Gender:** Male **Strain:** 57BL/6 (IL-6$^{+/+}$ and IL-6$^{-/-}$) **Age:** 6-8 wk **Weight:** 20-25 g	PM_{10} from ambient air in Düsseldorf, Germany **Particle Size:** PM_{10}	**Route:** IT Instillation **Dose/Concentration:** PM_{10}: 10 μg; Clodronate: 120 mg **Time to Analysis:** For alveolar macrophage depletion, clodronate instilled into mice lungs following endotracheal intubation 48 h prior to instillation of PM. Parameters measured 24 h post-exposure.	Mice treated with PM_{10} exhibited a shortened bleeding time, decreased prothrombin and partial thromboplastin times (decreased plasma clothing times), increased levels of fibrinogen, and increased activity of factors II, VIII, and X. This prothrombotic tendency was associated with increased generation of intravascular thrombin, an acceleration of arterial thrombosis, and an increase in BALF concentration of prothrombotic IL-6. IL-6$^{-/-}$ mice were protected against PM-induced intravascular thrombin formation and the acceleration of arterial thrombosis. Depletion of macrophages by the IT administration of liposomal clodronate attenuated PM-induced IL-6 production and the resultant prothrombotic tendency.
Reference: Nadziejko et al. (2002, 087460) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 16 wk	CAPs ($PM_{2.5}$) from Tuxedo, NY. (SO_2, NO_2 O_3 and NH_3 were removed prior to exposure). H_2SO_4 (fine and ultrafine) **Particle Size:** Ultrafine H_2SO_4 50-75 nm (MMAD)	**Route:** Nose-only Inhalation **Dose/Concentration:** CAPs: 80 and 66 μg/m^3 (avg 73); Fine H_2SO_4: 299, 280, 119, and 203 μg/m^3 (avg 225); Ultrafine H_2SO_4: 140, 565, 416, 750 μg/m^3 (avg 468) **Time to Analysis:** 4 h/exposure	Exposure to CAPs caused a striking decrease in respiratory rate that was apparent soon after the start of exposure and stopped when exposure to CAPs ceased. The decrease in respiratory rate was accompanied by a decrease in HR. Exposure of the same animals to fine-particle-size H_2SO_4 aerosol also caused a significant decrease in respiratory rate similar to the effect of CAPs. Ultrafine H_2SO_4 had the opposite effect on respiratory rate compared to CAPs.
Reference: Nadziejko et al. (2004, 055632) **Species:** Rat **Gender:** Male **Strain:** F344 **Age:** 18 mo	PM/CAPs (Tuxedo, NY) UFC (lab generated) SO_2 **Particle Size:** PM (Size Range): 0.5-2.5μm; UFC (MMAD): 30-50 nm	**Route:** Nose-only Inhalation **Dose/Concentration:** PM (μg/m^3): 161-200, avg. 180; UFC (μg/m^3): 500-1280, avg. 890; SO_2 (ppm): 1.2, 1.2, avg. 1.2 **Time to Analysis:** A total of 8 exposures were performed: 2 exposures to CAPs, 2 exposures to UFC, 4 exposures to SO_2. All three pollutants were tested w/ a crossover design so that each group alternated exposure to air and to pollutant. Exposures lasted 4 h and were performed at least 1wk apart. Parameters measured throughout duration of experiment.	Old F344 rats had many spontaneous arrhythmias. There was a significant increase in the frequency of irregular and delayed beats after exposure to CAPs. The same rats were subsequently exposed to UFC, SO_2 or air with repeated crossover design. In these experiments there was no significant change in the frequency of any category of spontaneous arrhythmia following exposure to UFC or SO_2.

Study	Pollutant	Exposure	Effects
Reference: Nemmar et al. (2008, 096566) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Weight:** 440 ± 14 g	DEP (SRM 2975) **Particle Size:** <1 µm	**Route:** Intravenous via the tail vein **Dose/Concentration:** DEP: 0.02mg or 0.1mg DEP/kg (corresponding to about 8 µg or 44 µg DEP/rat) **Time to Analysis:** 48 h following systemic administration of saline or DEP	Intravenous administration of DEP (0.1 mg/kg) triggered systemic inflammation characterized by an increase in monocyte an granulocyte numbers. Both doses of DEP caused a reduction of RBC numbers and hemoglobin concentration. TEM analysis of RBCs after in vitro incubation (5 µg/mL) or in vivo administration of DEP, revealed the presence of ultrafine-sized aggregates of DEP within the RBC. Larger aggregates were also taken up by the RBC. The myocardial morphology and capillary bed were not affected by DEP exposure.
Reference: Nemmar et al. (2007, 156800) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 16 wk **Weight:** 424 ± 8 g	DEP (SRM 2975) **Particle Size:** NR	**Route:** Tail Vein Injection **Dose/Concentration:** 8, 42, or 212 µg DEP/rat (150µl of 0.02, 0.1, or 0.5 mg/kg) **Time to Analysis:** 24 h	**Effect of DEP on Blood Pressure:** Significant decrease on BP in DEP-exposed rats at doses of 0.02 mg/kg, compared with mean BP observed in controls. **Effect of DEP on HR**: Doses of 0.02, 0.1, and 0.5 mg/kg in rats, resulted in significant reduction of HR compared to controls. **Effect of DEP on Tail Bleeding Time:** Shortening of tail bleeding time in rats exposed to 0.02, 0.1, and 0.5 mg/kg. The shortening was significant at the dose of 0.02 and 0.5 mg/kg compared w/ controls. Platelet counts in blood did not significantly increased post-DEP administration. **Effect of DEP on WBC and RBC Numbers:** No significant effect of DEP at doses of 0.02, 0.1 and 0.5 mg/kg on the numbers of granulocytes, monocytes, or lymphocytes compared with control.
Reference: Nemmar et al. (2003, 096567) **Species:** Hamster **Gender:** Male and Female **Weight:** 100-110 g	DEP (SRM 1650) **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 120 µl (5, 50, or 500 µg/animal) **Time to Analysis:** In-vivo: formation and embolization of thrombus were continuously monitored for 40 min. Ex-vivo: animals were ITly instilled w/ DEPs (0 or 50 µg per animal), and blood was collected 5, 15, 30, and 60 min post-instillation. In-vitro: Saline or saline-containing DEPs (0.1, 0.5, 1, and 5 µg/mL) was added to venous blood from untreated hamsters, and closure time was measured in the PFA-100 after 5 min/animal.	Doses of 5-500 µg enhanced experimental arterial and venous platelet-rich thrombus formation in-vivo. Blood samples taken from hamsters 30 and 60 min after instillation of 50 µg of DEPs yielded accelerated aperture closure (platelet activation) ex-vivo, when analyzed in the PFA-100. The direct addition of as little as 0.5 µg/mL DEPs to untreated hamster blood significantly shortened closure time in vitro.
Reference: Nemmar et al. (2004, 087959) **Species:** Hamster **Gender:** Male and Female **Weight:** 100-110 g	DEP (SRM 1650); Positively Charged Polystyrene Particles (PCPSP) **Particle Size:** PCPSP: 400 nm; DEP: NR	**Route:** IT Instillation **Dose/Concentration:** DEP: 50 µg/animal, or PCPSP: 500 µg/animal **Time to Analysis:** Pretreatment Phase: Hamsters were pretreated w/ Dexametasone IP (5 mg/kg) or IT (0.1 or 0.5 mg/kg) or Sodium Cromoglycate given IP (40 mg/kg), 1 h before DEP or vehicle instillation. Thrombosis: In-vivo thrombogenesis assessed 24 h post-instillation of DEP or vehicle.	DEP increased thrombosis without elevating plasma vWF. The IT instillation of PCPSP equally produced histamine release and enhanced thrombosis. Histamine in plasma resulted from basophil activation. IP pretreatment with Dexametasone abolished the DEP-induced histamine increase in BALF and plasma and abrogated airway inflammation and thrombogenicity. The IT pretreatment with Dexametasone showed a partial but parallel inhibition of all these parameters. Pretreatment with Sodium Cromoglycate strongly inhibited thrombogenicity, and histamine release.
Reference: Nemmar et al. (2003, 097487) **Species:** Hamster **Gender:** Male and Female **Weight:** 100-110 g	Ultrafine Particles: Unmodified Polystyrene Particles (UPSPs); Negatively Charged Carboxylate-Modified Polystyrene Particles (NCC-MPSPs); Positively-Charged Amine Modified Polystyrene Particles (PCA-MPSPs) **Particle Size:** UPSPs: 60 nm; NCC-MPSPs: 60 nm; PCA-MPSPs: 60 or 400 nm	**Route:** IT Instillation **Dose/Concentration:** 5, 50, and 500 µg/animal in 120 µl saline **Time to Analysis:** 1 h post-instillation	Unmodified and negative UFPs did not modify thrombosis. Positive UFPs increased thrombosis at 500 and 50 µg/animal, but not at 5 µg/animal. Positive 400 nm particles (500 µg/animal) did not affect thrombosis. PFA-100 analysis showed that platelets were activated by the in-vitro addition of positive UFPs and 400 nm particles to blood.

Study	Pollutant	Exposure	Effects
Reference: Nemmar et al. (2003, 087931) **Species:** Hamster **Weight:** 100-110 g	DEP (SRM 1650) **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 50 µg/animal in 120 µl saline **Time to Analysis:** 1, 3, 6, and 24 h	At 1, 6, and 24 h after instillation of 50 µg DEPs, the mean size of in-vivo induced and quantified venous thrombosis was increased by 480, 770, and 460%, respectively. Platelets activation in blood was confirmed by a shortened closure time in the PFA-100 analyzer. In plasma, histamine was increased only at 6 and 24 h. Pre-treatment with a H1 receptor antagonist (diphenhydramine, 30 mg/kg intraperitoneally) did not affect DEP-induced thrombosis or platelet activation at 1 h; however both were markedly reduced at 6 and 24 h.
Reference: Niwa et al. (2007, 091309) **Species:** Mouse **Gender:** Male **Strain:** LDLr/KO **Age,:** 6 wk (n = 20) **Use:** IT CB dispersion; 10-14 wk acute effect of CB dispersion on circulating CRP	Carbon Black **Particle Size:** 23-470 nm (mean size 120.7 nm)	**Route:** IT Dispersion **Dose/Concentration:** IT CB Dispersion Study: 1 mg per animal/wk; Acute Effect of CB Dispersion on Circulating CRP Study: 1mg/animal (single administration) **Time to Analysis:** IT CB Dispersion Study: 1x/wk for 10 wk Acute Effect of CB Dispersion on Circulating CRP Study: Single CB administration, blood samples collected 24 h post-administration	**IT CB Dispersion Study:** Although no difference in body weight (bw) between the four groups was observed at baseline, and all mice experienced an increase in bw with advancing age, the mice treated with CB tended to be smaller than those treated with vehicle (air). No significant differences were observed in cholesterol and TG levels among the for groups. Development of aortic lipid-rich lesions occurred in mice under a 0.51% cholesterol diet with or without CB infusion, but not in the mice fed a 0% cholesterol diet. **Acute Effect of CB Dispersion on Circulating CRP Study:** Circulating levels of CRP were significantly higher in mice exposed to CB versus those exposed to air, indicating an acute inflammatory response. Although the presence of CB in pulmonary macrophage-like cells in CB treated mice under 0.51% cholesterol diet was confirmed, CB was not detected in aortas, livers, kidneys, or spleens.
Reference: Niwa et al. (2007, 091309) **Species:** Mouse **Cell Types:** RAW264.7	Carbon Black (CB); Water-Soluble Fullerene ($C_{60}(OH)_{24}$); Fluoresbrite Carboxylate Microspheres; Ox-LDL; Acetylated-LDL **Particle Size:** Carbon Black and $C_{60}(OH)_{24}$: 7.1 nm (SD 2.4); Fluoresbrite Carboxylate Microspheres: 6 nm	**Route:** Cell Culture **Dose/Concentration:** CB: 1, 10, 100 µg/mL; $C_{60}(OH)_{24}$: 20, 100ng/mL **Time to Analysis:** RAW264.7+CB for 24 h, 13 days, and 50 days; RAW264.7+ $C_{60}(OH)_{24}$ for 24 h or 10 days; RAW264.7+ $C_{60}(OH)_{24}$ for 8 days, then co-treated w/ Ox-LDL for an additional 48 h; RAW264.7+Ox-LDL for 5 days, and then co-cultured w/ C60(OH)24 for an additional 48 h; RAW264.7+ 6 nm beads: 3 days, the Ox-LDL or acetylated-LDL added for 24 h	CB alone had no significant effects on RAW264.7 cell growth. $C_{60}(OH)_{24}$ alone or CB and $C_{60}(OH)_{24}$ together w/ Ox-LDL induced cytotoxic morphological changes, such as Ox-LDL uptake-induced foam cell-like formation and decreased cell growth, in a dose-dependent manner. $C_{60}(OH)_{24}$ induced LOX-1 protein expression, pro-matrix metalloprotease-9 protein secretion, and tissue factor mRNA expression in lipid-laden macrophages. Although CB or $C_{60}(OH)_{24}$ alone did not induce platelet aggregation, $C_{60}(OH)_{24}$ facilitated ADP-induced platelet aggregation. $C_{60}(OH)_{24}$ also acted as a competitive inhibitor of ADP receptor antagonists in ADP-mediated platelet aggregation.
Reference: Niwa et al. (2008, 156812) **Species:** Rat **Strain:** SD **Age:** 6 wk	CB from Kyoto, Japan **Particle Size:** Mean size (nm) ± SD determined at 1, 8, 15, 22, and 29 day post-exposure was 118.1 ± 2.4, 119.1± 2.7, 122.2 ± 2.0, 122.4 ± 2.5 and 121.0 ± 3.6 respectively	**Route:** Whole-body Inhalation **Dose/Concentration:** 15.6 ± 3.5 mg/m^3 **Time to Analysis:** 6 h/day, 5 days/wk, for a total of 4 wk. BP and HR were measured by tail-cuff plethysmography at 1, 14, and 28 day post -exposure. Sacrificed At 1, 7, 14, 28, and 30 day post-exposure	Although the presence of CB was confirmed in pulmonary macrophages, electron microscopic survey did not detect CB in other tissues including, liver, spleen and aorta. CB exposure raised blood pressure levels in a exposure-time dependent manner. Levels of circulating inflammatory marker proteins, including monocyte chemo attractant protein-1, IL-6, and CRP, were higher in the CB treated groups than in control groups.
Reference: Nurkiewicz et al. (2004, 087968) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** 7-8 wk	ROFA (from Everett, MA). Major metal contaminants are: Fe, Al, V, Ni, Ca, and Z. Main soluble metals are: Al, Ni, and Ca. **Particle Size:** 2.2 µm (ROFA mean count diameter)	**Route:** IT Instillation **Dose/Concentration:** ROFA group: 0.1, 0.25, 1, or 2 mg/rat. Vehicle control group: 300 µl saline. Particle control group: TiO_2 0.25 mg/rat. **Time to Analysis:** After single IT instillation of a particular dose, all rats recovered for 24 h.	**Saline Treated Rats:** A23187 dilated arterioles up to 72 ± 7% max. **ROFA and TiO_2 Exposed Rats:** A23187-induced dilation was significantly attenuated. **Sensitivity of Arteriolar Smooth Muscle to NO:** Similar in saline treated and ROFA exposed rats. **Other:** Significant increase in venular leukocyte-adhesion and rolling observed in ROFA exposed rats.

Study	Pollutant	Exposure	Effects
Reference: Nurkiewicz et al. (2006, 088611) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** 7-8 wk	ROFA from Everett, MA **Particle Size:** ROFA mean count diameter: 2.2 µm; TiO_2 mean diameter: 1.0 µm	**Route:** IT Instillation **Dose/Concentration:** ROFA group: 0.1 or 0.25 mg/rat. Vehicle control group: 300 µl saline. Particle control group: TiO_2 0.1 or 0.25 mg/rat. **Time to Analysis:** After single IT instillation of a particular dose, all rats recovered for 24 h.	**ROFA or TiO_2 Exposure and Arteriolar Dilation:** Exposure caused a dose-dependent impairment of endothelium-dependent arteriolar dilation. **ROFA or TiO_2 Exposure and Arteriolar Constriction:** Exposure did not affect microvascular constriction in response to PHE. **ROFA and TiO_2 and Leukocyte Rolling and Adhesion:** Exposure significantly increased leukocyte rolling and adhesion in aired venules, and these cells were identified as PMN leukocytes. **ROFA and TiO_2 and MPO:** MPO was found in PMN leukocytes, adhering to the systemic microvascular wall. Evidence suggests that some of this MPO had been deposited in the microvascular wall. There was also evidence of oxidative stress in the microvascular wall.
Reference: Nurkiewicz et al. (2008, 156816) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** 6-7wk **Weight:** NR	TiO_2 (DeGussa, Sigma-Aldrich) **Particle Size:** Fine- 1 µm, UF- 21 nm	**Route:** Whole-body Inhalation **Dose/Concentration:** Concentrations: Fine- 3-16 mg/m^3; UF- 1.5-12 mg/m^3; Dose: Fine- 8, 20, 36, 67, 90 µg; UF- 4, 6, 10, 19, 30 µg **Time to Analysis:** Acclimated 5 days. Exposed 4-12 h. Sacrificed 24 h post-exposure.	Particle accumulation within AMs, anuclear macrophages, particle-laden AMs intimately associated with the alveolar wall were all present in exposed rats. Calcium ionophore impaired arteriolar dilation in a dose-dependent manner in UF and fine exposed rats. UF produced greater systemic microvascular dysfunction. Microvascular dysfunction was the same for three groups of rats exposed to 30 µg UF TiO_2 under different conditions.
Reference: Nurkiewicz et al. (2009, 191961) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** 7-8 wk **Weight:** NR	Fine TiO_2 (Sigma-Aldrich, St. Louis, MO) (~99% rutile) TiO_2 nanoparticles (DeGussa-Aeroxide TiO_2 P25, Parsippany, NJ) (80% anatase, 20% rutile) **Particle Size:** Fine TiO_2- MMAD: 402 nm, Primary size: <5 µm, ,CMD: 710 nm; Nano-TiO_2- MMAD: 138 nm, Primary size: 21 nm, , CMD: 100 nm	**Route:** Aerosol Inhalation **Dose/Concentration:** 1.5-16mg/m^3 **Time to Analysis:** Acclimated 5 days. Exposed 240-720 min. Anesthetized 24 h post-exposure. Intravital microscopy, NO measurement, microvascular oxidative stress measurement, nitrotyrosine staining.	**Arteriolar Dilation:** Nano-TiO_2 significantly impaired endothelium-dependent arteriolar dilation. Equivalent levels of arteriolar dysfunction were found in fine and nano-TiO_2. Arteriolar dilation in response to abluminal microiontophretic application of SNP was not different from the controls or between the exposure groups. Arteriolar dilation was partially restored by radical scavenging with TEMPOL and catalase, NADPH oxidase with apocynin, and MPO inhibition with ABAH. **Microcirculation:** ROS increased in both groups. Nano-TiO_2 significantly increased the area of tissue containing nitrotyrosine in the lung and spinotrapezius microcirculation. **NO:** Fine and nano-TiO_2 significantly and dose-dependently decreased stimulated NO production in isolated microvessels. NO production was increased by radical scavenging with TEMPOL and catalase or NADPH oxidase with apocynin, and was largest in the fine TiO_2 group.

Study	Pollutant	Exposure	Effects
Reference: Okayama et al. (2006, 156824) **Species:** Rat **Cell Type:** Ventricular Cardiac Myocytes from Wistar Rats, approximately 3 days old	DEP (Tsukuba, Japan) DEPE: 5g of DEP in 5 mL PBS containing 0.05% Tween 80. Others: Catalase, LDH, MPG and SOD. **Particle Size:** DEP mass median diameter: 0.34 µm.	**Route:** In Vitro **Dose/ Concentration:** DEPE: 0-100 µg/mL; MPG: 0-1 mM; SOD: 800 U/mL; Catalase: 500 U/mL **Time to Analysis:** cells were incubated for 1, 2, 4, or 8, 24 or 48 h. LDH Activity of Supernatant: 24 h post-DEPE exposure. SOD, Catalase, MPG on DEPE-induced Toxicity: SOD, catalase or MPG was added to cells w/ or w/o DEPE & incubated for 4 or 24 h. Medium then replaced w/serum-free & cells incubated for another 24 h to analysis.	**Cytotoxic Effects of DEPE on Cardiac Myocytes:** DEPE above 20 µg/mL damaged cardiac myocytes in a time and concentration-dependent manner in both long- and short-term exposure conditions. However damage was greater after long-term exposure. LDH activity showed a concentration-dependent increase at higher levels of exposure (greater than 20 µg/mL). **Effects of ROS Scavenging Enzymes and Antioxidant on DEPE-induced Cell Damage:** SOD or catalase attenuated 50 µg/mL DEPE-induced cell damage compared with DEPE-treated groups lacking antioxidant enzymes. Co-incubation with SOD and catalase showed more protective effects towards DEPE-induced cell damage, although these effects were not statistically significant from cells treated with SOD only. MPG attenuated 50 µg/mL DEPE-induced cell damage in a concentration-dependent manner in both long and short-term exposure conditions. Especially in long-term exposure MPG showed strong protective effects against DEPE-induced cell damage. Cell viability was not affected by SOD, catalase, or MPG.
Reference: Proctor et al. (2006, 088480) **Species:** Rat **Gender:** Male **Age:** 12 wk **Use:** Thoracic Aorta from cp/cp and +/? Male Rats cp/cp = homozygous for cp gene. Prone to obesity and insulin resistant. +/? = heterozygous for either +/cp or +/+. Lean and metabolically normal.	ROFA from Birmingham, AL **Particle Size:** 1.95 ± 0.18 µm (aerodynamic diameter)	**Route:** Protocol 1: Used two aorta rings per each experimental treatment group (4 groups total). Protocol 2: Used four rings. **Dose/Concentration:** Protocol 1: exposed to 12.5 µg/mL ROFA-L (at 10 mg/mL). Protocol 2: exposed to 1.56, 3.25, 6.26, 12.5 µg/mL ROFA-L (at 10 mg/mL). **Time to Analysis:** Protocol 1: Cells treated with 12.5 µg/mL ROFA-L and/or 104mol/L L-NAME for 20 min Protocol 2: Parameters measured after ROFA-L only treatment Contractile response to phenylephrine (PE) was measured	ROFA-L (12.5 µg/mL) increased PE-mediated contraction in obese, but not in lean rat aortae. Effect was exacerbated by L-NAME, and it reduced ACh-mediated relaxation in obese and lean aortae. Initial exposure of aortae to ROFA-L caused a small contractile response, which was markedly greater on second exposure in the obese aortae but marginal in lean.
Reference: Radomski et al. (2005, 091377) **Species:** Rat **Strain:** Wistar Kyoto	Carbon Nano Particles (CNPs) (purchased from SES Research, Houston, TX): Multiplewall Nanotubes (MWNT); Single wall Nanotubes (SWNT); C60 Fullerenes (C60CS); Mixed Carbon Nanoparticles (MCN) PM: (SRM1648) (NIST) **Particle Size:** CNPs: NR; PM: 1.4 µm average size	**Route:** Simultaneous single PM injection into femoral vein as $FeCl_3$ injected to induce carotid thrombosis **Dose/Concentration:** 0.5 mL suspension of 50 µg/mL of PM in 0.9% NaCl solution. **Time to Analysis:** Blood flow continuously monitored for 900 s.	**Vascular Thrombosis:** $FeCl_3$ induced carotid artery thrombosis and MCN had an amplifying effect in the development of thrombosis. Infusions of MCN, SWNT, and MWNT significantly accelerated the time and rate of development of carotid artery thrombosis in rats. SRM1648 was less effective than CNPs in inducing thrombosis, while C60CS exerted no significant effect on the development of vascular thrombosis.
Reference: Radomski et al. (2005, 091377) **Species:** Human **Cell Types:** Platelets **Use:** Human platelet aggregation	Carbon Nano Particles (CNPs) (purchased from SES Research, Houston, TX): Multiplewall Nanotubes (MWNT); Singlewall Nanotubes (SWNT); C60 Fullerenes (C60CS); Mixed Carbon Nanoparticles (MCN); PM (SRM1648) **Particle Size:** CNPs: NR; PM: 1.4 µm average size	**Route:** Cell Culture (2.5×10^8 platelets/mL) **Dose/Concentration:** CNPs: 0.2-300 µg/mL; PM: 5-300 µg/mL **Time to Analysis:** Prostacyclin (PGI2), S-nitroso-glutathione (GSNO), aspirin, 2-methylthio-AMP, phenanthroline, EDTA and Go6976 were pre-incubated w/ platelets for 1 min before particle addition. Particles added to platelets and platelet aggregation studied for 8min.	**Platelet Aggregation:** All CNPs, except C60CS, stimulated platelet aggregation (MCN ≥ SWNT>MWNT>SRM1648). All particles resulted in upregulation of GPIIb/IIIa in platelets. In contrast, particles differentially affected the release of platelet granules, as well as the activity of thromboxane-, ADP, matrix metalloproteinase- and protein kinase C-dependent pathways of aggregation. Particle-induced aggregation was inhibited by prostacyclin and GSNO, but not by aspirin.

Study	Pollutant	Exposure	Effects
Reference: Reed et al. (2006, 156043) **Species:** Rat, Mouse **Gender:** Male and Female **Strain:** CDF (F344)/CrlBR (rat), SH (rat), A/J (mouse), and C57BL/6 (mouse) **Age:** 6-12 wk	HWS (burned mix of hardwood in noncertified wood stove using a Pineridge model 27000, Heating and Energy Systems, Inc. Clackamas, OR) Measured Components: EC, OM, NO_3, SO_4, NH_4, metals **Particle Size:** ~0.25 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** Low: 30 µg/m^3 Mid-low: 100 µg/m^3 Mid-high: 300 µg/m^3 High: 1000 µg/m^3 **Time to Analysis:** 6 h/day, 7days /wk for 1 wk or 6 mo. Immediate post-exposure analysis.	**Organ Weights:** Liver declined in rats of both genders at 1 wk and female rats at 6 mo. Lung volume increased and lung weight decreased in female rats at 6 mo. Spleen weight increased in female mice and rats at 1wk. Thymus weight decreased in male rats at 1wk. **Clinical Chemistry:** Cholesterol decreased at the high dose for male rats at 1wk and 6 mo and increased at mid-low and mid-high doses for female rats at 6 mo. ALP decreased for rats of both genders at 1wk and 6 mo for mid-low, mid-high and high dose levels (14-38%). AST decreased by 24% in male rats at 1wk with high dose. No effect on females. Creatinine serum levels decreased in males at 1wk at mid-high and high dose by 13%. No effect observed at 6 mo. BUN/Cre ratio decreased in females at 1wk (25%) and both genders at 6 mo at mid-high and high dose (18-19%). **Hematology:** Hemoglobin and hematocrit increased in 6 mo male rats. Bilirubin increased in female rats at 6 mo at high dose. Platelets increased for male and female rats at 1wk (21%, 19% respectively). No effect observed at 6m. WBC increased in males at 1wk.
Reference: Reed et al. (2004, 055625) **Species:** Rat, Mouse **Gender:** Male and Female **Strain:** CDF (F344)/CrlBR (rat), A/J (mouse) **Age:** 12 wk	DE: generated from two 2000 model 5.9 L Cummins ISM turbo diesel engines Co-exposure to 8 gas and 8 solid exhaust components measured **Particle Size:** 0.10 - 0.15 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** Low: 30 µg/m^3 Mid-low: 100 µg/m^3 Mid-high: 300 µg/m^3 High: 1000 µg/m^3 **Time to Analysis:** 6 h/day, 7 days/wk for 1wk or 6 mo. Analyzed 1 day post-exposure.	**Organ Weights:** Kidney weight increased after 6m for both males and female rats at the high dose. Kidney and liver weight increased for female mice at all dose levels at 6 mo. Lung weight increased at high dose at 6mo for female mice and male rats. Spleen weight decreased in male mice at the low and mid-high levels. **Clinical Chemistry:** There was a massive decrease in cholesterol (24%) for rats of both genders after 1 wk and a smaller decrease for male rats at 6 mo. GGT significantly increased at 6 mo for male and female rats at the mid-high and high dose. ALP increased in male rats at 1 wk by 10%. AST decreased at mid-high (15%) and high dose in female rats at 6 mo. BUN and BUN/Creatine declined (19%, 17%) in female rats at mid-high and high doses after 6 mo. BUN increased by 21% at mid-low, mid-high and high doses in male rats at 1wk. **Hematology:** WBC decreased in high females after 6 mo. Factor VII (blood clotting) decreased in MH and HR males after 1wk and male and female HR after 6 mo. Thrombin-antithrombin complex declined massively but only in males after 1wk.
Reference: Reed et al. (2008, 156903) **Species:** Rat **Gender:** Male, Female **Strain:** CDF (F344)/CrlBR, SH **Age:** NR **Weight:** NR	GEE (two 1996 General Motors 4.3-L V-6 engines; regular, unleaded, non-oxygenated, non-reformulated Chevron-Phillips gasoline, U.S. average consumption for summer 2001 and winter 2001-2002) **Particle Size:** 150 nm (MMAD)	**Route:** Whole-body Inhalation **Dose/Concentration:** PM: Low- 6.6 ± 3.7 µg/m^3, Medium- 30.3 ± 11.8 µg/m^3, High- 59.1 ± 28.3 µg/m^3 **Time to Analysis:** 2 wk quarantine period in chamber. Exposed 6 h/day, 7 days/wk, 3 day-6 mo. SH- surgery to implant telemeter in peritoneal cavity. 4 wk recovery. ECG data obtained every 15 min beginning 3 day pre-exposure, 7 day exposure, 4 day post-exposure.	**Organ Weight:** At 6 mo exposure, the heart weights of male and female rats increased and male rats' seminal vesicle weight decreased. **Clinical Chemistry:** Serum alanine aminotransferase, aspartate aminotransferase, and phosphorus decreased in medium and high-exposure females. **Hematology:** Hematocrit, red blood cell count, and hemoglobin dose-dependently increased for both genders at both time points. Plasma fibrinogen increased at 1wk in males. **CV Effects in SH Rat:** Lipid peroxides were significantly increased in males in the high exposure group. TAT complexes decreased in females in the high exposure group. **Removal of Emission PM:** The removal of emission PM strongly linked PM to increased seminal vesicle weight, red blood cell counts, LDH, lipid peroxides, and methylation.

Study	Pollutant	Exposure	Effects
Reference: Rhoden et al. (2005, 087878) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** Adult **Weight:** 300 g	Urban Ambient Particles (UAPs): SRM-1649; CAPs (Boston, MA) **Particle Size:** NR	**Route:** UAPs: IT Instillation. CAPs: Inhalation **Dose/Concentration:** UAPs: 750 µg suspended in 300 µl saline; CAPs: 700 ± 180 µg/m^3 **Time to Analysis:** UAPs: 30 min post-instillation. CAPs: immediately after 5 h exposure period	**Oxidative Stress and HR Function:** UAPs instillation led to significant increases in heart oxidants. HR increased immediately after exposure and returned to basal levels over the next 30 min. SDNN was unchanged immediately after exposure, but significantly increased during the recovery phase. **Role of ROS in Cardiac Response:** Rats were treated with 50 mg/kg NAC 1 h prior to UAPs instillation or CAPs inhalation. NAC prevented changes in heart rate and SDNN in UAPs-exposed rats. **Role of the Autonomic Nervous System in PM-induced Oxidative Stress**: Rats were given 5 mg/kg atenolol, 0.30 mg/kg glycopyrrolate, or saline immediately before CAPs exposure. Both atenolol and glycopyrrolate effectively prevented CAPS-induced cardiac oxidative stress.
Reference: Rivero et al. (2005, 088653) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 3 mo **Weight:** ~250 g	$PM_{2.5}$, collected from heavy traffic area in Sao Paulo, Brazil. $PM_{2.5}$ Composition (%): S (3.05), As (0.30), Br (0.21), Cl (2.09), Co (2.65), Fe (2.67), La (5.42), Mn (0.64), Sb (0.21), Sc (3.25), Th (8.14) **Particle Size:** $PM_{2.5}$	**Route:** IT Instillation **Dose/Concentration:** 100 or 500 µg of $PM_{2.5}$. **Time to Analysis:** 24 h post-instillation	**Hematology:** Total reticulocytes significantly increased at both $PM_{2.5}$ doses, while hematocrit levels increased in the 500 µg group. Quantification of segmented neutrophils and fibrinogen levels showed a significant decrease, while lymphocytes counting increased with 100 µg of $PM_{2.5}$. **Pulmonary Vasculature:** Significant dose-dependent decrease of intra-acinar pulmonary arteriole lumen/wall ratio was observed in both $PM_{2.5}$ groups. **Wet-to Dry Weight Ratio:** Significant increase in heart wet-to-dry weight ratio was observed in the 500 µg group.
Reference: Rivero et al. (2005, 088659) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 3 mo **Weight:** ~250 g	$PM_{2.5}$, collected from heavy traffic area in Sao Paulo, Brazil. $PM_{2.5}$ Composition (%): S (3.05), As (0.30), Br (0.21), Cl (2.09), Co (2.65), Fe (2.67), La (5.42), Mn (0.64), Sb (0.21), Sc (3.25), Th (8.14) **Particle Size:** $PM_{2.5}$	**Route:** IT Instillation **Dose/Concentration:** 50 and 100 µg of $PM_{2.5}$. **Time to Analysis:** HR and SDNN were assessed immediately before instillation, 30 and 60 min post-instillation.	HR decreased significantly with time, but no significant effect of treatment or interaction between time and treatment was observed. In contrast, there was a significant SDNN interaction between time and treatment. The SDNN decreased 60 min after instillation with $PM_{2.5}$ concentration of 50 and 100 µg.
Reference: Seagrave et al. (2008, 191990) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** 10-12 wk **Weight:** 250-300 g	GEE (2 1996 General Motors 4.3-L V6 gasoline engines; conventional Chevron Phillips gasoline, U.S. average composition) (CO, NO, NO_2, SO_2, THC) ($PM_{2.5}$ composition- EC, OC, SO_4, NH_4, NO_3) Simulated downwind coal emission atmospheres (SDCAs) (fly ash, gas-phase pollutants, sulfate aerosols, NO, NO_2, SO_2) Paved Road Dust (RD) (Los Angeles, CA; New York City, NY; Atlanta, GA) **Particle Size:** GEE: 150 nm (MMAD), RD: 2.6 ± 1.7 µm, SDCA: 0.1-1.0 µm	**Route:** Nose-only Inhalation **Dose/Concentration:** GEE: 60 µg/m^3, SDCAs: 317-1072 µg/m^3, RD: 306-954 µg/m^3; GEE: CO- 104 ppm, NO- 16.7 ppm, NO_2- 1.1 ppm, SO_2- 1.0 ppm, THC- 12ppm; SDCAs: CO- <1 ppm, NO- 0.19-0.62 ppm, NO_2- 0.10-0.37 ppm, SO_2- 0.07-0.24 ppm, THC- <1 ppm **Time to Analysis:** 6 h exposure. Cannula ligated into trachea and connected to rodent ventilator. Thorax and abdomen opened.	GEE produced CL in the lungs, heart, and liver. RD produced a significant effect in the heart at the low dose. SDCAs had no effect on CL. RD significantly increased the heart's oxidative stress, as demonstrated by the TBARS levels..
Reference: Simkhovich et al. (2007, 096594) **Species:** Rat **Gender:** Female **Strain:** Fischer 344 × Brown Norway hybrid **Age:** 4, 26 mo	Ultra Fine Particles (UFPs) isolated from industrial diesel reference PM 2975 **Particle Size:** UFPs ≤ 0.1 µm	**Route:** Heart Perfusion (ex-vivo) **Dose/Concentration:** UFPs 12.5, 25, and 37.5 mg. **Time to Analysis:** Hearts perfused w/ UFPs for 30 min and analysis conducted every 10 min.	Young adult and old hearts demonstrated equal functional deterioration in response to direct infusion of UFPs. Developed pressure in young adult UFPs-treated hearts fell from 101 ± 4 to 68 ± 8 mmHg. In the old UFPs-treated hearts developed pressure fell by 35%. Positive dP/dt was equally affected in the young adult and old UFPs-treated hearts and was decreased by 28% in both groups.

Study	Pollutant	Exposure	Effects
Reference: Smith et al. (2006, 110864) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** 8 wk **Weight:** 260-270 g	CFA: Coal Fly Ash (400 MW, Wasatch Plateau, Utah) (aerodynamic separation) **Particle Size:** 0.4-2.5 µm	**Route:** Nose-only Inhalation **Dose/Concentration:** 1400 µg/m^3 $PM_{2.5}$ including 600 µg/m^3 PM_1 **Time to Analysis:** 4 h/day for 3 consecutive days. Parameters measured 18 or 36 h post-exposure.	**Hematology:** Plasma protein increased at 18h. Lymphocyte and hematocrit percentage decreased at 36 h.
Reference: Stinn et al. (2005, 088307) **Species:** Rat **Gender:** Male and Female **Strain:** Crl: (WIU BR **Age:** 40 day	DE (generated from 1.6 L VW diesel under USFTP 72) CO: 10, 37 ppm CO_2: 2170, 6540 ppm NO: 7.0, 22.8 ppm NO_X: 8.6, 28.3 ppm SO_2: 0.83, 3.09 ppm NH_4: ND Measured Major Components: NO, SO_2, 1-nitropyrene, Zi. 50% by DE weight is EC. **Particle Size:** 0.19-0.21 µm (MMAD)	**Route:** Nose-only Inhalation **Dose/Concentration:** 3 and 10 mg/m^3 **Time to Analysis:** 6 h/day, 7 day/wk for 24 mo; 6 mo post-exposure	**Hematology:** Erythrocytes were unaffected (12, 24, 30) except in high dose females at 24 and 30 mo. Hemoglobin and hematocrit increased dose-dependently with no gender differences. Leukocytes increased in a dose- and time-dependent manner.
Reference: Sun et al. (2005, 087952) **Species:** Mouse **Gender:** Male **Strain:** ApoE$^{-/-}$ **Age:** 16 wk	CAPs: $PM_{2.5}$ from Tuxedo, NY. HFCD: High Fat Chow Diet NCD: Normal Chow Diet **Particle Size:** $PM_{2.5}$	**Route:** Whole-body Inhalation **Dose/Concentration:** $PM_{2.5}$: 85 µg/m^3; Daily concentration: 10.6 (SD 3.4) µg/m^3 (mean) Average exposure over 6 mo period: 15.2 µg/m^3. **Time to Analysis:** Study diets fed for at least 10 wk prior to exposure to $PM_{2.5}$ or FA. Exposed for 6 h/day, 5 days/wk for 6 mo. Sacrificed 15-47 days after exposure.	**Vasomotor Function:** Mice fed HFCD and exposed to $PM_{2.5}$ demonstrated an increase in the half-maximal dose for dilation to ACh with no changes in peak relaxation compared to the mice exposed to FA and fed HFCD and NCD. **Atherosclerosis Burden with $PM_{2.5}$:** In vivo MRI imaging of atherosclerosis burden in the abdominal aorta revealed significantly increased plaque burden in the mice fed HFCD compared with the mice fed NCD. Mean (SD) plaque areas in the mice exposed to $PM_{2.5}$ and fed HFCD vs. mice exposed to FA and fed HFCD were 33 (10) vs. 27 (13) units, respectively. **$PM_{2.5}$ and Vascular Inflammation:** A 2.6-fold higher inducible NOS content was apparent in the mice exposed to $PM_{2.5}$ and fed HFCD compared with the mice exposed to FA and fed HFCD chow and a 4-fold increase in the mice exposed to $PM_{2.5}$ and fed NCD compared with the mice exposed to FA and fed NCD.
Reference: Sun et al. (2008, 157033) **Species:** Mouse **Gender:** Male **Strain:** ApoE$^{-/-}$ **Age:** 6 wk	CAPs $PM_{2.5}$ Collected from Sterling Forest State Park, Tuxedo NY (40 miles NW of Manhattan) **Particle Size:** $PM_{2.5}$	**Route: Whole-body** Inhalation **Dose/Concentration:** Average Concentration of: 85 µg/m^3 CAPs in chamber. Average exposure over 6 mo was 15.2 µg/m^3. **Time to Analysis:** 6 h/day, 5 day/wk for 6 mo. Mice received two different diets, high-fat chow and normal-chow.	**Macrophage and Tissue Factor Expression in Aortic Segments**: Tissue Factor (TF) expression was noted predominantly in the extracellular matrix surrounding macrophages, foam cell-rich areas and around smooth muscle cells. **1. High-Fat Diet:** Increased TF and increased macrophage infiltration was observed in the plaques of high-fat chow mice exposed to PM compared to mice exposed to air and high fat diet. **2. Normal Diet:** PM-exposed mice saw an increase in CD68 expression compared to air-exposed. However TF expression was not significantly different in PM exposed normal diet mice compared to control normal diet mice.

Study	Pollutant	Exposure	Effects
Reference: Sun et al. (2008, 157033) **Species:** Human **Cell Lines:** BEAS-2B; Vascular Smooth Muscle Cells (hSMCs); and Monocytes (THP-1)	Ambient Particles collected from Sterling Forest State Park, Tuxedo, NY (24 h/day for 4 wk) **Particle Size:** Particle size ranges: 1. <0.18 µm 2. 1.8 - 2.5 µm or 3. 2.5 - 10 µm	**Route:** In vitro **Dose/Concentration:** 10-300 µg/ml **Time to Analysis:** Doses were tested for durations up to 24 h.	Dose durations tested for up to 24-h did not indicate detectable effects on cell viability. **Effect of PM on TF Expression and Activity in hSMCs:** In the PM size range of 1-3 µm, significant increases in TF expression was observed at doses of 100 and 300 µm /mL. In the <0.18 µm size range, significant increase in TF expression was observed at all doses. The particles with sizes 0.18 - 1.0 µm did not induce significant change in TF expression. **Effect of PM on TF Expression and Activity in Monocyte Cells:** TF protein expression increased with <0.18 µm and the 1- 3 µm range particles. Expression was increased in the 0.18-1.0 µm particle range but it was limited compared to the other PM size ranges. In general TF expression was higher in monocytes than in hSMCs cells, but not significantly. **Effect on TF Expression and Activity in Bronchial Epithelial Cells:** 100 µg/mL of the 1-3 µm and <0.18 µm particles significantly increased TF expression. **TF mRNA Expression:** TF mRNA was increased rapidly within the first hour in response to SRM-1694a PM. The lowest dose of SRM PM_{10} µg/mL induced highest levels of mRNA in hSMCs, no further increase was observed at higher concentrations.
Reference: Sun et al. (2008, 157032) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** 500-650 g	$PM_{2.5}$ or UFP **Particle Size:** $PM_{2.5}$; UFP: <0.1 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** Mean $PM_{2.5}$ concentration: 79.1 ± 7.4 µg/m^3. Normalized $PM_{2.5}$ over 10wk period: 14.1 µg/m^3. **Time to Analysis:** 6 h/day, 5 day/wk random exposure to $PM_{2.5}$, UFP, or FA for a total of 10 wk. At the end of wk 9 exposure, rats were infused w/ 0.75 mg/kg/day of AII for 7 days. $PM_{2.5}$, UFP, or FA, continued during AII infusion period. AII = angiotensin II	**Mean Arterial Pressure (MAP):** After AII infusion, MAP was significantly higher in $PM_{2.5}$ - AII vs. FA-AII group. Aortic Vasoconstriction to PE was potentiated with exaggerated relaxation to the Rho-kinase (ROCK) inhibitor Y-27632 and increase in ROCK-1 mRNA levels in the $PM_{2.5}$ - AII group. Superoxide production in the aorta was increased in the $PM_{2.5}$. AII group compared to FA-AII group, inhabitable by apocynin and L-NAME with coordinate upregulation of NAD(P)H oxidase subunits p22phox and p47phox and depletion of tetrahydrobipterin.
Reference: Sun et al. (2008, 157032) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** 500-650 g **Cell Line:** Primary Rat Aortic Smooth Muscle Cells (RASMCs)	$PM_{2.5}$ or UFP **Particle Size:** $PM_{2.5}$; UFP: <0.1 µm	**Route:** Cell Culture **Dose/Concentration:** UFP, $PM_{2.5}$: 10 or 50 µg/mL; AII: 100 nmol/L **Time to Analysis:** Exposed to UFP or $PM_{2.5}$ and parameters measured at 0, 1, 3, 6, and 15 min. AII = angiotensin II	Exposure to UFPs and $PM_{2.5}$ was associated with an increase in ROCK activity, phosphorylation of myosin light chain, and MYPT1. Pretreatment with N-Acetylcysteine and the Rho kinase inhibitors (Fasudil and Y-27632) prevented MLC and MYPT-1 phosphorylation by UFPs suggesting a superoxide-mediated mechanism for $PM_{2.5}$ and UFPs effects.

Study	Pollutant	Exposure	Effects
Reference: Sun et al. (2009, 190487) **Species:** Mouse **Gender:** Male **Strain:** C57BL/6, c-fmsYFP (transgenic, yellow fluorescent protein under monocyte-specific promoter) **Age:** 8, 10 wk **Weight:** NR	PM (concentrated- northeastern regional background; Tuxedo Park, NY) **Particle Size:** 2.5 µm (diameter)	**Route:** Whole-body Inhalation. IT Instillation. **Dose/Concentration:** Exposure chamber (mean): 72.7 µg/m^3, IT: 1.6mg/kg **Time to Analysis:** C57BL/6 mice, fed high-fat chow 10wk. Exposed in vivo 6 h/day, 5 day, 128 days. fmsYFP rendered diabetic or fed normal chow 10 wk. IT instilled with PM 2 times/wk for 10 wk.	**Metabolic Impairment:** PM induced insulin, homeostasis model assessment indexes, elevated glucose, and abnormalities in lipid profile consistent with the IR phenotype. **Vascular Endothelium:** PM decreased peak relaxation and ED50 to ACH and peak relaxation to insulin. Lower levels of NO release were seen. **Insulin Signaling:** PM reduced the phosphorylation of Akt in intact aorta. PKC-β11 was the only PKC isoform to increase. **Adipose Inflammation, Visceral Adiposity:** PM significantly increased TNF-α, IL-6, E-selectin, ICAM-1, plasminogen activator inhibitor-1, and restin. PM increased visceral and mesenteric fat mass. F4/80+ macrophages in fat tissue and adipocyte size increased. PM downregulated IL-10 and glactose-N-acetylgalactosamine-specific lectin. **YFP Cell Adhesion and Infiltration:** PM increased YFP cells in the adipose tissue, YFP cell infiltration in the mesenteric fat, and YFP cell adhesion to endothelium.
Reference: Tamagawa et al. (2008, 191988) **Species:** Rabbit **Gender:** Female **Strain:** New Zealand White **Age:** 12 wk **Weight:** Acute (average)- 2.4 ± 0.2 kg, Chronic (average)- 2.7 ± 0.3 kg	PM_{10} (urban; Ottawa, Canada) **Particle Size:**: 0.8 ± 0.4 µm (mean diameter)	**Route:** Intrapharyngeal Instillation **Dose/Concentration:** Acute- 2.6mg/kg, Chronic- 2mg/kg **Time to Analysis:** Acute animals exposed days 1, 3, 5. Chronic animals exposed 2 times/wk for 4 wk.	**Inflammation:** PM_{10} induced more macrophages, AMs, positive and activated AMs, and fewer tissue macrophages. NO, WBC and PMN were only significantly higher in the first two wk and IL-6 in the first wk. **Vascular endothelial function:** PM_{10} significantly reduced Ach-stimulated relaxation and did not alter SNP-stimulated relaxation. A significant inverse relationship between IL-6 and Ach-induced relaxation occurred at wk 1 in the acute model and wks 1 and 2 in the chronic model. **AMs:** The chronic model had a significant correlation between IL-6 and both positive and activated AMs at wk 1. A significant inverse relationship occurred between Ach and both the volume fraction of positive and activated AMs.
Reference: Tankersley et al. (2008, 157043) **Species:** Mouse **Gender:** Male **Strain:** C57BL/6, C3H/HeJ, B6C3F1 **Age:** 18, 28 mo **Weight:** NR	Carbon black (CB) (Wright dust feed particle generator-BGI, Waltham, MA) **Particle Size:** 0.1-1.0 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** Average $PM_{2.5}$ concentration- 401 ± 46 µg/m^3, Average PM_{10} concentration- 553 ± 49 µg/m^3 **Time to Analysis:** 3 h/day, 4 days	**Hemodynamics:** CB significantly elevated right atrial and ventricular pressures, pulmonary arterial pressure and vascular resistance, all of which were more pronounced in the 28 mo-old mice. RV contractility (specifically, the ejection fraction and maximum change in pressure over time) reduced in CB-exposed 28 mo-old mice. **Heart Tissue:** CB significantly declined Ca2+-dependent NOS activity and was more pronounced in 28 mo-old mice, who also had NOS2 upregulated. CB enhanced ROS generation and NOS-uncoupling and was greatest in 28 mo-old mice. CB also increased MMP-2, MMP-9, ANP, BNP, which were greatest in 28 mo-old mice. CB also reduced PKG-1 in 28 mo-old mice.

Study	Pollutant	Exposure	Effects
Reference: Tankersley et al. (2007, 097910) **Species:** Mouse **Gender:** Male **Strain:** C3H/HeJ and C57BL/6J **Age:** 10 wk **Weight:** 22-26 g	Carbon Black (CB) **Particle Size:** CB: 2.4 µm (MMAD) (GSD 2.75 µm).	**Route:** CB: Whole-body Inhalation; Sympathetic (S) & Parasympathetic (PS) blockade: IP Injection **Dose/Concentration:** CB: 159 ± 12 µg/m^3; PS (atropine): 0.5 mg/kg; S(propanolol): 1 mg/kg **Time to Analysis:** Successive 3 h CB and FA Exposures: conducted from 9 a.m. to 1 p.m., or at least 3 h after dark-to-light transition (exposure period selected based on the nadir in circadian pattern in HR responses). Subgroups of both strains exposed to PS & S blockade.	**FA Exposure with Saline:** A significantly greater 3 h average response occurred in C3 compared with B6 mice. **PS Blockade:** No evident strain difference between C3 and B6 was observed. **S Blockade:** 3 h average HR responses for C3 mice were significantly reduced compared with saline. **CB Exposure:** HR responses were significantly elevated in C3 compared with B6 mice, but these HR responses were not different relative to FA exposure. **S Blockade:** HR was significantly elevated in B6 mice during CB relative to FA, but was not changed in C3 mice.
Reference: Tankersley et al. (2004, 094378) **Species:** Mice **Strain:** AKR/J **Age:** ~180 days	Carbon Black (CB) and Filtered Air (FA) **Particle Size:** CB: 0.1 to 1 um.	**Route:** Whole-body Inhalation **Dose/Concentration:** CB average concentration: 160 ± 22 µg/m^3 **Time to Analysis:** FA exposure on day 1, CB exposure 3 h/day for 3 consecutive days (days 2-4)	On day 1, HR was significantly depressed during FA in terminally senescent mice. By day 4, HR had significantly slowed due to the effects of 3 days CB exposure. The combined effects of terminal senescence and CB exposure acted to depress HR to an average (± SEM) 445 ± 40 bpm, ~ 80 bpm lower compared to healthy HR responses. The change in rMSSD was significantly greater on day 1 and day 4 in terminally senescent mice, compared to healthy mice. LF/HF ratio was significantly depressed in terminally senescent mice on day 1. By day 4, significant increases in LF/HF were evident in healthy mice during CB exposure. Terminally senescent mice modulated a lower HR without change in the LH/HF ratio during CB exposure.
Reference: Thomson et al. (2005, 087554) **Species:** Rat **Gender:** Male **Strain:** F344 **Weight:** 200-250 g	Urban Ambient Particles (EHC-93) from Ottawa, Canada; O_3 **Particle Size:** Respirable Modes (aerodynamic diameter): 1.3 and 3.6 µm. Non-respirable Mode (aerodynamic diameter): 15 µm	**Route:** Nose-only Inhalation **Dose/Concentration:** EHC-93: 0, 5, 50 mg/m^3; O_3: 0, 0.4, 0.8 ppm **Time to Analysis:** 4 h to particles, O_3, or combination of particles and O_3.	Both pollutants individually increased preproET-1, ET-1 and endothelial NOS mRNA levels in the lungs shortly after exposure, consistent w/ the concomitant increase in plasma of ET-1[1-21]. Prepro-ET1 mRNA remained elevated 24 h post-exposure to particles but no after O_3. Both pollutants transiently increased ET-B receptor mRNA expression, while O_3 decreased ET-A receptor mRNA levels. Coexposure to particles plus O_3 increased lung preproET-1 mRNA but not plasma ET-1[1-21], suggesting alternative processing or degradations of endothelins. This coincided w/ an increase of MMP-2 in the lungs (this enzyme cleaves bigET-1 to ET-1[1-32]).
Reference: Thomson et al. (2006, 097483) **Species:** Rat **Gender:** Male **Strain:** F344 **Weight:** 200-250 g	Urban Ambient Particles (EHC-93) from Ottawa, Canada; O_3 **Particle Size:** NR	**Route:** Nose-only Inhalation **Dose/Concentration:** EHC-93: 0, 50 mg/m^3; O_3: 0, 0.8 ppm **Time to Analysis:** 4 h to particles, O_3, or combination of particles and O_3. Sacrificed immediately following exposure or following 24 h recovery.	Circulating levels of both ET-1[1-21] and ET-3[1-21] were increased immediately after exposure to PM and O_3. While expression of preproET-1 mRNA in the lungs increased, expression of preproET-3 mRNA decreased immediately after exposure. PreproET-2 mRNA was not detected in the lungs, and exposure to either pollutant did not affect plasma ET-2 levels. Coexposure to O_3 and particles, while altering lung preproET-1 and preproET-3 mRNA levels in a fashion similar to O_3 alone, did not cause changes in the circulating levels of the two corresponding peptides.

Study	Pollutant	Exposure	Effects
Reference: Totlandsdal et al. (2008, 157056) **Species:** Rat **Gender:** Male **Strain:** WKY/NCrl and Crl: WI (Han) **Age:** Adult **Weight:** Crl/WI, 250-300 g **Use:** Isolation of Rat Ventricular Cardiomyocytes and Cardiofibroblasts (RVCMs and RVCFBs)	Pigment Black Printex 90 (Frankfurt, Germany); PM: SRM 1648 **Particle Size:** Printex 90: 12-17 nm; PM: NR	**Route:** Cell Culture **Dose/Concentration:** Printex 90: 0, 50, 100, 200 or 400 µg/mL; PM: 0, 200 µg/mL **Time to Analysis:** 20 h	**Cardiac Cell Cultures**: IL-6 release was strongly enhanced upon exposure to conditioned media, and markedly exceeded the response to direct particle exposure. IL-1, but not TNF-α, seemed necessary, but not sufficient, for this enhanced IL-6 release. The role of IL-1 was demonstrated by use the use of an IL-1 receptor antagonist that partially reduced the effect of the conditioned media, and by a stimulating effect on the cardiac cell release of IL-6 by exogenous addition of IL-1 α and IL-1 β.
Reference: Tzeng et al. (2007, 097883) **Species:** Rat **Strain:** Wistar Kyoto **Cell Type:** Primary Vascular Smooth Muscle Cell Culture (VSMCs): isolated from thoracic aortas from 200-250 g rats.	Motorcycle Exhaust Particulate Extract (MEPE) collected from a Yamaha motorcycle with a 50 cm^3 two-stroke engine using 95% octane unleaded gasoline. **Particle Size:** PM_1, $PM_{2.5}$, PM_{10}	**Route:** In vitro **Dose/Concentration:** 10-100 µg/mL **Time to Analysis:** 3 days	Exposure of VSMCs to MEPE (10-100 µg/mL), enhanced serum-induced VSMC proliferation. The expression of proliferating cell antinuclear antigen was also enhanced in the presence of MEPE. VSCMs treated with MEPE induced increase COX-2 mRNA, protein expression, and PGE2 production, whereas the level of COX-1 protein was unchanged. MEPE increased the production of ROS in VSMCs, in a dose-dependent manner. MEPE triggered time-dependent ERK1/2 phosphorylation in VSMCs which was attenuate by antioxidants (NAC, PDTC). The level of translocation of NF-κB-p65 in the nuclei of VSMCs was also increased during MEPE exposure. The potentiating effect of MEPE in serum-induced VSMC proliferation was abolished by COX-2 selective inhibitor NS-398, specific ERK inhibitor PD98059, and antioxidants (NAC, PTDC).
Reference: Tzeng et al. (2003, 097247) **Species:** Rat **Strain:** Wistar Kyoto **Cell Type:** Primary Vascular Smooth Muscle Cell Culture (VSMCs)	Motorcycle Exhaust Particulate Extract (MEPE) collected from a Yamaha motorcycle with a 50 cm^3 two-stroke engine using 95% octane unleaded gasoline. **Particle Size:** NR	**Route:** In vitro **Dose/Concentration:** MEPE: 10 µg/mL; Nifedipine: 10 µmol; Manganese Acetate: 100 µmol; Staurosporine: 1-2 nM; Chelerythrine: 1 µm **Time to Analysis:** 18 h	MEPE induced a concentration-dependent enhancement of vasoconstriction elicited by phenylephrine in the organ cultures of intact and endothelium-denuded aortas for 18h. Nifedipine, manganese acetate, and staurosporine, but not chelerythrine, inhibited the enhancement of vasoconstriction by MEPE. ML-9 inhibited the enhancement of vasoconstriction by MEPE. MEPE enhanced the phosphorylation of 20k-Da in rat vascular smooth muscle cells. N-acetylcysteine significantly inhibited the enhancement of vasoconstriction by MEPE. A time-dependent increase in ROS production by MEPE was also detected in primary cultures of VSMCs.
Reference: Upadhay et al. (2008, 159345) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 6 mo **Weight:** NR	Ultrafine Carbon Particles (UFCP) **Particle Size:** Size- 31 ± 0.3 nm, MMAD- 46 nm, Surface area concentration- 0.139 m^2 particles/m^3, Mass specific surface area- 807m^2/g	**Route:** Whole-body Inhalation **Dose/Concentration:** 172 µg/m^3 **Time to Analysis:** Acclimatized 2 day. 1 day baseline. 24 h exposure. 4 recovery. Sacrificed 1st or 3rd day of recovery.	**Cardiophysiology:** The mean arterial BP and HR increased but returned to baseline levels by the 4th recovery day. SDNN and HRV decreased. RMSSD and LF/HF decreased but were not significant. **Pulmonary Inflammation:** UFCP did not cause pulmonary inflammation. **Pulmonary and Cardiac Tissue:** HO-1, ET-1, ETA, ETB, TF, PAI-1 significantly increased in the lung on the 3rd recovery day. HO-1 was repressed in the heart, but the other markers had slight, nonsignificant increases. **Systemic Responses:** Neutrophil and lymphocyte cell differentials significantly increased on the 1st recovery day. Other blood parameters were unaffected. The plasma renin concentration increased on the first 2 recovery days. Ang I and II concentrations increased on the 1st recovery day but was not significant.

Study	Pollutant	Exposure	Effects
Reference: Wallenborn et al. (2008, 191171) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 13 wk **Weight:** NR	Zinc Sulfate ($ZnSO_4$, aerosolized) **Particle Size:** NR	**Route:** Nose-only Inhalation **Dose/Concentration:** 9.0 ± 2.1 µg/m^3, 35 ± 8.1 µg /m^3, 123.2 ± 29.6 µg /m^3 **Time to Analysis:** Exposed 5 h/day, 3 days/wk, 16 wk. Half of the rats used for plasma/serum analysis, other half for isolation of cardiac mitochondria.	A trend toward increased BALF protein was seen. Cardiac mitochondrial ferritin had a small, significant increase. Mitochondrial succinate dehydrogenase and glutathione peroxidase had small, significant decreases. Subchronic exposure to 100 µg/m^3 caused expression changes of cardiac genes involved with cell signaling events, ion channels regulation, and coagulation. No pulmonary-related effects were seen.
Reference: Wallenborn et al. (2007, 156144) **Species:** Rat **Gender:** Male **Strain:** WKY, SH, and stroke-prone SH (SHRSP) **Age:** 12-15 wk	PM: precipitator unit power plant residual oil combustion **Particle Size:** PM: 3.76 µm (bulk) ± 2.15	**Route:** IT Instillation **Dose/Concentration:** WKY vs SHRSP: 1.11, 3.33, 8.33 mg/kg SH vs SHRSP: 3.33, 8.33 mg/kg **Time to Analysis: Single,** 24 h Note: 4 h post-exposure study done on WKY vs SHRSP but not published.	**Oxidative Stress - Cardiac:** SOD increased in the SHRSP vs WKY experiment only. Only SHRSP at 8.33 mg/kg showed a significant increase when compared to the control. **GPx:** No action but SHRSP levels were similar to SHR and, in the WKY vs SHRSP experiment, SHRSP exhibited higher activity level than WKY. **Ferritin:** Equivocal results were observed. Levels decreased at the high dose for WKY and SHRSP but increased at medium doses for SH and SHRSP. **ICDH:** Levels increased for WKY and decreased for SHRSP.
Reference: Wellenius et al. (2003, 055691) **Species:** Dog **Gender:** Female **Strain:** Mixed mongrel **Age:** NR **Weight:** 14-17 kg	CAPs **Particle Size:** 0.26 ± 0.04 µm	**Route:** Permanent Tracheostomy **Dose/Concentration:** Median: 285.7 µg/m^3, Range: 161.3-957.3 µg/m^3 **Time to Analysis:** Thoracotomy and tracheostomy performed. 5-13 wk recovery. Pairs of subjects: exposed 6 h/day either 2nd or 3rd exposure time and filtered air other days. 5 min preconditioning occlusion. 20 min rest interval. 5 min experimental occlusion. Some dogs exposed 6 h/d, 4 days (consecutive), filtered air on day 4.	CAPs increased the ST-segment elevation and remained elevated 24 h after exposure. This increase was seen in precordial leads V4 and V5. Multivariate regression analyses showed that the mass concentration of Si was significantly associated with the peak ST-segment elevation and integrated ST-segment change. Univariate regression analyses showed Pb to also be significantly associated with these measures. CAPs had no effect on peak heart rate during occlusion or the maximum occlusion-induced increase in heart rate.
Reference: Wellenius et al. (2004, 087874) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** Adult **Weight:** ~250 g **Use:** Rat Model for Acute Myocardial Infarction (AMI): Left-ventricular MI induced. Animals allowed to recover for at least 12 h after surgery.	CAPs (Boston, MA); exposures during the period of 07/2000 and 01/2003. CO **Particle Size:** $PM_{2.5}$	**Route:** Whole-body Inhalation **Dose/Concentration:** CO: 35ppm; CAPs (median concentration): 350.5 µg.m^3; CAPs+CO: (CAPs median concentration): 318.2 µg/m^3 **Time to Analysis:** 1 h exposure to CAPs or CAPs+CO for 1 h. Exposure to pollutants was preceded and followed by 1 h exposure to FA.	CO exposure reduced the ventricular premature beat (VPB) frequency by 60.4% during the exposure time compared to controls. This effect was modified by both infarct type and the number of pre-exposure VPBs, and was mediated through changes in HR. Overall, CAPs exposure increased VPB frequency during the exposure period, but this did not reach statistical significance. This effect was modified by the number of pre-exposure VPBs. In rats with a high number of pre-exposure VPB, CAPS exposure significantly decreased VPB frequency (67.1%). Overall, neither CAPs nor CO had any effect on HR, but CAPs increased HR in specific subgroups. No significant interactions were observed between the effects of CO and CAPs.

Study	Pollutant	Exposure	Effects
Reference: Wellenius et al. (2006, 156152) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** Adult **Weight:** ~250 g **Use:** Rat Model for Acute Myocardial Infarction (AMI): Left-ventricular MI induced. Animals allowed to recover for at least 12 h after surgery.	CAPs: (Boston, MA) **Particle Size:** $PM_{2.5}$	**Route:** Whole-body Inhalation **Dose/Concentration:** CO: 35 ppm; CAPs (median concentration): 645.7 $\mu g.m^3$; CAPs+CO: 37.9 ppm **Time to Analysis:** CAPs or CAPs+CO exposure for 1 h. Exposure to pollutants was preceded and followed by 1 h exposure to FA.	Among rats in the CAPs group, the probability of observing supraventricular arrhythmias (SVA) decreased from the baseline to exposure and post-exposure periods. The pattern was significantly different than that observed for the FA group during the exposure period. In the subset with one or more SVA during the baseline period, the change in SVA rate from baseline to exposure period was significantly lower in the CAPs and CO groups only, when compared to the FA group. No significant effects were observed in the group simultaneously exposed to CAPs and CO.
Reference: Wichers et al. (2004, 055636) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 75 day	HP-12 (oil-combustion derived PM obtained from inside wall of a Boston power plant stack burning residual oil number 6). Water-leachable constituents (µg/mg): SO4 (217.3); Zn (11.4); Ni (6.9); Fe (0.0); V (1.3); Cu (0.2); Pb (0.0) 1M HCl-leachable constituents (µg/mg): SO4 (220.6); Zn (15.5); Ni (14.8); Fe (15.6); V (32.9); Cu (1.1); Pb (1.7) **Particle Size:** 3.76 µm (MMAD) (GSD 2.16)	**Route:** IT Instillation **Dose/Concentration:** HP-12 (mg/kg): 0.00 (saline control), 0.83 (low), 3.33 (mid), 8.33 (high) **Time to Analysis:** 96 h or 192 h post-instillation.	Exposures to mid and high-dose HP-12 induced large decreases in HR, BP, and body temperature. The decreases in HR and BP were most pronounced at night and did not return to pre-instillation values until 72 h (HR) and 48 h (BP) after dosing. ECG abnormalities (rhythm disturbances, bundle branch block) were observed primarily in the high dose group.
Reference: Wold et al. (2006, 097028) **Species:** Rat **Gender:** Female **Strain:** SD **Use:** Left jugular vein and right carotid artery were cannulated.	UFPs from either ambient air (UFAAs) or diesel engine exhaust (UFDGs); UFIDs from industrial forklift exhaust and soluble fraction UFID suspension, particle free (SF-UFID) **Particle Size:** UFAAs diameter ≤ 150 nm; UFDGs diameter ≤ 100 nm	**Route:** IV Infusion **Dose/Concentration:** UFDG (50 µg/m) **Time to Analysis:** Infused w/UFAA or UFDG. Monitored continuously for 1 h then sacrificed.	Infusion of UFDGs caused ventricular premature beats (VPBs) in 2 out of 3 rats. Ejection fraction increased slightly in rats receiving UFAA and was unchanged in the UFDG and saline groups.
Reference: Wold et al. (2006, 097028) **Species:** Rat **Gender:** Female **Strain:** SD	UFPs from either ambient air (UFAAs) or diesel engine exhaust (UFDGs); UFIDs from industrial forklift exhaust and soluble fraction UFID suspension, particle free (SF-UFID) **Particle Size:** UFAAs diameter ≤150 nm; UFDGs diameter ≤ 100 nm	**Route:** Lagendorff Heart Perfusion **Dose/Concentration:** UFDG (100 µg/2ml); UFID (12.5 µg/l in perfusate); SF-UFID (12.5 µg/l) **Time to Analysis:** Lagendorff 1: Treated w/UFDG. Lagendorff 2: Treated with UFID & SFUFID. Both experiments were monitored continuously for 1 h after injection.	UFDGs caused a marked increase in left-ventricular and end-diastolic pressure (LVEDP) after 30 min of exposure. UFIDs caused a significant decrease in left-ventricular systolic pressure (LVSP) at 30min after the start of infusion. This effect was absent when SF-UFID was studied.
Reference: Yatera et al. (2008, 157162) **Species:** Rabbit **Gender:** Female **Strain:** WHHL **Age:** 42 wk **Weight:** 3.2 ± 0.1 kg (avg)	EHC-93 from Ottawa, Canada **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** PM_{10} suspension: 5 mg EHC-93 in 1 ml saline **Time to Analysis:** Exposed 2 times/wk for 4 wk. Acute effects observed at 0.5, 1, 2, 4, 8, 12, and 24 h after initial instillation. Subchronic effects observed once/wk for 4 wk.	Exposure to PM_{10} caused progression of atherosclerotic lesions in thoracic and abdominal aorta. It also decreased circulating monocytes expressing high levels of CD31 and CD49 day, and increased expression of CD54 (ICAM-1) and CD106 (VCAM-1) in plaques. Exposure to PM_{10} increased the number of BrdU-labeled (*) monocytes into plaques and into smooth muscle underneath plaques.

Study	Pollutant	Exposure	Effects
Reference: Ying et al. (2009, 190111) **Species:** Mice **Gender:** Male **Strain:** ApoE$^{-/-}$ **Age:** 16 wk	CAPs:,New York City (Manhattan), NY; May-Sept 2007 **Particle Size:** $PM_{2.5}$	**Route: Whole-body** Inhalation **Dose/Concentration:** 138.4 ± 83.7 µg/m^3 **Time to Analysis:** 6 h/day, 5 day wk, 4 mo	**Vascular Tone:** Significant decrease in PE-induced maximum contraction of aortic rings in CAPs-exposed mice. No difference in sensitivity to PE between groups. Treatment with the soluble guanylate cyclase inhibitor ODQ restored the response to PE in CAPs aortic rings. No significant differences in relaxation induced by ACh. CAPs abolished the relaxation induced by Ca ionophore A23187. CAPs exposure slightly (but significantly) decreased maximum relaxation induced by SNP. **Protein Expression:** iNOS mRNA expression was increased in the aortas of CAPs-exposed mice. eNOS and GTPCH levels were unchanged. Distribution of inOS protein expression was limited to plaque in air-exposed mice and was found in the plaque and media for CAPs-exposed mice. **Superoxide Production:** Superoxide levels in CAPs-exposed mice were increased in the aorta compared to air-exposed mice. The addition of L-NAME significantly increased superoxide production. Extensive protein nitration in aortas of CAPs mice. NADPH subunits Rac1 and p47 phox mRNA expression was increased in aortas of mice exposed to CAPs. **Atherosclerosis:** Significant increase in plaque area of CAPs-exposed mice. Higher levels of macrophage infiltration, collagen deposition, and lipid composition of plaques from CAPs-exposed mice.
Reference: Yokota et al. (2004, 096516) **Species:** Rat **Gender:** Male **Strain:** SD **Weight:** 345-498.2 g	DEP (obtained from the Japan Automobile Research Institute) **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** Group 1: DEP: 1 mg/0.1 ml; Group 2: DEP: 0.2 ml (10, 12.5 or 25 mg/ml); Group 3: DEP 2.5 or 5 mg/0.2 ml **Time to Analysis:** DEP pre-treatment 24-72 h before ischemia/reperfusion.	**DEP Effects on Mmyocardial Ischemia/Reperfusion-induced Arrhythmia:** An increased mortality was observed in the DEP group compared to the vehicle-treated group. 46% of the animals in DEP died during the first 3 min reperfusion period. The animals of other groups were intratracheally instilled with DEP at the beginning of ischemia/reperfusion experiment, or were pretreated with polyethylene glycol-conjugated SOD (1000 IU/kg, iv). In these animals, incidences of both arrhythmia and mortality were similar to those in the animals treated with the vehicle. **DEP Rffects on the Biochemical and Hematological Parameters:** Neutrophil count was elevated by a higher dose (5 mg) of DEP at 24 h after the IT instillation, and oxygen radical production, which was induced by 12-O-tetradecanoylphorbol 13-acetate, was enhanced at 72 h.
Reference: Yokota et al. (2005, 096003) **Species:** Rat **Gender:** Male **Strain:** SD **Weight:** 303-472.2 g	DEP from Japan **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** DEP: 5 mg/animal **Time to Analysis:** Single exposure 0.5, 1, 2, 3, 6, 12, 24, 48 h.	At 12 and 24 h post-instillation, circulatory neutrophil counts in the 5 mg DEP group were significantly elevated, and were 2.1-fold (12 h) and 2.3 fold (24 h) in vehicle treated animals. 1 mg DEP caused an increase of approximately 0.4-fold in CNC at 6 h. 12-O-tetradecanoylphorbol 13-acetate induced oxyradical production (ORP) in the isolated neutrophil was enhanced at 12 and 24 h after instillation with 5 mg DEP. In Serum, a marked elevation of CINC-1 and a slight elevation of MIP-2 were also observed, while TNF-α was not detected. GM-CSF was not detected in serum 24 h post-instillation.

Study	Pollutant	Exposure	Effects
Reference: Yokota et al. (2008, 190109) **Species:** Mouse **Gender:** Male **Strain:** ddy **Age:** NR **Weight:** 39.6-46.0 g	DEP (DMSC (dichloromethane soluble-component), RPC (residual particle-component)) **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 5 mg/kg, 10 mg/kg **Time to Analysis:** DMSC and RPC extracted from DEP. Mice acclimatized 7 day . DEP, DMSC, or RPC instilled. BALF and blood obtained and G-CSF, GM-CSF, IL-6 measured 2, 4, 12, 24 h post-instillation.	**Inflammation:** At 5 mg/kg DEP increased the total cell and macrophage count. DEP or RPC increased neutrophils at 5 and 10 mg/kg. 10 mg/kg DEP or RPC increased macrophages at 4 h and decreased at 12 h. **Hematology:** Compared to 5 mg/kg DEP, RPC increased RBC, WBC, and neutrophils. 10 mg/kg RPC or DEP caused sustained increases in RBC, WBC, and neutrophils. **Cytokines:** 5 mg/kg RPC markedly increased G-CSF and IL-6. Other cytokine increases at this dose were transient. 10 mg/kg DEP increased IL-6 at 4 h, and DEP or RPC increased G-CSF and IL-6 at 12 h. DEP or RPC also increased IL-1β. **Myocardium:** Myocardial MPO activity significantly increased in 5 mg/kg RPC at 12 and 24 h. Myocardial MIP-2 increased the most in 5 mg/kg RPC, while LIX tended to be lowered by RPC.

Table D-2. Respiratory effects: in vitro studies.

Study	Pollutant	Exposure	Effects
Reference: Aam and Fonnum (2007, 155123) **Species:** Human, Rat **Tissues/Cell Types:** Human-Neutrophil Granulocytes (NG); Rat- AM	DEP: SRM 1975 **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** NG: 8.8 - 280 µg/mL AM:140, 280 µg/mL Vitamin E = 5 µM **Time to Analysis:** 1 h	**ROS of NG:** Formation of ROS in NG decreased with increased doses of DEP. Lucigenin chemiluminescence of ROS formation diminished 25% at 8.8 µg/mL DEP and luminol chemiluminescence 32% with 17.5 µg/mL DEP. DCF fluorescence required much higher doses of DEP. Controls without PMA stimulation had highly reduced lucigenin and luminol with DEP dose of 140 µg/mL while DCF increased 116%. **ROS of AM:** 280 µg/mL of DEP decreased ROS level by 19% with DCF. DEP with PMA-unstimulated cells increased 24% with DCF. **Necrosis:** NG cell death was DEP dose-dependent. At 280 µg/mL, cell death increased 5.4% as compared to control. LDH concentration increased 1.6% with 70 µg/mL DEP and 3.9% with 280 µg/mL after 1 h.
Reference: Agopyan et al. (2003, 056065) **Species:** Human **Tissues/Cell Types:** BEAS-2B, NHBE, SAEC	PC: synthetic carboxylate-modified particles **Particle Size:** 2, 10 µm	**Route:** Cell Culture **Dose/Concentration:** PC2 = 0.83 g/mL or $3.4x10^9$ particles/mL PC10 = 0.8 g/mL or $3x10^6$ particles/mL **Time to Analysis:** PC2 = 12, 24, 8 h PC10 = 2, 6, 12, 24 h	**Calcium Imaging:** PC10 induced increase of Ca^{2+} concentration in all capsaicin-sensitive cells 100%. Similar reaction observed in cells exposed to PC2. However, more than 3-PC2s were required to induce a Ca increase unlike PC10. CPZ (10um) and amiloride could fully block PC-induced response. **cAMP:** Post 6 h, a dose-dependent increase in cAMP was observed. Again, CPZ blocked increase by 70-90% depending on cell type: SAEC >NHBE ~ BEAS-2B. **Apoptosis:** PC10 and PC2 induced apoptosis time-dependently. PC2 was slower in induction than PC10. Post 48 h, 80-95% cells were apoptotic in all cell types. Noncapaisin-sensitive cells (which did not bind to particles) did not exhibit apoptosis. CPZ reduced apoptosis by 97% BEAS-2B, 96% NHBE and 98% SAEC. Amiloride did not block apoptosis. **Necrosis:** Induction of necrosis by PC2 and PC 10 was negligible. A slight increase from 1% to 2% was observed at 24-48 h in NHBE and SAEC. BEAS-2B showed slight decrease from 3% to 4% in same time period.

Study	Pollutant	Exposure	Effects
Reference: Agopyan et al. (2004, 156198) **Species:** Human, Mouse **Tissues/Cell Types:** Human-NHBE, SAEC; Mouse-Wildtype and TRPV1(-/-) Terminal Ganglion Neurons (TG)	ROFA MSHA: Mt St Helen Ash **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 100 µg/mL ROFA or MSHA **Time to Analysis:** ROFA/MSHA in NHBE and SAEC = 2, 6, 24, 48 h ROFA/ MSHA in TG = 24 h cAMP measurements with NHBE and SAEC exposed to ROFA/MSHA = 6 h	**Calcium Imaging in NHBE and SAEC:** In 100% of reactive cells, ROFA/MSHA induced an increase in Ca^{2+}. Levels remained elevated as long as PM bound to plasma membrane. Washing and disjoining PM from membrane caused Ca^{2+} to slowly decline to baseline. CPZ (or CPZ and amiloride) reversibly inhibited PM-induced rises in Ca^{2+}. **Calcium Imaging in TRPV1(+/+) and (-/-) mice sensory neurons:** All sensitive neurons in TRPV1(+/+) increased Ca^{2+} in response to ROFA. No effect of ROFA in TRPV1(-/-). **cAMP:** ROFA and MSHA induced increases in Ca^{2+} in NHBE and SAEC cells, which was completely blocked by cAMP. **Apoptosis:** ROFA or MSHA induced time-dependent apoptosis, peaking at 24 h. CPZ again inhibited this response. Neurons bound to PM (<25um) induced apoptosis in TRPV1(+/+). Cells without bound PM or bound with PM (>25 µm) showed no effect. No apoptosis occurred in the absence of Ca^{2+}. **Necrosis:** Necrosis for any of the cell types was negligible. **PKA:** Inhibition of PKA resulted in 90+% apoptosis in NHBE and SAEC. Again, no apoptosis was observed in a Ca^{2+} free environment.
Reference: Ahn et al. (2008, 156199) **Species:** Human **Tissues/Cell Types:** A549	DEP: (6 cyl, 11L, turbo-charged, heavy-duty diesel engine, South Korea) Dex: anti-inflammatory (Sigma, St. Louis, MO) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentrations:** 0, 1, 5, 10, 50 and 100 µg/mL of DEP Some cells pre-treated with 10, 20, 40, 50 pg/mL of Dex. **Time to Analysis:** 24 h	**COX-2 Expression:** Cells expressed dose-dependent increases in COX-2 expression after treatment with 10-100 µg/mL of DEP. Treatment of 50 µg/mL for 24 h induced statistically significant COX-2 expression in both mRNA and protein levels. Pre-treatment with Dex significantly reduced expression of COX-2 mRNA and protein. Dex treatment induced dose-dependent suppression of DEP-induced protein levels. **PGE2 Levels:** Levels of the inflammatory mediator, PGE2, increased when were cells exposed to 50 µg/mL of DEP. Pre-treatment with 50 µg /mL Dex completely inhibited DEP-induced release of PGE2.
Reference: Ahsan (2005, 156200) **Species:** Human **Tissues/Cell Types:** Trx-1-transfected Clone of Murine L-929 cells; Control Clone (L-929-Neo1); A549	DEP: provided by Dr. Masaru Sagai, University of Health and Welfare, Aomori, Japan **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** DEP: 50 µg/mL hTrx-1- or L-929-Neo1: 40 µg/mL Pretreatment: rhTrx-1 (10 µg/mL) or DM-rhTrx-1 (NR) **Time to Analysis:** Pretreatment for 1 h. Parameters measured 3 h post exposure.	**ROS:** DEP induced significant increases of ROS in L929-Neo1 cells. hTRx-1 cells showed no affect. RT-PCR revealed hTrx-1 mRNA expression in transfected cells but not control L929-Neo1 cells. Endogenous murine Trx-1 mRNA expression increased in control cells, but not in hTrx-1 cells. A549 cells had increased ROS levels but these levels were suppressed with rhTrx-1 pretreatment. Pre-treatment with DM-rhTrx-1 increased ROS levels more. **Akt (antiapoptotic molecule):** Phosphorylated Akt prevents apoptosis. DEP induced phosphorylation of Akt in control cells after 3 h and dephosphorylation after 5 h. In hTrx-1 cells, Akt remained phosphorylated after 5 h. In A549 cells, Akt phosphorylated at 3 h and slowly turned off at 12-24 h. Pre-treatment with rhTrx-1 blocked dephosphorylation. This suggests that Trx-1 preserves active form of Akt and thereby protects against cytotoxicity from DEP.

Study	Pollutant	Exposure	Effects
Reference: Alfaro-Moreno et al. (2002, 156204) **Species:** Human, Mouse, Rat **Strain:** Human-A549; Mouse-J7 74A.1, BALB-c **Tissues/Cell Types:** HUVEC, Mouse Fibroblasts, Rat Lung Fibroblasts (RLF)	PM_{10}: Collected from 3 zones in Mexico City: North (industrial), Center (business) and South (residential) **Particle Size:** PM_{10}	**Route:** Cell Culture 15000 cells/cm^2 except: Cytotoxicity: Confluent Cultures 180,000 cells/cm^2. DNA Breakage: 20,000 cells/well. Cytokine Assays: 180,000 cells/cm^2 **Dose/Concentration:** Cytotoxicity: 10, 20, 40, 80, 160 µg/cm^2 Apoptosis: 160 µg/cm^2 DNA Breakage: 2.5, 5, 10, 20, 40 µg/cm^2 Cytokine Assays: 10, 20, 40, 80 µg/cm^2 E-Selectin Expression: 40 µg/cm^2 **Time to Analysis:** Cytotoxicity: 24, 48, 72 h; Apoptosis: 24 h; DNA Breakage: 72 h; Cytokine Assays: 24 h	**Cytotoxicity:** Cytotoxic effect exhibited dose-dependency after 72 h in proliferating cells of J774A.1, BALB-c and RLF cell lines. **Proliferating Cells:** Northern particles induced a statistically larger effect than central or southern particles. J774A.1 was more susceptible while BALB-c was less susceptible. A549 was most resistant to decreased viability during exposure. No significant variation in viability was observed when compared to the control. Particles were not cytotoxic among confluent cell growth for any cell lines when exposed to 20-160 µg/cm^2. **Apoptosis:** Overall, particles induced low rates of cell death via apoptosis. J774A.1 depicted similar levels of apoptosis when exposed to three PM zones, ~15% apoptotic cells measured. BALB-c was not reported. Results for the A549 measured apoptotic cells were: South- 4%, Central- 11% and North- 15%. HUVEC cells indicated an increase in apoptosis with northern particles. **DNA Breakage:** PM_{10} from all zones induced DNA breakage. A dose-dependent relationship was established with $PM_{2.5}$ particles at concentrations of 10 µg/cm^2. The Southern zone required a higher dose of PM (10 µg/cm^2) to produce the same effect as other zones (2.5 µg/cm^2). **Cytokines:** Particles induced TNF-α and IL-6 secretion in J774A.1 cells dose-dependently. IL-6 increased significantly with central particles. PGE2 secretion in RLF cells induced by exposure to PM showed dose-dependent responses. PM from the central zone induced the most PGE2 secretion. Max secretion was observed at doses of 40 µg/cm^2 from all three PM zones. **E-Selectin Expression:** HUVEC cells showed a 25% increase in E-selectin expression after exposure to 40 µg/cm^2 of PM.
Reference: Amakawa et al. (2003, 156211) **Species:** Mouse, Human **Strain:** Mouse-ICR **Tissues/Cell Types:** AMs **Gender:** Male **Age:** Mouse 6-7 wk; Human 20-24 yr	DEP (obtained from a 4JB1, Isuzu, 1500 rpm, 4cyl diesel engine) DEPE = DEP Extract (methanol) CB = Charcoal (Sigma) **Particle Size:** DEP- 0.4 µm, CB- 0.7 µm	**Route:** Cell Culture Mouse: 5×10^5 cells/mL; Human: 3×10^5 cells/mL **Dose/Concentration:** DEP = 1 or 10 µg/mL; DEPE = 1 or 10 µg/mL; CB = 1, 10, 100 µg/mL **Time to Analysis:** Human cells pre-treated with LPS 1 µg/mL. Murine cells pre-treated with SOD 300 IU/mL. Parameters measured 24 h post exposure.	**Cells:** For mice, more than 90% of the cells were macrophages and over 90% were viable. For humans, 96% of the cells were macrophages, 3% lymphocytes and 1% neutrophils; over 95% of the human cells were viable. **DEP Cytotoxicity:** None observed **Cytokines:** DEP (10 µg/mL) suppressed release of TNF-α and IL-6 for both mice and humans in a dose-dependent manner. Murine cells pre-treated with LPS or IFN-γ released even less TNF-α and IL-6. IL-10 was unaffected. Human macrophages pre-treated with LPS also released lower levels of TNF-α, IL-6 and IL-8. **ROS:** Pre-treatment of SOD on murine cells partially attenuated the suppressive effect of DEP as well as decreased the production of ROS generated by DEP (10 µg/mL). **Carbon:** Carbon particles did not suppress TNF-α or IL-6 release from murine AMs; however,100 µg/mL of CB stimulated TNF-α production. **Methanol:** No cytotoxicity nor cytokine release effects were observed. **DEPE:** DEPE suppressed TNF-α and IL-6 release in a similar way as DEP.

Study	Pollutant	Exposure	Effects
Reference: Amara et al. (2007, 156212) **Species:** Human **Cell Lines:** A549, NCI-H292	DEP = SRM 2975 CSC = cigarette smoke condensates (collected from Kentucky standard cigarettes, 2R4F; University of Kentucky) DC = DEP + CSC CB (Degussa, Frankfurt, Germany) **Particle Size:** CB: 95 nm; DEP: NR	**Route:** Cell Culture **Dose/Concentration:** DEP = 5-10 µg/cm^2 CB = 10 µg/cm^2 CSC = 10 µg/cm^2 **Time to Analysis:** 6 or 24 h	**Inflammatory Markers:** LDH of A549 was unaffected at either time point with DEP or CB. LDH increased with CSC at concentrations high than 10 µg/mL at both time points. DC had no effect. **Proteases:** MMP-1 mRNA expression showed a dose dependent increase with DEP in A549 cells. DEP also increased MMP-1 in NCI-H292 cells. CB and CSC had no effect. MMP-1 mRNA expressions were inhibited by N-acetylcysteine antioxidant. Similar inhibition was observed with NOX4 oxidase. DC induced a similar effect to DEP. MMP-1 protein expression increased post 24 h with DEP. MMP-2, TIMP-1, TIMP-2 mRNA expression was unaffected. **TGF:** TGF-β mRNA expression was unaffected. **ROS:** DEP and DC increased ROS formation after 1 h. DEP effect was inhibited by N-acetylcysteine antioxidant pre-treatment. **MAP-Kinase:** DEP induced MMP-1 expression increased ERK1/2 phosphorylation after 10 min, peaking at 30 min, and returning to normal levels at 60 min. Treatment with CBPs did not increase ERK1/2 phosphorylation whereas treatment with CSC resulted in phosphorylation. Only inhibitors of ERK1/2 reduced DEP induced MMP-1 activity. P38 and JNK inhibitors had no effect.
Reference: Anseth et al. (2005, 088646) **Species:** Human **Cell Lines:** A549; A549-p0 (lacking mitochondria)	s-ROFA: soluble portion **Particle Size:** 1.95 ± 018 µm	**Route:** Cell Culture (3X10^5 cells/mL) **Dose/Concentration:** 100 µg/mL **Time to Analysis:** Experiments conducted by spreading monolayer of Infasurf (calf lung surfactant extract on PBS, PBS+ROFA or conditioned media from A549 AEC. Parameters measured after one 6-h incubation period.	**Lung Surfactant Gelation:** ROFA alone and A549 conditioned media alone did not significantly alter Infasurf rheology. However, conditioned media from A549 AEC at 16 h induced a significant increase in elastic storage and viscous loss moduli. Inhibiting ROS production lowered effect, indicating s-ROFA gelation mediated through ROS. **ROS:** ROS mediated through mitochondria as evidenced by the effect of ROFA-AEC on surfactant gelation in the presence of mitochondria ROS inhibitors as well as A549-p0 cells.
Reference: Auger et al. (2006, 156235) **Species:** Human **Tissue/Cell Type:** Nasal Epithelial Cells	DEP: SRM1650 $PM_{2.5}$: obtained from a highway in Paris, France **Particle Size:** DEP: 400 nm (mean diameter); $PM_{2.5}$	**Route:** Cell Culture (2-3.5x10^4 cells/cm^2) **Dose/Concentration:** 10-80 µg/cm^2 **Time to Analysis:** Cells treated on apical side. Parameters measured 24 h following treatment.	**Cytotoxicity (LDH):** No cytotoxicity for DEP or $PM_{2.5}$ (80 µg/cm^2). **Cytokines:** In non-stimulated ALI cultures, IL-8 was the most abundantly secreted cytokine, followed by GM-CSF, TNF-α, and IL-6 in decreasing levels of production. Amphiregulin was moderately, but consistently, secreted. After treatment, both DEP and $PM_{2.5}$ induced IL-8 and amphiregulin release in a dose-dependent manner through the basolateral surface. $PM_{2.5}$ stimulated IL-6 and GM-CSF release through the apical surface. **ICAM-1 expression:** No effect from DEP or $PM_{2.5}$. **ROS:** DEP and $PM_{2.5}$ both increased ROS production in a dose-dependent manner.

Study	Pollutant	Exposure	Effects
Reference: Bachoual et al. (2007, 155667) **Species:** Mouse **Cell Type:** RAW 264.7	PM_{10} from two Paris, France subway sites: RER and Metro CB (Frankfurt, Germany) TiO_2 (Calais, France) DEP: SRM1650 (NIST) **Particle Size:** CB: 95 nm; TiO_2:150 nm; DEP: NR RER PM_{10}: 79% <0.5 µm, 20% 0.5-1 µm; Metro PM_{10}: 88% <0.5 µm, 11% 0.5-1 µm.	**Route:** Cell Culture (40,000 cells/mL) **Dose/Concentration:** All particles: 0.01, 0.1, 1, 10 µg/cm^2 **Time to Analysis:** 3, 8, 24 h	**Cell Viability:** No effects from any particulate at concentrations up to 10 µg/cm^2 for 24 h. **Inflammatory Effect:** Exposure of cells to 10 µg/cm^2 of RER or Metro induced time-dependent increase in TNF-α and MIP-2 protein release. This effect was similar to both locations. No effect was observed at low concentrations of PM_{10}. No effect of CB, TiO_2 or DEP was observed. **GM-CSF or KC production:** RER and Metro PM_{10} did not induce any effect at any concentration. **Effect on Protease mRNA Expression:** Exposure of cells to 10 µg/cm^2 RER or Metro PM_{10} did not modify mRNA expression of MMP-2 or -9 or their inhibitors TIMP-1 and -2. MMP-12 expression significantly increased after exposure to RER or Metro PM_{10} for 8 h. **Effects on HO-1 Protein Expression:** Exposure to 10 µg/cm^2 of RER or Metro PM_{10} for 24 h induced positive cytoplasmic staining for HO-1.
Reference: Baulig et al. (2007, 151733) **Species:** Human **Cell Line:** 16-HBE14o-	WUB: Winter Urban Background Particles (obtained from Vitry-sur-Seine, suburb of Paris, France) SUB: summer Urban Background Particles Vitry-sur-Seine) WC: Winter Curbside Particles, SRM1648 (obtained from Porte-d'Auteuil, ring road of Paris, France) SC: Summer Curbside Particles, SRM 1648 (Porte-d'Auteuil) DEP: SRM 1650a (NIST) DPL (control) **Particle Size:** WUB, SUB: $PM_{2.5}$; WC, SC, DEP: NR	**Route:** Cell Culture (20,000 cells/cm^2) **Dose/Concentration:** 10 µg/cm^2 **Time to Analysis:** 18 or 24 h	**EGF:** All native $PM_{2.5}$ induced similar AR secretion by bronchial epithelial cells (in decreasing order WC, WUB, SC, SUB), but this release was significantly greater than the release induced by DEP. β-cellulin increased with SC, WUB and WC. No data was available for SUB or DEP. **Interleukins:** IL-1α increased significantly with WUB, WC,SC, DEP, DPL (in decreasing order). No data was available for SUB. Exposure to WUB caused IL-1β to increase to induction factor of over 2. IL-11 R α decreased significantly with SUB. **Cytokines:** Exposure to WUB caused G-CSF to increase with an induction factor of over 2.Though not statistically significant, TNF-R1 also increased. **Proteases:** TIMP-2 decreased with WUB but significantly increased with SUB. Overall, SUB downregulated integrins and interleukins seen with other particles while upregulating neurotrophic factors, chemokine receptors and adhesion molecules. MMPs were not measured. **Chemokines:** CCR-3 significantly increased with SUB. GRO-γ and GRO-α increased with WC at both 18 and 24 h. DEP had no effect with GRO-α. Removal of metal from particles lowered response of GRO-α.

Study	Pollutant	Exposure	Effects
Reference: Bayram et al. (2006, 088439) **Species:** Human **Cell Type:** A549	DEP: (obtained from a 4JB1-type, light-duty, 4 cyl, 2.74-L Isuzu diesel engine) DEP-FCS: DEP + FCS DEP-NAC: DEP + N-acetylcystine, antioxidant DEP-A: DEP + AEOL10113, catalytic antioxidant DEP-S: DEP + SP600125, inhibitor of JNK DEP-N: DEP + SN50, inhibitor of NF-kB **Particle Size:** DEP: 0.4 µm (mean diameter)	**Route:** Cell Culture **Dose/Concentration:** DEP: 0, 5, 10, 50, 100, 200 µg/mL **Time to Analysis:** 24, 48, 72 h	**Cell Growth:** With 10% FCS (as a positive control), A549 cells exhibited time dependent growth. A mixture of FCS and DEP did not affect cell growth for up to 48 h. With DEP alone, cell growth was prevented from cell number reduction due to removal of serum at 48 and 72 h. A dose of 10 µg/mL induced a maximum proliferation effect. **Cell Cycle:** DEP increased the percentage of serum-starved cells in S phase at 48 h. DEP decreased the percentage in G0/1 phase and G2/M phase. **Apoptosis:** DEP prevented the increase in apoptotic, serum-starved cells. **Protein Expression:** p21CIP1/WAF1 expression increased at 48 h. DEP dose-dependently decreased this expression. **NAC:** NAC alone, at 33 mM, induced an increase in cell numbers. DEP-NAC inhibited cell numbers at 48 h. DEP-NAC inhibited cell numbers in S phase; thus, cells in G0/1 phase increased. DEP-NAC induced a further decrease of cells in G2/M phase. **AEOL10113:** DEP-A caused a dose-dependent decrease in cell numbers. **SP**600125**:** Alone, SP600125 increased cell numbers at 33 mM. DEP-S decreased cell numbers.
Reference: Becher et al. (2007, 097125) **Species:** Rat **Strain:** Crl/WKY **Cell Type:** AM, Alveolar Type II **Gender:** Male **Weight:** 200 g	SPM = suspended PM SRM-1648 **Particle Size:** 6-8 µm	**Route:** Cell Culture (1.5×10^6 cells/well AM; 6×10^6 cells/well Type II) **Dose:** 200 µg/mL = 20 µg/cm^2 **Time to Analysis:** 20 h	**Cytokines in Macrophages:** SPM increased TNF-α and MIP-2. NADPH inhibitor DPI reduced MIP-2 response, whereas iNOS inhibitor 1400W did not affect either. **Cytokines in Type 2 Cells:** SPM increased IL-6 and MIP-2 significantly. This SPM effect was inhibited by DPI, whereas1400W reduced the IL-6 response significantly. **ROS in Type 2 Cells:** SPM significantly increased ROS formation. DPI largely blocked this SPM effect. **ROS in Macrophages:** No significant increases were observed.
Reference: Becker et al. (2005, 088590) **Species:** Human **Gender:** Male and Female **Age:** 18-35 yr **Cell Types:** Alveolar Macrophages, NHBE	PM (Coarse, Fine, Ultrafine): Chapel Hill, NC **Particle Size:** PM-C: $PM_{2.5}$; PM-F: $PM_{0.1}$; PM UF: <0.1µm	**Route:** Cell Culture ($0.5\text{-}1\times10^5$ cells/well NHBE; $2\text{-}3\times10^5$/mL AM) **Dose/Concentration:** NH BE: 25, 50, 100, 250 µg/mL of PM; AMs: 50 µg/mL of DEP or 10 ng/mL of LPS **Time to Analysis:** 18h for NHBE; overnight for AMs	**Cytokines:** All 3 fractions induced dose-dependent increases in IL-8 secretion with PM-c, PM-F, PM-UF (in order of decreasing effects). TLR-2 antibody blocked these particle induced IL-8 effects. **Inhibitors of Endotoxin effects and TLR-4 activation:** No effects were observed in NHBE, but all 3 fractions repressed the IL-6 release in AMs. **TLR mRNA Expression:** PM did not affect TLR-2 mRNA in NHBEs. PM-C and PM-F induced a slight increase in TLR-4 mRNA in NHBEs while PM-UF induced a substantial increase. PM-C increased TLR-2 mRNA in AMs and decreased TLR-4 mRNA in AMs. **Induction of Hsp70:** PM-C and PM-F induced Hsp70 in NHBE dose-dependently. Hsp70 was not induced in AM following particle stimulator.

Study	Pollutant	Exposure	Effects
Reference: Becker et al. (2005, 088592) **Species:** Human **Gender:** Male **Age:** 18-35 yr **Cell Types:** AM, NHBE	PM (Coarse, Fine, Ultrafine): Chapel Hill, NC ROFA Fe, Si, Cr Components Oct 2001, Jan 2002, April 2002, July 2002 **Particle Size:** PM-C: 2.5-10 µm; PM-F: <0.1 µm; PM-UF: <0.1 µm	**Route:** Cell Culture (3-5×10^5 cells/well NHBE; 2-3×10^5 cells/mL AM) **Dose/Concentration:** NHBE: 11 µg/mL of PM; AM: 50 µg/mL of PM **Time to Analysis:** 18-24 h NHBE; 18 h AM	**IL-8 Release in NHBE:** PM-C and PM-UF induced effects. No effects from PM-F (all 4 dates). **IL-6 Release in AM:** All 3 fractions induced increase with later dates having generally lower effects. **ROS (DCF):** NHBE, at lower exposures, were observed to be more responsive to PM than AMs. AM exhibited highly variable results over time. **ROS (DHR):** NHBE cells were observed to be more responsive to PM than AMs. AM responsiveness to PM increased over 4 time periods; this was not observed in NHBE. **Seasonal Variability:** Coarse particles were more potent than F and UF regardless of the month, and the potency for PM to induce IL-6/IL-8 production varied significantly. Coarse particles induced a 5-25 fold change in IL-6 release for AMs and a 3-6 fold change in IL-8 release for NHBEs. **Metal Correlation to IL-6/8 induction:** Fe and Si were positively associated with IL-6 release in AMs incubated with the coarse fraction. Cr was positively associated with IL-8 release in NHBE cells incubated with F or UF.
Reference: Beck-Speier et al. (2005, 156262) **Species:** Human, Canine (Beagle) **Cell Types:** Human AMs, Canine AM (CAM)	DEP = SRM 1650a (NIST) EC = Ultrafine EC (spark discharge) P90 = Printex 90 (Carbon Black, Degussa) PG = Printex G (Carbon Black, Degussa) **Particle Size:** DEP: 20-40 nm; EC: 5-10 nm; P90: 14 nm; PG: 51 nm	**Route:** Cell Culture (1×10^6 cells/mL AM) **Dose/Concentration:** All particles: 1 (EC only), 3.2, 10, 32, 100 µg/mL **Time to Analysis:** 60 min	**Phagocytosis:** All particles were phagocytosed by CAM within 60 min. **Oxidative Potential:** EC showed a very high effect. DEP, P90 and PG had no effect **Formation of Lipid Mediators:** DEP, EC P90 and PG increased arachidonic acid and PGE2/TXB2 in CAM in a dose-dependent manner. Only EC increased LTB4 and 8-isoprostane. **ROS Activation:** All particles increased activity in canine macrophages with EC, P90 and PG increasing activity in a dose-dependent manner. DEP increased activity in canine macrophages. Similar results were observed human alveolar macrophages but only EC and P90 were tested. **Particle Mass vs Particle Surface Area:** PGE2/TXB2 effects were highly correlated with particle surface area.
Reference: Bitterle et al. (2006, 156276) **Species:** Human **Cell Type:** A549	C-UFP = ultrafine carbonaceous particles (obtained from a spark discharge aerosol generator GFG 1000, Palas, Karlsruhe, Germany) **Particle Size:** 90 nm (count median mobility diameter)	**Route:** Cell Culture (3×10^7 cells) **Dose/Concentration:** 44 ± 4 ng/cm^2; 87 ± 23 ng/cm^2; 230 ± 70 ng/cm^2 **Time to Analysis:** 6 h	**Cell Viability:** Exposure to clean air resulted in a 93.7 ± 9.1% viability. Exposure to low, mid and high doses of C-UFP resulted in a 94.9 ± 9.5% viability. Thus C-UFP had no effect on cell viability. **Interleukins:** Clean air controls induced a 2-3 fold increase in IL-6 and IL-8 production vs submersed control. U-CFP exposures induced a similar effect on IL-8 and IL-6 levels. **Antioxidant enzyme HO-1:** The mid dose increased transcription of HO-1 by 2.7 fold. There was no observed effect at the high dose level which indicates possible cytotoxicity.

Study	Pollutant	Exposure	Effects
Reference: Blanchet et al. (2004, 087982) **Species:** Human **Cell Type:** 16HBE	$PM_{2.5}$ (Vitry-sur-Seine, Paris, France) DEP = SRM 1650a CB = Carbon Black (Degussa) TiO_2 (Huntsman) **Particle Size:** CB: 95 nm; TiO_2: 150 nm	**Route:** Cell Culture (45,000 cells/cm^2) **Dose/Concentration:** All particles: 0.1, 1, 10, 30 µg/cm^2 **Time to Analysis:** 6, 18, 24, 30 h	**Amphiregulin Expression:** DEP and $PM_{2.5}$ both increased AR mRNA expression from 6 to 30 h, with $PM_{2.5}$ inducing higher expression levels than DEP. Both DEP and $PM_{2.5}$ increased AR protein secretion. No observed effect for CB and TiO_2. $PM_{2.5}$ induced protein secretion dose-dependently. **Signal Pathways in AR Secretion:** MAP kinase and tyrosine kinase inhibitors reduced effects of DEP and $PM_{2.5}$ but p38MAP kinase inhibitor did not. **Role of Oxidative Stress:** N-Acetylcysteine blocked AR secretion following $PM_{2.5}$. Antioxidant enzyme catalase had no effect. **Cytokines:** DEP induced a significantly high release of GM-CSF, higher than $PM_{2.5}$. EGFR antibody reduced GM-CSF release at 0.25 µg/mL dose.
Reference: Bonvallot et al. (2001, 156283), **Species:** Human **Cell Type:** 16HBE14o-	DEP: SRM 1650 OE-DEP: dichloromethane extract (2x) of DEP nDEP: native DEP sDEP: nDEP - OE-DEP CB: Carbon Black FR103 (Degussa) BaP: Benzo[a]pyrene CB: 95 nm NR **Particle Size:** CB: 95 nm; DEP: NR	**Route:** Cell Culture (3×10^6 cells) **Dose/Concentration:** DEP, sDEP, nDEP and CB = 10 µg/cm^2 OE-DEP = 15 µg/mL BaP = 0.25, 50 and 250 µg/mL **Time to Analysis:** 24 h	**Proinflammatory Response:** At 10 µg/cm^2, nDEP induced GM-CSF release by 4.7 fold. OE-DEP increased GM-CSF by 3.7 fold. BaP and sDEP also induced increases of CN-CSF but had smaller effect. CB had no effect. **NF-κB Activation:** nDEP and OE-DEP induced enhanced degradation of IκB at 2-4 h and 1 h respectively. NF-κB DNA binding was enhanced by OE-DEP (15 µg/mL, peak <1 h) and nDEP (10 µg/cm^2, peak at 2-h with plateau till 4 h). Both OE- and nDEP enhanced NF-kB DNA binding levels were higher than BaP enhanced binding levels. **CYP1A1 mRNA:** The CYP1A1 mRNA level was markedly increased in nDEP and OE-DEP treated cells in comparison with their respective controls. **Radical Scavengers (decreased ROS in situ):** Increases of GM-CSF and NF-κB DNA binding by nDEP and OE-DEP was attenuated by radical scavengers. **MAPK Activation:** Increases by nDEP and OE-DEP of GM-CSF was inhibited by Erk1/2 inhibitor but not by p38 inhibitors. Both nDEP and OE-DEP triggered Erk1/2 and p38 phosphorylation. sDEP affected p38 phosphorylation only.
Reference: Brown et al. (2007, 156300) **Species:** Human, Mouse **Cell Type:** PBMC, A549 (Human); J774A.1 (Mouse)	PM_{10} (London, England) CM from PM_{10}-treated human monocytes **Particle Size:** PM_{10}	**Route:** Cell Culture (1×10^6 cells/mL J774A.1; 5×10^6 cells/mL PBMC; 5×10^5 cells/well A549) **Dose/Concentration:** PM_{10}: 75 µl (10 µg/mL); CM: 250 µl; tBHP: 12.5 µm (in J774); TNF: 0, 500 pg, 1 ng, 10 ng **Time to Analysis:** tBHP:1, 2, 4 h; PM: 4 h; TNF: 18 h	**Cytokines:** PM_{10} induced release TNF-α protein from PBMCs at 10 µg/mL for 4 h. Further inhibited by verapamil and BAPTA-AM. Calmodulin inhibitor W-7 had no effect. CM increased IL-8 from A549 cells 3 fold. Verapamil, BAPTA-AM and W-7 significantly inhibited IL-8 release induced by CM. **ICAM-1:** A549 cells treated with TNF-α showed dose-dependently effect of TNF-α on ICAM-1 upregulation at 18 h. CM also induced upregulation. Verapamil, BAPTA-AM and W-7 fully inhibited CM-induced upregulation.

Study	Pollutant	Exposure	Effects
Reference: Calcabrini et al. (2004, 096865) **Species:** Human **Cell Type:** A549	$PM_{2.5}$ (Rome, Italy) **Particle Size:** $PM_{2.5}$	**Route:** Cell Culture (5×10^4 cells/well) **Dose/Concentration:** 30, 60 µg/cm^2 (aliquot of 0.1 µg/µl) **Time to Analysis:** 5, 24, 48, 72 h	**Particle Characterization:** Components measured include C-rich particles, Ca sulfates, silica, silicates, Fe-rich particles, metals. Carbonaceous particles made up majority of PM. **Cell Surface Changes:** PM deposited on the cell surface showed dose and time-dependent increases in microvilli rearrangement and cell shape alterations without affecting apoptotic markers for up to 72 h. **PM internalization:** At 24 h with the low dose, aggregates of PM in cytoplasm or surrounded by membrane was observed. With the high dose, large particle aggregates often close to nuclear envelopes were observed. **Cytoskeleton:** At 72 h PM induced dose-dependent alterations from rearrangement/interweaving of microtubules to bundling of microtubules with some shortening/disruption. **Cell Growth:** PM decreased cell growth in a dose and time-dependent manner **ROS:** PM increased ROS at the high dose for 5 h but not at 24 h or with the low dose. **Cytokines:** PM induced TNF-α peaked at 5 h at high dose and 48 h at low dose, both ND at 72 h. PM induced IL-6 starting at 24 h thru 72 h in time and dose dependent manner.
Reference: Cao et al. (2007, 156322) **Species:** Human **Cell Type:** HAEC	NIST-DEP: collected using a diesel forklift and hot bag filter system. (NIST, Minneapolis, MN) C-DEP: obtained from a 30-kw (40 hp) four-cylinder Deutz BF4M1008 diesel engine (U.S. EPA) Organic extract fraction of particles NIST- DEP 2% C-DEP 20 % **Particle Size:** NR	**Route:** Cell Culture (5×10^5 cells) **Dose/Concentration:** NIST-DEP, C-DEP: 0, 12.5, 25, 50, 100, 200 µg/mL **Time to Analysis:** 1-4 h	**Cell Viability:** DEP had no effect. **Stat3:** Both DEPs induced time-dependent phosphorylization of Stat3 in cytoplasm. NIST-DEP induced phosphorylization dose-dependently from 12.5 to 50 µg/mL but stayed level at 100 and 200 µg/mL. p-Stat3 induction was inhibited by antioxidant BHA though it was reactivated with exposure to H_2O_2. Reaction induced by H_2O_2 was similar to that of DEP. **pStat3 Nuclear Transport:** NIST-DEP induced cytoplasmic pStat3 to move from cytoplasm into nucleus. **pEGFR Dephosphorylation:** After 4 h of NIST-DEP exposure, dephosphorylation was inhibited for up to 90 min.
Reference: Chang et al. (2005, 097776) **Species:** Human **Cell Type:** A540, THP-1	UfCB (Printex 90, Degussa) **Particle Size:** 14 nm	**Route:** Cell Culture (7×10^5 cells) **Dose/Concentration:** 100 µg/mL **Time to Analysis:** 4 h	**ROS in THP-1 and A549**: UFCB increased ROS. NAC pretreatment blocked most of the UFCB-induced ROS production. **VEGF in THP-1:** UFCB increased VEG. NAC decreased the UFCB effects below those of the control. **VEGF in A549:** Produced similar, but less marked, results as with THP-1.

Study	Pollutant	Exposure	Effects
Reference: Chauhan et al. (2004, 096682) **Species:** Mouse **Strain:** BALB/c **Cell Type:** RAW 264.7; J774A.1; WR19M.1	EHC-T: total EHC-93 (Env Health Ctr, Ottawa, Canada) EHC-I: insoluble EHC EHC-S: soluble EHC SRM1648: urban particulate St. Louis (NIST) SRM1649: urban dust/organics Washington (NIST) VERP: fine $PM_{2.5}$ (Vermillion, Ohio) Cristobalite: SRM 1879 (NIST) TiO_2: SRM 154b (NIST) **Particle Size:** EHC-93: 0.5 µm (median diameter); Cristobalite, SRM 1648, SRM 1649, TiO_2,: NR; VERP: $PM_{2.5}$	**Route:** Cell Culture (15000 cells/well) **Dose/Concentration:** Particle suspensions: 20, 50, 100 µg/well LPS: 0-5 µg/mL IFN-y: 0-1000 U/mL **Time to Analysis:** Particles added to culture at 0h, LPS and IFN-γ added at 2 h. Parameters measured after 22 h incubation period.	**Stimulation with LPS/IFN-y:** LPS and IFN-y each induced NO release. Combination of LPS and IFN-y produced larger effect in all cell lines. L-NMMA, NOS inhibitor, suppressed most of the NO production with 100 nmol/L. **Cellular Viability and Cytotoxicity:** Exposure of cells to particulates did not result in overt cytotoxicity or excessive loss of cellular material. There was no correlation between the cytotoxicity of the particles in the surviving cells and the loss of protein mass in monolayers. **Nitrite Production:** EHC-T, EH-93-I, SRM1648 and SRM 1649 produced dose-dependent decreases. Cristobalite only decreased at higher doses. No effect from EHC-S, VERP or TiO_2. **iNOS:** EHC-I, EHC-T, Crisobalite and SRM1648 inhibited iNOS expression. TiO_2 had no effect. EHC sol, SRM 1649 and VERP were not tested.
Reference: Chauhan et al. (2005, 155722) **Species:** Human **Cell Type:** A549	EHC-T: total EHC-93 EHC-I: insoluble EHC EHC-S: soluble EHC Cristobalite (SiO_2): SRM-1879 TiO_2: SRM-154b **Particle Size:** EHC-93: 0.4 µm (median physical diameter); TiO_2, SiO_2: 0.3-0.6 µm	**Route:** Cell Culture (150000 cells/flask) **Dose/Concentration:** All particles: 0, 1, 4, 8 mg/5ml **Time to Analysis:** 24 h	**Cellular Viability:** Decreased after exposure to EHC-T, EHC-I and cristobalite. Rate of reduction was not consistent across doses. EHC-S and TiO_2 had no effect on viability. **ET-1:** Release of ET-1 peptide decreased dose-dependently for EHC-T, -S and -I. Fractions of EHC-S and EHC-I were more potent than EHC-T. TiO_2 and Cristobalite also reduced ET-1 secretion although this was not consistent across the dose range. **Cytokines:** Results showed no detectable amounts of GM-CSF, IL-1β or TNF-α in cell culture supernatants. IL-8 increased dose-dependently with EHC-T, EHC-I and cristobalite. **VEGF:** VEGF significantly increased dose-dependently with EHC-T, EHC-S and cristobalite. EHC-S induced a significant decrease in VEGF. **Gene Expression:** mRNA levels for preproET-1 reduced at 24 h for all particle types. EHC-S induced a significant decrease in ET-1 expression at this high dose. ECE-1 mRNA expression increased with EHC-T and EHC-I. Other particles had no effect. ETaR mRNA increased with EHC-T, EHC-S, and TiO_2 in biphasic manner where the highest expression of mRNA was seen at the middle dose levels. EHC-S had no effect. ETbR mRNA increased with a low dose of EHC-T and decreased with a high dose of EHC-T. EHC-S, EHC-I and cristobalite induced an increase of ETbR. TiO_2 induced a significant decrease. **Proteases:** mRNA levels for MMP-2 reacted similarly to preproET-1. mRNA levels for TIMP-2 was significantly induced with EHC-I. EHC-T and EHC-S induced small effects.
Reference: Cheng et al. (2003, 156337) **Species:** Human **Cell Type:** A549	DEP-h: DEP with high sulfur DEP-LS: DEP with low sulfur GEP: gasoline engine exhaust particles Primed cells pretreated with TNF-α **Particle Size:** DEP-h: 15.9 nm; DEP-LS: 17.7 nm; GEP: 8.3 nm	**Route:** In Vitro Cellular Exposure (Exhaust flow-through cell culture with air-cell-interface, exhaust diluted 10-15x with 8×10^5 cells/mL) **Dose/Concentration:** DEP (total): 1.5-3.5×10^6 particles/cm^3; GEP (total): 1-2×10^6 particles/cm^3; TNF-γ: 5ml (25 ng/ml) **Time to Analysis:** 60-360 min	**IL-8:** DEP-h induced a 3 fold increase in IL-8 than that of the control. DEP-LS also induced increases. Primed cell cases had higher levels (10x) than unprimed when exposed to DEP-LS. DEP-h induced higher levels of IL-8 than DEP-LS. This response lasted for up to 6 h. GEP induced a statistically insignificant increase of IL-8 in unprimed cells. With primed cells, GEP induced levels of IL-8 that exceeded those of DEP-h and DEP-LS. This response lasted for 1-2 h.

Study	Pollutant	Exposure	Effects
Reference: Chin et al. (2003, 156340) **Species:** Rat, Human **Cell Line/Type:** RAW 264.7, MHS (Alveolar Macrophage Cell Line), A549	CB: (N339, with benzo[a]pyrene absorbed on surface. Manufactured in Cabot, Boston, MA) BaP Benzo [a] pyrene 1, 6-quinone: BP-1,6-Q (obtained from NCI, Kansas City, MO) **Particle Size:** CB 0.1 µm (mean diameter)	**Route:** Cell Culture **Dose/Concentration:** CB: 1, 2, 4 µg/mL BaP: 2 µg/mL BP-1,6-Q: 1 µM **Time to Analysis:** 1-24 h	**HO-1 mRNA Expression:** In RAW264.7, HO-1 mRNA levels increased with 2 and 4 µg/mL at 2 h. Increases continued to 8 h and declined by 24 h. BaP had no effect. BP-1,6-Q increased HO-1 mRNA after 1 h and was maintained until 8 h. In A549 and MHS, HO-1 mRNA increased after 1 h, peaking at 8 h in A549 and 4 h in MHS. **HO-1 Protein Expression:** An increase of protein was observed from 4-8 h in RAW264.7. **AP-1:** Increases in binding activity were observed in RAW 264.7 cells at 2 h.
Reference: Churg et al. (2005, 088281) **Species:** Rat **Strain:** SD **Weight:** 250 g **Cell Type:** Epithelial Cells of Tracheal Explants	EHC93 (Ottawa Urban Air Particles) TiFe = Iron-loaded fine TiO_2 (obtained from Aldrich Chemicals, Milwaukee, WI) **Particle Size:** EHC-93: 3-4 µm (MMAD); TiFe: 0.12 ± 1.4 µm (geometric mean diameter)	**Route:** Cell Culture **Dose/Concentration:** EHC-93, TiFe: 500 µg/cm^2 **Time to Analysis:** 1, 24 h. Some experiments (referred to as 2 h) explants transferred to different dish and incubated for additional hour. Pre-treated with Inhibitors/Chelators for 2 h.	**Activation of NF-κB:** Both particle types increased nuclear translocation of NF-κB. TiFe and EHC-93 increased NF-κB 1.5 fold at 1 h. TiFe increased NF-κB 3.5 fold at 2 h. EHC-93 increased NF-κB more than 2 fold. TiO_2 by itself did not increase NF-κB at any exposure duration. **Morphological changes in tracheal epithelial cells:** No evidence of dust particles was observed (EHC-93 or TiO_2) in the epithelial cell cytoplasm at 2 h. No evidence of morphologic cell damage from particles was observed. **Colchicine:** Treatment with colchicine did not prevent NF-κB activation. **Inhibitors/Activators:** Tetramethylthiourea (TMTU) (membrane-permeable active oxygen scavenger), Deferoxamine (redox-inactive metal chelator), PPS (Src inhibitor) AG1478 (epidermal growth factor receptor inhibitor) prevented NF-κB activation in both EHC93 and TiFe exposed-cells. Iron-containing citrate extract of both dusts increased NF-κB activation in both EHC93 and TiFe exposed-cells.
Reference: Courtois et al. (2008, 156369) **Species:** Rat **Strain:** Wistar **Cell Line:** Dissected intrapulmonary arteries from rats used in corresponding in vivo experiments	PM (SRM 1648) (63% in, 4-7% , mass fraction >1%: Si, S, Al, Fe, K, Na) UF carbon black (FW2, P60) **Particle Size:** SRM 1648 mean diameter 0.4 µm; ultrafine carbon black: FW2- 13 nm, P60- 21 nm	**Route:** Cell Culture **Dose/Concentration:** 100, 200 µg/mL **Time to Analysis:** 24 h incubation	**NO:** Generally, Ach-induced relaxation in intrapulmonary arteries decreased, Ach-induced cGMP accumulation decreased, and relaxation by SNP or DEA-NO also decreased. UF carbon black did not affect NO responsiveness. **Oxidative Stress, Inflammatory:** Dexamethasone prevented SRM 1648-induced impairment of the Ach relaxation response but antioxidants did not. TNF-α, MIP2, IL-8 increased. ROS was not affected.
Reference: Dagher et al., (2007, 097566) **Species:** Human **Cell Type:** L132 (Normal Lung Epithelial Cells)	LC10, LC50 = $PM_{2.5}$ (collected Jan-Sept in Dunkerque, France) **Particle Size:** cumulative frequency: 0.5 µm: 34%; 1 µm: 64%; 1.5 µm: 79%; 2 µm: 87%; 2.5 µm: 92%; 5 µm: 98%; 10 µm: 100%	**Route:** Cell Culture (3×10^6, 1.5×10^6, 0.75×10^6 cells/20mL) **Dose/Concentration:** LC10: 19 µg/mL; LC50: 75 µg/mL **Time to Analysis:** 24, 48 or 72 h	**p65 Protein:** Phosphorylation of p65 increased in PM-exposed L132 cells in dose-dependent manner. **IκBα Protein:** Phosphorylated IκBα protein concentrations increased in cytoplasm with both particle types at all time points. **p65 and p50 DNA:** p65 DNA binding increased at 24 h with LC10 and LC50, at 48 h with LC10, and at 72 h with LC10 and LC50. p50 DNA binding increased at all time points with LC10 and LC50.

Study	Pollutant	Exposure	Effects
Reference: Dai et al. (2003, 087944) **Species:** Rat **Strain:** SD **Weight:** 250 g **Cell Type:** Tracheal Explants	EHC-93 (Environmental Health Center, Ottawa) DEP: SRM 1650a (NIST) **Particle Size:** EHC-93: 3-4 µm (MMAD); DEP 1.55 ± 0.04 µm (CMD)	**Route:** Cell Culture **Dose/Concentration:** ECH, DEP: 500 µg/cm^2 **Time to Analysis:** Exposed for 1 h. Parameters measured following a 7 day incubation period.	**Hydroxyproline:** EHC93 induced an almost 3 fold increase in explant hydroxyproline. DEP increased tissue hydroxyproline 2.5 fold. **Procollagen:** EHC-93 doubled gene expression of procollagen. Procollagen gene expression could be fully inhibited by SN50, TMTU or treatment of the PM with DFX. Treatment of explants with p38 or ERK (inhibitors) had no effect on procollagen expression. DEP induced an increase in procollagen gene expression but this increase was completely prevented by SN50 and MAP kinase inhibitors (SB203580 and PD98059). Neither TMTU or DFX has any effect. **TGFβ1:** Treatment of explant with EHC93 approximately doubled gene expression for TGFβ1. Treatment with SN50, TMTU and fetuin (TGFβ antagonist) blocked increase. DFX, MAP kinase inhibitors (SB203580 and PD98059) had no effect. DEP roughly doubled TGFβ1 expression.SN50 and MAP kinase inhibitors (SB203580 and PD98059) fully blocked this effect. TMTU and DFX had no effect.
Reference: Doherty et al. (2007, 096532) **Species:** Rat **Strain:** NR8383 **Cell Types:** AMs	Ratios of: V: Fe; Al: Fe; Mn: Fe V = sodium vanadate ($NaVO_3$) Al = aluminum chloride hexahydrate ($AlCl_3$) Mn = manganese chloride tetrahydrate ($MnCl_2$) Fe = ferric chloride hexahydrate ($FeCl_3$) Ratios based on $PM_{2.5}$ measurements from NYC, LA and Seattle **Particle Size:** Metals from $PM_{2.5}$ samples	**Route:** Cell Culture (2×10^5 cells/mL) **Dose/Concentration:** Fe = 16 µmol (equivalent to urban NYC 500 µg $PM_{2.5}$); V and Mn tested in molar rations of 0.02 to 0.4 relative to Fe; Al tested in molar ratios of 0.125 to 8 relative to Fe. **Time to Analysis:** 20 h	**IRP:** Addition of V increased IRP activity 5 to 9 fold. Though there was no seeming dose responsivity, IRP activity remained strongly elevated over the range of V:Fe ratios tested. Addition of Mn only resulted in an effect at 0.1 molar ratio (two-fold), not at higher or lower ratios. Al resulted in peak increases of 5 fold at molar ratios 2 while declining to 2 fold at molar ratios 4 and 8. **Cytotoxicity:** Al was cytotoxic at molar ratios of 4 and 8. All other Al, V, Mn ratios had no effect. **Mixtures:** The combination of metals tested at NYC PM ratios and V drove all the Fe transport activity. Combinations of V+Mn and V+Al increased activity more than V:Fe alone.
Reference: Doornaert, et al. (2003, 156410) **Species:** Human **Cell Line/Type:** 16HBE14o-; P-HBE	DEP: SRM 1650 (NIST) CB: (Sigma, France) DPC: Dipalmitoyl phosphatidylcholine (positive control) 0.5 um **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** DEP and CB: 1-100 µg/mL **Time to Analysis:** Parameters measured 24, 48, 72 h post exposure. 1-HBE Cell Deadhesion Capacity: 24 h, evaluation of detachment performed every 5min for 40 min after. Cell Wound Repair Capacity: 24 h, repair evaluated 3.5, 7, 24 h after.	**Cytotoxicity:** DEP was cytotoxic at 100 µg/mL at all time points in a time-dependent manner. CB and DPC cytotoxicity was substantially lower but significant at 72 h. **Phagocytosis:** 1-HBE cell levels that were in contact with DEP or CB or have phagocytized those particles increased in a dose-dependent manner. DEP induced greater levels of cell contact and phagocytosis than CB. **F-actin:** Only DEPs were engulfed by F-actin stained cell fragments. **Actin CSK Stiffness:** DEP (5, 20, 100 µg/mL) induced net dose-dependent decrease in cytoskeleton stiffness and a dose-dependent decrease in actin cytoskeleton stiffness. CB produced no significant decrease. **Adhesion Molecules**: DEP induced a concomitant reduction of both CD49 (α3) and CD29 (β1) integrin subunits and a decrease in level of CD44 (HBE cell-cell and cell-matrix adhesion molecule) at both 20 and 100 µg/mL. **Proteases:** DEP also induced an isolated decrease in MMP-1 expression without change in tissue inhibitor of TIMP-1 or TIMP-2 at 100 µg/mL. CB produced no change or insignificant results. **1-HBE Cell Deadhesion Capacity:** DEP exposure induced a dose-dependent amplification of cell detachment at 5 min of incubation and onward. **Cell Wound Repair Capacity:** DEP inhibited wound repair/wound closure in a dose-dependent manner.

Study	Pollutant	Exposure	Effects
Reference: Dostert et al. (2008, 155753) **Species:** Human **Cell Line/Type:** THP1, monocyte-derived macrophages (MM)	Asbestos Silica DEP CSE: cigarette smoke extract MSU: monosodium urate crystals **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** Asbestos: 0.1, 0.2 mg/mL; Silica: 0.1, 0.2, 0.25, 0.5 mg/mL; DEP: 0.2, 0.25, 0.5 mg/mL; CSE: 5%, 10% in solution mg/mL; MSU: 0.1, 0.2 mg/mL **Time to Analysis:** 1, 3, 6 h	**IL-1β:** Increased levels of IL-1β with asbestos and silica were observed in THP1 at 6 h. CSE and DEP had no effect. MM also had increased levels with asbestos, silica and MSU at high dose levels only. **Caspase-1:** Asbestos increased caspase-1 activity. **ROS:** Asbestos doses in THP1 exhibited an increase in ROS formation.
Reference: Doyle, et al. (2004, 088404) **Species:** Human **Cell Type:** A549 from non-smoking adults	BD: 1,3-butadiene, known carcinogen Acrolein: photochemical and NO product of BD in atmosphere Acetaldehyde: photochemical and NO product of BD in atmosphere Formaldehyde: photochemical and NO product of BD and ISO in atmosphere ISO: isoprene, 2-methyl analog of BD Methacrolein: photochemical and NO product of ISO in atmosphere Methyl vinyl ketone: photochemical and NO product of ISO in atmosphere **Particle Size:** NR	**Route:** Environmental Irradiation (smog) Chambers **Dose/Concentration:** 50 ppb NO; 200 ppbV ISO, BD **Time to Analysis:** Exposed to gases for 5 h. Analysis 9 h post exposure.	**Cytotoxicity:** ISO+NO and BD+NO induced small increases of LDH in A549. However, ISO+NO+light and BD+NO+light increased LDH levels 4-6 fold indicating photochemical products of ISO and BD are highly cytotoxic. LDH levels of each combination were equivocal. **IL-8 Protein:** Methacrolein, methyl vinyl ketone and formaldehyde (products of ISO) increased IL-8 protein levels significantly. ISO+NO had no effect. BD photochemical products (acrolein, acetaldehyde and formaldehyde) also increased IL-8 protein, more than doubling the photochemical products induced by ISO. BD+NO had no effect. **IL-8 mRNA:** IL-8 mRNA expression also increased with photochemical products of ISO and BD but did not reach a statistically significant level.
Reference: Duvall et al. (2008, 097969) **Species:** Human **Cell Type:** Airway Epithelial Cells	PM-F, -C, -UF Particles collected from: Seattle, WA (PM-S); Salt Lake City, UT (PM-SL); Phoenix, AZ (PM-P); South Bronx, NY (PM-SB); Hunter College, NY (PM-Sterling Forest, NY (PM-SF) **Particle Size:** Coarse: >2.5 µm; Fine: <2.5 µm; UFP: <0.1 µm	**Route:** Cell Culture (100,000 cells/cm^2) **Dose/Concentration:** 5 mg/ml **Time to Analysis:** 1, 24 h post exposure	**Particle Characterization:** PM-HR, PM-SL and PM-S contained the highest UF, F, and C concentrations. PM-SB and PM-HR had similar F and C concentrations. Sulfate was highest in PM-F for all sites except in PM-SB and PM-HR. Wood combustion was highest in PM-SL, PM-S, PM-P. Soil dust was highest in PM-SL and PM-S. **IL-8:** PM-UF induced a greater increase in IL-8 than other types of PM except PM-P. PM-UF is associated with vanadium, lead, copper, sulfate. PM-F-HR caused the greatest increase followed by PM-SB. PM-F-SF and PM-F-P was least effective. PM-C also caused an increase in IL-8 levels and was associated with vanadium and EC. **COX-2:** PM-F-S induced the greatest increase in COX-2 expression. Other PM-F sites induced similar increases. UF PM had no effect. PM-C, associated with EC, induced increases. **HO-1:** PM-F-SF induced the greatest increase in HO-1. PM-F-SL was the least effective. UF PM had no effect. PM-C, associated with copper, barium and EC, caused an increase.
Reference: Dybdahl et al. (2004, 089013) **Species:** Human **Cell Type:** A549	DEP: SRM 1650 (NIST) **Particle Size:** 90 nm (MMAD)	**Route:** Cell Culture (10^5 cells/mL) **Dose/Concentration:** 0, 10, 50, 100, 500 µg/mL **Time to Analysis:** 2, 5, or 24 h	**Cytokines:** DEP induced dose-dependent increases of IL-1α, IL-6, IL-8 and TNF-α at 24 h. Cytokines increased between 4 and 18 fold at the highest DEP dose as compared to controlled cells. DEP also increased IL-6 mRNA expression levels in a dose and time-dependent manner.IL-6 mRNA levels increased 14 fold at 24 h, 8 fold at 5 h, and 2 fold at 2 h. **Cell Viability:** DEP exposure did not decrease cell viability at any dose tested.

Study	Pollutant	Exposure	Effects
Reference: Fritsch et al. (2006, 156452) **Species:** Mouse **Cell Type:** RAW 264.7	$MAFO_2$: incinerator fly ash (collected by electrostatic precipitation in commercial municipal waste incinerator facility) composition representing 12% of total mass (mg/g): Fe (9.1); Pb (23.3); Zn (75.7); C (7.5) **Particle Size:** 165 nm (modal value)	**Route:** Cell Culture (1×10^6 cells/well) **Dose/Concentration:** 6.3-188 µg/cm^2 for Toxicity; 2.6, 6.5, 13.2 µg/cm^2 for Arachidonic Acid; 13.2 µg/cm^2 for MAPK Pathway; Other doses noted in Effect of Particles **Time to Analysis:** 1, 2.5, 5, 24 h	**Toxicity:** Viability decreased from 99% to 18% at 62.5-188 µg/cm^2. Lower doses had no effect. **Arachidonic Acid:** At 2.5 h, AA level increased 2 fold for 6.5 µg/cm^2 and 6 fold for 13.2 µg/cm^2. No increase was observed after 5 h. **MAPKs:** Cells pretreated with PD98059, an inhibitor of MEK-1, inhibited AA liberation due to $MAFO_2$ treatment of 13.2 µg/cm^2 **COX-2:** A time-dependent increase of COX-2 protein expression was exhibited at 2.5 and 5 h. **ROS:** A dose-dependent increase in ROS formation was observed at concentrations greater than 31.3 µg/cm^2 after 3 h. **GSH:** There was an observed increase of production at 20 h. Doses greater than 60 µg/cm^2 reduced total glutathione. **HO-1:** There was an observed dose-dependent increase in expression at 4 h.
Reference: Fujii et al. (2002, 036478) **Species:** Human **Cell Type:** HBEC (from current smokers), AMs, Co-Culture: AMs+HBEC **Age:** HBEC: 48-70 yr	PM_{10}: EHC-93 (Ottawa, Canada) **Particle Size:** PM_{10}	**Route:** Cell Culture (HBEC: 2.5-3× 10^6 cells/well); (AMs: 1.0×10^7 total) **Dose/Concentration:** 100, 500 µg/mL **Time to Analysis:** 2, 8, 24 h	**Viability:** Over 90% of HBEC were viable after a 24 h exposure of up to 500 µg/mL of PM. AMs incubated with and without 100 µg/mL saw no significant difference in viability. **Cytokine mRNA:** TNF-α, GM-CSF, IL-1β, IL-6, LIF, OSM and IL-8 mRNA expression increased in co-culture with 100 µg/mL at 2 and 8 h. In AMs, TNF-α, IL-1β, IL-6 mRNA expression increased with 100 µg/mL at 2 h. IN HBECs, IL-1β and LIF increased with 100 µg/mL at 2 h. HBECs added to AMs exposed to PM_{10}, further increase in mRNA of IL-1β, LIF and IL-8. **Cytokine Protein:** In co-culture and AMs, significant increase in protein production of GM-CSF, IL-8, IL-1β, IL-6 and TNF-α in dose-dependent manner. GM-CSF and IL-6 production significantly higher in co-culture then AM or HBEC alone. **Bone Marrow:** Co-culture instillation of supernatants increased circulating band cell counts at 6 and 24 h with 100 µg/mL.
Reference: Fujii et al.. (2001, 156455) **Species:** Human **Cell Type:** HBEC from current smokers **Age:** 48-70 yr	PM_{10}:EHC93 (Ottawa, Canada)99% <3.0um **Particle Size:** PM_{10}(99% < 3.0 µm)	**Route:** Cell Culture ($2.5\text{-}3\times10^6$ cells/dish) **Dose/Concentration:** 10, 100, 500 µg/mL **Time to Analysis:** 2, 8, 24 h	**Phagocytosis:** 18.6% of cells engulfed particles when exposed to 100 µg/mL. Over 90% remained viable. **Cytokine mRNA:** LIF mRNA increased dose-dependently at 2 h but declined at 8 and 24 h. GM-CSF increased dose-dependently at 8h and peaked at 24 h. IL-1α increased at 2 h, increased dose-dependently at 8 h and peaked at 24 h. M-CSF, MCP-1, IL-8 were unaffected. **Cytokine Protein:** LIF, GM-CSF, IL-1β and IL-8 increased dose-dependently. Soluble fraction of 100 µg/mL PM_{10} did not affect cytokine production.

Study	Pollutant	Exposure	Effects
Reference: Garcon et al. (2006, 096633) **Species:** Human **Cell Type:** L132	$PM_{2.5}$ (collected in Dunkerque, France for 9mo, Jan-Sept) **Particle Size:** $PM_{2.5}$- 0-0.5 µm (33.63%), 0.5-1.0 µm (30.61%), 1.0-1.5 µm (14.33%), 1.5-2.0 µm (8.69%), 2.0-2.5 µm (4.89%), >2.5 µm (7.87%)	**Route:** Cell Culture: 3×10^6 cells/20ml (24 h); 1.5×10^6 cells/20ml (48h); 0.75×10^6 cells/20ml (72 h) **Dose/Concentration:** 18.84, 37.68, 56.52, 75.36, 150.72 µg/mL; LC10- 18.84 µg/mL; LC50- 75.36 µg/mL **Time to Analysis:** 24, 48 or 72 h	**Cytotoxicity:** PM induced dose-dependent (R_2 =.9907) cytotoxic effect in proliferating L132 cells. **LDH:** Increase at 72 h with 56.52 and 75.36 µg/mL. **Oxidative Stress:** A decrease in MDF activity was observed at all exposure levels at 24, 48, and 72 h (72-h <5 % of control). MDA levels showed increase concentration after 72 h, both LC10 and LC50. LC10 and LC50 saw an increase in SOD activity at 24 h; LC50 saw a decrease in activity after 48 and 72 h. 8-OHdG and PARP exhibited increases at all time points with LC10 and LC50. **Inflammatory Response:** Increases of TNF-α concentration was exhibited at 24 h at LC50, and at 48 h and 72 h at LC10 and LC50. iNOS activity increase at all time points at LC10 and LC50.NO concentration exhibited increases at all time points after exposure to LC10 and LC50.
Reference: Geng et al. (2005, 096689) **Species:** Rat **Strain:** Wistar Kyoto **Tissue/Cell Type:** Lung macrophages	BPM: Blowing $PM_{2.5}$; PM collected from Wuwei City, Gansu Province, China (Blowing days correspond to desert storm days) NPM: Non-blowing (normal) $PM_{2.5}$ **Particle Size:** $PM_{2.5}$	**Route:** Cell Culture **Dose/Concentration:** 0, 33, 100, 300 µg/mL **Time to Analysis:** 4 h	**Cytotoxicity**: Dosages greater than 150 µg/mL decreased cell viability. **Plasma Membrane Fluidity**: Dose-dependent decrease had no effect on membrane lipid hydrophilic region. **Plasma Membrane Permeability**: LDH enzyme activity and extracellular AP activity increased dose-dependently, indicating increased membrane permeability, but this was only statistically significant at 300 µg/mL dose. NPM may affect some parameters at 100 µg/mL. Overall, NPM induced a slightly higher increase than BPM. **Intracellular Ca2+:** A dose-dependent increase was observed. **Lipid Peroxidation (TBA):** An increase was observed only at 300 µg/mL. **Antioxidant (GSH):** A decrease was observed only at 300 µg/mL.
Reference: Geng et al. (2006, 097026) **Species:** Rat **Strain:** Wistar Kyoto **Tissue/Cell Type:** Lung macrophages	DPM: dust storm samples; PM collected from Baotou City, Inner Mongolia, China in March 2004 NPM: normal PM **Particle Size:** $PM_{2.5}$	**Route:** Cell Culture **Dose/Concentration:** 0, 33, 100, 300 µg/mL **Time to Analysis:** 4 h	**Cytotoxicity**: MTT reduction assay revealed a significant decrease in cell viability at 150 µg/mL and 300 µg/mL. LDH enzyme activity significantly increased at 150 and 300 µg/mL. **GSH levels:** Significant decreases were seen in cellular GSH levels and increases in TBARS levels in both groups with a 300 µg/mL dose. **Plasma Membrane Activity:** In the plasma membrane, Na, K-ATPase were significantly inhibited. $Ca^{2+}Mg^{2+}$-ATPase were unaffected. **Plasma Membrane Lipid Fluidity**: Results indicate that DPM could increase the surface fluidity of membrane lipid. **Intracellular Ca2+:** A dose-dependent increase in free intracellular Ca2+ levels was observed.
Reference: Ghio et al. (2005, 088272) **Species:** Human **Cell/Tissue Type:** BEAS-2B	FAC: ferric ammonium citrate (component of ROFA) $VOSO_4$: vanadyl sulfate (component of ROFA) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 100 µM FAC - preexposed before metal compounds or oil fly ash 50 µM $VOSO_4$ - preexposed before metal compounds or oil fly ash 100 µg/mL ROFA **Time to Analysis:** 0-1 h, 4 h	**IRE DMT1:** FAC increased mRNA and protein expression for -IRE DMT1. $VOSO_4$ decreased mRNA and protein expression for -IRE DMT1. +IRE DMT1 unaffected by any treatment. **Metal transport:** Uptake of iron increased after pre-exposure to FAC and decreased after pre-exposure to $VOSO_4$. Pre-exposure to FAC again increase the uptake of both iron and vandium. $VOSO_4$ induced opposite effect, decreasing Fe uptake. **ROS:** Increased acetaldehyde, indicating increased oxidative stress. ROS decreased with FAC pretreatment. ROS increased with $VOSO_4$ pretreatment.

Study	Pollutant	Exposure	Effects
Reference: Gilmour et al. (2004, 057420) **Species:** Rat **Strain:** SD **Cell/Tissue Type:** AM	Coal Fly Ash MU = Montana Ultrafine MF = Montana Fine MC = Montana Coarse KF = West Kentucky Fine KC = West Kentucky Coarse Coal combustion using a laboratory-scale down-fired furnace rated at 50kW. Montana subbituminous coal and western Kentucky bituminous coal **Particle Size:** Coarse: >2.5 µm; Fine: <2.5 µm; UFP: <0.2 µm	**Route:** Cell Culture (2×10^5 cells/mL) **Dose/Concentration:** 125 µg/mL or 250 µg/mL **Time to Analysis:** 4 or 24 h	**LDH:** Mid and high doses of Montana ultrafine particles showed significant increase after 4 h exposure vs control. Other particle types had no effect. After 24 h, LDH level was not statistically significant between particles tested and control. **Cytokines:** Treatment with Montana ultrafine particles resulted in a significant production increase of TNF-α. MIP-2 showed increases in all the fine and ultrafine treatments, with Montana ultrafine and W. Kentucky fine PM showing the highest increases. IL-6 increased with Montana ultrafine particles although there was some variability and the increases were not statistically significant.
Reference: Gilmour et al. (2005, 087410) **Species:** Human **Cell/Tissue Types:** monocyte derived macrophages, HUVECs, A549, 16HBE	PM_{10}: Collected from the Marylebone and Bloomsbury monitoring sites in London, UK **Particle Size:** PM_{10}	**Route:** Cell Culture **Dose/Concentration:** 50 µg/mL **Time to Analysis:** 4 h, 6 h, 20 h	**IL-8**: PM_{10} at 50 µg/mL induced a significant increase in IL-8mRNA and protein expression in PMM and 16HBE at 6 and 20h. A less substantial increase was also observed in A549. **Procoagulant Activity**: PM_{10} induced a significant decrease in macrophage mediated clotting time in 16HBE. Other cell types were unaffected. **Annexin V Binding**: At 100 µg/mL, PM_{10} induced a significant increase in binding macrophages at 4 and 20 h. There was no effect at 50 µg/mL. **Tissue Factor mRNA Expression**: Expression was increased in macrophages at 6 h only. **tPA Expression**: mRNA expression decreased at 6 h. Protein expression decreased at 4 h and 20 h in a dose-dependent manner. **TF Expression:** TF mRNA expression increased in a dose-dependent manner at 6 h in HUVECs. Protein levels also increased at 4 h but declined to basal levels by 20 h.
Reference: Gilmour et al. (2003, 096959) **Species:** Human **Cell/Tissue Type:** A549	PM_{10}: Collected from the Marylebone and Bloomsbury monitoring sites in London, UK TSA H_2O_2 NAC Mannitol Provided by Sigma Chemical, Poole, UK or GIBCO-BRL, Paisley, UK **Particle Size:** PM_{10}	**Route:** Cell Culture **Dose/Concentration:** PM_{10}: 100 µg/mL; TSA: 100 ng/mL; $H2O_2$: 200 µM; NAC and Mannitol: 5 mM **Time to Analysis:** 24 h	**IL-8:** PM_{10}, TSA and $H2O_2$ treatment induced an increase of IL-8. Concomitant exposure of TSA with PM_{10} or H_2O_2 significantly increased IL-8 release when compared to PM_{10} or H_2O_2 alone. IL-8 mRNA expression with PM_{10} or H_2O_2 exposure and TSA coincubation caused significant increases. Silver staining of PCR products indicated that the IL-8 gene promoter was associated with acetylated H4 following TSA, PM_{10} and TNF treatment. **H4:** PM_{10} exposure significantly increased acetylation levels of H4 over controls. Increased acetylated H4 was mediated by PM_{10} in a dose-dependent manner. Treatment with PM_{10} and H_2O_2 increased HAT activity associated with H4 by 245% and 166% respectively. Significant increases in acetylation of H4 following treatment of cells with TSA, PM_{10} and H_2O_2 for 24 h was observed. PM_{10}induced HAT activity was significantly decreased in the presence of NAC and mannitol. Nuclear presence of HDAC2 protein was significantly reduced by exposure to both HDAC inhibitor and PM_{10}. There was a decreasing trend in HDAC2 gene expression following TSA and PM_{10} treatment. **NF-κB:** The activation of the transcription factor NF-κB was enhanced following the inhibition of HDAC with TSA and by treatment with

Study	Pollutant	Exposure	Effects
Reference: Graff et al. (2007, 156488) **Species:** Human **Cell/Tissue Type:** HAEC	PM -UF: ultrafine -F: fine -C: coarse Particles collected from Seattle, WA (-S), Salt Lake City, UT (-SL), Phoenix, AZ (-P), South Bronx, NY (-SB), Hunter College, NY (-H), Sterling Forest, NY (-SF) **Particle Size:** UF: <0.1 µm; F: 0.1- 2.5 µm; C: 2.5-10 µm	**Route:** Cell Culture **Dose/Concentration:** 250 µg/mL **Time to Analysis:** 6 h, 24 h	**Gene Expression:** PM-UF, PM-F, and PM-C both upregulated and downregulated genes in the HAECs though downregulation was far more common for all the three PM fractions. PM-F affected the greatest number of transcripts, followed by the UF and C fractions. **IL-8:** mRNA expression increased, with PM-F-S having the greatest impact. Aluminum, strontium, manganese and potassium were highly associated with expression. Wood combustion was moderately associated. **HOX-1:** mRNA expression increased, with PM-F-SF having the greatest impact. Potassium, manganese, strontium and wood combustion were highly associated with expression. Aluminum and vanadium were moderately associated.
Reference: Gualtieri et al. (2005, 097841) **Species:** Human **Cell Type:** A549	TD: Tire debris extracted in methanol, constituent of PM_{10} (generated by spinning a new automotive tire against abrasive surface) **Particle Size:** 10-80 µm	**Route:** Cell Culture **Dose/Concentration:** 10, 50, 60, 75 µg/mL **Time to Analysis:** 24, 48, 72 h	**Cytotoxic Effect:** Treated cells presented inhibitory effect on reduction of MTT which appeared to be dose and time-dependent. A statistically significant reduction was observed at 48 and 72 h. Trypan blue showed a significant PM lethality as well as a dose-dependent increase in mortality. **DNA Damage:** At 24 and 72 h, DNA damage increased dose dependently in damaged and ghost cells. **Cell Cycle Analysis:** At 24 h, TD extract-treated cells presented a significant increase in the percentage of cells in G1 phase when compared with control. This increase was associated with a decrease in the percentage of cells in S phase. At 48 and 72 h, the increase in percentage of cells in G1 was associated with a decrease in the percentage of cells in both S and G2/M phases. Cells exposed to TD extracts presented changed morphology. Modifications most obvious at 72 h. The highest dost produced increased vacuolization in cytoplasm and apoptotic nuclear images.
Reference: Hetland et al. (2005, 087887) **Species:** Rat **Gender:** Male **Strain:** Crl/Wky **Cell Type:** AMs	PMC = Coarse PMF = Fine -A = Amsterdam -L = Lodz -R = Rome -O = Oslo Coexposures PAH, Fe, Al, Zn, Cu, V **Particle Size:** PMC: 2.5-10 µm; PMF: 0.2-2.5 µm	**Route:** Cell Culture (1.5×10^6 cells/well) **Dose/Concentration:** 50, 100 µg/mL PM **Time to Analysis:** 20 h	**IL-6:** PMC from all cities exhibited increases in IL-6 release with spring and summer roughly equal and both inducing higher levels than the winter PMC. For the Spring and Summer samples, PMC-L exhibited the highest IL-6 releases (440% and 460% respectively) followed by Rome, A'dam/Oslo, and Oslo/A'dam. For the winter samples, Rome and Amsterdam induced higher IL-6 levels (340% and 300% respectively) than Lodz and Oslo (165% and 160%). The fine fractions did not induce any significant cytokine release. **TNF-α:** PMC from all cities increased TNF-α release with 50 µg/mL generally inducing a slightly higher increase than 100 µg/mL. **Constituent Correlation:** Levels of Fe, Al, Zn, Cu and V as well as PAH (total and fractions) showed no correlation with IL-6 release. **Endotoxin Correlation with IL-6 release:** A confirmatory test revealed no correlation.

Study	Pollutant	Exposure	Effects
Reference: Hetland et al. (2004, 097535) **Species:** Rat, Human **Cell Type:** Alveolar Macrophages (Rat), A549 **Strain:** Wky/NHsd **Gender:** Male **Weight:** 180-230 g	AMC = Ambient Coarse AMF = Ambient Fine AMUF = Ambient Ultrafine (AM samples taken at a suburban site, without a dominating PM source, near Utrecht, Netherlands) Road PM: PM_{10}, (collected in a road tunnel with predominating road abrasion due to use of studded tires in Trondheim, Norway) **Particle Size:** AMC: 2.5-10 µm; AMUF: <0.1 µm	**Route:** Cell Culture (1×10^6 cells/well) **Dose/Concentration:** 0, 100, 200, 400, 600, 800, 1000 µg/mL **Time to Analysis:** 20h (Type 2 cells); 40h (A549 cells)	**IL-8:** All 3 AM fractions showed dose-dependent increases in A549 cells until 600 µg/mL; at that concentration, levels declined. AMC showed the most pronounced decline which correlates with decreased viability. Road PM showed a near linear response until 1000 µg/mL, whereas DEP plateaued at 600 µg/mL in A549. **MIP-2:** AMC and AMUF had no effect on Type 2 cells. DEP induced increases at 200 µg/mL, whereas Road PM induced the strongest increase, peaking at 600 µg/mL in Type 2 cells. **IL-6:** AMC induced increases at 100 µg/mL in Type 2, but levels declined below normal at 200 µg/mL. AMUF induced a decline of IL-6 levels. Road PM induced significant increases in Type 2. DEP had a slight effect. AM fractions induced increases in A549 cells, peaking at 600 µg/mL with AMF. DEP and Road PM induced a dose-dependent increase. **Cell Survival:** AMC showed major effects at 200 µg/mL in Type 2. AMUF showed effects at 400 µg/mL. Road PM and DEP showed a gradual decline from 75% to 50% at 800 µg/mL in Type 2. All AM fractions induced a decrease in viability after 600 µg/mL in A549 with AMC inducing a larger decrease than AMUF and AMF; AMUF and AMF induced similar levels. Road PM and DEP had no effect on A549. **Apoptosis:** AMC elicited a marked induction of apoptosis 200 µg/mL in Type 2 cells. AMF showed a dose-dependent increase in A549. Other AM fractions showed some slight increases in both cell types. Statistical significance was reached for all particles except for Road PM.
Reference: Holder et al. (2008, 093322) **Species:** Human **Cell Type:** 16HBE14o	DEP: generated from a single cylinder diesel engine using , commercial certified #2 diesel fuel Copollutants: NO_X 7 ppm, CO_2 0.1% **Particle Size:** Suspension: 223 nm (mean diameter); ALI: 122 nm (mean diameter)	**Route:** Suspension (1×10^5 cells/cm^2), Air Liquid Interface (ALI, 1×10^5 cells/cm^2) **Dose/Concentration:** Suspension: 0.13, 0.24, 1.88, 2.5, and 12.5 µg/cm^2; ALI: 1 g/cm^3 (total number of particles: 2.3×10^7 particles/cm^2) **Time to Analysis:** Exposure for 6 h. Parameters measured 20 h post-exposure.	**ALI vs Tracheal Bronchial (TB) Deposition:** The TB region deposition is 1.5 nominally x ALI, but particle diameter deposited in the TB was 62 nm (geometric mean diameter) as compared to the particle deposition in the ALI, measuring 260 nm. **Inflammatory Response:** Suspended DEP decreased viability at concentrations of 2.5 µg/cm^2 or higher. IL-8 release (corrected for viability) increased at concentrations of 1.88 µg/cm^2 or higher in a dose-dependent manner. IL-8 exhibited intermediate levels of secretion between in vitro levels of 0.25 and 1.88 µg/cm^2. No statistically significant results were observed in ALI. Viability for ALI was near 100% (75% uncorrected).
Reference: Huang et al. (2003, 087376) **Species:** Human, Mouse **Cell Type:** BEAS-2B, RAW 264.7	PMC: PM coarse PMF: PM fine PMSM: PM submicron Collected between September-December 2000 from 4 ambient monitoring stations in Taiwan that represented background, urban, traffic, and industrial sites **Particle Size:** PMC: 2.5-10 µm; PMF: 1-2.5 µm; PMSM: <1 µm	**Route:** Cell Culture (5×10^5 cells/mL) **Dose/Concentration:** All PM: 50, 70, 100 µg/mL **Time to Analysis:** BEAS-2B: 8h; RAW 264.7: 16 h	**Viability:** None of the PM fractions affected cell viability. **IL-8:** Only PMSM induced a significant IL-8 increase in BEAS-2B. IL-8 response was associated with a combination of Mn and Cr (R_2 = 0.28). Response was also correlated with nitrate, although significance disappeared when 1 extreme nitrate value was removed. **Lipid Peroxidation:** Only PMSM enhanced lipid peroxidation in BEAS-2B, correlating with both elemental and . **TNF-α:** In RAW264.7, PMSM increased TNF-α production. Polymixin pretreatment significantly reduced TNF-α levels for all 3 PMs which indicates an endotoxin role in macrophage response. TNF-α production (after polymixin pretreatment only) was associated with Cr and Fe content.

Study	Pollutant	Exposure	Effects
Reference: Hutchison et al. (2005, 097750) **Species:** Mouse **Cell Line:** J774.1A	PM_{10}: Samples collected for 7 day during closure (-C) and reopening of steel plant (-R) PMT: PM total (aqueous sonicate) PMS: PM soluble aqueous PMI: PM insoluble aqueous **Particle Size:** PM_{10}	**Route:** Suspension **Dose/Concentration:** 500 µl (estimated concentrations of 112, 143, 156, 180, 233, 255 µg/1ml water) **Time to Analysis:** 4 h	**Particle Characterization:** Reopening of the plant showed a significant increase in the total and acid extractable metal content of PM. Aqueous extractable metal content did not change. Soluble zinc, copper and manganese also increased significantly post reopening. Iron was the most abundant in acid extractable metals and increased greatly at the reopening. **TNF-α:** PMT-R and PMT-C induced a statistically significant increase. Treatment with chelation agent reduced effect to control levels.
Reference: Imrich et al. (2007, 155859) **Species:** Rat **Gender:** Female **Age:** 12-14 wk **Cell Type:** AM	UAP: SRM 1649 (positive control) TiO_2: Particle control CAPs (Boston, MA) All cells primed with LPS Coexposure with NAC, dimethylthiourea (DMTU), $H2O_2$ or catalase **Particle Size:** CAPs: ≤2.5 µm; UAP: $PM_{2.5}$; TiO_2: ~1 µm	**Route:** Cell Culture ($2×10^5$ cells/well) **Dose/Concentration:** Caps 100 µg/mL; UAP: 50 or 100 µg/mL; LPS 250 ng/mL; NAC, DMTU: 2, 10, 20 mM; Catalase: 1, 5, 10 mM; H_2O_2 0-50 µm/hr **Time to Analysis:** 18-20h	**TNF-α:** DMTU at 20 mM reduced TNF in LPS-primed cells in control and UAP-treated groups. NAC at 20 mM reduced TNF release but this was not statistically significant. Catalase significantly inhibited TNF in control and UAP-treated groups. CAPs (especially the insoluble portion) significantly increased TNF unless co-exposed with NAC, DMTU or catalase. All three reduced levels back to around basal levels. DMTU was particularly effective at diminishing TNF release. H_2O_2 increased TNF release in CAPs-exposed cells. TiO_2 had no increased ability to induced cytokine release when mixed with H_2O_2. **Cell Death:** Viability decreased substantially when exposed to H_2O_2 + CAPs. The soluble fraction of CAPs showed to be more effective with H_2O_2 than the insoluble portion. TiO_2 had no significant effect. **NO:** Some CAPs induced slight increases when mixed with H_2O_2. No difference was observed between soluble and insoluble portions of CAPs. **DFO:** DFO at 0.05 mM completely inhibited oxidation induced with soluble CAPs + H_2O_2. Insoluble CAPs + H_2O_2 was also DFO-sensitive. DFO was ineffective against the insoluble CAPs induction of TNF and MIP-2.
Reference: Ishii et al. (2004, 088103) **Species:** Human **Cell Type:** A549 (collected from 6 lobectomy or pneumonectomy smokers), HBEC	EHC-93:PM_{10} (obtained from Environmental Health Directorate, Ottawa, Ontario, Canada) **Particle Size:** PM_{10}	**Route:** Cell Culture ($1×10^7$ cells) **Dose/Concentration:** 100 µg/mL **Time to Analysis:** 3, 6, 24 h	**Cytokines:** TNF-α, IL-1β, GM-CSF, IL-6, and IL-8 levels were significantly increased in A549 cells. **mRNA Expression:** MCP-1, ICAM-1 and IL-8 mRNA expression increased in untreated AM supernatants at 3 h. Only the MCP-1 levels were statistically significant at 3 h. Levels declined by 6 h. When A549 cells were exposed to PM_{10} exposed AM, levels of RANTES, TNF-α, ICAM-1, IL-1β, and LIF increased. Except for RANTES mRNA, these differences were less in the 6 h samples. VEGF increased as well, but this increase was not statistically significant. **TNF-α and IL-1β-neutralizing Antibodies:** IL-1β antibody alone or in combination with TNF-α significantly reduced expression of all eight mRNAs. Combinations for some mRNAs reduced expression by up to 1/2. This effect was not observed when A549 was treated with the control AM. **Transcription Factor Binding Activity:** Binding of AP-1 and Sp1 increased when A549 treated with supernatants from PM_{10}-exposed AM, but not from control AM.

Study	Pollutant	Exposure	Effects
Reference: Ishii et al. (2005, 096138) **Species:** Human **Cell Type:** AMs (obtained from 10 smokers who stopped smoking 6 wk prior), HBEC	EHC-93: PM_{10} (obtained from Environmental Health Directorate, Ontario, Canada) **Particle Size:** PM_{10}	**Route:** Cell Culture (HBEC: 2.5-3.0×10^6 cells; AM: 1×10^7 cells; co-culture of AM/HBEC: 5×10^6 cells) **Dose/Concentration:** 100 µg/mL **Time to Analysis:** 2, 24 h	**mRNA Expression After 2 h Exposure:** AM or HBEC exhibited no effect. In contrast, co-culture increased expression of MIP-1β, GM-CSF, M-CSF, IL-6, MCP-1 and ICAM-1-mRNA. **mRNA Expression After 24 h Exposure:** AMs exhibited no effect. HBEC increased levels of GM-CSf, LIF and ICAM-1. Co-culture, on the other hand, increased expression of MIP-1β, GM-CSF, M-CSF and ICAM-1 mRNA. **Protein Levels:** AM and HBEC both increased GM-CSF, IL-6 and MIP-1β release into the supernatant. Co-culture effect was not additive but synergistic (i.e., higher than expected). MCP-1 levels did not increase significantly. Co-culture appeared to decrease protein levels for both the control and PM values. M-CSF levels increased for co-culture only. **Surface Expression of ICAM-1:** Upon 24 h exposure to PM, HBEC exhibited an increase in expression. Expression in AMs were not affected by 2 h PM stimulation. **ICAM-1 Inhibitors:** IgG or anti-CD11b antibody was unaffected in co-culture.
Reference: Jalava et al. (2005, 088648) **Species:** Mouse **Cell Type:** RAW 264.7	UPM: SRM1649a (Washington, DC) DEP: SRM1650 (NIST) EHC-93: Ottawa dust (Environmental Health Center, Ottawa, Canada) HFP-00: Pooled ambient air $PM_{2.5}$ sample from Helsinki, Finland M-UPM: methanol extract of UPM **Particle Size:** SRM 1649a, SRM 1650, EHC-93: NR; HFP-00: $PM_{2.5}$	**Route:** Cell Culture (5×10^5 cells/mL) **Dose/Concentration:** 150 µg/mL **Time to Analysis:** Methanol treatment of PM samples: 24 h; Exposure to ambient PM samples: 2, 4, 8, 16, or 24 h.	**TNF-α:** All the PM samples increased TNF-α. **Cell Viability:** SRM1649a exhibited the most cytotoxicity, followed by HFP-00 and EHC-93. Methanol significantly affected cytotoxicity of the EHC-93 sample only. **Cytokines:** TNF-α concentrations in the cell culture medium significantly increased at all time points between 2 and 24 h. The highest increase was seen in EHC-93. IL-6 production also increased at different levels with the highest increase observed in EHC-93. No response was observed for IL-10. **Cell Viability:** Duration of exposures had no significant effect on any of the samples. A 2 h exposure time was sufficient to induce the typical reductions in cell viability.
Reference: Jalava et al. (2006, 155872) **Species:** Mouse **Cell Type:** RAW 264.7	PM: Collected east of Helsinki, Finland between Aug 23 and Sept 23, 2002 Divided in 12 groups (4 sizes by 3 exposure types): -S: seasonal average -W: wildfire -M: mixed -B: blank **Particle Size:** $PM_{10-2.5}$; $PM_{2.5-1}$; $PM_{1-0.2}$; $PM_{0.2}$	**Route:** Cell Culture (5×10^6 cells/mL) **Dose/Concentration:** 15, 50, 150 and 300 µg/mL **Time to Analysis:** 24 h	**Particulate Mass Concentrations in HVCL Size Ranges:** The largest increase of PM concentrations was observed in $PM_{1-0.2}$. **NO:** All 12 samples increased NO production when compared to corresponding unexposed controls. Peaks were observed at 150 µg/mL, except in $PM_{1-0.2}$. **Cytokines:** All 12 samples increased TNF-α and IL-6 production. $PM_{10-2.5}$ and $PM_{2.5-1}$ produced a much larger response than $PM_{1-0.2}$ and $PM_{0.2}$. IL-6 production for $PM_{0.2}$ was not measured. MIP-2 production also increased with similar trends. **Cytotoxicity:** All 12 samples induced dose-dependent decreases in cell viability. $PM_{10-2.5}$ were the least active inducers of apoptosis while PM0.2 showed the highest activity (4-17% of apoptotic cells).

Study	Pollutant	Exposure	Effects
Reference: Jalava et al. (2007, 096950) **Species:** Mouse **Cell Type:** RAW 264.7	Urban background PM PM_{10}, $PM_{2.5}$, and PM0.2 collected from 6 European cities during different times of the year from October 2002 to July 2003: -D: Duisburg (Fall) -P: Prague (Winter) -A: Amsterdam (Winter) -HR: Helsinki (spring), -B: Barcelona (spring) -AT: Athens (summer) **Particle Size:** PM_{10}: 2.5-10 µm; $PM_{2.5}$: 0.2-2.5 µm; $PM_{0.2}$: <0.2 µm	**Route:** Cell Culture (5×10^5 cells/mL) **Dose/Concentration:** 15, 50, 150, 300 µg/mL **Time to Analysis:** 24 h	**PM Characterizations:** The highest mass concentrations of PM_{10} and $PM_{0.2}$ were measured in Athens. Prague had the highest $PM_{2.5}$ concentrations. **NO:** All PM fractions induced statistically significant NO production in macrophages. $PM_{2.5}$ -P and $PM_{2.5}$ -AT produced significantly larger responses, though all samples at 150 and 200 µg/mL induced statistically significant production. When compared to the other $PM_{0.2}$ samples, -P and -HR produced significantly larger responses. **Cytokines:** PM_{10} showed average cytokine production to be 7.8 fold and 83 fold for TNF-α, and 4.4 fold and 530 fold for MIP-2 when compared to $PM_{2.5}$ and $PM_{0.2}$ respectively. PM_{10} induced statistically significant increases in production of TNF-α, MIP-2 and IL-6. $PM_{2.5}$, with exception of Prague, caused significant increases in cytokines. $PM_{0.2}$-A and -AT showed small yet statistically significant increases in TNF-α. An increase in MIP-2 was observed with -P and -HR. IL-6 increased significantly with PM_{10} and slightly with $PM_{2.5}$. In the $PM_{0.2}$ range, only the -A and -AT samples caused a small, statistically significant TNF- α production. MIP-2 production was only detected from the -P and -HR samples. $PM_{0.2}$ effects on IL-6 response were negligible. **Cytotoxicity:** The average cytotoxicity of PM_{10} and $PM_{2.5}$ were roughly equal, but $PM_{0.2}$ were less cytotoxic with the exception of -P. The dose-response trends for most of the samples were linearly declining, with PM_{10} and $PM_{2.5}$ exhibiting statistically significant declines in viability.
Reference: Jimenez et al. (2002, 156610) **Species:** Human **Cell Type/Line:** A549, THP-1, Mono Mac 6 (DSMZ)	PM_{10}: Collected from London and Edinburgh air particulate monitoring stations. TiO_2: Tioxide Europe (London, UK) and Degussa-Huls (Cheshire, UK) $UFTiO_2$: Tioxide Europe (London, UK) and Degussa-Huls (Cheshire, UK) **Particle Size:** PM_{10}, TiO_2: 200 nm; $UFTiO_2$: 20 nm	**Route:** Cell Culture (110,625 cells/well) **Dose/Concentration:** PM_{10}, TiO_2, $UFTiO_2$: 100 µg/mL; TNF-α: 10 ng/mL **Time to Analysis:** 4 h	**NF-κB and AP-1 DNA Binding**: NF-κB DNA binding increased in PM_{10} and TNF-α exposed macrophages by 9.5 and 12 fold. NF-κB activity remained unaltered in TiO_2 and $UFTiO_2$ exposed macrophages. **IL-8:** Cells treated with PM_{10} conditioned media increased transcription binding of NF-kB to IL-8 promoter sites. Increases were observed in gene expression after exposure to TNF-α and PM_{10}. TiO_2 or $UFTiO_2$ had no effect. Increases observed in IL-8 production with PM_{10}. **IL-8 Promoter CAT Activity:** PM_{10} media increased CAT expression by 65% over control. No differences observed with TiO_2 or $UFTiO_2$ media. **Neutrophil Chemotaxis:** PM_{10} conditioned media induced a 2.3 fold increase compared to control. **TNF-α and IL-1β Production:** PM_{10} media increased TNF-α and IL-1β production. No increases were observed in TiO_2 and $UFTiO_2$ media.

Study	Pollutant	Exposure	Effects
Reference: Jung et al. (2006, 132421) **Species:** N/A **Type:** Surrogate Lung Fluid	Soot Particles: Generated using a co-flow, laminar, diffusion flame system CB (Degussa) $PM_{2.5}$: Collected using IMPROVE air pollution samplers **Particle Size:** Soot: 185 nm; CB: 25 nm, $PM_{2.5}$	**Route:** Surrogate Lung Fluid **Dose/Concentration:** Soot: 0-30 mg; CB: 5-10 mg; $PM_{2.5}$: 50 or 100 µg/mL **Time to Analysis:** Parameters measured continuously over 2 h.	**OH Radical Formation:** Formation occurred with linear dependence on soot mass. Average response was 0.89 nmol OH produced per mg of soot. Formation also occurred with soot + hydrogen peroxide. Hydrogen peroxide alone did not form OH radicals. **Fe:** Average Fe concentration in soot particles was 305 ± 172 nM. Observed negative correlation between amount of Fe and amount of OH radical formation. DSF inhibited iron-induced increase in OH radical formation. **Carbon Black:** OH radical generation by carbon black was significantly less than soot. OH generation by CB was observed to be linearly proportional to PM mass, but CB was much less efficient at generating the OH radical. **$PM_{2.5}$:** A high variability in the increase of OH radicals was observed with $PM_{2.5}$. Pretreatment with DSF partially blocked OH radical production, but a significant level remained. This may be due to $PM_{2.5}$ containing high levels of Fe and Cu.
Reference: Kafoury and Madden (2005, 156617) **Species:** Mouse **Cell Type:** RAW 264.7	DEP: SRM 1975 (purchased from NIST, Rockville, MD) BAY11-7082, NF-κB inhibitor (coexposure) IL-1ß: obtained from Santa Cruz Biotechnology (Santa Cruz, CA) **Particle Size:** DEP: 0.3 µm (mean diameter)	**Route:** Cell Culture (3-4×10^5 cells) **Dose/Concentration:** DEP 25, 100, or 250 µg/mL; IL-1ß: 100 ng/mL **Time to Analysis:** DEP: 4 h pre-treated with BAY11-7082 for 1.5 h; IL-1β: 4 h	**TNF-α:** DEP induced a significant release of TNF-a at 100 and 250 µg/mL dose-dependently. Exposure at 25 µg/mL had no effect. IL-1β containing PM samples at 100 µg/mL also resulted in a significant release of TNF-α. **NF-κB Binding Activity:** Treatment of RAW 264.7 with BAY11-7082 significantly inhibited IL-1β-induced TNF-α release. Similar effects observed with DEP-induced TNF-α release. **Apoptosis:** Inhibition of NF-kB binding activity by BAY11-7082 resulted in DEP-induced apoptotic response. Without BAY11-7082, apoptosis was not induced even at the DEP dose of 250/µg/mL for 4 h. The control, U937 cells with campothecin, induced apoptosis.
Reference: Karlsson et al. (2006, 156625) **Species:** Human **Cell Type:** A549, Monocytes (isolated from heparinized whole blood)	PM (W1: wood burning in old-type boiler; W2: wood burning in modern boiler; P: wood pellets burning in pellets burner; T1: PM_{10} tire debris with studded tires and ABT pavement; T2a: PM_{10} tire debris with studded tires and ABS pavement; T2b: $PM_{2.5}$ tire debris with studded tires and ABS pavement; T3: PM_{10} tire debris with friction tires and ABS pavement; St: PM_{10} from busy street in Stockholm, Sweden; Su: PM_{10} from platform of subway station in Stockholm) **Particle Size:** W: NR, T1, T2a, T3, St, Su: PM_{10}, T2b: $PM_{2.5}$	**Route:** Cell Culture **Dose/Concentration:** Suspension: 40 µg/cm^2; Culture: 100 µg/cm^2 (1 ml/well) **Time to Analysis:** Suspension: 4 h; Culture: 18 h	**PM Characterization:** Boiler emitting PM-W1 led to 4 times higher emission of particles when compared to PM-W2 and 8 times higher emissions when compared to PM-P. Total concentration and CO was substantially higher in the old-type wood boiler. **Effects with Filter Fibers:** No increase of DNA damage was observed compared to the water control. Filter fibers led to the induction of cytokines in human macrophages. **Genotoxicity:** All particulate samples induced DNA damage in A549 cells. PM-Su exhibited the most genotoxicity and induced 4-5 times more DNA damage than others. **Cytokines on Glass Fiber Filters:** PM-W2 induced a significant increase in IL-8. PM-St induced the highest increases of IL-6, IL-8, and TNF-α. **Cytokines on Teflon Filters:** PM-2a and PM-2b samples caused significant increases of IL-6, IL-8, and TNF-α.

Study	Pollutant	Exposure	Effects
Reference: Katterman et al. (2007, 096358) **Species:** Rat **Cell Type/Line:** RLE-6TN (Alveolar Epithelial Cell Line)	PM: Oils: OAAF, Oil Q, OII I II, NF2 PM: Coal Germany and Ohio Diesel particulates: ZODDA (doped with Zn), ZSDDA (doped with Zn and S): S: PMs washed in solution; F: Fresh samples; L: Leached Al_2O_3, Fe_2O_3, SiO_2, TiO_2, ZnO also tested **Particle Size:** NR	**Route:** Cell Culture (cytotoxicity: 50,000 cells/well; SEM: 25,000 cells) **Dose/Concentration:** Oils 0.2 mg/mL; Coals 0.7 mg/mL; Diesel 0.01 mg/mL; Al_2O_3 0.5 mg/mL; Fe_2O_3 0.7 mg/mL; SiO_2 0.7 mg/mL; TiO_2 0.7 mg/mL; ZnO 0.05 mg/mL **Time to Analysis:** 24 h	**Metabolic Activity:** For oils comprised of 3/4 fresh and 1/4 leached, metabolism decreased. Coals (fresh and leached) had no effect. ZODDA-F and ZSDDA-F both induced decreases in activity. ZSDDA-L had no effect. **Cellular Morphology:** PM-S had a minimal effect. PM-F induced widespread cell damage. **Constituent Differences between PM-F and PM-L:** In oil samples Cu, Ti and Ca salts were removed upon washing. Fe, Al, Si remained constant. **Grinding Effects:** Coal toxicity increased upon grinding, whereas diesel PM toxicity decreased upon grinding. **Metal Oxide Effects:** Only SiO_2, and ZnO (much higher at lower concentrations than other metal oxides) decreased metabolic activity. Fresh, washed and sonicated samples exhibited similar results. Grinding only affected TiO_2 (increase) and ZnO (decrease).
Reference: Kendall et al. (2004, 156634) **Species:** Human **Tissue Type:** BALF (obtained by bronchoscope from 6 nonsmokers and 3 smokers)	$PM_{2.5}$ sample sites; 2 schools in Bronx, NY, 6 background urban, 6 urban roadside. Sampling occurred 24 h/day for 12 days. Particle Surface Chemistry: 79-87% carbonaceous material (Ch, COO, C-(O,N)), 10-17% O (O1s), 1.5-4% N (NH_4^+, N-C, NO_3^{2-}), 0.6-1% S, and 0.3-2 % Si. Only NO_3 - higher in roadside samples. NH_4 and NO_3 - correlated with NO and NO_X in air but not NO_2. **Particle Size:** $PM_{2.5}$	**Route:** BALF interaction **Dose/Concentration:** 5-10 ml of 0.5 M NaCl or BALF **Time to Analysis:** Filters treated with BALF for 4 h	**Saline Washing:** Removed particles and decreased NH_4, NO_3, O and S relative to C1. **BALF treatment (XPS):** $PM_{2.5}$ surfaces interacted strongly with BALF within hours of contact. Specific surface components of $PM_{2.5}$ immersed in BALF were desorbed while biomolecules from BALF were adsorbed to particles. N-C on the PM surface increased 3 fold for smokers and 4 fold for nonsmokers (range 1.4-7.4). This is most likely related to protein-like adsorption on PM. Treatment also induced a slight increase in COO and decreases in NH_4, NO_3, O and S. **ToF-SIMS - Organics:** Particle loading and surface hydrocarbons showed a linear correlation. Loss of hydrocarbons from $PM_{2.5}$ surface averaged 55% (10-75) after undergoing saline and BALF washes. In only 3/12 samples BALF removed less hydrocarbon. BALF treatment increased the amino acid and phospholipid content of the $PM_{2.5}$ surface. **ToF-SIMS - Inorganic:** Saline washing appeared to increase Al and Si but with extreme variability; this increase was not statistically significant. Both saline and BALF washing decreased NH_4 and Na levels to a similar extent. BALF washing did not affect Al or Si.
Reference: Kim et al. (2005, 088454) **Species:** Human **Cell Type/Line:** BEAS-2B	Zn^{2+} **Particle Size:** NA	**Route:** Cell Culture **Dose/Concentration:** 15, 50, 100 µmol **Time to Analysis:** 1-20 h	**Cell Viability:** At 50 µM for 20 h, no apoptosis was induced. **IL-8:** At 12 h, IL-8 increased in dose-dependent manner. At 15 or 50 µM, Zn^{2+} increased protein 1.6 and 4.6 fold respectively. IL-8 mRNA expression increased dose-dependently, reaching statistical significance at 2 h and continuing until 4 h. **EGFP (adenoviral IL-8 promoter):** Levels increased 2.4 fold with 50 µM Zn^{2+}. **Proteases:** With 50 µM Zn^{2+}, phosphorylation of MAPKs ERK, JNK and p38 increased by 15 min and continued increasing up to 2 h. Pre-exposure of inhibitors of MEK, JNK, before Zn^{2+} exposure caused inhibition of Zn-induced IL-8 mRNA and protein production. Inhibitor of p38 had no effect. Dephosphorylation of ERK and JNK was partially inhibited with exposure to Zn^{2+}.

Study	Pollutant	Exposure	Effects
Reference: Kleinman et al. (2003, 087938) **Species:** Rat **Strain:** Wistar Kyoto, F344 **Age:** 22-24 mo, 10 wk **Cell Type/Line:** AM	UF1: Utrecht 1 Fine (urban freeway) UC1: Utrecht 1 Coarse UF2: Utrecht 2 Fine (urban, freeway, light industrial) UC2: Utrecht 2 Coarse SRM 1650 SRM 1648 **Particle Size:** UF1: 0.2-2.5 µm; UC1: 2.5-10 µm; UF2: 0.2-2.5 µm; UC2: 2.5-10 µm	**Route:** Cell Culture (10^5 cells/well at 10^6 cells/mL) **Dose/Concentration:** 1.2 to 1200 ng/10^6 cells **Time to Analysis:** 4, 18 h	**Macrophage PMA-stimulated respiratory burst activity:** SRM 1648 and 1650 induced dose-dependent decreases approaching 0 at 50 -100 µg/10^5 cells. Large dose-dependent decreases from old rat AMs exposed to fine PM exposure were followed by young rat AMs exposed to fine PM. However, no age-related effects were statistically significant. **Free radical production:** All coarse particles depressed free radical production in a semi-dose-dependent manner, with UC2 exhibiting more potency than UC1. Both fine particles also showed dose-dependent responses but UF1 and UF2 responses were greater than the control at 3 µg/10^6 cells. **PM Characterization:** Ratios between coarse and fine PM were similar for metals tested (Al, Fe, Mn, Zn). Al was higher in coarse samples and Zn higher in fine PM, although large variability was observed. Fe and Mn results were roughly equivalent for all samples.
Reference: Kocbach et al. (2008, 198874) **Species:** Human **Cell Type/Line:** THP-1	PMW: Wood smoke particles Collected from conventional Norwegian wood stove burning birch PMT+: Traffic-derived particles; collected from road tunnel in winter when studded tires were used PMT-: Traffic-derived particles; collected from road tunnel in summer without studded tires DEP: SRM2975 Porphyr: fine grain syenite porphyry (prepared by SINTEF, Trondheim, Norway) Polymyxin B Sulphate (endotoxin inhibitor) **Particle Size:** PMW, PMT, DEP: NR; Porphyr 8 µm (mean)	**Route:** Cell Culture (1×10^6 cells/mL) **Dose/Concentration:** 30-280 µg/mL **Time to Analysis:** 2, 5, 12 h	**Particle Characterization:** PMT+ contained a high mineral particle content. PMT- contained carbon aggregates, and polycyclic aromatic hydrocarbons (PAH). PMW and DEP contained carbon aggregates. PAH content of PMW was greater than DEP. Porphyr was not included in the analysis. **Cytokines:** PMT± induced releases of TNF-α, IL-1β, and IL-8 with 30 or 70 µg/mL. PMW similarly induced TNF-α and IL-8. DEP induced IL-1β and IL-8. Porphyr induced IL-8 increases. IL-4, IL-6 and IL-10 were unaffected. Overall, the order of effective cytokine induction from most to least effective was PMT±, PMW, DEP, and Porphyr. mRNA expression of TNF-α, IL-1β, IL-8, and IL-10 increased with 140 µg/mL of PMT± and slightly for PMW. **LDH:** PMT ± induced small but statistically significant increases at low doses. DEP increased LDH at 280 µg/mL only. **Polymyxin B Sulphate:** The endotoxin inhibitor significantly inhibited LPS-induced cytokine release by 80-90% and reduced PMT± induction by 50-60%. **Organic Extraction:** PMT+ washed and native particles showed equivocal induction of cytokine release. PMT+ organic extract had no effect. PMT- and PMW organic extracts significantly increased TNF-α and IL-8. Washed particles induced less significant increases of IL-8. DEP organic extract had no effect.

Study	Pollutant	Exposure	Effects
Reference: Kristovich et al. (2004, 087963) **Species:** Human **Cell Type/Line:** HUVEC, HPAEC, HPMVEC, HPBMC	CP: carbon particle (carbonaceous negative image of zeolite) CFE: C/Fe particulate (synthesized) CFE+: C-Fe/F-Al-Si particulate (synthesized) CFA: Coal Fly Ash (Coal-fired power plant, NOS) DEP: (exhaust pipe of diesel powered truck) CP, CFE, CFE+ approx 1 µm (resembling zeolite) Particle Characterization (Surface chemistry): CP = 88% C, 1% Si, 10% O, 1% N. CFE = 80% C, 2% Fe, 2% Si, 16% O. CFE+ = 20% C, 6% Al, 3% Si, 50% F, 6% O, 11% N, 4% Na. CFA = 25% C, 3% Fe, 13% Al, 17% Si, 41% O, 1 % N. DEP = 70% C, 3% Fe, 24% O, 1% N, 2% S. **Particle Size:** CP, CFE, CFE+: approximately 1 µm (resembling zeolite); CFA: <2 µm; DEP: 150 nm	**Route:** Cell Culture (4×10^6 cells/well) **Dose/Concentration:** CP: 5-50 µg/cm^2; CFE: 2.5-25 µg/cm^2; CFE+: 2.5-25 µg/cm^2; CFA: 10-100 µg/cm^2; DEP: 2.5-25 µg/cm^2 **Time to Analysis:** 4, 8, or 24 h	**Cytotoxicity:** CP exhibited no effects. DEP and CFE exhibited intermediate toxicities in the range of 50-70 µg/cm^2. No toxicity was apparent when treated with CFA (up to 200 µg/ cm^2) or synthesized C particulates. **Endothelial Activation:** ICAM-1, VCAM-1, and E-selectin were activated dose-dependently by DEP, CFE, and CFE+. No effects observed for CFA or CP. These effects were not the result of endotoxin release. **Individual Variability:** Donors (humans) showed variability in responses especially for CFA. 3/9 had a medium response negated by ND responses in 6/9.
Reference: Kubatova et al. (2006, 198835) **Species:** Rat, Human **Cell Type/Line:** RAW 264.7, BEAS-2B	PMW: Wood Smoke Collected from airtight wood stove burning hardwoods -P: Polar (fraction extracted from 25-50 C) -MP: Mid Polar (fraction extracted from 100-150 C) -NP: Nonpolar (fraction extracted from 200-300 C) -C: P + MP + NP **Particle Size:** NR	**Route:** Cell Culture (RAW 264.7: 10^6 cells/mL; BEAS-2B: 10^5 cells/mL) **Dose/Concentration:** 50, 100, 200 µg/mL **Time to Analysis:** 12 h	**GSH:** PMW-MP and PMW-NP induced GSH depletion substantially in a dose dependent manner starting at 50 µg/mL in both cell types. DMSO had no effect. **Cytotoxicity:** PMW-MP and PMW-NP increased cytotoxicity at 200 µg/mL in RAW 264.7. BEAS-2B was unaffected. **Particle Characterization:** PMW-MP contained higher concentrations of oxy-PAHs, disyringyls, syringylguaiacyls and PAHs. oxy-PAHs include 9-fluorenone, 1-phenalenone, 9,10-anthraquinone and hydroxycadalene. PAHs included phenanthrene, fluoranthene and pyrene. **Effects of Individual Components of PMW-MP on GSH:** 1,8-dihydroxy-9-10anthraquinone and 9,10-phenanthraquinone depleted GSH. 9,10-anthraquione, anthrone, 1-hydroxypyrene increased GSH. Phenanthrene, 1-methylpyrene, 9-fluorenone and xanthone had no effect.
Reference: Kubatova et al. (2004, 087986) **Species:** Monkey **Cell Type/Line:** African green monkey kidney cells designated COS-1 (CV-1 cells with origin - defective mutants of SV40), E coli PQ 37 (SOS Chromotest)	DEP: Obtained from diesel bus PMW: Wood smoke particulates obtained from airtight wood stove burning hardwood HSF: Hot pressure fractionation -C: P + MP + NP -P: Polar -MP: Mid Polar -NP: Nonpolar OE: Organic Extraction -HNP: n-hexane nonpolar -MEP: methanol polar **Particle Size:** NR	**Route:** Cell Culture (10,000 cells/180 µl) **Dose/Concentration:** 0, 50, 100, 150, 200, 250, 300 µg/mL **Time to Analysis:** Cytotoxicity: 24 h; Chomotest: 2 h SOS	**Cytotoxicity:** PMW induced cytotoxicity in a dose-dependent manner. PMW-HNP induced low cytotoxicity, followed by PMW-C (intermediate) and PMW-MEP (highest). Levels above 25 µg/mL were cytotoxic. DEP-HNP induced cytotoxicity but was not dose-dependent. Results similar for all 3 fractions (highly variable). All fractions with concentrations higher than 100 µg/mL were cytotoxic. **Extraction Water Temperature Effect:** PMW was cytotoxic at temperatures over 50 C. DEP was cytotoxic at temperatures higher than 200˚ C. At 250˚, cytotoxicity between DEP and PMW was similar. At 300˚ C, PMW cytotoxicity declined and DEP stayed high, resulting in DEP inducing higher cytotoxicity than PMW. **SOS Chromotest:** β-Galactosidase formation increased, peaked at 200˚ C with DEP and declined to control at 300˚ C. Individual fractions showed linear dose response from 25-200 µg/mL with 150˚ C and 200˚ C extracts significantly higher.

Study	Pollutant	Exposure	Effects
Reference: Lee et al. (2005, 156682) **Species:** Human **Cell Type/Line:** A549	MEP: Motorcycle Exhaust Particles (Yamaha Cabin engine, 95 octane unleaded gasoline,150 rpm) MEPE: MEP Particle Free **Particle Size:** MEP 0.5 µm; MEPE<0.2 µm	**Route:** Cell Culture (1×10^5 cells/well) **Dose/Concentration:** MEP 0.02, 0.2, 0.2, 2, 20 µg/mL; MEPE 20 µg/mL **Time to Analysis:** 24 h	**IL-8:** MEP induced IL-8 at concentrations greater than 0.2 µg/mL. Levels increased 2fold at 24 h with 20 µg/mL. MEPE induced similar responses at 20 µg/mL. Induction of IL-8 mRNA expression was dose-dependent with MEP and MEPE. **Cytotoxicity:** Exposure to particles did not affect cytotoxicity. **NF-κB:** MEP (20 µg/l) induced time-dependent activation for 2 h and continued at same level for up to 6 h. Pretreatment of PDTC (1mM) fully inhibited MEP induction. **MAP Kinase:** MEP induced time-dependent activation up to 30 min and stayed elevated for at least 60 min. **ROI:** MEP treatment induced a time-dependent increase in ROI for up to 1 h and then continued the at same level for up to 6 h.
Reference: Lee and Kang (2002, 198864) **Species:** Mouse **Cell Type/Line:** Peritnoeal Macrophages, RAW 264.7	MEP Yamaha 2-stroke engine using unleaded gas) MEPE(particle-free MEP) **Particle Size:** 0.5 µm	**Route:** Cell Culture (5×10^5 cells/mL (Cytotoxicity), 3×10^5 cells/mL (Apoptosis), 2×10^6 cells (MMP and ROI), 1×10^7 cells (GSH) **Dose/Concentration:** 5, 10, 50, 100, 300, 1000 µg/mL **Time to Analysis:** 6, 12, 18, 24 h	**Cytotoxicity:** Viability decreased dose and time-dependently in all cell types at 24 h. **Apoptosis:** subG1 significantly and dose-dependently increased at the 300 MEP µg/mL dose in all cell types, indicating increased apoptosis. MEPE induced similar results. Inhibition was successful against MEP-induced apoptosis by calcium chelators EGTA, BAPTA-AM, cyclosporin A and antioxidants NAC, GSH, catalase and SOD. **Ca2+**: MEP and MEPE increased Ca^{2+} at 300 µg/mL. BAPTA-AM completely inhibited induction. **ROI:** MEP increased ROI in a time-dependent manner. Calcium chelators and antioxidants substantially attenuated induction. **GSH:** MEP significantly decreased GSH. **MMP:** Mitochondria membrane potential decreased dose-dependently with MEP 100 µg/mL and 300 µg/mL. Calcium chelators and antioxidants partially inhibited reduction.
Reference: Li et al. (2002, 042080) **Species:** Mouse **Cell Line:** RAW 264.7, THP-1	VACES (Biosampler PM_{10} in Downey, CA -DEP concentrate in water) DEPM (DEP methanol extract) DEPME (DEP methylene chloride extracts) DEPAL (DEPME aliphatic (hexane)) DEPAR (DEPME aromatic (hexane/methlene chloride)) DEPPO (DEPME polar (methylene chloride/methanol)) **Particle Size:** NR	**Route:** Cell Culture (2×10^6 cells/well Mouse RAW 264.7 and THP-1; 0.67×10^6 cells/well Murine RAW 264.7) **Dose/Concentration:** 10-200 µg/mL JNK Activation and IL-8 Production: THP-1 cells- 0, 10, 25, 50, 100 µg/mL DEPM; THP-1 cells- 0, 10, 25, 50, 100 µg/mL of DEP; RAW264.7 cells- 10 -100 DEP µg/mL Cytotoxicity: 1, 10, 25 (THP-1 cells only), 50, 100, 200 µg/mL GHS/GSSG: 0, 10, 25, 50, 100 µg/mL HO-1 Expression: 0, 25, 50, 100, 200 µg/mL **Time to Analysis:** GHS/GSSG: DEPM, whole DEP (RAW 264.7 only) 8 h. HO-1, MnSOD Expression: RAW 264.7, THP-1 7h. RAW 264.7 cells exposed to whole DEP 16 h. JNK Activation, IL-8 Production: THP-1 cells 30 min, 16 h. RAW 264.7 cells 90 min. Cytotoxicity: RAW264.7, THP-1 18 h.	**GSH/GSSG Ratio:** DEPM induced dose-dependent decrease in GSH/GSSG ratios in both cell lines. DEP induced decreases at comparable doses to DEPM. **HO-1 Expression:** Cells exhibited dose-dependent increases in HO-1 expression. **HO-1 Expression in Murine RAW 264.7:** VACES-F consistently induced HO-1 expression over a 9m period, whereas VACES-C was effective in inducing HO-1 during fall and winter. HO-1 induction positively correlated to higher OC and PAHs that were represented in VACES-F, but also seen with a rise in PAHs in VACES-C during winter months. **MnSOD:** At doses of 2.5 µg/mL, DEPM increased MnSOD in THP-1 cells. **JNK Activation:** DEPM dose-dependently increased JNK phosphorylation but did so without a change in the JNK expression level. DEP-exposed mouse RAW264.7 cells exhibited similar increases in JNK phosphorylation but without increasing JNK expression. **IL-8:** Exposure to DEPM elicited dose-dependent increase in IL-8 levels of THP-1 cells.

Study	Pollutant	Exposure	Effects
Reference: Li et al. (2002, 087451) **Species:** Human **Cell Line:** BEAS-2B, NHBE, THP-1 macrophages	DEPM (DEP methanol extract) DEPME (DEP methylene chloride extracts) DEPAL (DEPME aliphatic (hexane)) DEPAR (DEPME aromatic (hexane/methlene chloride)) DEPPO (DEPME polar (methylene chloride/methanol)) **Particle Size:** 0.05-1 µm	**Route:** Cell Culture (10^6 cells/mL) **Dose/Concentration:** 0, 10, 25, 50, 100 µg/mL **Time to Analysis:** 30, 60, 120 min	**ROS:** BEAS-2B cells demonstrated increased HE fluorescence, indicating increased ROS formation. THP-1 cells were unaffected. **GSH/GSSG Ratio:** DEPM dose-dependently decreased GSH/GSSG in THP-1 and BEAS-2B cells. Similar changes occurred with NHBE cells. THP-1 cells maintained a higher ratio of GSH/GSSG than BEAS-2B and NHBE cells. **NAC on GSH/GSSG Ratio:** Exposure to DEPM in the presence of NAC did not affect the GSH/GSSG ratio in BEAS-2B and NHBE cells. In THP-1 cells, NAC prevented a decline in the GSH/GSSG ratio. **MnSOD and HO-1:** THP-1, BEAS-2B and NHBE cells showed constitutive MnSOD expression and dose-dependent expression of HO-1 protein and mRNA. No change occurred in the expression of β-actin. **DEPAL, DEPAR, DEPPO, CoPP on HO-1 Expression:** DEPPO was more potent than DEPAR. DEPAL lacked activity for THP-1 and BEAS-2B cells. The potency of DEPPO was sufficient to affect cellular viability and HO-1. CoPP induction of HO-1 failed in THP-1 cells, but succeeded in BEAS-2B cells. However, it did not protect against the oxidizing effects of DEPM. **JNK:** JNK activation increased in DEP-exposed THP-1 and BEAS-2B cells. JNK isoforms were observed at doses of ≥ 25 µg/mL. In BEAS-2B cells a high rate of cell death diminished this response at 100 µg/mL. NHBE also showed increased JNK phosphorylation at doses 50 - 100 µg/mL. **NAC on JNK:** NAC led to inhibition of JNK activation. **IL-8:** THP-1 cells showed dose-dependent increases of IL-8. NHBE cells showed incremental increases followed by rapid decline at 100 µg/mL attributed to apoptosis. BEAS-2B cells responded to 10 µg/mL with increased IL-8, but cellular toxicity and cell death led to a drop in IL-8 production at higher doses. **Cytotoxicity:** Comparing cytotoxicity at 25 µg/mL DEP, BEAS-2B cells had a higher rate of cell death than THP-1 cells. BEAS-2B cells showed a significant rise in cell death at doses larger than 10 µg/mL. In THP-1 cells, it took doses of 25 µg/mL or more before significant increases occurred. In BEAS-2B, cell death began at 2 h. In THP-1, increases in cell death prolonged for 8h or longer. NHBE cells also showed increase rates of cytotoxicity compared to macrophages. NAC in THP-1 interfered with a generation of cytotoxicity, but NAC did not have any decreasing effect on cell death in BEAS-2B or NHBE cells.

Study	Pollutant	Exposure	Effects
Reference: Lindbom et al. (2007, 155934) **Species:** Mouse **Cell Line/Type:** RAW 264.7	PM_{10}: -ST: Street -S: Subway -G: Granite -Q: Quartzite (-G and -Q generated by road simulator at Swedish National Road and Transport Research Institute) **Particle Size:** PM_{10}: Bimodal with peaks around 4-5 um and 7-8 um.	**Route:** Cell Culture (130,000 cells/cm^2) **Dose/Concentration:** 1, 10 or 100 µg/mL **Time to Analysis:** 18, 24 h Analysis of Arachidonic Release (AA): Cells pre-incubated w/ 1 µCI tritium marked for AA and washed exposed to 10, 50, 100 and 250 µg/mL	**Cellular Viability:** Viability was not influenced by any particle types and in all cases exhibited 90% or higher viability, except for the combination of subway particles and NAC where viability dropped to 20%. **Cytokines:** All particles induced TNF-α secretion in a dose-dependent fashion. PM-S was most potent at 1 µg/mL. PM-G and PM-ST induced effects at 10 µg/mL. PM-Q induced increase of TNF-α at 100 µg/mL.PM-ST induced IL-6 release at 10 µg/mL. PM-G, PM-Q, PM-S induced IL-6 secretion at 100 µg/mL. DFX inhibited TNF-α in cells exposed to PM-S and PM-ST. DFX induced increase of TNF-α with PM-Q. For all PM types (except PM-ST) DFX inhibited induced IL-6 secretion. **NO:** PM-ST and PM-G induced a significant release of NO, with PM-ST inducing a higher NO release than PM-G. **NAC:** NAC treatment significantly inhibited both TNF-α and IL-6 secretion with all PM particles. **L-NAME**: L-NAME caused a decrease in NO secretion at 100 µg/mL of PM-ST. L-NAME did not have an effect on granite-induced NO secretion at 100 µg/mL. **Cytokine Gene Expression:** TNF-α mRNA showed a trend to increase for -ST, but this did not reach significance. IL-6 gene expression increased for PM-Q, PM-ST, PM-S but not for PM-Q. **AA Release:** PM-S exposure at 100 and 250 µg/mL was the only PM to induce AA release. **Lipid Peroxidation:** All particle types induced lipid peroxidation. PM-S and PM-ST induced significantly higher lipid peroxidation as compared to PM-Q and PM-G. **ROS:** All particle types induced ROS formation. PM-S and PM-ST induced significantly higher formation at 10 µg/mL. PM-Q and PM-G induced small but significant decreases in absorption at 100µg/mL. Both PM-ST and PM-S had significant dose responses for all concentrations tested. No difference was observed between PM-G and PM-Q. PM-S and PM-ST pretreated with DFX had a lower ability to induce ROS formation. **Endotoxin Content:** Only PM-ST showed positive results for endotoxin content.

Study	Pollutant	Exposure	Effects
Reference: Liu et al. (2005, 088304) **Species:** Human **Cell Type:** HPAECs	SE: Wood Smoke Extract; generated using a stainless steel receptacle containing 100g of dry wood dust **Particle Size:** NA	**Route:** Cell Culture **Dose/Concentration:** 40 µg/mL **Time to Analysis:** 0-4 h; Mitochondrial Membrane Destabilization: 0-60 min; DNA Defragmentation: 0-6 h; Cytotoxicity: 24 h	**Viability:** SE exposure reduced cell viability dose-dependently. Reduction reached ~38% of control. **Effect on Oxidative Stress/ Antioxidant Enzymes:** SE caused an increase in ROS levels, in particular O_2- and $H2O_2$ in a time-dependent manner. Exposure to SE for up to 4 h caused a decrease in GSH levels in a time-dependent manner. Increased expression of Cu/Zn SOD mRNA and HO-1 mRNA was observed. Catalase or GPx mRNA expression was unaffected. Upregulation of Cu/Zn SOD and HO-1 occurred in a time-dependent manner **Mitochondrial Translocation/ Capsase-Independent Apoptosis/DNA fragmentation:** Exposure for up to 60 min caused an increase in the percentage of annexin V-FITC-pos cells but not PI-pos cells. At 4 h, FDA-pos cells was unaffected. SE exposure caused a loss of mitochondrial membrane potential (indicated by the change in JC-1 fluorescence). Cytosolic bax levels increased after exposure for 1 or 2 h and returned to basal level at 4 h after exposure. Levels of procaspase-3 and caspase-9 were unaltered by SE exposure after 4 h. Procaspase-3 increased and caspase-9 decreased by $H2O_2$ exposure. SE exposure increased levels of AIF and EndoG (exposure up to 4 h). At 6 h, increased DNA defragmentation was observed. Pre-treatment with caspase inhibitors (CMK and Z-VAD-FMK) failed to suppress SE-induced apoptosis. **NAC:** Treatment with NAC prevented ROS increase in cells exposed to SE for 60 min. NAC addition prevented the reduction of GSH by SE. NAC decreased nuclear levels of AIF and EndoG and completely reduced DNA-fragmentation. NAC alleviated the SE-induced reduced viability. GSH and DNA fragmentation were unaffected by NAC.
Reference: Long et al. (2005, 087454) **Species:** Human **Cell Types:** Human, Peripheral blood mononuclear cells (PBMCs) differentiated into MDMs (90-95 % CD14+) and T lymphocytes	Synthetic C and C/Fe particles (phenol and paraformaldehyde polymers on a zeolite template) C/Fe analysis Al 1.38 %, Si 0.33 %, Fe 0.46% **Particle Size:** 1 µm	**Route:** Cell Culture (5×10^6 cells, 2 mL /well MDMs) **Dose/Concentration:** 5 µg/cm^2 **Time to Analysis:** 2-24 h	**ROS release:** Oxidative burst form C/Fe maxes out at 20 min with no effect from C particles. **Cellular particulate actions:** C particulates were present within lysosomes with small clumps forming after 24 h outside of lysosomes with no evidence of organelle lysis and/or agglomeration. C/Fe particulates showed similar initial effects progressing at 24-h total organelle lysis extending to the outer cell membrane. **T cell effects:** No effects from C or C/Fe particles Medium Effect: Particle agglomeration appears to be a direct result of serum present within a cell free medium **Hydroxyl radical formation:** C/Fe particles showed an order of magnitude of higher hydroxyl formation as compared to C particles

Study	Pollutant	Exposure	Effects
Reference: Ma et al. (2004, 088417) **Species:** Mouse **Cell Line:** JB6P+ (Epidermal Cell Line)	DEP: SRM 1975 **Particle Size:** 0.5 µm	**Route:** Cell Culture **Dose/Concentration:** Non-cytotoxic: 5, 10, 20 µg/mL; Cytotoxic: 0, 10, 20, 40, 80, 100, 160 µg/mL **Time to Analysis:** 24, 48 h; NF-κB and AP-1: 12 h Phosphorylation of Akt: 5- 120 min. Effect of LY294002 on DEP: Cells pretreated with LY294002 (0 or 10 µM) for 30 min and then exposed to DEP for 0-60 min.	**Viability:** Below 20 µg/mL, DEP had no effect. At concentrations greater than 20 µg/mL, DEP caused apoptosis. **NF-κB and AP-1:** DEP stimulated NF-κB activity at 5 and 10 µg/mL. At 20 µg/mL, NF-κB activity decreased, but was still greater than the control. DEP had no effect on AP-1 activity. **PI3K/Akt Signaling Pathway:** DEP induced phosphorylation of Akt on both Thr-308 and Ser-473. LY294002 (an inhibitor of P13K) blocked phosphorylation of Akt, p70/p85 s6 kinase and GSK 3b. LY294002 eliminated DEP-mediated phosphorylation of Akt. Inhibition of P13K by expressing p85 also blocked DEP-induced Akt phosphorylation. DEP induced phosphorylation on GSH-3B on Ser-9 without affecting tyrosine phosphorylation and enhanced phosphorylation of p70/p85 S6 kinase on Thr-389. DEP had no effect on phosphorylation of FKHR. **SAPK/JNK Pathway:** DEP slightly activated the pathway. Increased transient activation of MKK4 (a signal component of the SAPK/JNK pathway) and thus enhanced phosphorylation of SAPK/JNK. DEP promoted phosphorylation of c-Jun and ATF-2. DEP did not affect p38 MAPK or ERK phosphorylation. **LY294002:** Treatment with LY294002 (P13K inhibitor) eliminated DEP-induced NF-κB activity. A similar effect was observed with the use of another P13K inhibitor, wortmannin. TDZD-8 (GSK-3B inhibitor), D-JNKI(a JNK inhibitor), SB202190 (inhibitor for p38 MAPK) or PD98059 (inhibitor for MEK1) had little effect on DEP-mediated NF-κB activation.
Reference: Maciejczyk and Chen (2005, 087456) **Species:** Human **Cell Type:** BEAS-2B	CAPs: $PM_{2.5}$ Collected via cyclone inlet on side of building in Tuxedo, NY. Weekdays 9-3 March 4 to September 5, 2003 Mass contributions of the Regional Sulfate, Soil, Oil- Combustions and Unknown/other categories to CAPs are: Regional Sulfate- 65%, Soil- 20%, Unknown/Other- 13% and Oil Combustion- 2%. Composition: * Regional Sulfate characterized by high concentrations of S, Si and . * Soil characterized by high concentrations of Ca, Fe, Al and Si. * Oil-Combustion characterized by high concentrations of V, Ni and Se. **Particle Size:** $PM_{2.5}$	**Route:** Cell Exposure (subchronic exposures); Cell Culture (NF-κB) (9×10^4 cells/well) **Dose/Concentration:** CAPS 109 ± 178 $\mu g/m^3$ (air exposure); 300 µg PM/ml (culture) **Time to Analysis:** 24 h	**NF-κB:** NF-κB response most notably correlated with V and Ni - elements associated with oil combustion source category (oil combustion makes up the group that is the smallest percentage of CAP mass).

Study	Pollutant	Exposure	Effects
Reference: Madden et al. (2003, 198877) **Species**: Human **Cell Type:** NHBE	DEP(SRM 2975) Diesel Exhaust Extracts from a High load (HL~75% engine load) or Low load (LL 0% engine load): Obtained from Caterpillar diesel engine, 4 cycl, 4 stroke, model 3304 Particle Characterization: LL extract has greater amount of low-molecular-weight carbonyls (2-5 carbons). HL had more intermediate size carbonyls (6-9 carbons). Largest carbonyls analyzed (11-12 carbons) found in similar ratios in the two types of extract (number of carbons is indicative of differences in boiling points). **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 0, 10, 50, 100, 250, 500 µg/well **Time to Analysis:** 24 h (after 2 h of treatment, 0.5 ml of BEGM added to each well and cells incubated for an additional 22 h) .	**Cytotoxicity:** LL, HL and SRM had no effect on LDH release. **51Cr:** Incubation of cells with LL or SRM (10 to 500 µg/well) had no effect. 500 µg/well of HL induced a significant increase in 51Cr release. **IL-8:** HL induced a 5-fold increase in IL-8 at 500 µg/well. A decrease was observed at the highest dose of LL extract. SRM did not significantly alter IL-8 production. **PGE2:** Production of PGE2 (inflammatory/immune mediator) increased in cells treated with HL extract at 500 µg/well. LL had no effect. Stimulation with melittin caused LL extract to have inhibitory effect on PGE2 at 500 µg/well. SRM had no effect.
Reference: Matsuo et al. (2003, 198879) **Species:** Human **Cell Type:** NHBE, NHPAE, TIG-1, TIG-7 (normal human lung embryonic fibroblasts)	DEP: prepared at National Institute for Environmental Studies (Tsukuba, Japan) RDEP: residual DEP (after sequential extraction with hexane (NOS), benzene, dichloromethane, methanol, 1N ammonium hydroxide) **Particle Size:** 0.4 µm (MMAD)	**Route:** Cell Culture (NHBE: 5×10^4 cells/cm^2; NHPAE: 3×10^3 cells/cm^2; TIG-1 and TIG -7: 3×10^3 cells/cm^2; Apoptosis: 2×10^5 cells/cm^2; ROS/NO: 2×10^4 cells/cm^2; Cytotoxicity Modulating Agent: 3×10^4 cells/cm^2; GSH: 3×10^4 cells/cm^2) **Dose/Concentration:** 25, 50, 100, 200, 300, 400, 500 µg/mL **Time to Analysis:** 1 h	**Cytotoxicity in NHBE:** Both DEP and RDEP exhibited dose-dependent cytotoxicity at concentrations beginning from 50 µg/mL and higher. RDEP was less cytotoxic than DEP. DEP exposure resulted in necrosis, not apoptosis. **Comparative Cytotoxicity:** The order of LC50 values (50% lethal concentration) was: NHBE (118 µg/ml), NHPAE (137 µg/ml), TIG (270 µg/ml). NHBE's susceptibility was higher than the susceptibility of NHPAE and TIG cells. **ROS/NO:** DEP induced dose-dependent increases at 25 and 50 µg/mL. **Reduced Glutathione:** DEP induced dose-dependent decreases. At 200 or 300 µg/mL, GSH levels decreased by 55.2 or 97.3%, respectively. **Antioxidant Effects:** Various antioxidants either decreased DEP cytotoxicity (PMC, Ebselen, EUK-8) or had no effect on DEP cytotoxicity (SOD, catalase, GSH, α-tocopherol) **Chelating Agents:** DEP became less cytotoxic when Ion-chelating agents were preincubated for 24 h. No effect on DEP cytotoxicity was observed when chelating agents were administered to cells immediately after sonication. **Endocytosis inhibitors:** Decreased DEP toxicity was observed in a dose-dependent manner.
Reference: Matsuzaki et al. (2006, 199517) **Species:** Human **Cell Type:** Peripheral neutrophils **Gender:** Male and Female **Age:** 20-40 yrs	DEP: generated from a 4JB1-type, 4 cyl Isuzu diesel engine me-DEP: methanol extract of DEP (40 % of DEP by dry weight) **Particle Size:** 0.4 µm	**Route:** Cell Suspensions (5×10^5 cells/mL) **Dose/Concentration:** all me-DEP f-actin: 1, 5, 10 µg/mL CD11b: 5, 10, 30 µg/mL IL-8: 5, 10, 30 µg/mL H_2O_2: 5, 10, 30, 60 µg/mL MMP-9, LTB-4: 5, 10, 30, 60 µg/mL **Time to Analysis:** f-Actin: 15 min CD11b: 2 h IL-8: 2 or 24 h H_2O_2: 30 min MMP-9, LTB-4: 2 or 24 h	**F-Actin:** Treatment with me-DEP showed a dose-dependent increase in the f-actin content of neutrophils and this increase was significantly higher at 5 and 10 µg/mL. **CD-11b:** Treatment increased CD-11b expression two-fold at 30 µg/mL. **IL-8:** Minimal response was observed after 2 h. A significant increase was observed (243%) at 24 h with 30 µg/mL. **LTB-4:** At 2 h, LTB4 increased to 115% and 119% with 30 and 60 µg/mL me-DEP respectively. At 24 h with 60 µg/mL me-DEP, LTB-4 increased to153%. **H_2O_2:** Exposure to 30 and 60 µg/mL of me-DEP induced large dose-dependent increases of 563% and 1220%, respectively. **MMP-9:** A significant increase at 2 and 24 h were observed. In both exposure periods, 30 µg/mL induced larger increases than 60 µg/mL.

Study	Pollutant	Exposure	Effects
Reference: Molinelli et al. (2006, 198949) **Species:** Human **Cell Type:** NHBE, BEAS-2B	PMH: PM_{10} extracts in hexane PMA = PM_{10} extracts in acetone of residue after hexane extraction -G: Guaynabo(Urban) and -F: Fajardo (Preservation Area) **Particle Size:** PM_{10}	**Route:** Cell Culture (3×10^3 cells/well) **Dose/Concentration:** NHBE exposed to 0-100 µg/mL of PM_{10} BEAS-2B exposed to 10,100, 250 µg/mL of PM_{10} **Time to Analysis:** 48 h	**Metal analysis:** Hexane extracts Cu, V, Ni all higher in winter than summer. For hexane extracts within the same season, metal concentrations were higher in the Fajardo extracts. On the other hand, the acetone extracts from Guaynabo generally had higher metal concentrations than Fajardo. **Cytotoxicity NHBE:** The order of most to least toxic for PM extracted with hexane is: winter-G, winter-F, summer -G , summer-F. The order of most to least toxic for PM extracted with acetone is: summer-G, summer-F, winter-g. **Cytotoxicity BEAS-2:** For PM extracted with hexane, the cytotoxicity order is: winter-G, winter-F, summer-G, summer-F. The order for acetone extracted PM is: summer-G , summer-F, winter-F, winter-G. Effects trend similar to metal levels (no analysis). Summer extracts showed linear dose-response curves. Winter extracts exhibited more equivocal results, especially for Fajardo. Results suggest that NHBE cells are more sensitive than the BEAS-2B cells to PM extracts.
Reference: Moller et al. (2002, 036589) **Species:** Canine, Mouse **Cell Type:** Beagle-Dog Alveolar Macrophages (BD-AM), J774A.1	$fTiO_2$ (origin NR) $ufTiO_2$ (origin NR) ufP-G: carbon black (Printex-G, Degussa, Frankfurt, Germany) ufP90: carbon black (Printex90, Degussa, Frankfurt, Germany) ufEC90: EC (produced by electrical spark generator under standardized conditions with low impurities) DEP (SRM 1650) UrbD: Urban Dust (SRM 1649a) **Particle Size:** (in diameter) TiO_2: 220 nm; $ufTiO_2$: 20 nm; ufP-G: 51 nm; ufP90: 12 nm; ufEC90: 90 nm; DEP: 120 nm; UrbD: NR	**Route:** Cell Suspension **Dose/Concentration:** 10, 32, 100, 320 µg/mL **Time to Analysis:** 24 h	**Cytoskeleton of J774A.1:** At doses of 32 µg/mL or less, the particles did not significantly influence relaxation and stiffness. $fTiO_2$and ufP90 had no effect at any dose. $ufTiO_2$ at 320 µg/mL induced retarded relaxation and significant stiffening. ufEC90 induced dose-dependent retardation of relaxation and increased stiffening. DEP and UrbD induced similar results. **Cytoskeleton of BD-AM:** $ufTiO_2$ and $fTiO_2$ both induced some retarded relaxation and increased stiffening at 100 µg/mL dose. $ufTiO_2$ appears to increase stiffening in a dose-dependent manner. ufEC90 induced dose-dependent acceleration of relaxation due to the carbon content of ufEC90. DEP also induced acceleration of relaxation as well as a decrease in stiffness. **Phagocytosis:** At 24 h, $ufTiO_2$ and $fTiO_2$ significantly reduced phagocytic ability in J774A.1 but not in BD-AM. All carbonaceous particles induced significant impairment in J774A.1. All ultrafine carbon particles inhibited BD-AMs. **Cell Proliferation:** $ufTiO_2$ significantly inhibited proliferation compared to the control and $fTiO_2$ at 100 µg/mL in J774A.1. ufEC90 and ufP90 inhibited proliferation slightly with ufEC90 inducing slightly greater inhibition than ufP90. UrbD and DEP also significantly reduced proliferating. **Apoptosis:** All particles induced decreased viability at 100 µg/mL in both cell types. With $ufTiO_2$ inducing greater apoptosis than $fTiO_2$, ufEC90 than ufP90 and ufEC90 than ufP-G.
Reference: Mutlu et al. (2006, 155994) **Species:** Human, Rat **Cell Type:** A549	PM_{10} (Collected by baghouse from ambient air in Dusseldorf, Germany) **Particle Size:** PM_{10}	**Route:** Cell Culture **Dose/Concentration:** 0.05, 0.5, 5. 50 $\mu g/cm^2$ **Time to Analysis:** 24 h	**Na, K-ATPase Plasma Membrane Protein:** PM_{10} induced a decrease of protein in the plasma membrane of A549 cells. Total Na,K-ATPase levels were unaffected. **ROS:** Pretreatment with EUK-134, superoxide dismutase and catalase mimetic, inhibited the decrease of GSH. Furthermore, it attenuated the decrease of NA,K-ATPase in A549 cells. **NA, K-ATPase Activity:** PM_{10} induced a dose-dependent decrease in ouabain-sensitive liberation of 32P from AT32P in primary rat alveolar type II cells. This effect was inhibited with pretreatment with EUK-134.

Study	Pollutant	Exposure	Effects
Reference: Nam et al. (2004, 198887) **Species:** Human **Cell Type:** A549	$PM_{2.5}$ Collected from hospital rooftop, Seoul, South Korea **Particle Size:** $PM_{2.5}$	**Route:** Cell Culture **Dose/Concentration:** 0.5, 1, 10, 25, 50 µg/cm^2 **Time to Analysis:** 6, 24 h	**NF-κB/IκBα:** 50 µg/cm^2 DEP induced IκBα degradation which peaked at 2 h and recovered after 4 h. Treatment with increasing amount of $PM_{2.5}$ resulted in a dose-dependent decrease in IκBα. $PM_{2.5}$ increased NF-κB in a dose-dependent manner up to 10 µg/cm^2. NF-κB induction peaked at 12 h. **IL-8:** $PM_{2.5}$ treatment increased protein level more than 3 fold with 100 µg/cm^2 $PM_{2.5}$. mRNA levels also increased. **iNOS Inhibitor:** $PM_{2.5}$ induced IL-8 elevation was completely blocked by iNOS inhibitor. iNOS inhibitor also negated $PM_{2.5}$ induction of NF-κB activity. Antioxidants and iNOS inhibitor reduced PM-induced IκBα degradation.
Reference: Nozaki et al. (2007, 097862) **Species:** Mouse **Cell Line:** LA-4 (Alveolar Epithelial Cells)	PM: Rooftop of 5 story building, urban, Japan PME: dichloromethane extract of PM filtered P90: Printex 90 (carbon black) (Degussa) **Particle Size:** PM: 0.22 µm; PME: 2.5 µm; P90: 14 nm	**Route:** Cell Culture (1.4×10^4 cells/cm^2) **Dose/Concentration:** 1.1 µg/cm^2 **Time to Analysis:** 24, 28, 72 h	**Cytotoxicity:** P90 had no effect. PM and PME were cytotoxic at similar levels. **Protein Expression:** All particles affected protein expression (no specific protein- 2D gel electrophoresis).
Reference: Obot et al. (2002, 042370) **Species:** Mouse **Cell Line:** BALB/c **Cell Type:** AM	PM: SRM 1648 PM-100: PM heated to 100° C PM-500: PM heated to 500° C PM-PH: PM acid digestion PMAC: Acetone extraction PMCH: Cyclohexane extraction PMH2O: Water extraction All extract fraction used as residual particles **Particle Size:** NR	**Route:** Cell Culture (5×10^5 cells/mL) **Dose/Concentration:** PM: 200 µg/mL; PM-100: 188 µg/mL; PM-500: 130 mg/l; PM-PH: 94 µg/mL; PMAC: 173 µg/mL; PMCH: 171 µg/mL; PMH2O: 188 µg/mL Fraction doses adjusted for mass loss during fraction treatment **Time to Analysis:** 4 h	**Cytotoxicity:** All 7 fractions had cytotoxic effects. PM had highest cytotoxicity. PM-500, PM-PH, PMAC less toxic than PM. **Apoptosis:** All 7 fractions significantly increased apoptosis. The PM fractions that induced the greatest apoptosis in descending order are: PM, PMH2O, PM-100, PM-500, PMAC, PMCH and PM-PH. PM-induced apoptosis (only PM, PM-500 and PMAC tested) was blocked by poly I or 2F8 antibody (scavenger receptors). **Particle Characterization:** Untreated PM and PM-100 did not have measurable amounts of transition metals on its surface. Measured components include carbon, O_2, N, S, Si, Ca, Al, P, Cl. PM-PH mostly contained O_2 and Si. PM-500 had increased O_2, Si compared to PM and measurable amounts of Na, K., Zn, Co, Pb, Fe. Included increased surface density of S, P, Al. PMCH lacked nonpolar organic compounds.
Reference: Obot et al. (2004, 095938) **Species:** Mouse (7-9wk), Human **Cell Line:** Mouse-BALB/c **Cell Type:** AM	PM: SRM 1648 (collected by bag-house in St. Louis, MO). PM-100: PM heated to 100˚ C PM-500: PM heated to 500˚ C PM-PH: PM acid digestion PMAC: Acetone extraction PMCH: Cyclohexane extraction PMH_2O: Water extraction All of the 6 extract fractions from PM1648 $PM_{2.5}$: Collected in Houston, TX **Particle Size:** PM1648: NR; $PM_{2.5}$	**Route:** Cell Culture (5×10^5 cells/mL) **Dose/Concentration:** PM: 200 µg/mL; PM-100: 188 µg/mL; PM-500: 130 mg/l; PM-PH: 94 µg/mL; PMAC: 173 µg/mL; PMCH: 171 µg/mL; PMH2O: 188 µg/mL Fraction doses adjusted for mass loss during fraction treatment $PM_{2.5}$ = 50, 100, 150, 200 µg/mL **Time to Analysis:** Mouse-4 h; Human-24 h.	**Human AM Viability:** Only PM, PM-100, PMAC and PMH2O decreased viability. **Human AM Apoptosis:** PM, PM-100 and PMH2O increased apoptosis. PM induced greater apoptosis than PM-100 and PMH2O. **Regression Analysis Mouse vs Human:** Although individual fractions differed somewhat, cell viability and apoptosis of all 7 fractions showed linear regression **Human and Mouse AM Viability with PM2.5:** Nearly identical dose-dependent decrease was exhibited starting at 50 µg/mL **Human and Mouse AM Apoptosis with $PM_{2.5}$:** Nearly identical dose-dependent increases were exhibited with human AM responses peaking at 150 µg /mL and declining at 200 µg/mL (no mouse data for 200 µg/mL). **Regression Analysis with PM2.5:** Excellent correlation of mouse and human responses for viability and apoptosis was exhibited.

Study	Pollutant	Exposure	Effects
Reference: Okeson et al. (2003, 042292) **Species:** Rat **Cell Type:** RLE-6TN (Type II Alveolar Epithelial Cells)	CG: Coal ash, Germany CU: Coal ash, USA 5C: PM # 5 Oil fly ash coarse 5F: PM #5 Oil fly ash fine 6MSC: PM #6 Oil med sulfur fly ash coarse 6HSC: PM # 6 Oil high sulfur fly ash coarse 6HSF: PM # 6 Oil high sulfur fly ash fine **Particle Size:** CG, CU: NR; 5C, 6MSC, 6HSC: >2.5 µm; 5F, 6HSF: <2.5 µm	**Route:** Cell Culture **Dose/Concentration:** Coal Fly Ash 12.5, 25, 50, 125, 250 µg/mL Oil Fly Ash - 100 µg/mL **Time to Analysis:** 24 h	**Oil PM Characterization:** Generally, the fine fractions had higher metal levels than the coarse fractions except for Zn. High sulfur had a higher metal content than med sulfur. Carbon percent weight was stable across all 5 fractions. **Coal Ash Cytotoxicity:** CG treatment exhibited similar cytotoxic results as CU. Cytotoxic effects were exhibited at concentrations of 12.5 µg/mL and above. Effects remained steady at concentrations above 50 µg/mL. **Oil Ash Cytotoxicity:** Cytotoxic effects were induced by all. The order of PM fractions inducing the most cytotoxicity to the least is the following: 5F, 6HSF, 6HSC, 5C, 6MSC. **Correlation of Metal Content and Cytotoxicity:** Fe, V showed a reasonable correlation. Zn had no correlation. **Cell Metabolism:** An inhibitory effect was observed with 100 µg/mL coal ash after 6 h. After 12 h of exposure, CU, unlike CG, does not continue to inhibit cell metabolism. Oil ash was generally less effective than coal ash. The order of PM fractions inhibiting metabolism the most to the least is the following: 5F, 6HSC, 5C, 6MSC. 6HSF not tested.
Reference: Okeson et al. (2004, 087961) **Species:** Rat **Cell Type:** RLE-6TN (Type II Alveolar Epithelial Cells)	Zn, V, Fe chloride as salts (valence state not reported) **Particle Size:** NR	**Route:** Cell Culture (50000 cells/well) **Dose/Concentration:** 0.001, 0.01, 0.1, 1.0, 10 mM **Time to Analysis:** 24 h	**Cytotoxicity:** All metals cytotoxic at concentrations greater than 0.1 mM. V is 5 times less cytotoxic than Zn, and Fe is 7 times less cytotoxic than Zn with a EC50 of 3mM and 4mM, respectively. At 10 mM of each metal, no surviving cells were present. **NCS:** Incubation with NCS (5 or 10 %) decreased toxicity of Zn, especially at 0.1 mM, but had no effect on Fe or V toxicity. **Albumin:** BSA decreased Zn toxicity at equivalent concentrations but to a lesser extent than NCS.
Reference: Osornio-Vargas et al. (2003, 052417) **Species:** Mouse **Cell Line/Type:** J774A.1, L929 (Mesenchymal Cells)	PM_{10} $PM_{2.5}$ -N = Northern (industrial) -SE = Southeastern (lake basin dust) sites, both heavy vehicular traffic, Mexico City, Mexico **Particle Size:** PM_{10}; $PM_{2.5}$	**Route:** Cell Culture (J774A.1: 15000 cells/cm^2; L929: 30,000 cells/well) **Dose/Concentration:** 20, 40, 80 µg/cm^2 **Time to Analysis:** 24-72 h	**PM Characterization:** Elements similar in particle types with elements in PM_{10} more abundant. Northern particles contained more Co, Zn, Ni, Pb. **Endotoxin:** All PM samples had detectable amounts of endotoxin. $PM_{2.5}$ -N had 22 EU/mg. PM_{10}-N had 30 EU/mg. $PM_{2.5}$ -SE had 12 EU/mg. PM_{10}-SE had 59 EU/mg. **Cytotoxicity (J774A.1):** The two northern samples, $PM_{2.5}$ and PM_{10}, both induced similar cytotoxic effects at 40% survival. PM_{10}-SE and $PM_{2.5}$ -SE induced dose-dependent responses. In general, the northern samples had a higher cytotoxic effect than the southern samples. **Apoptosis (J774A.1):** Northern samples induced more apoptosis than did the southeastern samples. There was no difference between PM_{10} and $PM_{2.5}$ induced apoptosis. **TNF-α and IL-6 (J774A.1):** TNF-α and IL-6 induced dose-dependent increases. At 80 µg/cm^2, PM_{10} -SE induced the most production of IL-6 followed by $PM_{2.5}$ -SE, PM_{10}-N , and $PM_{2.5}$ -N. **J774A.1 Supernatant Toxicity (L929):** Conditioned medium from J774A.1 pre-exposed to each PM type reduced cell viability in L929 cells. This was correlated with TNF-α level in supernatants.

Study	Pollutant	Exposure	Effects
Reference: Penn et al. (2005, 088257) **Species:** Human **Cell Type:** BEAS-2B	BDS: Butadiene soot (created on-site by passing BD through a back-flash protected stainless steel two-stage regulator to a stainless steel Bunsen burner) -P1: <2.5 µm -P2: 2.5-10 µm -P3: >10 µm BDS-W: solvent washed Graphite Composition: <2.5 µm = 92%, 2.5-10 µm = 5%, >10 µm = 3% **Particle Size:** BDS-P1: <2.5 µm; BDS-P2: 2.5-10 µm; BDS-P3: >10 µm	**Route:** Cell Culture (1-1.5×10^6 cells) **Dose/Concentration:** 3 mg BDS **Time to Analysis:** 5 min-72 h	**Particle Characterization:** By weight, EC makes up 94% of BDS, hydrogen 2%, nitrogen and sulfur 1%, and oxygen less than 0.1%. **PAH Components of BDS: 13 prominent PAHs:** acenaphthylene, fluorene, anthracene, cyclopentaphenanthrene, fluoranthene, acephenanthrylene, pyrene, benzofluorenes, acepyrene, chrysene, benzopyrenes, perylene, benzoperylene. **BDS Activity:** At 60-120 min, BDS was observed in the cells. At 4 h, fluorescence observed in cytoplasmic vesicles and increased during the first 24 h then plateaued for the next 72 h. BDS-W appeared in vesicles sooner than BDS.
Reference: Pozzi et al. (2005, 088610) **Species:** Mouse **Cell Type:** RAW 264.7	PM: Collected continuously for 15 days, 8-10 m from street, Sept 1999, Rome, Italy -F = Fine particulate -C = Coarse particulate CB (Degussa Huber NG90) **Particle Size:** PM-F: 0.4-2.5 µm; PM-C: 2.5-10 µm; CB: 200-250 nm	**Route:** Cell Culture (1.3×10^5 cells/well) **Dose/Concentration:** 30 µg/mL; 14 µg/cm^2 120 µg/mL; 54 µg/cm^2 **Time to Analysis:** 5, 24 h	**Cytotoxicity:** For 24 h, lower levels of PM-F, PM-C, and CB had no effect on cell viability. Higher levels of PM-C and CB induced a significant release of LDH. **Arachidonic Acid (AA):** Both fractions of PM increased AA release in a dose-dependent manner at 5 h. CB increased a release only at the higher concentrations although, in terms of magnitude, the CB-induced release was much less than the ambient PM-induced release. Pretreatment with deferoxamine was not effective in decreasing AA release. **TNF-α:** TNF-α levels increased significantly for both concentrations and time periods for PM. PM-C at 24 h was significantly lower than at 5 h for both concentrations. PM-C at 30 µg/mL induced a much greater TNF-α release than PM-F at 5 h. **IL-6:** PM-F significantly increased at 5 h for both concentrations. Elevated IL-6 levels were exhibited at both PM-C doses at 24 h. At 5 h, only the high dose elevated IL-6 levels. CB was devoid of an effect on IL-6. LPS-induced IL-6 response was similar to coarse PM at the high dose, with the response being greater at 24 h than at 5 h.
Reference: Prophete et al. (2006, 156888) **Species:** Rat **Cell Type:** NR8383 AMs	Ambient $PM_{2.5}$ NYC: 1st and 26 St, NYC LA: San Gabriel foothills, Claremont, CA SEA: 15th Ave S and S. Charleston, Seattle, WA V, Mn, Al, Fe levels in PM added metals to cells V: Na_3VO_4 Al: $AlCl_3•6H_2O$ Mn: $MnCl_2•4\ h_20$ Fe: $FeCl_3•6H_20$ **Particle Size:** $PM_{2.5}$	**Route:** Cell Culture (2×10^5 cells/mL) **Dose/Concentration:** Fe(III) 16 µmol V, Mn, and Fe(III) mixtures with V or Mn in molar ratios 0.02, 0.08, 0.2 and 0.4 × Fe(III) Al and Fe(III) mixtures with Al in molar ratios 0.37, 0.75, 2, 7.5 × Fe(III) **Time to Analysis:** 20 h	**Particle Characterization:** Fe and metal to F ratios based on ratios observed in $PM_{2.5}$ from LA, SEA and NYC sites. V: Fe ratios remarkably similar among sites. Fe levels fixed at NYC level of 16 µm (highest). **IRP:** Coexposure with 3 metals increased IRP binding activity relative to Fe(III) alone, by up to 3.5 fold for Al (1.5-3 ratio), 2 fold for Mn (0.08-0.2 ratio) and 7 fold for V (0.2 ratio). IRP activity dropped at higher ratios. A drop in IRP activity at higher ratios may be result of cytotoxicity for Al, but not for V and Mn. **iNOS:** Al induced iNOS expression dose-dependently. There was no observed effect for Mn and V. **Induction of Hypoxia-inducible Factor (HIF-1α):** Only V and Al induced HIF-1α. **Activation of ERK1 and -2:** V and Al induced pERK1, but only V induced pERK2. Mn had no increasing effects, but data indicated a decreasing induction.

Study	Pollutant	Exposure	Effects
Reference: Ramage and Guy (2004, 055640) **Species:** Human **Cell Type:** A549	PM_{10}: Collected in Wolverhampton, UK ufCB: Ultrafine Carbon Particles (Origin not reported) **Particle Size:** PM_{10}, ufCB: <100 nm (diameter)	**Route:** Cell Culture **Dose/Concentration:** 80 µg/mL **Time to Analysis:** 0, 0.5, 3, 6, 18 h	**CRP:** Treatment with ufCB or PM_{10} produced an increase in CRP expression with similar effects noted after 6 h. PM_{10} induced greater increases than ufCB. Both the cytoplasm and nucleus contained CRP. **Hsp70:** PM_{10} and ufCB induced increased levels at all time points with ufCB inducing greater levels than PM_{10}. Hsp70 expression was observed in the cytoplasm and nucleus. **Antioxidants of CRP and Hsp70:** Coincubation of ufCB with Nacystelin and Trolox caused a small reduction in CRP and Hsp 70.
Reference: Rao et al. (2005, 095756) **Species:** Rat **Strain:** SD **Cell Type:** AMs and cultured lung fibroblasts	DEP: SRM 2975 (NIST) **Particle Size:** 0.5 µm	**Route:** Cell Culture **Dose/Concentration:** 200 µg/mL **Time to Analysis:** 4 h	**mRNA Expression:** No change in IL-1β or iNOS were observed. Data suggests that the lung fibroblasts is the main source of IL-6 and MCP-1 in BAL fluid because of their comparatively high message levels. Due to the extreme variability in results, the cause of an increase on co-culture with AMs and/or DEPs was not assessed.
Reference: Reibman et al. (2003, 156905) **Species:** Human **Cell Type:** HBEC, BEAS-2B	UFPM: Ultrafine PM FPM: Fine PM IPM: Intermediate PM CPM: Coarse PM CB: Carbon black All PM collected 8th floor, 26th St and 1st Ave, New York City, NY **Particle Size:** UFPM: <0.18 µm; FPM: 0.18 - 1.0 µm; IPM: 1.0 - 3.2 µm; CPM: >3.2 µm	**Route:** Cell Culture **Dose/Concentration:** 11 µg/cm^2; 100 µg/mL **Time to Analysis:** 6, 18 h	**Cytotoxicity:** After treatment, cells were more than 90% viable. UFPM and FPM caused no gross alterations in cell morphology or adhesion. **MIP3α/CCL20 mRNA (6 h):** Stimulation of mRNA released by HBEC upon exposure to UFPM appeared similar to that provided by TNF-α (5 µg/mL) and IL-1β (10 mg/mL). **MIP3β/CCL20 protein in HBEC (18 h):** TNF-α and IL-1β induced a dose-dependent increase in MIP3α/CCL20 protein (0-10 ng/mL), whereas Il-4 and IL-13 induced MIP3α/CCL20 protein release that reached maximum levels at 1 ng/mL. No release of MIP1α/CCL3 nor RANTES/CCL-5 was observed upon stimulation with cytokines. **Secretion of MIP3α/CCL20 in response to PM (18 h):** All PM fractions less than 2.5 µm resulted in the release of MIP3α/CCL20 protein in HBEC roughly equivalent amounts. CB similar in size to UF/fine PM did not result in the release of MIP3α/CCL20, nor did LPS (0.01-1.0 µg/mL). No release of MIP1α/CCL3 nor RANTES/CCL 5 was observed upon stimulation by PM fractions. **Activation of MAPK (ERK1/2 and p38):** ERK1/2 and p38 was activated by TNF-α, IL-1β, IL-4 and IL-13 within 15 min and was sustained for at least 60 min. Erk1/2 and p38 inhibitors reduced MIP3α/CCL20 release in BEAS-2B cells in response to cytokines.

Study	Pollutant	Exposure	Effects
Reference: Riley et al. (2003, 053237) **Species:** Rat **Cell Type:** RLE-6TN (Type II Alveolar Epithelial Cells)	Zn: $ZnCl_2$ Cu: $CuCl_2$ Fe: $FeCl_2$ V: VCl_4 Ni: $NiCl_2$ **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 0.01, 0.1, 1.0, 10 mM **Time to Analysis:** 2, 4, 24, 72 h	**Cytotoxicity (SDH):** All particles were cytotoxic in a dose-dependent manner. Zn and V were cytotoxic at 0.05 mM, Cu at 0.5 mM, Ni at 0.8 mM and Fe at 2 mM. For Zn, cell death (LDH) had a biphasic response: a slow logslope until approx 0.1 mM at which point it rapidly accelerated to a peak at 5 mM with a small decline at 10 mM. Most of Zn cytotoxicity was not due to apoptosis. LPS did not affect either Zn or Cu cytotoxicity. **Metabolism Inhibition Time Course Response (Cu and Zn only):** At high (1 mM) concentrations, Zn toxicity peaked at 36-48 h followed by a 2-fold recovery by 72 h. Cu showed a faster, steady decline plateauing after 36 h. At low concentrations (0.1 mM), Cu showed a steady slow decline. At 48 h, Zn decreased faster to max activity and returned to control by 72 h. **IL-6 Secretion:** Zn and Cu both decreased IL-6 secretion. Decreases were very similar for both metals and concentrations when expressed as secretion per viable cell ratio except for Zn at 1.0 mM. **Metal Combinations:** Zn and Cu gave variable results. Zn protected against V cytotoxicity. Zn and Cu had an additive response. Zn did not affect Fe toxicity.
Reference: Riley et al. (2005, 096452) **Species:** Rat, Human **Cell Type:** RLE-6TN, NR8383 Alveolar Macrophages, A549	Fe: $FeCl_2$ Ni: $NiCl_2$ Cu: $CuCl_2$ V: VCl_2 **Particle Size:** NR	**Route:** Cell Culture (5×10^4 cells/well Alveolar Cells; 1.2×10^5 cells/well NR8383) **Dose/Concentration:** AMs: 0.02, 0.05, 0.07, 0.08 mM; RLE-6TN: 0.1, 0.2, 0.6, 1.0, 6.0 mM; A549: 0.5, 0.8, 4.4, 4.8 mM **Time to Analysis:** 2-48 h	**Relative Sensitivity of Cell Strains to Metal Chloride:** NR8383 was more sensitive than RLE-6TN and A549 except for V where NR8383 and RLE-6TN were both more sensitive than A549. **Relative sensitivity of Cell Strains to Metal Chloride vs Sulfate:** With the exception of Cr, sulfate was generally more cytotoxic than chloride (note V valence state). **A549 Cytotoxicity Time Course:** Zn cytotoxicity takes 24 h to develop whereas Cu cytotoxicity develops within 2 h. LDH release for Cu, however, develops in 24 h. **RLE Cytotoxicity Time Course:** Zn starts at 2 h and develops until 24 h. Cu develops within 2 h and continues until 24 h where it is less toxic than Zn. Both release equivalent amounts of LDH after 24 h. **NR8383 Cytotoxicity Time Course:** Both Zn and Cu exhibit time dependent toxicity beginning as early as 4 h. LDH release maximizes at 12 h and either remains steady or declines.
Reference: Ritz et al. (2007, 198901) **Species:** Human **Cell Type:** BEAS-2B, NHBEC	DX: Extract of DEP (generated from a light duty four-cylinder diesel engine 4JB1 type Isuzu Automobile) **Particle Size:** <1 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** 0, 20, 50, 100 µg/mL **Time to Analysis:** 24 h	**NQO1 (Sentinel Phase II Enzyme):** Cells transfected with NQO1 reduced induction of IL-8 by DX exposure. **Sulfurophane:** Increased gene expression of phase II enzymes, particularly NQO1, was observed in both cell types. Gene expression in BEAS-2B was greater than that of NHBEC. Sulfurophane did not upregulate GSTM1 in BEAS-2B but induced a 2-fold increase in NHBEC. Pretreatment also inhibited DX-induction of IL-8 in both cell types. **Cytokines:** DX induced significant increase of IL-8 in both cell types at concentrations of 10 µg/mL or higher. GM-CSF and IL-8 remained unaffected in BEAS-2B. GM-CSF and IL-8 Increased in NHBECs and reached statistical significance at 25 µg/mL.

Study	Pollutant	Exposure	Effects
Reference: Rosas Perez et al. (2007, 097967) **Species:** Mouse **Cell Type:** J774A.1	PM_{10} Collected in Mexico City, Mexico from January-June, 2002 North: Iztacala, manufacturing industry; Center: Merced, heavy traffic; South: Ciudad Universitaria, residential Principal Component Analysis of Air Pollution Data: Group 1:S/K/Ca/Ti/Mn/Fe/Zn/Pb (43% of variance); Group 2: Cl/Cr/Ni/Cu (16%); Group 3: Endotoxins/OC/EC (14%). For all 3 sites: Averages of Group 1 is statistically different among the center, north and south sites with the central site producing the highest values. Group 2 is similar among the sites and, for Group 3, the north had a lower average than the center and south sites. **Particle Size:** PM_{10}	**Route:** Cell Culture (1.5×10^4 cells/cm^2) **Dose/Concentration:** 20, 40 or 80 µg/cm^2 **Time to Analysis:** 72 h	**Cytotoxicity:** Responses were dose-dependent; there was no observed site interaction. Cytotoxicity seems to be a result of the following components: S/K/Ca/Ti/Mn/Fe/Zn/Pb. **IL-6:** Only the center site at 40 µg/cm^2 induced an increase. Induction of higher IL-6 levels seems to be related to high values of S/K/Ca/Ti/Mn/Fe/Zn/Pb and endotoxins/OC/EC. **TNF-α:** Production was induced by all samples in a dose-dependent manner. Similar to IL-6, induction of higher TNF-α levels seems to be a result of high values of S/K/Ca/Ti/Mn/Fe/Zn/Pb and endotoxins/OC/EC. **p53:** Only south PM had effect. Induction of p54 seems to depend on high levels of Cl/Cr/Ni/Cu and low levels of S/K/Ca/Ti/Mn/Fe/Zn/Pb.
Reference: Sakamoto et al. (2007, 096282) **Species:** Human **Age:** 58-82 yr (Smokers) **Cell Type:** HBEC	PM_{10}: EHC-93 (Obtained from Health Canada, Canata) **Particle Size:** PM_{10}	**Route:** Cell Culture **Dose/Concentration:** 100, 300 and 500 µg/mL **Time to Analysis:** Calcium responses: up to 60 min; cytokines: 6 or 24 h	**Intracellular [Ca2+]:** [Ca] concentration slowly increased, elevating after 10 and 30 min for 500 and 300 mg/mL, respectively. The response plateaued at 35 min for 500 µg/mL. **Extracellular [Ca2+]:** Starting at 20 min, the removal of extracellular Ca decreased the PM_{10} response significantly. Calcium channel blocker (10µM or 1mM) LaCl3 and (5mM) NiCl2 significantly blocked the PM-induced intracellular Ca. Lacl2 administration (1mM) inhibited the PM-induced Ca2+ response in a dose-dependent manner. **Mode of Action:** Intracellular Ca induced by ATP declined more slowly in the cells exposed by PM_{10}. This indicates that PM_{10} blocks Ca clearance via the calcium pumps. **Cytokines:** PM_{10} induced a dose-dependent increase in cytokine mRNA levels and cytokines IL-1β, LIF, IL-8 and GM-CSF. Cytokine expression was unaffected by the reduction of extracellular Ca2+ . Preincubation with the calcium chelator reduced responses for IL-1β and IL-8 but not LIF or GM-CSF.
Reference: Salnikow et al. (2004, 087469) **Species:** Human **Cell Line:** 1 hAEo-	$FeSO_4$ $FeCl_3$ $NiSO_4$ **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 0.25 and 0.5 mM Fe exposures also contained 60 µg/mL apotransferrin **Time to Analysis:** 24 h	**Cytotoxicity:** Both Fe had no effect. $NiSO_4$ caused marginal cytotoxicity (75%). **Hypoxic Stress:** At 20 h, $NiSO_4$ (at concentrations of 0.25 or 0.5 mM) induced NDRG-1/Cap43 protein production indicating hypoxic stress. DFX and DMOG induced a similar effect. **IL-8:** $NiSO_4$ induced IL-8 time-dependently for up to 48 h. At 48 h, the increase was 6+ fold. **Coexposure (Ni + Fe) on Fe uptake:** Fe(III) uptake was greater than Fe(II) uptake. $NiSO_4$ had no effect. Ni uptake was greater than Fe uptake but was decreased by coexposure to Fe. Coexposure also did not effect hypoxic stress. Coexposure with Fe did reduce Ni-induced IL-8 production.

Study	Pollutant	Exposure	Effects
Reference: Salonen et al. (2004, 187053) **Species:** Mouse **Cell Type:** RAW 264.7	PM_{10} (urban traffic) Finland Pooled as winter (W), spring I (SI), or spring II (SII) based on component/time considerations **Particle Size:** PM_{10}: 0.12-10 µm	**Route:** (2×10^6 cells/well) **Dose/Concentration:** 15, 50, 150, 500, 1000 µg/mL **Time to Analysis:** 0, 24 h	Air quality parameters: Winter and spring I did not differ. SII much lower $PM_{2.5}$ Metal data equivocal as well as highly variable resuspension rates. Total PAHs: W=303; SI=233; SII=204 ng/mg **Inflammation (IL-6, TNF-α, NO)/Cytotoxicity:** A dose-dependent increase was observed for TNF-α, IL-6 and NO except for SI. The IL-6 levels, of those particles exposed to SI, decreased at 1000 µg/mL. **TNF-α, IL-6:** SI = SII>>W>control. **NO production:** W≥SI≥SII **Cell Viability:** W=SI=SII toxic at 500 and 1000 µg/mL **Water-soluble vs Insoluble:** TNF-α and IL-6 were nearly entirely the result of insoluble components of PM_{10}. Cytotoxicity was driven by both soluble and insoluble components. **Metal Chelation:** The addition of metal chelators did not modify IL-6, TNF-α or cytotoxicity **LPS inhibitor:** Treatment with the LPS inhibitor eliminated the IL-6 response and, perhaps, slightly reduced the TNF-α response but not cytotoxicity **Hydroxyl radicals:** A dose-dependent induction of hydroxyl radicals and induction of hydroxyl radical lesions (at 500 and 1000 $\mu g/m^3$) in the calf thymus DNA were observed.
Reference: Samet et al. (2003, 113782) **Species:** Human **Cell Type:** A431 (Epidermoid Cells)	As: $NaASO_3$ V: $VOSO_4$ Zn: $ZnSO_4$ **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 500µM **Time to Analysis:** 20, 30 or 90 min	**EGFR Dimerization:** Zn, V or As did not induce EGFR dimerization in a cell free system i.e., no direct crosslinking. Zn did not induce dimerization in whole cells either. **Phosphorylation of EGFR:** Zn induced phosphorylation at 3 sites similar to EGF. As and V had no effect. **EGFR Kinase Inhibitor:** While EGF action was blocked, Zn continued to induce phosphorylation and was independent of EGFR kinase activity. **c-Src:** Blocking of c-Src tyrosine kinase (transactivator of phosphorylation) negated all Zn-induced phosphorylation but only had a slight effect on EGF stimulated cells. **ERK1/2 Phosphorylation:** Zn increased levels of ERK1/2. Pretreatment with EFGR kinase inhibitor reduced both Zn and EGF effect. This effect was not blocked by the c-Src blocker.
Reference: Santini et al. (2004, 087879) **Species:** Mouse **Cell Type:** RAW 264.7	DEP: Collected adjacent to moderate traffic in Rome, Italy **Particle Size:** $PM_{2.5}$	**Route:** Cell Culture (2.5×10^5 cells/mL) **Dose/Concentration:** 0.01, 0.1, 1.0 µg/mL **Time to Analysis:** 24 h	**500 MHz Results (no 1 µg/mL):** DEP induced a dose-dependent increase in choline compounds, α- and βgamma- glutamine/glutamate (0.01 >0.1 µg/mL), lactate, and CH_2, CH_3 moieties of fatty acids. DEP decreased inositol and phosphoreatinine. **700 MHz Results (no 1 µg/mL):** DEP induced similar results, except α-, βgamma-glutamine were dose-dependent. Inositol showed no effect. Taurine slightly increased. Results were confirmed after eliminating biological interferences via perchloric acid. **Growth Curves/Cell Cycle Analyses/Cell Morphology:** DEP had no effect. **Cytokines:** IL-6 levels increased at 0.1 and 1 µg/mL. TNF-α was unaffected.

Study	Pollutant	Exposure	Effects
Reference: Saxena et al. (2003, 096986) **Species:** Mouse **Cell Type:** RAW 264.7	DEP: SRM 1650 CO: Crude Organic Extract of DEP Fractionated into asphaltene (pentane/hexane), saturated hydrocarbon, less polar (aromatic) hydrocarbon, more polar (aromatic) hydrocarbon, resins, residual (resins) **Particle Size:** NR	**Route:** Cell Culture (2.5×10^4 cells/mL) **Dose/Concentration:** DEP, CO 5, 10, 15, 20, 25 µg/mL IFN-y: 10 ng/mL LPS: 1 mg/mL **Time to Analysis:** 1-3 days	**Cytotoxicity:** No cytotoxic effects were observed. **NO:** DEP alone induced NO in a dose-dependent manner which peaked after 1 day and plateaued for days 2 and 3. IFN-y + DEP showed dose- and time-dependency. LPS + DEP showed no effect at 1 day, but dose-dependently reduced NO production on days 2 and 3. Addition of Bacillus Calmette-Guerin (BCG) eliminated the effect of DEP at 2 days but showed a dose-dependent decrease at 3 days. **Effectiveness of Particulate Components:** The carbonaceous core of DEP did not affect BC G-stimulated NO production. CO significantly inhibited BCG-stimulated NO production. Study indicated that the extract of aromatic hydrocarbons and resins caused an inhibitory effect in a dose-dependent manner.
Reference: Seagrave et al. (2007, 097549) **Species:** Human **Gender:** Male (3 donors) **Age:** 16, 23 yr **Cell Type:** A549	DE: Generated by DE 5500 watt generator using #2 certification oil performed under 5000w load. Emissions diluted to 3 mg/m^3 total particulate matter. **Particle Size:** 0.14-0.5 µm	**Route:** Air Liquid Interface **Dose/Concentration:** 8.33 mL/min/well **Time to Analysis:** 3 h exposure; 1 or 21 h post-exposure	**Particle Deposition:** 140 and 500 nm microspheres demonstrated uniform deposition of approx. 10%. **Transepithelial Electric Resistance:** No effect of DE; rather, more effect was observed from air controls. **Macromolecular permeability:** DE caused an increase 1 h but returned to control at 21 h. **LDH/Cytotoxicity:** DE had a highly variable(donor specific) effect at 1 h and returned to control levels at 21 h **Mitochondrial activity (WST):** DE reduced activity at 1 h and possibly increased activity at 21 h (high donor-to-donor variability) **Mucus Like Substance Excretion:** There was high donor to donor variability; no overall effects were observed. **Alkaline Phosphatase (AP):** DE decreased at 1 h and perhaps increased at 21 h **Glutathione:** DE caused a large decrease at 1 h but returned to normal at 21 h. **HO-1:** After DE exposure, levels increased but were still lower than air exposed controls **Cytokines:** No differences for IL- 8 or 12, TNF-α, GM-GSF, IL-1α, or IFN-γ were observed. IL-4 and -6 were decreased upon DE exposure.
Reference: Seagrave et al. (2004, 087470) **Species:** Human **Cell Type:** A549	DPM: SRM2975 (NIST) DPM-O: DPM organic extract (acetone/DCM) CB: Carbon Black (Elftex-12, Cabot) **Particle Size:** CB: 37 nm; Stokes diameter 198 nm	**Route:** Cell Culture (1×10^5 cells/well) **Dose/Concentration:** 0.03 -1,000 $\mu g/cm^2$ **Time to Analysis:** 0, 18 h	**IL-8 release:** DPM increased semi dose-dependently (perhaps steady based on error range) up to 1 $\mu g/cm^2$ after which IL-8 declined dose dependently to zero (control = 100%) at 300 and 1000 $\mu g/cm^2$. LDH release was steady which indicates no cytotoxicity. **DPM interaction with IL-8:** DPM depletes IL-8 from solution in a dose-dependent manner (cell free). BSA preincubation reduced the slope of the dose response but not the final result. CB has no effect. DPM-O residuals act identical to DPM. Increasing NaCl concentrations reduced DPMs depletion of IL-8 **Neutrophil responses:** DPM and bound IL-8 together caused a marked aggregation of cells resulting in spindle shapes. DEM or IL-8 alone did not cause this aggregation although DEP did recruit neutrophils

Study	Pollutant	Exposure	Effects
Reference: Seagrave et al. (2003, 054979) **Species:** Human, Rat **Cell Line:** F344/Crl BR (mouse) **Age:** 11 wk (mouse) **Weight:** 250 g **Cell Type:** A549, AMs	PM filter collection Collected from diesel or gasoline powered vehicles as follows: BG: BS Gasoline G30: Normal Emitter gasoline (30F) G: Normal emitter gasoline (72F) HD: High Emitter Diesel D30: current technology diesel (30F) D: current technology diesel (72F) WG: White Smoke Gasoline **Particle Size:** NR	**Route:** Cell Culture (1×10^5 cells/well) **Dose/Concentration:** 0.03-10,000 µg/cm^2 **Time to Analysis:** 16-18 h	**Cytotoxicity:** LDH activity increased in A549 cells. The types of pollutants that are most toxic, in decreasing order of cytotoxicity, are the following: BG, G30, and G which are significantly different from HD, D30, D, WG which are also significantly different from DS. LDH activity also increased in rat macrophages. G, G30, and BG were the most toxic. HD and D30 were intermediately toxic and D, WG, and DS were the least toxic. In both cell types, gasoline was more cytotoxic than diesel. **Cytokines:** All particle types except DS increased IL-8 levels in A549 though not all increases were statistically significant. Also, many particle samples at high concentrations produced an apparent suppression of IL-8 release. **Alkaline Phosphatase:** G30 and G were more potent than the other particle samples in A549. WG and D30 induced no significant effects. For A549 cells, activity increased at low concentrations and was suppressed at higher concentrations. **Macrophage Peroxide Production:** In rat AMs, peroxide production was often the highest at the lowest concentrations and the lowest production caused by the highest concentrations. D30 followed this trend and induced the highest production as well as the greatest suppression. Using two different statistical methods, D30 >6 others which in turn >DS. Using the second method D30 and D >all other 6. Order of potency between two methods completely different. Authors noted that in vitro potency quite different from in vivo potency (previous paper).
Reference: Seaton. et al. (2005, 198904) **Species:** Human **Cell Type:** A549	$PM_{2.5}$ from London PM_{10} from Manchester (positive control) PM from Holland Park, Hampstead and Oxford Circus stations (HP, HR and OC) **Particle Size:** $PM_{2.5}$, PM_{10}, Holland Park, Hampstead and Oxford Circus PM had a median diameter of 0.4 µm. 80% of the particles had a diameter less than 1 µm.	**Route:** Cell Culture **Dose/Concentration:** 1-100 µg/mL **Time to Analysis:** Cytotoxicity: 24 h; IL-8: 8 h; Generation of hydroxyl radicals: 8 h	**Cytotoxicity:** Dust from all three tunnels (Holland Park, Hampstead and Oxford Circus) were able to cause cell death (LDH). The release of LDH indicated a dose-dependent relationship. The highest dose of Holland Park PM induced the ~17% release of LDH, Hampstead triggered ~ 13% and Oxford Circus ~3% (no different than control). PM_{10} from Manchester caused a 7% LDH release at the highest dose. The negative control (TiO_2) caused no response (2% release at highest dose). **IL-8:** All three tunnel PMs induced a dose-dependent release of IL-8. At the highest dose, all three tunnel dusts induced IL-8 stimulation more so than the control site $PM_{2.5}$. HP induced a 3 fold increase. Also, the highest TiO_2 concentration caused the least IL-8 stimulation. **Hydroxyl Radical Generation/ DNA Plasmid assay:** The plasmid assay indicated that the tunnel dusts induce more free radical activity than the Manchester PM_{10} and TiO_2. HP nearly doubled the percentage of DNA damage with intermediate results for HR and OC. Results for PM_{10}, TiO_2 and control were identical

Study	Pollutant	Exposure	Effects
Reference: Singal and Finkelstein (2005, 198905) **Species:** Human, Mouse **Cell Type/Line:** A549Luc1 lung adenocarcinoma epithelial cell line (human), MLE15Luc1 and MLE15Luc2 (mouse) All cells contain human cytokine IL-8 controlling firefly luciferase	AE2: Aerosil 200, amorphous silica (Degussa) CI: Carbon iron particles (25% Fe) **Particle Size:** AE2: 12 nm surface area ~200 ± 25 m^2/g; CI: ~40 nm	**Route:** Cell Culture (5×10^5 cells/well) **Dose/Concentration:** 18 µg/mL, 36 µg/mL, 72 µg/mL all in 1 mL /well **Time to Analysis:** 24 h	**Luc Activity:** Luciferase enzyme activity is significantly less in MLE15Luc2 cells than in MLE15Luc1 cells. For both cells, luciferase activity is time- and dose-dependent peaking at 4-8 h. **Aerosil 200:** AE2 induced dose- and time-dependent Luc response which peaked at 3 h and decreased thereafter in a similar way as TNF-α. Contrary to TNF-α, AE2 induced much cytotoxicity starting at 6 h. **Effect of Proteasomal Inhibitors (MG-132):** Inhibitor reduced AE2 Luc activity to near control levels. Similarly, LDH-cytotoxicity was halved **A549 Human Cell Response:** AE2 acted similarly to the MLE response. CI particles showed slightly less activity without peaks. AE2 increased cytotoxicity after 12 h, whereas CI had no effect. Contrary to MLE mouse, MG_132 did not affect Luc activity but PD98059 (selective noncompetitive inhibitor of the MAP pathway) and SN50 (NF-κB inhibitor) reduced AE2 and CI-induced activity.
Reference: Song et al. (2008, 156093) **Species:** Rat **Cell Type:** RAW 264.7	DEP collected from a 4JB1-type, light-duty (2740 cc), four-cylinder diesel engine operated using standard diesel fuel at speeds of 1500 rpm under a load of 10 torque. **Particle Size:** 0.4 µm (mean diameter)	**Route:** Cell Culture (5×10^5 cells seeded on a 24-well plate) **Dose/Concentration:** 50 µg/mL **Time to Analysis:** 72 h	**Nitrite Production:** 50 µg/mL of DEP induced production when compared to the control. Over the 72 h period, a general trend was not observed, but maximal induction of nitrite occurred at 4 h after stimulation.
Reference: Steerenberg et al. (2006, 088249) **Species:** Rat, Human **Cell Type:** AM (rat), Type 2 cells (rat), A549	PMC: PM Coarse PMF: PM fine Ambient air samples collected from Rome, Italy; Oslo, Norway; Lodz, Poland; Amsterdam, the Netherlands; De Zilk, the Netherlands. **Particle Size:** PMC: 2.35-8.5 µm; PMF: 0.12-2.35 µm	**Route:** Cell Culture **Dose/Concentration:** NR **Time to Analysis:** 20 h	Crustal material (metals and endotoxin but not Ti, As, Cd, Zn, V, Ni, Se) were positively associated with AM IL-6 and TNF-α and Type 2 MIP-2 and IL-6. Sea spray (Na and Cl) was also correlated with AM IL-6.
Reference: Tal et al. (2006, 108588) **Species:** Human **Cell Type:** HAEC	100 mM Zn(II) or V(IV) stock solutions **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 500 µmol **Time to Analysis:** 5, 20 min	**Zn-mediated EGFR Phosphorylation:** EGFR kinase activity was required but not EFGR ligand binding. EGFR Kinase inhibition reduced Zn mediated EGFR activation. (authors NOTE: complete reverse of results in B82L and A431 cells). Src Kinase is not required. Zn inhibiting Src kinase was nearly total after 20 min. **EGFR-Specific Protein Tyrase Phosphatase (PTP):** Zn inhibited PTPs, similar to V(IV) resulting in a decrease of exogenous EGFR dephosphorylation
Reference: Tamaoki et al. (2004, 157040) **Species:** Human **Cell Type:** HBEC	UFCB: Ultrafine Carbon Black - (Tokai Carbon, Japan) FCB: Fine Carbon Black (Tokai Carbon, Japan) **Particle Size:** UFCB: 11 ± 0.5 nm (mean diameter) FCB: 250 ± 16 nm (mean diameter)	**Route:** Cell Culture (10^4 cells/well) **Dose/Concentration:** 6.1, 12.3, 18.4, 24.5, 30.7 µg/cm^2 **Time to Analysis:** Up to 72 h	**DNA Synthesis/ Protein Synthesis:** Synthesis increased by UFCB (30.7) for up to 72 h and flattened after 48 h. FCB had no effect. UFCB also showed a dose-dependent response beginning at 12.3 µg/cm^2 up to 24.5 after which the response plateaued. The addition of Cu/Zn Super oxide dismutase (SOD) or a NADPH oxidase inhibitor completely inhibited the UFCB effects. Similarly, two different EGFR tyrosine kinase inhibitors, and a Me inhibitor all reduced UFCB response to control levels. **ERK activation:** UFCB caused phosphorylation of ERK beginning at 2 min, peaking at 5 min and decreasing at 10 min. ERK activation was inhibited by EGFR tyrosine kinase inhibitor Cu/Zn SOD and neutralizing body for HB-EGF but not by PDGF-R kinase inhibitor. **HB (polyclonal heparin binding)-EGF release:** UFCB induced rapid cell surface loss with recovery after 20 min and nearly full recovery at 360 min. Metalloproteinase inhibitor and Cu/Zn SOD both prevented HB-EGF release.

Study	Pollutant	Exposure	Effects
Reference: Tao and Kobzik (2002, 157044) **Species:** Rat **Cell Type:** RLE-6TN (Alveolar Type II Epithelial Cells), Fetal Lung Fibroblasts (RFL), AMs	UAP: Urban Air Particles (SRM 1649) TiO_2 SiO_2 ROFA **Particle Size:** TiO_2: ~1 µm; SiO_2: ~1 µm; ROFA: NR	**Route:** Cell Culture (1×10^5 cells AM 1.4×10^5 cells RLE/RFL) **Dose/Concentration:** 1-50 µg/mL **Time to Analysis:** 24 h	**Cytokines:** TNF-α and MIP-2 in RLE was unaffected by any particle samples. TNF-α and MIP-2 in AM significantly increased with 25 µg/mL UAP. TNF-α and MIP-2 in the co-culture of AM + RLE increased with each particle. The order of particles in decreasing order are as follows: SiO_2 at 25µg/mL, UAP at 12.5 µg/mL, ROFA at 25 µg/mL, and TiO_2 at 50 µg/mL. Except for SiO_2, the blocking of effects caused by LPS absorbed on the particles did not affect the cytokine response. For SiO_2, the response was reduced but still above the control. **Co-culture:** Physically separating AM and RLE cells and adding PM completely negated the co-culture's response to PMs. This indicates that cell to cell contact is required for co-culture potentiation of PM effects. **Inhibitors:** Various inhibitors of cell adhesion molecules (heparin, β -1, 2 or 3 integrin) had no effect on UAP-induced cytokine release.
Reference: Veranth et al. (2007, 090346) **Species:** Human **Cell Type:** BEAS-2B, A549, NHBE	Artificial particles and PMs N-Al: nano alumina Al_2O_3 M-Al: Micro Al_2O_3 N-Ce: nano CeO_2 M-Ce: micro CeO_2 N-Fe: nano Fe_2O_3 M-Fe: micro Fe_2O_3 N-Ni: nano NiO M-Ni: micro NiO N-Si: nano SiO_2 M-Si: micro SiO_2 N-Ti: nano TiO_2 M-Ti: micro TiO_2 KLN: kaolin MUS: Min-U-Sil (ground crystalline silica) DD: desert rural soil Utah $PM_{2.5}$ JE: Juarez, urban street $PM_{2.5}$ MNC: Mancos, rural Utah $PM_{2.5}$ LPS: lipopolysaccharide V: $VOSO_4$ (soluble) (19 µg/mL) **Particle Size:** (Surface mean diameter) N-Al: 6 nm (261 m^2/g) M-Al: 210 nm (7.7 m^2/g) N-Ce: 14 nm (71 m^2/g) M-Ce: 1500 nm (0.6 m^2/g) N-Fe: 5 nm (221 m^2/g) M-Fe: 100 nm (12 m^2/g) N-Ni: 6 nm (145 m^2/g) M-Ni: 16 nm (57 m^2/g) N-Si: 19 nm (127 m^2/g) M-Si: 440 nm (5.4 m^2/g) N-Ti: 6 nm (242 m^2/g) M-Ti: 410 nm (3.5 m^2/g) KLN: 100 nm (24.3 m^2/g) MUS: (NOS <5 µm) DD: 400 nm (6.2 m^2/g) JE: (NOS <3 µm) MNC: 200 nm (13.0 m^2/g)	**Route:** Cell Culture (35,000 cells/cm^2 BEAS; 2500 cells/cm^2 NHBE; 20,000 cells/cm^2 A549) **Dose/Concentration:** 0.53, 5.3 and 53 µg/cm^2 (= 1, 10, 100 µg/mL) **Time to Analysis:** 24 h	**Cell Viability:** Except for Ni and V no cytotoxicity was observed at the highest concentration. **IL-6 Secretion in BEAS-2 B Cells:** Nano and micro sizes of the same metal showed no differences in response (high experiment to experiment variability). In general, the soil-derived dusts (JE, DD, MNC) were more potent than the metal and ceramic oxide particles. In KGM media, BEAS-2B cells are more responsive to vanadium and other soluble metals and less responsive to LPS, but this relationship is reversed in LHC-9 media. **IL-8 Secretion in BEAS/LHC vs NHBE in BEGM Cells:** Levels were much higher in NHBE cells than BEAS-2B cells. For BEAS-2B, the nano size Si and both sizes of Ni induced levels statistically greater than the control. For NHBE, only Si and Ni (for both sizes) were statistically greater than control. **IL-6 in NHBE:** The nano and micro sized particles of Al, Ce, Fe and nano sized Si all induced statistically significant increases. Control levels of IL-6 were much higher in NHBE cells than in BEAS-2B cells. Secretion induced by pure oxide particles was small for both the mid and high concentration levels (5.3 and 53 µg/cm^2). **BSA/ Bovine Serum Addition Effect:** In a fixed solution nano-Ni, nano-Ti and KLN all reduced the measured IL-6 by 60+ percent. Addition of BSA or bovine serum dose dependently reduced the action of the particles to near control levels. **PM Effects (without added protein) on IL-6 In Solution:** Increasing metal concentration did not affect a fixed IL-6 concentration until the 100 or 316 µg/mL levels.

Study	Pollutant	Exposure	Effects
Reference: Veranth et al. (2007, 090346) **Species:** Human, mouse, rat **Cell Type:** A549, BEAS-2B (types E and U), RAW 264.7, Primary macrophages	S: desert dust (collected from unpaved desert road in Utah, $PM_{2.5}$ enriched) V: vanadium soluble (prepared from $VOSO_4$, Alfa Aesar, Ward Hill, MA) C: Coal fly ash ($PM_{2.5}$ enriched and derived from commercial power plant burning Utah bituminous coal) D: Diesel PM (tail-pipe particles collected from high emitting BSr on-road light duty truck) L: Lipopolysaccharide T: Titanium dioxide (Alfa Aesar) K: Kaolin (purchased from Capitol Ceramics, UT) **Particle Size:** BET surface (m^2/g) S: 6.2 ($PM_{2.5}$ enriched) V: NA C: 5.4 ($PM_{2.5}$ enriched) D: NR L: NA T: 3.5 (1-2 µm) K: 24 (<200 mesh = 74 µm)	**Route:** Cell Culture **Dose/Concentrations:** Maximum concentrations: S = 100 µg/cm^2 V = 100 µg/cm^2 C = 100 µg/cm^2 D = 32 µg/cm^2 L = 1000 EU/mL T = 100 µg/cm^2 K = 100 µg/cm^2 **Time to Analysis:** 24 h	**Viability:** Generally, cell viability was greater than 75% of the control post treatment. Vanadium, at the highest concentration, induced less than 50% of control viability whereas kaolin, also at the highest concentration, induced cell death. **IL-6:** BEAS-2B E or U in LHC-9 showed a response to S and L. BEAS-2B (U) was in LHC-9 medium with added serum (FBS). This resulted in a doubling of response coupled with at least an 8 fold increase in control levels. BEAS-2B (E) showed response for S and V but not L. A549 showed response to S and K. RAW 264.7 and Rat macrophages showed responses to S(very low) and L. In general, the IL-6 responses in A549 and RAW 264.7 were similar and significantly lower than the responses in rat macrophages or BEAS-2B. **Effect of Culture Media Composition (BEAS-2B):** Varying ratios of LHC-9 and KGM media resulted in a near 10 fold increase in control rate once LHC was 33% or more of the media. Upon Soil Dust (NOS) exposure IL-6 increased linearly with % LHC-9 in culture/exposure media. Addition of calf serum (0.1-10 %) raised control IL-6 levels at least 40 fold. At a steady PM concentration, the addition of serum resulted in a log-linear increase in IL-6 release which blocked any PM effect. **Reversibility of Media Effect:** Changing media with every passage showed that media effects do not persist once media are changed. **Culture Well Size:** Going from a 6 well to 96 well plate (decreasing well size) increased IL-6 control values about ten fold, while the positive control (TNF) response increased 3 fold. Hence the sensitivity of the test (i.e., positive/control response) declined from 11 fold to 3 fold with increasing well number / decreasing well size. Because cell seeding density and the like were held constant, these changes suggest that edge effects are the cause of the IL-6 changes.
Reference: Veranth et al. (2006, 087479) **Species:** Human **Cell Type:** BEAS-2B	$PM_{2.5}$ samples from 28 samples from 8 locations in Utah, New Mexico and Texas (rural, industrial, road side, military) 2 coal fly ash samples (a product of combustion using Utah bituminous coal and New Mexico bituminous coal) TiO_2 kaolin clay **Particle Size:** $PM_{2.5}$; TiO_2: 1-2 µm	**Route:** Cell Culture (35,000 cells/ cm^2) **Dose/Concentration:** 10, 20, 40, 80 µg/cm^2 **Time to Analysis:** 24 h	**Cell Assays:** In sample soils viability declined dose dependently while IL-6 increased dose-dependently. IL-8 was highly variable (peak at 20 µg/l, dose-dependent increase or flat response.) **IL-6 Assays for All Soil PMs:** Soils ranged across an order of magnitude greater than LPS, coal fly ash, TiO_2 or kaolin samples. One soil even exceeded the pos V control at equal concentrations **Correlation with Cell Viability:** Correlation was strong for Mn ($p<0.001$) and weak for EC3, K, Se, and Hg ($0.01<p<0.05$). **IL-6, 10 µg/cm^2:** Correlation was medial for OC-1(OC) and P at $0.001<p<0.01$. **IL-6, 80 µg/cm^2:** Correlation was strong for OC3, OP (pyrolized Carbon), OC, EC1, TC and intermediate for OC2, OC4, Zn and weak for Ca2+, EC2, Si, Ca, Ca: Al. **IL-8, 10 µg/cm^2:** Correlation was weak for EU (Endotoxin), CO_3, Si, and Br. **IL-8, 80 µg/cm^2:** Correlation was medial for CO_3, Sr and weak for K+, EC3, Mg, Si. **IL-8 trend (corr over 10-80 range):** Correlation was strong for EC, intermediate for OC4, EC1, EC2, EC3, TC, Ni and weak for OP, OC, Cr, and Sr. IL-6 and Il-8 were not correlated nor were IL-6 and cell viability. Authors noted that weak correlations ($0.01<p<0.05$) contained false positives.

Study	Pollutant	Exposure	Effects
Reference: Veranth et al. (2004, 087480) **Species:** Human **Cell Type:** BEAS-2B	$PM_{2.5}$ enriched soil samples DD: desert dust, unpaved road, Utah WM: West Mesa, sandy grazing site, NM R40: Range 40 gravel soil, TX UN: Uinta, sandy soil, UT **Particle Size:** 0.4-3 µm	**Route:** Cell Culture (20,000/cm^2) **Dose/Concentration:** 10, 20, 40, 80, 160 µg/cm^2 **Time to Analysis:** 24 h	**Elemental Analysis of PM**: Major differences UN generally lower in major minerals but high Fe content and high EC. High Mn. Low Pb and Zn **Cytotoxicity:** UN and WM were the most cytotoxic at all dose levels, followed by R40 and DD. All particles showed a dose-dependent cytotoxic response. **IL-6 Release:** DD and R40 (up to the 160 µg/cm^2) showed dose-dependent responses and induced an 8-fold increase at the highest concentration levels. WM peaked at 40 µg/cm^2 and UN induced similar responses above 10 µg/cm^2. **IL- 8 Release:** DD induced a dose-dependent response. WM peaked at 10 µg/cm^2. Release induced by DD and WM seemed to be limited by toxicity. There was no treatment with R40. **TNF-α:** DD, WM and UN induced release was not detected at the 40 or 80 µg/cm^2 concentrations. **LPS:** LPS was the primary factor in inducing IL-6 release when exposed to LPS-containing mixtures. LPS alone induced lesser responses than treatment to the environmental dust particles. TiLPS induced a less than two-fold increase in IL-6 versus the over seven-fold increase induced by soil dust positive control. LPS treatments were less cytotoxic than DD. Limited IL-6 and IL-8 responses were observed at 2000 EU/mL compared with DD at 80 µg/cm^2 **Endotoxin:** Inverse relationship between endotoxin content and IL-6 release was observed. **Viability vs Physical Modification of Dust Sample (no UN):** Only leaching in a variety of water based vehicles increased viability minimally (generally <25 %). Heat treatment (150-, 300, 550° F) and methanol extraction had no effect **IL-6 Release vs Physical Modification of Dust Sample (no UN):** One hour thermal treatment at 150° F had no effect on IL-6 response. All other treatments reduced IL-6 release (heat 350°, 500° and extractions).
Reference: Veronesi et al. (2002, 024599) **Species:** Human **Cell Type:** BEAS-2B	Ambient PM - St. Louis: Urban particulates - Ottawa: Urban particulates -MSH: Volcanic dust from Washington state's Mt. St. Helen -Woodstove: Woodstove particles from conventional fireplace burner -CFA: Coal fly ash from western U.S. power plant -OFA: Oil fly ash from Niagara, NY - A: Total Fractions - B: Soluble Fractions - C: Washed Fractions **Particle Size:** PM >2.5 µm; PM: 2-10 µm; PM >10 µm	**Route:** Cell Culture **Dose/Concentration:** 50 µg/mL; 30 µg/cm^2 100µg/mL; 60 µg/cm^2 **Time to Analysis:** 4, 16 h	**Ca:** Calcium increased significantly with all particles types. **IL-6:** At 50 and 100 µg/mL, IL-6 increased with all particle types at 4 and 16 h. Overall, fraction -A was the most potent. **Surface charge:** Surface charge correlated strongly with increases in both Ca^{2+} and IL-6 levels. OFA, however, was unmeasurable due to technical difficulties.

Study	Pollutant	Exposure	Effects
Reference: Vogel et al. (2005, 087891) **Species:** Human **Cell Type:** U937 (ATCC) monocytes (macrophage differentiation)	UDP: SRM 1649 (NIST) UDP-OE: DCM extract of SRM-1649, 0.45 µm filter sUDP: stripped particles UDP DEP: SRM 2975 (NIST) DEP-OE: DCM extract of SRM-2975, 0.45 µm filter sDEP: stripped particles DEP CB95: Carbon Black (Degussa) **Particle Size:** UDP, DEP: NR; CB95: 95 nm	**Route:** Cell Culture (2×10^5 - 2×10^6 cells/mL) **Dose/Concentration:** DEP, UDP: 2.5, 10 or 40 µg/cm^2 (eq to 12.5, 40, 200 µg/mL) DEP-OE, UDP- OE: 10 µg/cm^2 (particle equivalent) **Time to Analysis:** 24 h	**Effect On mRNA Expression (COX-2, TNF-α, IL-6, IL-8, C/EBPβ, CRP, CYP1a1):** All DEP and UDP induced dose-dependent increases. IL-6 tended to plateau at 10 µg/cm^2. Generally, with the exception of COX-2, UDP effects on genes were stronger than DEP. **Cytotoxicity:** Both DEP and UDP were cytotoxic at 40 µg/cm^2 **Fractionation and mRNA Expression:** For COX-2, TNF-α, IL-8 mRNA fractions were much more active than parent particles and consequently stripped particles were much less active than parent particles. CB95 had no effect. The reverse effect occurred for IL-6 and CRP mRNA expression. The particles that induced mRNA expression in decreasing order are: sUDP, UDP, UDP-OE. **Inhibition Of mRNA Expression:** CRP: pretreatment with IgG and wortmannin (Fcγ receptor binding and ingestion dependent inhibitors resp) blocked the effects of DEP, UDP and sDEP and sUDP. Luteolin (AhR inhibitor) had no effect. **COX-2:** Only luteolin inhibited COX-2 expression for DEP, DEP-OE, UDP, and UDP-OE. **CYP1a1:** Luteolin also inhibited OE-DEP and OE-DUP effects (only those two particles tested). **Cholesterol Accumulation:** DEP, UDP and UDP-OE and DEP-OE at 10 µg/cm^2 all increased cholesterol accumulation by at least 2 fold
Reference: Wang et al. (2003, 157106) **Species:** Rat **Cell Type:** Lung Myofibroblasts	V_2O_5: (Aldrich Chemical Co., Wisconsin) **Particle Size:** NR	**Route:** Cell Culture (1×10^5 cells/100 mm dish; 3.2×10^4 cells/cm^2) **Dose/Concentration:** 400 µm **Time to Analysis:** 0.5, 1, 4, 24 h	**H_2O_2 Drives STAT-1 Activation:** Pretreatment with NAC or catalase reduced V_2O_5-induced STAT activation by more than 90% and completely abolished H_2O_2-induced STAT activation. Within 5 min of V_2O_5 treatment, H_2O_2 was significantly decreased in the supernatants of cultured myofibroblasts and suppression of H_2O_2 levels continued for up to 24 h post V_2O_5 treatment. This supports the findings that myofibroblast-generated H_2O_2 is required for V_2O_5-induced STAT activation. **Temporal STAT-1 Activation:** H_2O_2 induced rapid activation within minutes whereas activation by V_2O_5 occurred more slowly (beginning 8h post treatment). **p38, ERK, EGFR:** p38 and EGFR are required for H_2O_2- or V_2O_5-induced STAT-1 activation whereas ERK is not required
Reference: Whitekus et al. (2002, 157142) **Species:** Mouse **Cell Line:** RAW 264.7	DEP (light-duty, four-cylinder engine-4JB1 type, Isuzu Automobile, Japan; standard diesel fuel) (extracts) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 50 µg/mL **Time to Analysis:** 5 h	DEP significantly reduced the GSH:GSSG ratio**.** This effect was prevented by adding thiol antioxidants NAC or BUC. DEP increased lipid peroxide levels, but the addition of all antioxidants decreased these levels. DEP increased carbonyl groups. NAC, BUC, and luteolin reduced HO-1 expression.

Study	Pollutant	Exposure	Effects
Reference: Wilson et al. (2007, 097268) **Species:** Mouse **Cell Type:** J774	CB: Carbon Black, Printex 90 (Degussa) $FeCl_3$ $ZnCl_2$ **Particle Size:** CB: 14 nm	**Route:** Cell Culture (4×10^5 cells/mL at 1mL/well) **Dose/Concentration:** CB 1.9 -31 µg/mL; $FeCl_3$, $ZnCl_2$ 0.01-100 µmol **Time to Analysis:** 4 h	**ROS Production in Cells:** CB alone increased ROS. Coexposure with $ZnCl_2$ did not affect ROS. **ROS Production - Cell Free:** CB induced a significant increase in ROS. $ZnCl_2$ had no effect. Coexposure CB/Zn also had no effect. **TNF-α Production (Fe -Zn 0.01-100 µmol):** Coexposure of CB over a range of metals gave no change over CB alone for Fe. For Zn, only at the concentration of 100 µmol was there a small interaction between Zn and CB. Similar results were seen at metal concentrations between 20 -100 µmol. Synergism was observed between Zn and CB and no observed effect of Fe. **Macrophage Cytoskeleton:** CB resulted in black vacuoles. Co-treatment of cells with Zn and CB increased the severity of Zn effects. Fe exhibited no synergism. **Apoptosis /Necrosis:** No synergism of CB with either Fe or Zn. **Phagocytosis:** Only at 31 µmol CB and 50 µmol Zn did a synergistic effect occur; it resulted in a 4-fold reduction.
Reference: Wottrich et al. (2004, 094518) **Species:** Human **Cell Type:** A549, THP-1, Mono Mac 6	Fe: hematite α-Fe_2O_3 Si60: silicasol (SiO_2, amorphous silica) Si100: silicasol Q: crystalline quartz DQ12 **Particle Size:** Fe: 50-90 nm; Si60: 60 nm; Si100: 80-110 nm; Q <5 µm	**Route:** Cell Culture (2×10^4 cells/well. Co-culture: 2×10^4 A549 and 2×10^3 Macrophages) **Dose/Concentration:** A549 light microscopy hematite 100µg/mL (23 µg/cm^2) TEM hematite 50 µg/mL (16 µg/cm^2) Cytotoxicity 10, 50, 100 and 200 µg/mL (6.1, 30, 61 and 121 µg/cm^2) Cytokines 50 and 200 µg/mL **Time to Analysis:** 24 h	**Particle Uptake:** Hematite agglomeration was observed in all 3 cell lines. TEM confirmed cytosol aggregates as well as single particles, which includes particles transported intracellularly to basolateral membrane of epithelial cells. **Cytotoxicity:** LDH increased significantly in A549. In decreasing order, Q , Fe, S60, and S100 (which exhibited levels similar to controls) all induced cytotoxicity. THP-1 cells appeared the most sensitive with Q, Fe, S60, S100, control inducing cytotoxicity in decreasing order. Mono Mac 6 cells were the least sensitive with Fe, S60, Q, S100. **Cytokines:** IL-6 and IL-8 released from A549 cells upon exposure to all particles. No response was observed in Mono Mac 6 or in THP-1 cells. **Co-cultures:** Mix of A549 with either Mono Mac 6 or THP-1 led to a large (ten fold) increase in response to particles. Ten fold increases were observed in IL-6 and IL-8 levels with the Mono Mac 6 co-culture and the THP-1 co-culture, respectively.

Study	Pollutant	Exposure	Effects
Reference: Wu et al. (2007, 098412) **Species:** Human **Cell Line:** B82L **Cell Type:** B82L- par (parental fibroblasts), B82L-wt (wild type EGFR), B82L-K721M (kinase defective EGFR), B82L-c'958 (COOH-terminally truncated EGFR at Tyr-958)	$ZnSO_4$ (Sigma) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** Zn: 500 µmol EGF: 100 ng/mL **Time to Analysis:** 20 min	**EGFR Mutations:** EGFR-wt has a functional tyrosine kinase domain, intact Src phosphorylation (Tyr 845) and 5 tyrosine autophosphorylation sites. EGFR-c'958 lacks all 5 tyrosine autophosphorylation sites. EGFR-K721M lacks tyrosine kinase (ATP binding). EGFR-Y845F lacks Src autophosphorylation (Tyr 845) and, instead, has a receptor at Tyr 845 that is phosphorylated by nonreceptor Tyrosine kinase Src. **Zn Induced Ras (MAPK signaling protein):** No effect was observed in B82L-par cells. Zn had an effect in -wt, -c'958, and -K721M which confirms the need for EGFR. This indicates that neither tyrosine kinase nor autophosphorylation sites were required for Zn effects. No observed increase for Y845F indicated that EGFR tyrosine 845 (phosphorylated by c-Src) is required for Zn effects. However, it was not required for EGF effects. **Src Kinase Requirement:** Using a Src blocker drastically reduced Zn effect but not the EGF effect. Src activation occurred independent of EGFR Tyr-845. **Zn Induced Association of EGFR with Src:** Zn induced a physical association in all 4 mutants; EGF did not. **Zn Induced Phosphorylation of EGFR at Tyr-845:** Zn induced phosporylation of EGFR at Tyr-845 in B82L-wt,-c'958 and -K721M. EGF exhibited similar effects. Src blockers significantly reduced phosphorylation induced by Zn but not for EGF. Neither Zn or EGF induced phosphorylation in B82L-Y845F cells.
Reference: Wu et al. (2003, 199749) **Species:** Human **Cell Type:** BEAS-2B	Zinc Ion: Zn^{2+} **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 10, 25, 50 µmol **Time to Analysis:** 0-8 h	**Cytotoxicity:** Exposure to 50 µmol Zn^{2+} for 8 h did not result in significant alterations in cell viability. **PTEN Protein Levels:** 50 µmol Zn^{2+} for 4 and 8 h significantly decreased levels in a dose-dependent manner. Exposure to 50 µM vanadyl sulfate (tyrosine phosphatase inhibitor) had minimal effects on PTEN. 100 ng/mL of non-specified EGF receptor ligand for 1-8 h did not exhibit any significant effects on PTEN levels. **P13K/Akt:** Zinc induced Akt activation in a dose- and time- dependent fashion. Active Akt levels were the highest at 1 h post exposure to Zn^{2+}, corresponding with the time period when there was a minimal effect on PTEN protein level. When treated with LY294002 (inhibitor of P13K activity), Akt phosphorylation was significantly inhibited. **PTEN mRNA Levels:** Decreased PTEN mRNA expression was observed in cells exposed to 50 µmol Zn^{2+} for 8 h whereas PTEN protein levels declined as early as 4 h. **Proteasome-mediated PTEN Degradation:** Use of MG132 (proteasome inhibitor) had no significant effect on Zn^{2+} induced PTEN mRNA expression. Therefore mRNA expression may not play a critical role in PTEN protein reduction. Instead data suggested that 26 S proteasome played a vital role in Zn^{2+} induced PTEN degradation. PI3K inhibitor blocked Zn-induced PTEN degradation, but failed to prevent significant Zn-induced down-regulation of PTEN mRNA.

Study	Pollutant	Exposure	Effects
Reference: Wu et al. (2004, 096949) **Species:** Human **Cell Type:** NHBE	Zinc Ion: Zn^{2+} **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 100 µmol **Time to Analysis:** 2 h	**Cell Viability:** After 2 h of exposure, Zn^{2+} induced effects in NHBE cells at 100 and 200 µmol levels (but not 50 µmol). Continuing exposure to 100 µmol Zn^{2+} for 4 and 6 h did not significantly alter cell viability. Thus, in all subsequent studies, NHBE cells were treated with 100 µmol Zn^{2+}. **Induced EGFR Phosphorylation:** Exposure to 100µM Zn^{2+} for 1-4 h induced phosphorylation of EGFR in NHBE cells. EGFR kinase inhibitor PD153035 (to determine if phosphorylation of EGFR was the result of autophosphorylation of activated EGFR tyrosine kinase activity) caused Zn^{2+} -induced phosphorylation to subside. Zn^{2+} activity requires tyrosine kinase activity. **EGFR Phosphorylation Pathway:** To test whether Zn^{2+} exposure results in ligand release, which in turn can activate phosphorylation, NHBE cells were pretreated with LA1 blocking antibody. Results showed significant suppression of Zn^{2+} induced phosphorylation, therefore Zn^{2+} phosphorylation might be initiated by the release of EGFR ligands. **HB-EGF, TGF-α, EGF:** To examine the involvement of specific ligands (HB-EGF. TGF-α and EGF) in the phosphorylation pathway, cells were exposed to anti-HB-EGF, anti-TGF-α and anti-EGF. Results showed that anti-HB-EGF reduced Zn^{2+} induced phosphorylation significantly, anti-TGF-α produced partial inhibition and anti-EGF had no inhibitory effect. Exposure with blocking antibody LA1 was tested to determine if it caused an increase in soluble HB-EGF. HB-EGF mRNA expression was also elevated in cells exposed to Zn^{2+}. Previous studies indicate metalloproteinase (MMP) involvement in cleaving ligand precursors. It was found that MMP-3 inhibitor partially blocks Zn^{2+} induced HB-EGF release. (MMP-2 and MMP-9 did not show similar inhibition patterns) Zn^{2+} exposure increased the release of MMP-3 from HNBE cells.

Study	Pollutant	Exposure	Effects
Reference: Wu et al. (2005, 097350) **Species:** Human **Cell Line:** Subclone S6 **Cell Type:** BEAS-2B	Zinc Ion: Zn^{2+} **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 50 µmol **Time to Analysis:** 4 or 8 h; EGFR phosphorylation: 30, 60, 120, 240 min	**Cell Viability:** Exposure to 50 µmol Zn^{2+} for 8 h did not result in significant alterations in cell viability (assessed by LDH release). **P13K/Akt Signaling Pathway:** To evaluate P13K's on COX-2 Zn^{2+} induced expression, LY-294002 (a P13 inhibitor) and another unnamed P13 inhibitor were used. Exposed cells indicated suppressed levels of Zn^{2+} induced COX-2. To determine Akt role, ad-DN-Akt (AAA) was used. Infected cells indicated over-expression of Akt and significant reduction of Zn^{2+} induced GSK-3α/β phosphorylation. Over expression of DN-Akt(AAA) blocked Zn^{2+} induced COX-2 expression. **PTEN's Role in Blocking Zn2+ Induced COX-2 mRNA Expression:** PTEN is an antagonist of P13/Akt pathway. Overexpression of wildtype PTEN blocked Zn^{2+}-induced mRNA COX-2 expression, suggesting PTEN inhibits PIP3 signal transduction to Akt. **Analysis of the Src/EGFR Signaling Pathway:** Zn^{2+} induced a time-dependent increase in Src and EGFR phosphorylation in cells. Blockage of Src activity via PP2 (Src inhibitor) decreased Zn^{2+} induced EGFR phosphorylation. The EGFR tyrosine inhibitor completely blocked Zn^{2+}-induced EGFR phosphorylation. EGF (a ligand of EGFR signaling) induced COX-2 expression, suggesting that EGFR regulated Zn^{2+} -induced COX-2 expression. **p-38 and EGFR Kinase Activity:** Use of PD-153035 (EGFR inhibitor) and PP2 (Src inhibitor) and SB-203580 (p38 inhibitor) all blocked Zn^{2+}-induced Akt phosphorylation of Src., EGFR and p38. It is thought that p38 is a critical kinase in regulation of Zn^{2+} -induced COX-2 protein expression.
Reference: Yacobi et al. (2007, 156166) **Species:** Rat **Cell Type:** L2 (Lung epithelial cells)	PNP: Polystyrene nanoparticles, negatively charged (Molecular Probes, Eugene, OR) PNPA: Amidine modified PNP, positively charged SWCNT: Single-wall carbon nanotubes (Carbon Nanotech, Houston, TX) QDC: Chitosan coated (CdSe/ZnS) Quantum dots, positively charged (made) QDA: Alginate coated QD, negatively charged UAPS: Ultrafine Ambient particulate suspensions (VACES) (48 % OC) **Particle Size:** PNP20: 20 nm; PNP100: 100 µm; SWCNT: 0.8-1.2 nm (diameter); SWCNT: 100-1000 nm; QD: 30 nm; UAPS: <150 nm	**Route:** Cell Culture (1.2×10^6 cells/cm^2) **Dose/Concentration:** PNP up to 706 µg/mL QD up to 176 µg/mL SWCNT up to 88 µg/ mL UAPS up to 36 µg/mL **Time to Analysis:** on days 4, 5 or 6 by replacing monolayer apical fluid with PM in suspension for up to 1440 min. Intermediate measurements at 15, 30, 60, 120, 240 and 1440 min.	**UAPS and Rt (transmonolayer resistance):** Rt declined up to 60% within 1 h at 36 µg/mL. Rt plateaued (or exhibited a very slight upgradient) for up to 24 h (last measurement). No cytotoxicity was observed. Replacement of apical fluid with fresh media after 2 h of exposure restored Rt to near control values within 24 h. **UAPS and Leq (short-circuit current):** Peak decline of 30% after 4 h followed by gradual recovery over 24 h. Replacing media after 2 h exposure returned Ieq to control values within 24 h. **UAPS and Apparent Permeability:** Permeability measured via C14 mannitol and inulin showed no effect of UAPS. **QD and Rt:** QD depressed Rt by nearly 55% at 4 h for positively charged and 30% for negatively charged QDs. Recovery towards control values started at 4 h and was near complete at 24 h **SWCNT and Rt:** SWCNT depressed Rt by ~ 40% at 1 h (same for 22, 44, and 88 µg/mL). Recovery was near complete at 4 h and complete at 24 h. **PNP and Rt:** No statistically significant effects were observed.

Study	Pollutant	Exposure	Effects
Reference: Yun et al. (2005, 088302) **Species:** Human **Cell Type:** A549	DEP: Collected using a 6 cyl 11L, heavy duty (2001 yr) bus engine (South Korea) **Particle Size:** NR	**Route:** Cell Culture (3×10^4 cells/well) **Dose/Concentration:** 1, 10, 100, 250, 500 and 1000 µg/mL; main testing 250 µg/mL **Time to Analysis:** 12 h	**NF-κB Transcription Activation:** DEP induced dose-dependent activity up to 250 µg/mL. After peaking at 250 µg/mL, concentrations above 250 induced dose- dependent declines. Activity peaked at 12 h for 250 µg/mL and declined to control at 24 or 48 h. The mechanism of DEP action was the degradation of IκBα which is an intracellular inhibitor of nuclear translocation of NF-κB. **TAK1 and NIK Required for NF-κB Activation by DEP:** Dominant negative mutants of TAK1 and NIK reduced DEP induced response to basal level. TAK1 was phosphorylated after DEP exposure and was sustained for at least 90 min.
Reference: Zhang et al. (2007, 156179) **Species:** Human, Rat **Cell Type:** A549, RLE-6TN	$PM_{2.5}$: Collected by baghouse from Dusseldorf, Germany Particle Characterization: Carbon 20%, Hydrogen 1.4%, Nitrogen <0.5%, Oxygen 14.1%, Sulfur 2.1%, Ash 63.2%. **Particle Size:** $PM_{2.5}$	**Route:** Cell Culture **Dose/Concentration:** 100 µg/cm^2 **Time to Analysis:** 24 h	**Apoptosis:** At 100 µg/mL for 24 h, PM induced a 2.5 fold increase in apoptosis in A549. **Mitochondrial Membrane Potential:** A significant reduction in AEC mitochondrial membrane potential was observed. **Caspase -3 & -9:** Increased activity of both enzymes in both cell types was observed. More specifically, a 2- to 2.5-fold increase of caspase -3 and -9 in A549 and an 8-fold increase of caspase-9 and 4-fold increase of caspase-3 in RLE-6TN were observed. **BIM:** Downregulation of BIM by RNA interference inhibited PM-induced apoptosis. An inhibited decrease in mitochondrial membrane potential and activation of both caspases were observed.
Reference: Zhang et al. (2004, 157183) **Species:** Mice **Cell Line/Type:** C10 (alveolar Type II-like epithelial cell line)	DEP: SRM 1650a **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 5 or 25 µg/mL **Time to Analysis:** 30-360 min	**fra Expression:** DEP induces fra-1 but not fra-2 expression. mRNA induction peaks around 180 min DEP affects fra-1 mRNA expression at the transcriptional level. **ERK/JNK/p38 MAPK signaling pathways:** 3 inhibitors (PD-98059, SB-202190 or SP-600125) all reduced DEP stimulated fra-1 induction to near control levels. DEP stimulated phosphorylation of the MAPKs which peaks at 60 min but stays elevated at 180 min. **MMP-9 promoter activity:** fra-1 upregulation may play a role in DEP induced increases in MMP-9 promoter activity as fra-1 appears to bind at the -79 TRE sequence of the MMP-9 promoter.

Table D-3. Respiratory effects: in vivo studies.

Reference	Pollutant	Exposure	Effects
Reference: Adamson et al. (2003, 087943) **Species:** Rat **Gender:** Male **Strain:** SD **Weight:** 150 g	PM_{10}: EHC-93W (whole dust) EHC-93S (soluble) EHC-93L (leached) EHC-2KW, -S, -L Measured components Zn, Mg, Pb, Fe, Cu, Al **Particle Size:** EHC-93W, -93S, -93L, -2KW, -2KS, -2KL: PM_{10}	**Route:** IT Instillation **Dose/Concentration:** 5 mg/rat; 33.3 mg/kg **Time to Analysis:** 4 h, 1 day, 3 day, 7 days, 14 days	**BALF Cells:** The greatest increase in cell numbers was observed with EHC-93W. Activity peaked at 1 day with a return to normal levels by 7 days. EHC-93L also induced an increase in cell numbers, more so than EHC-93S, but both particles induced statistically significant increases. However, these increases were mostly attributable to an increase in the AM and PMN populations. **BALF Inflammatory/Injury Markers:** Metallo-proteinase (MMP) 2 and 9 both increased, peaking at 1 day and 4 h respectively. MMP2 activity appears related to the soluble fraction whereas MMP-9 activity appears to be related to the leachable fraction.

Reference	Pollutant	Exposure	Effects
Reference: Ahn et al. (2008, 156199) **Species:** Mouse **Gender:** Male **Strain:** BALB/C1 **Age:** 6 wk **Weight:** 19-24 g	DEP: Collected using a turbo-charged, intercooler, 6-cylinder, heavy-duty, diesel engine (model year 2000 DPBS: control **Particle Size:** NR	**Route:** Oropharyngeal Aspiration **Dose/Concentration:** 1, 10, 25 mg/kg per day; Those receiving 25 mg/kg DEP also received pre-treatment of Dex (1, 5 mg/kg) 1 h prior **Time to Analysis:** 5 consecutive days; 72 h post final exposure	**BALF Inflammatory/Injury Markers:** Lung injury was more severe in mice exposed to 25 mg/kg of DEP than when compared to mice exposed to 1 mg/kg DEP. However, lung injury caused by exposure to 25 mg/kg DEP could be completely prevented with pre-treatment of 5mg/kg Dex. Treatment with 1 mg/kg Dex prior to exposure to 25 mg/kg DEP depicted partial reduction in lung injury. **BALF Cells:** Treatment with DEP over a 5 day period caused an increase in total number of cells (macrophages, neutrophils and lymphocytes) when compared to control. Total Cells: Control - 5.33 ± 0.44 cells 1 mg/kg DEP - 6.26 ± 0.87 cells 10 mg/kg DEP - 14.40 ± 1.90 cells 25 mg/kg DEP - 47.20 ± 3.40 cells **COX-2 Expression:** Exposure to DEP lead to a dose-dependent increase in COX-2 levels; specifically, treatment with 25 mg/kg significantly increased COX-2 levels. This effect was completely reduced by treatment with 5mg/kg of Dex.
Reference: Ahsan et al. (2005, 156200) **Species:** Mouse **Gender:** Male and Female **Strains:** hTrx-1-transgenic and C57BL/6 (control) **Age:** 8-8.5 wk	DEP: Obtained from Dr. Masaru Sagai (Amori, Japan) **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** Lung Damage: 0.1 mg/mouse; Survival Analysis: 0.2 mg/mouse; ESR: 0.05 mg/mouse **Time to Analysis:** 24 h	**ESR:** hTrx-1 induced 0.05 mg generation of hydroxyl radicals in the lungs (mid thorax ESR spectra) compared to control. **BAL Inflammatory/Injury Markers:** hTrx-1 attenuated cellular damage from 0.1mg DEP. Control mice showed massive edema with neutrophilic infiltration, hemorrhagic alveolar damage and collapsed air spaces. hTrx-1 mice showed mild/moderate edema with clear demarcation of air spaces. **Viability:** After 4, 12 and 24 h, survival was 32, 24 and 12% respectively as compared to 80, 52 and 40% for hTrx-1 mice.
Reference: Andre et al. (2006, 091376) **Species:** Mouse **Gender:** Female **Strain:** BALB/cJ **Age:** 10-12 wk	UFCP: Ultra Fine Carbon Particles (electric spark generator, Model GFG 1000; Palas, Karlsruhe, Germany) Measured Component: UFCP>96% EC **Particle Size:** 49 nm	**Route:** Whole-body Inhalation **Dose/Concentration:** 380 µg/m^3 **Time to Analysis:** 4 and 24 h; 0 and 24 h post-exposure	**BALF Cells:** A small increase in PMN number suggests a minor inflammatory response after 24 h exposure. Number of macrophages did not increase. **BAL Inflammatory/Injury Markers:** Total protein concentration significantly increased post 24 h inhalation. Post 4 h, heat shock proteins were induced. Post 24 h, immunomodulatory proteins (osteopontin, galectin-3 and lipocalin-2) significantly increased in alveolar macrophages and septal cells. 236 (1.9%) genes was increased and 307 (2.5%) genes were decreased with upregulated genes being primarily related to the inflammatory process.
Reference: Antonini et al. (2004, 097199) **Species:** Rats **Gender:** Male **Strain:** SD **Weight:** ~250 g	ROFA-P: Precipitator -S: Soluble (0.22 µm filter), Components: Fe, Al, Ni, Ca, Mg, Zn -I: insoluble, Components: Fe, Al, Ni, Ca, Mg, Zn, V -T: total ROFA-AH: Air Heater -S: Soluble (0.22 µm filter), Components: Fe, V, Ni, AL -I: Insoluble, Components: Fe, V, Ni, AL -T: Total **Particle Size:** < 3 µm (mean diameter)	**Route:** IT Instillation **Dose/Concentration:** 1mg/100g bw in 300 µl saline; 60 mg/kg **Time to Analysis:** 24 h; Clearance Experiment: two single exposures day 0 and 3 observed at day 6, 8 and 10	**ESR:** Only ROFA-P contained free radicals, primarily in ROFA-P-S. **BALF Cells:** No effects on alveolar macrophages were observed, but all ROFA-P fractions increased lung neutrophils. ROFA-P-S and ROFA-P-I effects combined roughly equaled ROFA-P-T. **BAL Inflammatory/Injury Markers:** ROFA-AH-T and ROFA-AH-I increased LDH. ROFA-P and -AH increased albumin for T and I fractions. **Pulmonary Clearance (Listeria Monocytogenes):** ROFA-P-T and ROFA-P-S significantly slowed bacteria clearance from lungs. ROFA-AH and ROFA-P-I had no effect.

Reference	Pollutant	Exposure	Effects
Reference: Arimoto et al. (2007, 097973) **Species:** Mouse **Strain:** ICR **Gender:** Male **Age:** 6 wk **Weight:** 29-33 g	DEP (collected using a 4JB1 4-cyl, 2.74L Isuzu diesel engine) DEP-OC: organic chemical extracts LPS DL = DEP + LPS DOL = DEP-OC + LPS **Particle Size:** 0.4µm	**Route:** IT Instillation **Dose/Concentration:** DEP or DEP-OC: 4 mg/kg; LPS: 2.5 mg/kg; DL or DOL: NR **Time to Analysis:** 24 h	**Cytokines:** DEP-OC or DEP alone did not change levels of MIP-1α, MCP-1 or MIP-2. DL induced significant increases in MIP-1, MIP-2 and MCP-1. **LPS:** LPS and DOL induced increases in MCP-1 though the increase induced by DL was greater. No effect on MIP-1α or MIP-2 was observed.
Reference: Bachoual et al. (2007, 155667) **Species:** Mouse **Strain:** C5B17 **Gender:** Male **Age:** 7 wk **Weight:** 22.3 ± 073 g	RER: PM_{10} Paris, France subway CB TiO_2 DEP **Particle Size:** RER: 79% < 0.5 µm; 20%: 0.5-1 µm CB: 95 nm TiO_2: 150 µm DEP: NR	**Route:** IT Instillation **Dose/Concentration:** 5, 50, 100 µg/mouse, 0.22, 2.2, 4.5 mg/kg **Time to Analysis:** 8 or 24 h	**BALF Cells:** 100 µg RER and 100 µg DEP increased total cell count and neutrophil influx after 8 h and returned to normal by 24 h. Smaller doses of RER and DEP induced no effect. CB induced no effect. **BAL Inflammatory/Injury Markers:** 100 µg RER increased BALF protein after 8 h. No effect was observed after 24 h nor with smaller doses of PM. RER significantly increased MMP-12 mRNA level after 8 h and HO-1 total lung mRNA content. No effects on MMP-2 or -9 or TIMP-1 or -2 expression were observed. No effects from CB or DEP were observed. **Cytokines:** 100 µg RER increased BAL, TNF-α and MIP-2 protein content after 8 h.
Reference: Batalha et al. (2002, 088109) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** NR **Weight:** 200-250 g	CAPs (Harvard Ambient Particle Concentrator) **Particle Size:** Mean: 2.7 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** Range: 73.5-733 µg/m^3 **Time to Analysis:** CAPs exposure 5 h/day, 3 days (consecutive). SO_2 exposure to induce CB 5 h/day, 5 days/wk, 6 wk. Killed 24 h postexposure.	**Histopathology:** CAPs slightly increased the wall thickness of small pulmonary arteries and edema in the adventitia and hyperplasia of the terminal bronchiole and alveolar ducts epithelium. **L/W ratio:** The L/W ratio decreased in CAPs-exposed rats as particle mass, Si, Pb, SO42-, EC and OC increased. Univariate analyses showed significant negative correlations between the L/W ratio and Si and SO42- in normal rats and Si and OC in CB rats. Multivariate analysis showed only Si to be significant in both groups.
Reference: Becher et al. (2007, 097125) **Species:** Mouse **Strain:** Crl/Wky (iNOS(-/-)) and C57Bl/6 **Gender:** Male **Age:** 8-14 wk **Weight:** 25 g	Suspended PM: SRM-1648 **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 1.6 µg/lung; 64 mg/kg **Time to Analysis:** 20 h	**Cytokines:** In both wild and KO strains, all particles caused increases of IL-6, MIP-2 and TNF-α levels. NADPH-oxidase KO mice showed significantly lower levels of IL-6 and MIP-2 responses to SPM comparatively to wildtype. iNOS KO mice showed significantly reduced IL-6, TNF-α, MIP-2 responses to SPM comparatively to wildtype. **Free Radicals:** SPM induced significant increases in free radical formation in alveolar type 2 cells but could be inhibited by DPI.
Reference: Bhattacharyya et al. (2004, 088095) **Species:** Mouse **Strain:** SD **Weight:** 200-250 g	Douglas Fir Wood Smoke (generated by burning wood at 400˚C in crucible oven) **Particle Size:** NR	**Route:** Nose-only Inhalation **Dose/Concentration:** 25 g/mouse **Time to Analysis:** Various exposure periods (0, 5, 1 0, 15, 20 min). Parameters measured after 24 h recovery period.	**Biochemical Parameters:** Lipid peroxidation increased after 20 min of wood smoke inhalation as did Myeloperoxidase at 20 min. No effects were observed at other times or for total antioxidant status, reduced or oxidized glutathione. **Antioxidant Enzyme Activities:** No effect was observed. **Histology:** Dose-dependent damage progressing from loss of cilia (5 min), degeneration of mucosal epithelium, loss of mucosal epithelium to disrupted mucosal epithelium with submucosal edema and inflammation. Changes persisted for up to 4 days.

Reference	Pollutant	Exposure	Effects
Reference: Cao et al. (2007, 097491) **Species:** Rat **Strain:** SH and WKY **Age:** 12 wk	$PM_{2.5}$ (Shanghai, China) Components: As, Cd, Cr, Cu, Fe, Ni, Pb, Zn, V, Ba, Se, Mg, Co, Mn **Particle Size:** $PM_{2.5}$	**Route:** IT Instillation **Dose/Concentration:** 1.6, 8.0 and 40 mg/kg **Time to Analysis:** Exposed 1/day for 3 days, sacrificed 24 h following last exposure	**BALF Cells:** PM decreased macrophages and increased neutrophils and lymphocytes in a dose-dependent manner. For the same exposed dose, WKY rats had a higher percentage than SH but a smaller percentage of neutrophils and lymphocytes. **BAL Inflammatory/Injury Markers:** LDH activity and TBARs increased a in dose-dependent manner. Notably, activity in SH rats was much higher than WKY at the same dose exposed for each dose level. **Cytokines:** PM induced pro-inflammatory cytokine release (IL-1β, TNF-α, CD44, MIP-2, TLR-4, OPN). Again, SH cytokine level was greater than WKY at all dose levels. PM induced anti-inflammatory cytokines CC16 and HO-1 in a similar manner but at much lower rate.
Reference: Carter et al. (2006, 095936) **Species:** Rat, Mouse, Hamster **Gender:** Female (all) **Strain:** F-344 (rat), B6C3F1 (mouse), Syrian Golden (hamster) **Age:** 7-10 wk	CB: Printex 90 **Particle Size:** primary size: 17 nm; 1.2-1.6 µm (aerosol aerodynamic diameter)	**Route:** Whole-body Inhalation **Dose/Concentration:** 1, 7, 50 mg/m^3 **Time to Analysis:** 6 h/day for 5 days/wk for 13 wk; 1 day, 3 m, 11 m post-exposure	**Superoxide:** Levels rose in all species at 50 mg dose. Hamsters had no increase at 7 and 1 mg doses. Mice also increased at 7 mg. Rats significantly increased at all dose levels. Rats maintained elevation except for the 50 mg dose at 11 mo postexposure; it declined but was still higher than control. Mice maintained elevation at 50 mg while 7 mg returned to control levels by 3 mo postexposure. **H_2O_2:** At 50 mg, increased levels in all species, with the highest in rat, were observed. At 7 mg, increased levels in rats and mice were initially seen but levels returned to baseline by 11 mo. Hamster levels were not significant. At 1 mg, no significant changes were observed. **NO:** Induced similar reactions as H_2O_2. Rat response continued through the study while mice and hamsters returned to baseline by 11 mo postexposure. Rats produced significantly higher levels at all times than other species. **BALF Cells:** CB induced significant increases in neutrophils at 7 and 50 mg for all species. Rats had the highest and most prolonged PMN response. Mice and hamsters had very similar reactions. **Cytokines:** TNF-α, MIP-2 and IL-10 increased in a dose-dependent manner in rats and mice. Hamsters increased for IL-10 only. MIP-2 levels were highest in rats. TNF-α level were similar in all three species at 50 mg, but hamsters started with a markedly higher basal level. **Glutathione Peroxidase:** Hamsters were the most responsive with significant increases at all levels. Rats and mice increased at 50mg and continued to increase for up to 11mo. Hamster levels declined with time but continued to be higher than control. **Glutathione Reductase:** Rats increased only at 50mg and remained elevated for up to 11mo. Mice increased at 7 and 50mg and remained elevated for up to 11mo. Hamsters increased at all levels at 11mo, but at 50mg, levels only increased post 1 day. **Superoxide Dismutase:** All species reacted in a dose-dependent manner. Rats were the least responsive. Rat SOD activity increased over time while rat and mouse activity decreased at 50mg. Data were consistent with cytokine data. **Summary:** Rats appear to produce proinflammatory responses while mice and hamsters produce antiinflammatory responses.

Reference	Pollutant	Exposure	Effects
Reference: Cassee et al. (2005, 087962) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto and SH/NHsd **Age:** 7 wk and 8-12 wk	CAPs: $PM_{2.5}$ Netherland suburban, industrial and freeway tunnel site collections Wistar rats pre-exposed to O_3 SO_4, NO_3 and NH_4 ions: 54 ± 4% suburban, 53 ± 7% industrial and 35 ± 5% freeway site conc. of total CAPS mass **Particle Size:** $PM_{2.5}$ (0.15<PM<2.5 µm)	**Route:** Nose-only Inhalation **Dose/Concentration:** PM 365-3720 µg/m^3 (results from 16 different exposures 2000, 2002); O_3: 1600 µg/m^3 (0.8 ppm) **Time to Analysis:** 8 h O_3 pre-exposure; 6 h CAPS exposure; 48 h post-exposure	**BALF Cells:** Wistar exhibited increased protein, albumin, NAG and decreased ALP activity and macrophage numbers. Wistar showed increased PMNs due to O_3, but was not significantly increased with additional CAPs exposure. SH showed no effect of CAPS except for the increased PMNs. **BAL Inflammatory/Injury Markers:** No effect on AL, LDH, Glutathione, GSSG, GSH, Uric Acid was observed. **Cytokines:** No effect on IL-6, MIP-2 or TNF-α was observed. CAPs induced an increase in CC16 plasma of SH rats. **Hematology:** CAPS induced an increase in RBC, HGB and HCT of Wistar rats and fibrinogen of SH rats. **Histology:** Wistar and SH rats had no obvious lung abnormalities. Small changes include increased macrophages and cellularity of centriacinar septa of O_3-only rats. Both O_3-only and O_3+CAPS showed bronchial epithelium hypertrophy and perivascular influx of PMNs. **BrdU Labeling Index of Terminal Bronchiolar Epithelium:** No CAPs effects were observed.
Reference: Chang et al. (2005, 097776) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 5 wk **Weight:** 25-30 g	UFCB: Ultrafine Carbon Black - Printex 90 (Degussa) **Particle Size:** 14 nm	**Route:** IT Instillation **Dose/Concentration:** 200 µg/100 uµ/mouse **Time to Analysis:** Parameters measured 4, 16, 21, 42 h post single exposure	**BALF Cells:** Neutrophil number was at control level at 4 h, increased after 16 h, peaked at 21 h and returned to normal at 42 h. No effect was observed for the macrophage count. **BAL Inflammatory/Injury Markers:** UfCB increased total protein with peak at 21 h. TNF-α increased at 4 h and returned to normal at 16 h. **VEGF (Vascular Endothelial Growth Factor):** Increased at 4 h and peaked at 16 h but remained elevated at 21 and 42 h. VEGF and total protein in BALF were correlated (R_2 = 0.7352). **ROS:** Pretreatment with NAC (ROS inhibitor) decreased induction of BALF VEGF and total protein by UfCB but did not fully block its effect. **Histology:** Thickened alveolar walls in lungs of UfCB-treated mice 16 h post-IT was observed.
Reference: Chang et al. (2007, 097475) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 5 wk **Weight:** 25-30 g	UFCB: Ultrafine Carbon Black - Printex 90 (Degussa) **Particle Size:** 14 nm diameter	**Route:** IT Instillation **Dose/Concentration:** 200 µg/mouse; 8 mg/kg **Time to Analysis:** Pretreatment with NAC (N-acetylcysteine) ip 320 mg/kg, 2 h before UFCB IT instillation. Parameters measured 24 h post exposure.	**BALF Cells:** Increased relative lung weight, total protein (2 fold), total cells (11 fold) and number of neutrophils were observed. BALF AM count was not affected. **BAL Inflammatory/Injury Markers:** Of the 33 identified proteins, the following 6 were confirmed and validated: Cp (ceruluplasmin), albumin, EGFR, LIFR (leukemia inhibitory factor receptor), α2M and β-actin. All were increased following UFCB exposure. The following were also identified: 3 membrane proteins, 3 intracellular proteins, 10 protease inhibitors and 6 antioxidants. UfCB increased LIFR and EGFR in BALF. UfCB significantly reduced EGFR and LIFR in lung homegenate. UfCB did not affect EGFR protein but down-regulated LIFR in A549 cells treated with UfCB. **Antioxidant:** Pretreatment with NAC reduced the intensity of albumin and α2M bands in BALF as well as most other proteins. Statistical analysis showed positive correlation between VEGF and albumin (R_2 = 0.796) and VEGF and α2M (R_2 = 0.7331) in BAL.

Reference	Pollutant	Exposure	Effects
Reference: Cho et al. (2005, 156344) **Species:** Mouse **Gender:** Male **Strains:** DBA/2J, 129P3/J, C57BL/6J, BALB/cJ, A/J, C3H/HeJ, C3H/HeOuJ **Age:** 6-8 wk	ROFA: Obtained from Power unit 4, Boston, MA Absent of LPS **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 6 mg/kg bw (150 µg in 50µl/ 25 g) **Time to Analysis:** 24 h; Additional HeJ and OuJ mice: single: 1.5, 3 and 6 h (compare TLR-mediated molecular events)	**BALF Cells:** Significant genetic effects on number of macrophages and PMNs after ROFA challenge. For PMNs, DBA/2J, C57BL/6J, BALB/cJ, and 129P3/J all induced increases significantly higher than C3H/HeJ. For macrophages, only the A/J strain induced increases significantly higher than C57BL/6J. Total protein, PMNs and macrophages all increased with HeOuJ inducing increases significantly different from HeJ. **BAL Inflammatory/Injury Markers:** Significant genetic effect on mean total protein concentration was observed. In decreasing order, DBA/2J, 129P3/J and C57BL/6J all induced increases significantly higher than C3H/HeJ. **TLR4 mRNA Expression:** A significant decrease was observed in TLR4 transcript level in HeJ- ROFA exposed mice post 1.5 h. Post 6 h, TLR4 levels were greater than the control levels. OuJ expression increased beginning 1.5 h post exposure. **TLR4 Protein Level:** Protein level of OuJ mice significantly exceeded (~2-3 fold) HeJ mice at 1.5, 3 and 6 h. **Activation of Downstream Signal Molecules:** Greater activation of MYD88, TRAF6, IRAK-1, NF-KB, MAPK, and AP-1 was observed in OuJ mice than in HeJ mice before the development of ROFA- induced pulmonary injury. **Cytokines:** IL-1β, LT-β, IL-1α, IL-7, IL-13, IL-16 increased in both strains (OuJ and HeJ). Levels of all cytokines above were significantly higher in OuJ than in HeJ.
Reference: Churg et al. (2003, 087899) **Species:** Human **Gender:** Female (Mexico City); Male, Female (Vancouver) **Age:** 66 ± 9yr (Mexico City); 76 ± 11yr (Vancouver) **Weight:** NR	PM (Mexico City- high PM region, Vancouver- low PM region) **Particle Size:** Geometric mean size of individual particles in tissue: 0.040-0.067 µm; Aggregates in tissue: 0.34-0.54 µm; Mexico City: 2.5, 10 µm	**Route:** Ambient Air Exposure. Autopsy Tissue. **Dose/Concentration:** 10 - >1000×10^6 g dry tissue; Mexico City: PM_{10}: 66 µg/m^3, Vancouver: PM_{10}: 25 µg, $PM_{2.5}$: 15 µg **Time to Analysis:** Lung samples taken from deceased lifelong Mexico City residents and Vancouver residents >20 yr. Subjects were never-smokers, did not work in dust occupations or cook with biomass fuels.	The lungs from Mexico City residents showed increased muscle and fibrous tissue in the membranous bronchioles and respiratory bronchioles compared to the Vancouver residents. Pigmented dust, lumental distortion and carbonaceous aggregates of UFPs were present in the Mexico City lungs.
Reference: Costa et al. (2006, 088438) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** 60 day	ROFA FP&L plant #6 oil, 1% sulfur **Particle Size:** ~1.95 µm	**Route:** IT Instillation, Nose-only Inhalation (IH) **Dose/Concentration:** IT instillation = 110 µg/rat IH = 12 mg/m^3 **Time to Analysis:** IT instillation: single; IH: 6 h 24, 48, 96 h (histopathology 24 and 48 only)	**ROFA distribution:** IH and IT instillation resulted in equivocal distribution (µg/g lung tissue) in 5 different lung lobes. **Airway Hyperactivity:** IT instillation resulted in doubled airway hyperreactivity at 24 h which was sustained for 96 h. IH hyperreactivity did not reach statistically significant level. **BALF Cells:** Neutrophils peaked at 24 h and slowly declined at 48 and 96 h. **BAL Inflammatory/Injury Markers:** IH and IT instillation showed very similar responses (R_2 = 0.98). Time-dependent increases were observed for protein and LDH. **Lung Pathology:** IT instillation showed more alveolitis, bronchial inflammatory and fibrinous fluid infiltrate. IH showed relatively more congestion of small airways and alveolar hemorrhage.

Reference	Pollutant	Exposure	Effects
Reference: Courtois et al. (2008, 156369) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 12-14 wk **Weight:** NR	PM (SRM 1648; 63% inOC, 4-7% OC, >1% mass fraction- Si, S, Al, Fe, K, Na) Carbon black (FW, P60) UF, fine TiO_2 **Particle Size:** PM mean diameter: 0.4 µm; Carbon black: FW- 13 nm, P60- 21 nm; TiO_2 mean diameter: 0.14 µm	**Route:** IT Instillation **Dose/Concentration:** 5 mg PM or TiO_2 **Time to Analysis:** 6-72 h	Particles were present in lung parenchyma that was removed 12 and 72 h post-instillation.
Reference: Dick et al. (2003, 036605) **Species:** Mouse **Gender:** Female **Strain:** CD1 **Age:** 8-10 wk **Weight:** 20-25 g	CO: PM Coarse FI: PM Fine FU: PM ultrafine PM collected in RTP, NC **Particle Size:** CO: 3.5-20 µm; FI: 1.7- 3.5 µm; FU: <1.7 µm	**Route:** IT Instillation **Dose/Concentration:** 10 µg, 50 µg, 100 µg/mouse; 0.5, 2.5, 5.0 mg/kg **Time to Analysis:** DMTU 500 mg/kg bw 30 min pre-exposure for some mice. Parameters measured 18 h post-exposure.	**Particle Characteristics:** S increased (CO-33.20 µg/mg, FI- 49.44 µg/mg FU- 122.79 µg/mg) with decreasing particle size (mostly in the water-soluble fraction). Fe and Cu higher in coarse and fine fractions (mostly present in the insoluble). CO PM contained more nickel (in both soluble and insoluble) than FI or FU particles. Also, endotoxin levels similar in CO and FI; much lower in FU (0.165 EU/mg). **BALF Cells:** PMN increased with exposure for all 3 fractions except 100 µg FI. **BAL Inflammatory/Injury Markers:** Albumin increased only at 100 µg FI. No differences in NAG or LDH observed. **Cytokines:** IL-6 increased at 100 µg dose for all 3 fractions with similar responses. TNF-α increased a 100 µg dose of fine PM vs control. **Effect of PM After Pre-treatment w/DMTU:** Systemic administration of DMTU alone depicted a two-fold increase in total antioxidant capacity. **DMTU halved neutrophil response observed with PMs alone:** No fractions were increased over DMTU alone which was at least two-fold saline control. IL-6 concentrations were drastically reduced in the DMTU group for the mice exposed to coarse particles (all fractions were reduced but only coarse had a significant response). TNF-α levels were decreased after treatment with particles and DMTU but treatment with particles and saline (control) produced similar results.
Reference: Dybdahl et al. (2004, 089013) **Species:** Mouse **Gender:** Female **Strain:** BALB/CJ or trans-genic (MutaMouse) **Age:** 9-10 wk **Weight:** ~20 g	DEP: SRM 1650 (NIST) **Particle Size:** DEP: NR; Control: PM 0.13 µm diameter	**Route:** Nose-only Inhalation **Dose/Concentration:** I: 20, 80 mg/m^3 II: 5, 20 mg/m^3 **Time to Analysis:** I: single exposure 90 min; II: 90 min/day for 4 days; I & II: parameters measured 1, 3, or 22 h post exposure	**Cytokines:** A single 90 min DEP exposure increased IL-6 gene level dose-dependently in the lung. For 80 mg/m^3 DEP, significantly higher IL-6 gene level was observed, both 1 and 22 h post exposure. For 20 mg/m^3 DEP, a significantly higher IL-6 level was observed at 1 h post exposure but normalized at 3 h. **BALF Cells:** Inhalation of DEP did not decrease viability of BALF cells. For mice exposed to 20 mg/m^3 DEP, at 1 h post exposure in BAL fluid there was 3 fold increase in total cell number. **DNA Damage:** Level of 8-oxodG increased post single exposure with 80 mg/m^3 inducing levels significantly higher than controls. Repeated exposures were associated with significantly higher DNA strand breaks.
Reference: Elder et al. (2004, 055642) **Species:** Rat **Gender:** Male **Strain:** F344, SH **Age:** 23 m (Fisher), 11-14 m (SH)	UFP: argon-filled chamber with electric arc discharge (TSI, Inc., St. Paul, MN) **Particle Size:** 36 nm	**Route:** Whole-body Inhalation. **Dose/Concentration:** UFP: 150 µg/m^3 bw; LPS: 2 mg/kg **Time to Analysis:** 6 h, 18 h	**BALF Cells:** Neither inhaled UFP nor LPS cause a significant increase in BALF total cells or percentage of neutrophils in either rat strain. No significant exposure-related alteration in total protein concentration was observed. In both rat strains LPS induced a significant increase in the amount of circulating PMNs. When combined with inhaled UFP, PMNs decreased; for F-344 rats, this decrease was significant. **ROS in BALF:** In F-344 rats, both UFP and LPS have independent and significant effects on DCFD oxidation. Effects were in opposite directions; particles decreased ROS whereas LPS increased ROS.

Reference	Pollutant	Exposure	Effects
Reference: Elder et al. (2004, 087354) **Species:** Rat **Gender:** Male **Strain:** F344 **Age:** 21 mo	Freshly generated vehicle exhaust emissions from I-90 between Rochester and Buffalo, NY **Particle Size:** NR	**Route:** Whole-body Inhalation; IT Instillation (Influenza) **Dose/Concentration:** Vehicle exhaust: 0.95-3.13×10^5 particles/cm^3 Endotoxin: 84 EU Influenza (IV): 10, 000 EID 50 in 250 µl **Time to Analysis:** 1×6 h, 3×6 h or both. Parameters measured 18 h post-exposure. 48 h prior to on-road exposures, instilled intratracheally with IV. Immediate pre-exposure of priming agent endotoxin. EXPERIMENTS 1: LPS + PM 6 h 2: LPS + PM 6 h, 3×6 h 3: IV + PM 6 h 4: IV + PM 6 h, 3×6 h	No departures from normal baseline cellular or biochemical values were observed, suggesting that on-road exposures were well tolerated by the rats. **BAL Inflammatory/Injury Markers:** Increase in total protein concentration, LDH and B-glucuronidase activities were observed. **Specific results according to groups 1-4 are as follows:** **Experiment 1:** No endpoints revealed significant differences between groups of rats exposed to gas phase only versus the gas-phase/particle mixture. **Experiment 2:** Combination of endotoxin and particles produced greater inflammatory responses than those treated with saline and particles post 1 day. After 3 days, no statistically significant changes were noted. **Experiment 3:** Influenza virus significantly increased ROS release in BALF cells. **Experiment 4:** Influenza virus significantly increased both percentage of PMNs in BALF and BALF cell ROS release.
Reference: Elder et al. (2005, 088194) **Species:** Rat, Mouse, Syrian Golden Hamster **Gender:** Female **Strain:** F-344, B6C3F1, FIB	HSCb: Printex-90 high surface area carbon black, Deguss-Huels (Trostberg, Germany). LSCb: Sterling V, low surface area carbon black, Cabot (Boston, MA) **Particle Size:** HSCb = 14 nm, LSCb = 70 nm	**Reference:** Whole-body Inhalation **Dose/Concentration:** 0, 1, 7, 50 mg/m^3 HSCb; 50 mg/m^3 LSCb (rats only) **Time to Analysis:** 6 h/day, 5 daus/wk for 13 wk. Parameters measured 1 day, 3 mo, 11 mo post-exposure	**Body Weight:** Environmental changes pre and post-exposure affected test subjects' life spans, particularly hamsters. Hamsters also experienced significant loss of body weight when exposed to high doses of HSCb. **Effects of Carbon Black:** In rats, lung weight of the high dose HSCb doubled. After 11mo, analysis of all lungs showed no significant difference. Mice had the highest relative lung burdens at the end of exposure time but also cleared particles faster at high doses than rats. However, clearance slowed over the 11mo recovery period, especially in high dose mice. Hamsters showed significant elevations in lung carbon black burden for all exposures at all time points. Hamsters exposed to high dose HSCb exhibited impaired clearance. **BALF Cells:** Presence of PMNs was limited to the mid and high dose groups. Overall maximal response was reached in mice and hamsters, but not in rats with increasing mass dose of HSCb.
Reference: Evans et al. (2006, 097066) **Species:** Rat **Gender:** Male **Strain:** SD	DEP: collected under dry, outdoor, ambient conditions from tractor exhaust pipe (1985, Japanese ISEKI 1500 cc tractor) burning Esso 2000 diesel and 20/30 mixture of Esso light engine oil. 10% UF, 90% fine Cabosil: amorphous silicon dioxide 16% UF, 84% fine **Particle Size:** DEP: 30 nm; Cabosil: 7 nm	**Route:** IT Instillation **Dose/Concentration:** 1 mg/rat DEP; 1 mg/rat Cabosil **Time to Analysis:** Pretreatment with 0.5 unit of bleomycin; IT 3 or 7 days after pre-treatment; 1wk post-IT	**Lung permeability:** In bleomycin-treated group, obvious inflammatory status and edema within the lung was observed. This was shown by significant increases in acellular protein and free cells. **Changes in lung:** Body weight ratio, lung surface protein content, free cell counts, and apical surface protein of rat type I cells were only altered by bleomycin treatment and not particle exposure.

Reference	Pollutant	Exposure	Effects
Reference: Finnerty et al. (2007, 156434) **Species:** Mouse **Gender:** Male **Strain:** C57BL/61 **Age:** 12 wk **Weight:** 24.3 ± 0.3 g	Coal Fly Ash (generated at U.S EPA National Risk Management Research Laboratory by burning Montana subbituminous coal under conditions simulating full-scale utility boiler conditions) Transition metals of Coal Fly Ash: Fe, Mg, Ti, Mn, V **Particle Size:** >$PM_{2.5}$	**Route:** IT Instillation **Dose/Concentration:** PM: 200 mg/mouse; 9.1 mg/kg PM+LPS10: 200 mg PM+10 mg LPS PM+LPS100: 200 mg PM+100 mg LPS LPS: 100 µg **Time to Analysis:** 18 h	**BALF Cells:** No significant differences in platelet concentration or white blood cell count in any groups were observed. The percentage of neutrophils increased significantly with PM+LPS100. PMN rose in PM groups and increased further with LPS treatment. Increases in PM+LPS were groups statistically significant. More leukocytes were present in the alveolar space in PM+LPS10 compared to the PM group. The most severe response was in the PM+LPS100 group. **Cytokines:** Plasma TNF-α and IL-6 significantly increased for the PM+LPS100 group. An additive effect of LPS and PM for IL-6 was observed. For saline and PM groups, pulmonary TNF-α was below detection range. A synergistic effect for TNF-α was observed. A less than additive effect for IL-6 was observed. Pulmonary TNF-α significantly increased in the PM+LPS100 group. Pulmonary IL-6 significantly increased in both PM+LPS groups.
Reference: Fujimaki et al. (2006, 096601) **Species:** Mouse **Gender:** Male **Strain:** IL-6(-/-) and WT: B6J129Sv (control) **Age:** 5-6 wk	DEP: collected from a 4-cylinder, 2.74 L, Isuzu diesel engine **Particle Size:** 0.4 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** 1.0, 3.0 mg/m^3 **Time to Analysis:** 12 h/dayfor 4 wk. Parameters measured 1 day post-exposure	**BALF Cells:** Treatment significantly increased BAL cells from WT mice at both dose levels. The increase of macrophages and neutrophils were dose-dependent. An increase in lymphocytes were present in WT mice with the low dose. No significant increase in cells were observed from IL-6 (-/-). **Cytokines:** TNF-α largely increased in IL-6(-/-) mice exposed to 3 mg/m^3 compared to WT mice. IL-6 production increased in WT mice exposed to 3 mg/m^3. CCL3 increased in both WT and IL-6(-/-) at high dose. IL-1β remained at the control level.
Reference: Gerlofs-Nijland et al. (2005, 088652) **Species:** Rat **Gender:** Male **Strain:** SH/NHsd **Age:** 11-12 wk **Weight:** 250-350 g	RTD: road tunnel dust (obtained from a Motorway tunnel in Hendrik-Ido-Ambacht, Netherlands) EHC-93 (Ottawa, Canada) **Particle Size:** Coarse: 2.5- 10 µm; fine: 0.1- 2.5 µm	**Route:** IT Instillation **Dose/Concentration:** 0.3, 1, 3, 10 mg/kg; EHC-93: 10 mg/kg **Time to Analysis:** 4, 24, 48 h	**BALF Cells:** PMN significantly increased in RTD (3 and 10 mg/kg dose) and EHC-93 exposed animals at 24 h and decreased by 48 h but remained statistically significant. AM numbers decreased for 3 mg/kg RTD group at 4 h. **BAL Inflammatory/Injury Markers:** Myeloperoxidase (measured at 24 h in 1, 3, 10 mg/kg RTD groups) was elevated in a dose-dependent manner. RTD induced time-dependent increases in LDH activity at 24 and 48 h, although these increases were less than EHC-93 values at the same time points. Alkaline phosphatase increased dose-dependently for RTD at 48 h. GSH decreased at 24 h to approximately the same levels in 0.3, 1, and 3 mg/kg RTD dose groups. Uric acid only decreased in 1 mg/kg RTD group at 24 h. **Cytokines:** IL-6 levels were elevated only at 10 mg/kg for RTD and EHC-93 at 4 and 24 h; it remained elevated for EHC-93 at 48 h. A dose-dependent increase in TNF-α at 4 h for RTD was observed. TNF-α levels remained elevated only for the 10 mg/kg groups at 24 h and returned to control levels by 48 h. A dose-dependent increase in MIP-2 for all RTD dose groups were observed and remained elevated through 48 h for both PM types (although values were returning to control levels). **Pulmonary Histopathology:** A dose-dependent increase in the number of inflammatory foci at 24 and 48 h for 3 and 10 mg/kg RTD groups was observed. The response was even greater for the EHC-93 exposed group at similar time points.

Reference	Pollutant	Exposure	Effects
Reference: Gerlofs-Nijland et al. (2007, 097840) **Species:** Rat **Gender:** Male **Strain:** SH/NHsd **Age:** 13 wk **Weight:** 250-350 g	PM samples collected from: 1. MOB high traffic density 2. HIA high traffic density 3. ROM high traffic density 4. DOR moderate traffic density 5 MGH low traffic density 6 LYC low traffic density **Particle Size:** Coarse: 2.5 - 10 µm; Fine: 0.1 - 2.5 µm	**Route:** IT Instillation **Dose/Concentration:** 3, 10 mg/kg **Time to Analysis:** 24 h	**BALF Cells:** Pulmonary inflammation was induced in a significant and dose-dependent manner for both dose levels. Inflammation in the BALF included airway neutrophilia, increased macrophage numbers and mild lymphocytosis. Both coarse and fine PM caused dose-dependent alveolitis. Fine PM from LYC (10 mg/kg dose) also caused some bronchiolitis. **BAL Inflammatory/Injury Markers:** LDH was significantly increased for all doses of coarse PM and for the high dose of fine PM. BALF protein concentration was observed predominantly at the high dose of coarse PM. Location ROM had evidence of attenuated responses with fine PM. Ascorbate concentrations were reduced but were only significant for rats exposed to the highest dose of coarse PM fractions from the locations MOD, HIA, and LYC. **Cytokines:** TNF-α concentrations increased for all coarse samples with the exception of DOR and LYC. Fine PM induced similar responses for all sites. MIIP-2 concentrations increased only at certain sites for coarse but not fine PM. **Location-related Differences:** Coarse PM from MOB, HIA and MGH induced higher LDH responses than other locations. Coarse PM from HIA produced BALF protein concentrations higher than LYC and ROM. MGH induced greater amounts of BALF protein than ROM. Coarse PM from LYC lowered fibrinogen values more than PM from location MOB, HIA, and MGH. Fine PM showed less differences among the various sites. **Particle Correlation:** Fine PM exhibited significant correlation between zinc content and BALF cytotoxicity markers protein and LDH - mainly from HIA. Fine PM also exhibited positive correlations with copper and barium. Coarse PM showed positive correlation with barium and copper, mainly from MOB.
Reference: Gerlofs-Nijland et al. (2009, 190353) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 12 wk **Weight:** 200-300 g	PM (Prague, Czech Republic; Duisburg, Germany; Barcelona, Spain) (Prague and Barcelona coarse PM organic extracts) **Particle Size:** Coarse: 2.5-10 µm, Fine: 0.2-2.5 µm	**Route:** IT Instillation **Dose/Concentration:** 7mg/kg **Time to Analysis:** 24 h	Cytotoxicity (LDH, protein, albumin) and inflammation (NAG, MPO, TNF-α were increased by PM, and were greatest in the coarse PM fraction. Metal-rich PM had greater inflammatory and cytotoxic effects. PAH content influenced greater inflammation (including neutrophils), and cytotoxicity. Generally, whole PM and coarse PM were more potent than organic extracts and fine PM, respectively.
Reference: Ghio et al. (2005, 088272) **Species:** Rat **Gender:** Male **Strain:** N8 b/b Belgrade rats and N8+ Ib Belgrade controls	Oil Fly Ash (Southern Research Institute, Birmingham, AL) **Particle Size:** 1.95 ± 0.18 µm (MMAD)	**Route:** IT Instillation **Dose/Concentration:** 500 µg/rat; 2 mg/kg **Time to Analysis:** 24 h	**BALF Cells:** Homozygous Belgrade with mutation G185R had higher levels of Fe and V 24 h post-exposure. This may demonstrate a decreased ability to remove Fe and V from the lower respiratory tract than heterozygous +Ib littermates. This also indicates that DMT1 is normally responsible for at least some Fe and V uptake; thus, a defective DMT1 transports less. **BAL Inflammatory/Injury Markers:** Increased protein and LDH concentrations in the homozygous strain were observed when compared to control
Reference: Ghio et al. (2005, 088275) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** 60 day **Weight:** 250-300 g	Ferric ammonium citrate (FAC) Vanadyl sulfate ($VOSO_4$) **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 0.5 mL 100 µm FAC/rat; 0.5 mL 10 µm $VOSO_4$/rat; 500 µg oil fly ash; 2 mg/kg **Time to Analysis:** Single or double exposure with 24 h rest period. Parameters measured 15, 30, 60 min, 24 h post-exposure.	**DMT1 Immunohistochemistry and Lung Injury:** FAC increased and $VOSO_4$ decreased -IRE DMT1 staining. Same exposures had no effect on +IRE DMT1. -IRE DMT1 expression in macrophages, airway and alveolar epithelial cells increased with increased Fe exposure. Vanadium nearly eliminated staining except in alveolar macrophages. Increased metal clearance with pre-exposure to FAC. Less metal clearance with pre-exposure to $VOSO_4$. Pre-exposure to iron diminished lung injury whereas pre-exposure to vandium increased lung injury after oil fly ash instillation. Lung injury measured by concentration of protein and LDH in BAL.

Reference	Pollutant	Exposure	Effects
Reference: Gilmour et al. (2007, 096433) **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 10-12 wk **Weight:** 20-22 g	PM - CO, FI, UF (obtained from U.S. Seattle (S), Salt Lake City (SL), South Bronx (SB), Sterling Forest (SF)) SB: included 35% sulfate, 22% gasoline, diesel and brake wear. SF: 48% sulfate. SL: 34% wood combustion and 28% sulfate S: 39% wood combustion and 29% sulfate Residual oil combustion and soil dust less than 5% for all sites. **Particle Size:** CO: 2.5-10 µm; FI: ≤ 2.5 µm; UF: ≤ 0.1 µm	**Route:** Oropharyngeal Aspiration **Dose/Concentration:** 25 µg or 100 µg PM; 1.25 or 5 mg/kg **Time to Analysis:** 18 h	**BALF Cells:** PMN increased with the high dose of CO samples from SB, SL, S, but not SF. No significant increases from FI were observed, though the high dose induced increased PMN. UF from SL caused a highly variable response. **BAL Inflammatory/Injury Markers:** Seattle CO fractions showed no dose-dependent effect on protein concentration. Results for other locations were distinctly higher with 100 µg dose than 25 µg and saline doses. SL CO high dose induced the most significant increase. LDH response was weakly dose-related. Only SB showed a statistically significant increase for LDH with the high dose UF. **Cytokines:** MIP-2 was similar to PMN response. SB CO induced the most significant response. SL UF was highly variable. **Particle Characteristics:** LPS was higher in S (CO, FI, UF) and SL (CO, FI, UF). Zn levels were highest in SB (CO, FI, UF). Fe was higher in all CO and FI samples with SB CO inducing the highest.
Reference: Gilmour et al. (2004, 057420) **Species:** Mouse **Gender:** Female **Strain:** CD1 **Age:** 8-10 wk **Weight:** 20-25 g	Coal Fly Ash MU: Montana Ultrafine MF: Montana Fine MC: Montana Coarse KF: W. Kentucky Fine KC: W. Kentucky Coarse Particle Characteristics: Montana Sulfur 0.83%, Ash 11.72%. Trace amounts of Ba, P, Sr, V, Nb, Cd, Se, Ga, Cu. Depleted in Si, Al, Fe, Mg, Ti. Kentucky Sulfur 3.11%, Ash 8.07% **Particle Size:** Coarse: >2.5 µm; Fine: <2.5 µm; Ultrafine: <0.2 µm	**Route:** Oropharyngeal Aspiration **Dose/Concentration:** 25 ug or 100 µg/mouse **Time to Analysis:** 18 h	**BALF Cells:** PMN highly increased for MU at both doses. The level was comparable to the positive control. PMN also increased with KF at high dose. Coarse particles caused no significant increase in PMN. Number of macrophages did not change, but NAG increased significantly with MU for both dose levels and with KF and MF at high dose level. **BAL Inflammatory/Injury Markers:** Total protein and LDH was not significantly elevated. Albumin concentration increased significantly after treatment with the fine high dose of both particle types. **Cytokines:** MU particles caused a significant increase in TNF-α. MIP-2 increased in all fine and ultrafine PM-instilled animals with the highest in the MU and KF at both doses. IL-6 was detectable only in the BALF of MU and KF with substantial variability. The IL-6 levels were not significant.
Reference: Gilmour et al. (2004, 087948) **Species:** Rat **Gender:** Male **Strain:** SH/NQIBR, WKY **Age:** 12 wk **Weight:** 280-340 g	PM (collected from precipitator unit of an oil burning power plant in Boston) Measured Components of PM: S, Zn, Ni, V, Al, Cu, Pb, Fe, Ca, Na, K, Mg, Endotoxin **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 0.0, 0.83, 3.3, and 8.3 mg/kg in SH rats; 0.0 or 3.3 mg/kg in WKY and SH rats **Time to Analysis:** 24 h	**BALF Cells:** No increase in macrophage number was observed in either rat strain following saline or PM exposure at 24 h. **BAL Inflammatory/Injury Markers:** LDH activity increased in a dose-related manner; this was observed in SH rats after exposure to 0.83, 3.33 and 8.3 mg/kg PM. SH rats showed greater lung permeability following PM exposure than WKY rats. SH rats showed acute lung inflammatory response after exposure to PM when compared to WKY rats. **Cytokines:** MIP-2 mRNA expression increased significantly in SH PM exposure group only. No significant differences in TNF-α RNA expression in either WKY, SH rats or control treatment groups were observed. **CD14:** A significant increase in lung CD14 protein was observed only in SH rats exposed to PM. **TLR4:** A significant increase in TLR4 protein in SH rats exposed to PM was observed. **NF-κB:** A significant increase in NF-κB binding protein in the nuclei of SH rats exposed to PM was observed. This effect was not observed in the control of PM-exposed WKY rats.

Reference	Pollutant	Exposure	Effects
Reference: Gilmour et al. (2004, 054175) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 12 wk	ufCB: Ultrafine carbon black (Printex 90 (Degussa) CB: (Huber 990, HR. Haeffner and Co) **Particle Size:** ufCB: 14 nm; CB: 260 nm (primary particle diameter)	**Route:** Whole-body Inhalation **Dose/Concentration:** ufCB: 1.66 mg/m^3 fCB: 1.40 mg/m^3 Number concentrations ufCB: 52380 particles/cm^3 fCB: 3800 particles/cm^3 **Time to Analysis:** Exposed for 7 h. Sacrificed 0, 16 or 48 h post-exposure.	**BALF Cells:** Total number of cells increased significantly in UfCB-exposed rats at 0 and 16 h. Recruitment of cells did not occur in response to CB exposure. PMNs increased significantly in the BALF of ufCB-exposed rats at 16 h. Leukocytes remained unchanged following CB exposure but increased significantly at 0 and 48 h post exposure to ufCB. **Cytokine mRNA:** A significant increase in BALF MIP-2 mRNA expression was observed at 48 h. No differences in MIP-2 mRNA levels were observed in the whole lung tissue.
Reference: Godleski et al. (2002, 156478) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** NR **Weight:** 200-250 g	CAPs (Boston; Harvard Ambient Particle Concentrator) **Particle Size:** 0.27 ± 2.3 µm (diameter)	**Route:** Whole-body Inhalation **Dose/Concentration:** 73.5-733 µg/m^3 **Time to Analysis:** Exposed 5 h/days, 3 days (consecutive). BAL 24 h post-exposure	**BALF Cells and Inflammatory Markers:** PMNs significantly increased with CAPs exposure and also in relation to CAPs mass, Br, SO_4^{2-}, EC, OC and Pb. An overall increase in pro-inflammatory mediators and decrease in immune enhancer and evidence of vascular endothelial responses occurred with CAPs exposure.
Reference: Gottipolu et al. (2009, 190360) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto, SH **Age:** 14-16 wk **Weight:** NR	DE (30-kW (40hp) 4-cylinder indirect injection Deutz diesel engine) (O_2- 20%, CO- 1.3-4.8 ppm, NO- <2.5-5.9 ppm, NO_2- <0.25-1.2 ppm, SO_2- 0.2-0.3 ppm, OC/EC- 0.3 ± 0.03) **Particle Size:** Number Median Diameter: Low- 83 ± 2 nm, High- 88.2 nm; Volume Median Diameter: Low- 207 ± 2 nm, High- 225 ± 2 nm	**Route:** Inhalation **Dose/Concentration:** Low- 507 ± 4 µg/m^3, High- 2201 ± 14 µg/m^3 **Time to Analysis:** Exposed 4 h/day, 5 days/wk, 4 wk. Necropsied 1 day post-exposure.	DE increased neutrophils in a concentration-dependent manner, and GGT activity at the high dose. Particle-laden macrophages were found in DE-exposed rats.
Reference: Gunnison and Chen (2005, 087956) **Species:** Mouse **Gender:** Male **Strain:** DK (ApoE$^{-/-}$, LDLr$^{-/-}$) **Age:** 18-20 wk	CAPS (Northeastern regional background) Ambient air copollutants measured O_3, NO_2 **Particle Size:** 389 ± 2 nm	**Route:** Whole-body Inhalation **Dose/Concentration:** CAPS = 131 ± 99 µg/m^3 including O_3 = 10 ppb and NO_2 = 4.4 ppb **Time to Analysis:** 6 h/day, 5 days/wk for 4 mo (5/12/03-9/5/03). Sacrificed 3-4 days post-exposure.	**Microarray Data:** 13 genes in the heart tissue and 47 genes in the lung tissue were identified as possibly affected. Strict standards (1.5 fold response, 10% false discovery rate) resulted in responses by only 1/13 genes (Rex3 - no known heart physiology) in the heart tissue and 0/47 genes in the lung tissue. Using more liberal response (nonstatistical) standards (1.5 fold only) and comparison of each CAPS animal with all 3 control animals (3x3 array) resulted in possible effects on 7 additional genes in the heart tissue and 37 genes in the lung tissue.
Reference: Gurgueira et al. (2002, 036535) **Species:** Rat **Gender:** Male **Strain:** SD **Weight:** 250-300 g	CAPs (Harvard Ambient Particle Concentrator) CB (C198 Fischer Scientific, Pittsburg, PA USA) Composed of 85.9 ± 0.2% Carbon, 13.0 ± 0.2% O_2, 1.17 ± 0.2% Sulfur ROFA (Boston, MA USA oil-fired power plant) **Particle Size:** CAPs: 1-2.5 µm; CB: <2.5 µm; ROFA: <2.5 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** 300 ± 60 µg/m^3 **Time to Analysis:** 1, 3, 5 h CAPs Exposure followed by immediate post-exposure analysis. 5 h CB, immediate analysis. 30min ROFA, Immediate analysis.	**In situ Chemiluminescence(CL):** Data show a significant increase in lung and heart CL at 5 h. Lung CL increased linearly with time of exposure. **Oxidants:** CAPs-initiated oxidative stress was not detectable in those rats allowed to recover in room air after the simulated "peak" in particulate air pollution. Rats breathing particle-free filtered air for 3 days had significantly lower levels of oxidants. Exposure to inert CB did not exert oxidant effects on the heart and lung. **BAL Inflammatory/Injury Markers:** The water content of the lung and heart increased significantly upon exposure to CAPs but not to filtered air and increased as a function of length of exposure. Rats breathing CAPs also showed increases in LDH and CPK as a function of length of exposure. **Antioxidant Enzymes:** Data showed an increase in SOD and catalase activities in both the lung and heart. The pattern of increase was tissue specific.

Reference	Pollutant	Exposure	Effects
Reference: Hamoir et al. (2003, 096664) **Species:** Rabbit **Strain:** New Zealand **Age:** 12-16 wk **Weight:** 2.8 ± 0.5kg	PSC: Polystyrene particles, Carboxylate modified, 3 types PSA: Polystyrene particles, Amine modified, 1 type **Particle Size:** PSC: 24, 110 or 190 nm (PSC24, PSC110, PSC190); PSA: 190 nm	**Route:** IT Instillation **Dose/Concentration:** PSC24: 0.04 or 4 mg/rabbit PSC110, PSC190, PSA190: 4 mg/rabbit **Time to Analysis:** 0, 30, 60, 90, 120 min	**Capillary Filtration Coefficient:** A time-dependent increase correlating to total number of particles/surface area, not particle size, was observed. PSA induced a significant increase in microvascular permeability as compared to PSC. This suggests that the number of particles exposed should be considered an important parameter for measuring air quality rather than total particle surface area.
Reference: Happo et al. (2007, 096630) **Species:** Mouse **Gender:** Male **Strain:** C57BL/6J **Weight:** 19-30 g **Age:** 10-11 wk	PMC (Coarse) PMF (Fine) PMUF (Ultrafine) Collected in 6 European cities: Duisburg, Prague, Amsterdam, Helsinki, Barcelona, Athens **Particle Size:** PMC: PM_{10}-2.5; PMF: $PM_{2.5}$-0.2; PMUF: PM0.2	**Route:** IT Instillation **Dose/Concentration:** 1, 3, 10 mg/kg Time course: 10 mg/kg **Time to Analysis:** 1. Dose-Response study: parameters measured 24 h post exposure. 2. Time course study: parameters measured 4, 12, 24 h post single exposure (at 10 mg/kg).	**BALF Cells:** 1. For the dose-response study, all the PMC samples exhibited dose-dependent increases of total cell numbers. The 3 and 10 mg/kg doses of PMC induced statistically significant increases. At 10 mg/kg, only 2/6 samples induced statistically significant increases. No PMUF samples induced effects at any dose. 2. For the time-response study, no increases in cell numbers were shown at 4 h. Though the levels induced by PMC at 24 h were lower than at 12 h, both levels were statistically significant. PMF induced statistically significant increases only at 12 h for 4/6 samples. PMUF induced only 1 significant increase at 12 h; the 24 h time point was not tested. **BAL Injury Markers:** 1. The lower doses of 1 and 3 mg/kg did not induce significant increases in any of the PM samples, except for PMUF-Athens. All 6 samples of PMC, at 10 mg/kg, induced significant increases. At 10 mg/kg, 4/6 PMF samples induced significant increases. 2. At 4 h, none of the samples increased protein concentration. The PMC samples, excluding Prague, induced significantly higher concentrations at 12 h. At 24 h, only 3/6 PMC samples induced significant increases. Only 2 PMF samples induced significant increases at 12 and 24 h. At 12 h, effects induced by PMUF were minimal and inconsistent; the 24 h time point was not tested. **Cytokines:** 1. Only PMC induced dose-dependent responses that reached statistical significance at 10 mg/kg. PMF and PMUF induced minimal and inconsistent responses. 2. TNF-α levels increased significantly at 4 and 12 h by PMC. At 24 h, TNF-α levels returned to near control levels. PMF, at 4 h, induced statistically significant increases for 3/6 samples and significant increases in 2/6 samples at 12 h. No PMUF samples significantly increased TNF-α levels. PMC induced the highest IL-6 levels at 4 h. Levels at 12 and 24 h were reduced with 6/6 and 3/6 samples showing statistically significant increases, respectively. PMF showed a similar trend with 4 h inducing the highest levels that were reduced at 12 and 24 h. Of the PMUF samples, only the Helsinki and Duisburg samples induced statistically significant results at 4 and 12 h. Generally, the PMUF responses were negligible when compared to PMC and PMF. 2. All PMC samples induced the highest levels of KC production at 4 h. At 12 and 24 h, levels were reduced but 4/6 samples induced statistically significant levels. PMF showed a similar trend- the highest levels were induced at 4 h (in 3/6 samples). PMUF at 4 h showed small, though not significant, increases. At 12 h, only 2 samples showed statistically significant differences from the control; the 24 h time point was not tested.
Reference: Harder et al. (2005, 087371) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 14-17 wk **Weight:** NR	Carbon UFP **Particle Size:** 37.6 ± 0.7 nm (diameter)	**Route:** Inhalation **Dose/Concentration:** 180 µg/m^3 **Time to Analysis:** 24 h exposure. 3 day recovery.	UFP induced mild pulmonary inflammation, significantly increased PMN, and increased the total protein and albumin concentrations. Particle-laden macrophages sporadically accumulated in the alveolar region.

Reference	Pollutant	Exposure	Effects
Reference: Harkema et al. (2004, 056842) **Species:** Rat **Gender:** Male **Strain:** F344, BN **Age:** 10-12 wk **Weight:** NR	CAPs (Detroit; July-Sept. 2000; Harvard Ambient Fine Particle Concentrator) **Particle Size:** 2.5 µm (diameter)	**Route:** Inhalation, IT Instillation. **Dose/Concentration:** 4 day concentration: 676 ± 288 µg/m^3, 5 day concentration: 313 ± 119 µg/m^3, July concentration: 16-185 µg/m^3, September concentration: 81-755 µg/m^3; IT Instillation- 200 µL (soluble and insoluble) **Time to Analysis:** F344 rats sensitized to endotoxin, BN rats to OVA. Exposed 10 h/day 1, 4, 5 days (consecutive). Another group of rats IT instilled. Both groups killed 24 h post-exposure.	The retention of PM in the airways was enhanced by allergic sensitization. Recovery of anthropogenic trace elements was greatest for CAPs-exposed rats. Temporal increases in these elements were associated with eosinophil influx, BALF protein content and increased airway mucosubstances. A mild pulmonary neutrophilic inflammation was observed in rats instilled with the insoluble fraction but instillation of total, soluble or insoluble $PM_{2.5}$ in allergic rats did not result in differential effects.
Reference: Hiramatsu et al. (2003, 155846) **Species:** Mouse **Gender:** Female **Strain:** BALB/c and C57BL/6 **Age:** 8 wk **Weight:** 17-22 g	DE: generated by 2369-cc diesel engine (Isuzu) at 1050 rpm and 80% load with commercial light oil **Particle Size:** NR	**Route:** Whole-body Inhalation **Dose/Concentration:** DEP: 100 µg/m^3 or 3 mg/m^3; SO_2<0.01 ppm; NO_2 2.2 ± 0.3 or 15 ± 1.5 ppm; CO 3.5 ± 0.1 or 9.5 ± 0.6 ppm **Time to Analysis:** 7h/d, 5 days/wk for 4 or 12 wk, Immediate	**BALF Cells:** Alveolar macrophages (AMs) increased dose-dependently at 30 and 90 day. High DE exposure resulted in bronchus-associated lymphoid tissue (BALT) around DEP-AMs; this was less conspicuous in C57BL/6 than in BALB/c mice. B- and T-cell populations were found in the BALT with no significant differences observed between the strains. Lymphocytes and neutrophils increased time- and dose-dependently with a greater increase in BALB/c than C57BL/6 observed. No eosinophils or basophils were observed. Mac-1-positive cells exposed to high DE levels increased in both strains at 1 month (33.8%) and 3 mo (20.3%) vs. low dose group (5.3 and 7% respectively). **Cytokines:** At 30 days, TNF-α, IL-12p40, IL-4 and IL-10 mRNA increased, IL1b and iNOS decreased. IFN-γ increased in BALB/c but decreased in C57BL/c. IL-6 mRNA was not affected. At 90 day, IL-4 and IL-10 mRNA similarly increased in C57BL/6 mice exposed to low DE level but decreased at high DE level.
Reference: Hollingsworth et al. (2004, 097816) **Species:** Mouse **Gender:** Male **Strains:** C57BL//6TLR$^{+/+}$, C57BL//6TLR$^{-/-}$ **Age:** 8-9 wk	ROFA **Particle Size:** NR	**Route:** Oropharyngeal Aspiration **Dose/Concentration:** 50 µl of 1µg/mL suspension per mouse **Time to Analysis:** Parameters measured post single exposure of 6 and 24 h.	**Methacholine sensitivity:** No ROFA effect was observed in wild type or knockout mice. **BALF Cells:** ROFA increased total cell number. Total number of neutrophils with lavage fluid increased 24 h post-exposure in both strains.
Reference: Hutchison et al. (2005, 097750) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 3 m **Weight:** 250-300 g	PM_{10} United Kingdom samples collected before (-B), during closure (-C) and reopening of steel plant (-R) PMT = PM total (aqueous sonicate) PMS = PM aqueous supernatant PMI = PM insoluble pellet **Particle Size:** PM_{10}	**Route:** IT Instillation **Dose/Concentration:** 112 to 180 µg PM in 500 µl; 0.44-0.72 mg/kg **Time to Analysis:** 18 h	**BALF Cells:** PMT-R neutrophil cell number and percentage were significantly higher than PMT-C or control. PMS-R and PMI-R were also higher than their respective controls. The neutrophil cell numbers induced by PMI-R were greater than PMI-C and the control. Total cell count unchanged. **BALF Inflammatory/Injury Markers:** Only albumin increased after PMT-R. Upon exposure, total protein and LDH did not increase. **Cytokine mRNA expression:** Only PMT-R increased IL-1ß mRNA expression. No effects on TNF-α and TGF-ß expression levels were observed. IL-6, MIP2, and GM-CSF mRNA was not detected in BAL cell extracts from either the control or treated groups.
Reference: Inoue et al. (2006, 097815) **Species:** Mouse **Gender:** Male **Strains:** C3H/HeJ (TLR-4 point mutant) and C3H/HeN (Control) **Age:** 6 wk	DEP (derived from 4 cyl, 2.74l light duty diesel engine) **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 12 mg/kg **Time to Analysis:** 24 h	**BALF Cells:** DEP induced an increase in total cells, neutrophils, and mononuclear cells. TLR4 knockout mice (C3H/HeJ) showed a much lower response. **Cytokines:** DEP induced a massive increase in MIP-1x, IL-1β and KC. However, levels of MIP-1x were significantly less in the knockout than the wild type while levels of IL-1β and KC were significantly higher in knockouts than the wild type.

Reference	Pollutant	Exposure	Effects
Reference: Inoue et al. (2005, 097481) **Species:** Mouse **Gender:** Male **Strain:** NC/Nga **Age:** 10 wk	DEP (derived from 4 cyl, 2.74l light duty diesel) **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 100 µg/mouse **Time to Analysis:** 1/wk for 6 wk. Parameters measured 24 h after last administration	**BALF Cells:** DEP significantly increased total cells, neutrophils and mononuclear cells but did not induce an effect on eosinophils. **Cytokines:** DEP increased IL-4, KC and MIP-1. The increase in IL-5 was not statistically significant.
Reference: Ishihara et al. (2003, 096404) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 5 wk	DE (from 2 engines, produced on site) -L = low level DE -M = medium level -MG = DE w/o particulates -HR = high level Measured Components: NO_2, SO_4, SO_2, CO, CO_2, NO_X, NO, HTHC, HCHO, O_2 **Particle Size:** L: 0.33 -0.50 µm M: 0.35 - 0.40 µm HR: 0.42 - 0.45 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** L: 0.18 - 0.21 mg/m^3 M: 0.92- 1.18 mg/m^3 MG: 0.01 mg/m^3 HR: 2.57 - 2.94 mg/m^3 **Time to Analysis:** 16 h/day, 6 days/wk, for 6, 12, 18 & 24 mo. Parameters measured immediately following last exposure.	**Morbidity and Mortality:** Weight gain in HR group was less than other groups at 18 and 24 mo. This indicates a significant difference between the HR and C group. Mortality during the study was frequent. C group experienced an 8% mortality rate, L group 12%, M group 15%, MG group 12% and HR group 23%. **BALF Cells:** The HR group showed a significant increase in total cell count from 6 to 18 mo. The percentage of PMN increased at 6mo in M, MG and HR group. M group lymphocytes significantly increased at 6, 12, and 24 mo of exposure. Macrophages decreased at 6 mo for the M and HR groups. **BAL Inflammatory/Injury Markers:** Significant differences were seen among groups with respect to number of total cells and percentages of cell differential, total protein, fucose, sialic acid, phospholipid and prostoglandin E2. Total protein increase was observed in both M and HR dose groups with the HR group increasing time-dependently. **Mucus and Surfactant:** The HR group showed a significant increase from 12 to 18 mo.
Reference: Jones et al. (2005, 198883) **Species:** Rabbit **Strain:** New Zealand **Weight:** 2.5- 3.5 kg	ASP: Amorphous silica particles (Hypersil) MCSP: Microcrystalline silica particles **Particle Size:** ASP: 5 µm; MCSP: 5 µm	**Route:** Intrapulmonary Instillation (Right upper lobe of lung) **Dose/Concentration:** 50mg in 0.5 mL saline **Time to Analysis:** Parameters measured at varying times from 6 h to 91 days post treatment.	**MCSP:** At 6 h, neutrophils increased. Macrophages increased 3 fold. At 60 h, neutrophils were pyknotic and the lungs displayed a thickened interstitium containing silica particles. At 5 days, collagen deposition appeared. At 8 days, fibroblastic activity and necrosis were observed. At 15 days, aggregation of silica particles and necrotic debris were apparent. At 8 wk, fibroblasts were still present. At 13 wk, active scarring and raised neutrophil macrophage counts were still present. **ASP:** At 15 h, neutrophils increased. Macrophages tripled and remained increased for 3wk. At 4 day, macrophages bore particles. At 13 day, neutrophils decreased significantly. By 25 day, silica spheres were gradually removed from lungs. **PET Scanning:** 18F-fluoroproline showed increased activity beginning at 14 days and peaking at 41-54 days. **Microautoradiography:** 3 h-proline at 13 wk showed radiolabel localization to fibroblasts in the challenged lung.

Reference	Pollutant	Exposure	Effects
Reference: Kato and Kagawa (2003, 089563) **Species:** Rat **Gender:** Male **Strain:** Jcl Wistar **Age:** 5 wk	Roadside air (Prefectural Tokyo-Danishi-Yokohama highway, Yokohama-Haneda Airport Metropolitan expressway and Satsukibashi-Mizuecho city road, Japan) **Particle Size:** NR	**Route:** Whole-body Inhalation **Dose/Concentration:** Exposed group: 62.7 µg/m^3 PM, 55.7 ppb NO_2,; Control group: 14.3 µg/m^3 PM, 5.1 ppb NO_2 **Time to Analysis:** Exposed for 24, 48, 60 wk. Parameters measured immediately following exposure.	**Respiratory Tissue:** Post 24 wk, the lung surface was light gray with some BC particle deposits. Post 48-60 wk, however, the surface was scattered with particle deposits in addition to its light gray color. **Airway Changes:** After 60 wk, no remarkable changes seen in the epithelium. The structure of the airways remained normal. **Cells:** No proliferation or ectopic growth of goblet cells were noted. Mast cells increased in epithelial intercellular space. No mast cell degranulation was observed. Lysosomes increased in ciliated cells post 48 wk. Clara cells were unaffected. **Lymph Nodes:** Deposition of carbon particles were noted in the trachea and bronchiole-associated lymph nodes post 24 wk. **Alveolar Changes:** No changes in morphology of broncho-alveolar junctions were noted. Anthracosis observed within alveolar walls and pleura post 24 wk and became progressively marked with increased exposure. No change in the number of alveolar holes between exposure and control groups were observed.
Reference: Kato et al. (2003, 198882) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** 7 wk **Weight:** 190-220 g	Polystyrene latex suspension of latex beads (Japan Synthetic Rubber Co.), uncoated or coated with lecithin **Particle Size:** 240 nm	**Route:** IT Instillation with nebulizer **Dose/Concentration:** 5 ml of 0.2% suspension administered over 20 min at flow rate of 0.25 ml/min **Time to Analysis:** Exposed for 20 min. Parameters measured 30 min following treatment.	**Alveolar Macrophages:** Following treatment, AMs appeared undamaged. AMs ingested more uncoated than coated beads, but both were ingested. Ingestion of beads differed as coated beads were engulfed individually while uncoated beads were engulfed individually or in aggregates. **Epithelial Cells:** Type I cells incorporated coated beads within a layer of cytoplasm. Type II cells incorporated beads in lamellar bodies. Uncoated beads were not incorporated. **Other:** Neither type of beads were incorporated into endothelial cells, fibroblasts or interstitium of alveolar wall **Monocytes:** Only the coated beads were incorporated by the monocytes. They were found inside and outside phagosomes and lysosomes of monocytes. PMNs did not incorporate any beads.
Reference: Kleinman et al. (2003, 053535) **Species:** Rat **Gender:** NR **Strain:** F344n-NIA **Age:** 22-24 m	O_3 CCL: O_3 + Ammonium bisulfate (ABS) + Elemental Carbon (EC) CCH: O_3 + ABS + EC Purified Air (control) **Particle Size:** CCL: 0.30 ± 2.5 µm; CCH: 0.29 ± 2.3 µm	**Route:** Nose-only Inhalation **Dose/Concentration:** O_3: 0.2 ppm CCL: 50 µg/m^3 EC + 70 µg/m^3 ABS + 0.2 ppm O_3 CCH: 100 µg/m^3 EC + 140 µg/m^3 ABS + 0.2 ppm O_3 **Time to Analysis:** 4 h/days, 3 consecutive days/wk for 4 wk	**BALF Cells:** CCL and CCH induced macrophage respiratory burst activity. The effect induced by O_3 was not significant. **BAL Inflammatory/Injury Markers:** Total protein, mucus glycoprotein and albumin were somewhat elevated in all exposure groups but only reached statistically significance for CCL and protein (very high variability). CCL and CCH both depressed Fc receptor side binding. No effect for O_3 was observed. **DNA Replication:** O_3 caused a slight effect of 20-40% increase. CCL and CCH caused between 250 - 340% increase for interstitial and epithelial cells. CCL induced greater reactions than the high dose.
Reference: Kleinman and Phalen (2006, 088596) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** 6 wk **Weight:** 200 g	LO_3: Low O_3 HO_3: High O_3 LS: Low H_2SO_4 HS: High H_2SO_4 LOLS: Low O_3 + Low H_2SO_4 LOHS: Low O_3 + High H_2SO_4 HOLS: High O_3 + low H_2SO_4 HOHS: High O_3 + high H_2SO_4 **Particle Size:** LS = 0.23 µm ± 2.3 HS = 0.28 µm ± 2.1 LOLS = 0.23 µm ± 2.3 LOHS = 0.28 µm ± 2.1 HOLS = 0.23 µm ± 2.3 HOHS = 0.28 µm ± 2.1	**Route:** Nose-only Inhalation **Dose/Concentration:** LO_3 = 0.30 ppm HO_3 = 0.61 ppm LS = 0.48 mg/m^3 HS = 1.00 mg/m^3 LOLS = 0.31 ppm + 0.41 mg/m^3 LOHS = 0.31 ppm +1.04 mg/m^3 HOLS = 0.60 ppm + 0.52 mg/m^3 HOHS = 0.60 ppm + 0.86 mg/m^3 **Time to Analysis:** Exposed for 4 h. Parameters measured 42 h post-exposure.	**Inflammatory Lesions in Lung Parenchyma:** Neither Type 1 or 2 lung lesions were affected by sulfuric acid alone. HO_3 doubled Type 1 lesions and increased Type 2 lesions 25-fold. Additions of H_2SO_4 to O_3 appeared to have a dose-dependent protective effect for both types of lesions. **DNA Synthesis in Nasal, Tracheal and Lung Tissue:** Increased DNA synthesis was observed at all high O_3 exposures but was not affected by coexposure to H_2SO_4. **Macrophage FcR binding:** No effects were observed (no data for LO_3 and HO_3). **Macrophage Phagocytosis:** All levels of exposure (no data for LO_3 and HO_3) decreased phagocytosis.

Reference	Pollutant	Exposure	Effects
Reference: Kodavanti et al. (2005, 087946) **Species:** Rat **Gender:** Male **Strain:** WKY and SH/NCrlBR **Age:** 11-14 wk	CAPs (EPA, NC) Measured components included Al, Be, Ba, Co, Cu, Zn, Pb, Mn, Ni, Ag, Ti, As. **Particle Size:** 1 day: 1.07-1.19 µm; 2 days: 1.27-1.48 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** 1 day study: 1138-1765 µg/m^3 2 day study: 144-2758 µg/m^3 **Time to Analysis:** 4 hr (SH only); 4 hr/day, 2 day (WKY and SH) Post-exposure: 1 day: 3 h except study #4, 18-20 h; 2 day: 18-20 h	**Breathing Parameters:** In a paired analysis of control SH and treated SH, treated SH showed an increase in expiratory and inspiratory time due to CAPs. The treated and control groups of WKY rats did not show significant differences. **BALF Cells:** In the 2 day study, WKY rats showed decreases in total cells; this decrease was associated with decreased macrophages. WKY showed an increase in neutrophils. **BAL Inflammatory/Injury Markers:** Total protein and albumin in WKY rats decreased whereas SH rats maintained the same approximate level. LDH activity lowered slightly in both strains. **Cell Membrane Integrity:** SH rats showed increased GGT (membrane bound enzyme) activity and plasma fibrinogen for 5/7 exposures but these increases did not appear to be dose-dependent. **Cytokines:** Levels were undetermined in SH rats. WKY showed slight increases in IL-6, TNF-α, and MIP-2 but these increases were not statistically significant.
Reference: Kooter et al. (2006, 097547) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 12-14 wk	CAP-F = fine (Site I) CAP-UF = fine + ultrafine (Site II) (Netherlands) Some measured components: Ammonium, nitrate, sulfate ions: 56 ± 16% CAP-F mass, 17 ± 6% CAP-UF mass **Particle Size:** 0.15<CAP-F<2.5 0.65-0.75 µm CAP-UF<2.5 0.58-1.41 µm	**Route:** Nose-only Inhalation **Dose/Concentration:** CAP-F 399- 3613 µg/m^3 CAP-UF 269-556 µg/m^3 **Time to Analysis:** 6 h/day for 2 days consecutive, 18 h	**BALF Cells:** A decrease in absolute neutrophils as well as percentages of reticulocytes and percentages of neutrophils were observed with CAP-F. Increased percentages of lymphocytes were observed with CAP-F. **BALF Inflammatory/Injury Markers:** Based on unchanged levels of LDH and ALP, no cytotoxicity was noted. No significant change in the levels of total cells were observed. MDA (malondialdehyde) decreased with CAP-UF. Ho-1 increased with CAP-UF and CAP-F. **Cytokines:** CC16 decreased at 457µg/m^3 of CAP-F and increased at 3613 µg/m^3 of CAP-F. **Pathology.** No changes were observed.
Reference: Kumar et al. (2004, 096655) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Weight:** 150 ± 20 g	Fly Ash (Obra Thermal power Station, India) **Particle Size:** PM <5 µm (90%)	**Route:** Whole-body Inhalation **Dose/Concentration:** 14.4 ± 1.77 mg/m^3 (fluid bed generator) **Time to Analysis:** 4 h/day for 28 day. Parameters measured immediately following last exposure.	**Lung Weight:** Lung body weight increased 25.58% relative to controls. Total body weight slightly decreased in the treated group. **BALF Cells:** Only eosinophils(%) increased 95% over controls. Congestion and focal infiltration of monocytes in alveolar area was seen. Fly ash laden macrophages in alveoli combined with hypertrophy of epithelial lining cells was observed. **BAL Inflammatory/Injury Markers:** LDH, GGT, ALP and lavagable protein increased by 140, 450, 160 and 50%, respectively.
Reference: Lei et al. (2004, 087999) **Species:** Rat **Gender:** Male **Strain:** SD **Weight:** 318 ± 8 g	CAPs (Yaipei, Taiwan) **Particle Size:** 0.01- 2.5 µm	**Reference:** Nose-only Inhalation **Dose/Concentration:** 371 ± 208 µg/m^3 **Time to Analysis:** 6 h/day for 3 day, 5 h post-exposure pulmonary function. 2 day post-exposure for BALF collection Pulmonary hypertension induced 2 wk pre-exposure	**Respiratory Effects:** Decreased respiratory frequency and increased tidal volume for both experimental and control groups were observed. However, only the experimental group levels were statistically significant. There was an increase in airway responsiveness (Penh/methacholine) for CAPs group when compared to the control. **BALF Cells:** A massive increase in total cell number and percent neutrophils was observed. There were no changes in percent macrophages, lymphocytes and eosinophils. **BAL Inflammatory/Injury Markers:** Total protein and LDH increased in the CAPs group. **Cytokines:** TNF-α and IL-6 were not affected.

Reference	Pollutant	Exposure	Effects
Reference: Lei et al. (2004, 087884) **Species:** Rat **Gender:** Male **Strain:** SD **Weight:** 300-350 g	CAPs from Asian dust storm (Taiwan) Measured Components: Si, Al, S, Ca, K, Mg, Fe, As, Ni, W, V, OC, EC, SO_2, NO_2, nitrate, sulfate **Particle Size:** 0.01- 2.5 µm	**Route:** Nose-only Inhalation **Dose/Concentration:** 315.6 µg/m^3 (Low) or 684.5 µg/m^3 (High) **Time to Analysis:** Low: Exposed for 6 h. Sacrificed 36 h post-exposure High: Exposed for 4.5 h. Sacrificed 36 h post-exposure Pulmonary hypertension induced 2 wk pre-exposure.	**BALF Cells:** PM induced dose-dependent increases in total cells and percentage of neutrophils. No change in macrophages, lymphocytes or eosinophils occurred. Basophils were highly variable. **BALF Inflammatory/Injury Markers:** Dose-dependent increases were observed for total protein and LDH. **Cytokines:** IL-6 increased dose-dependently. (control: 33.5 ± 7.5, low 165.1 ± 117.2, 273.6 ± 62.8 pg/mL).
Reference: Li et al. (2007, 155929) **Species:** Mouse **Gender:** Female **Strain:** BALB/c, C57BL/6 **Age:** 9 wk **Weight:** NR	DEP (2369-cc diesel engine manufactured by Isuzu Motor, operated at 1050 rpm, 80% load, commercial light oil) **Particle Size:** NR	**Route:** Inhalation **Dose/Concentration:** DEP: 103.1 ± 9.2 µg/m^3, CO: 3.5 ± 0.1 ppm, NO_2: 2.2 ± 0.3 ppm, SO_2: <0.01 ppm **Time to Analysis:** Protocol 1: Exposed 7h/day, 5 days/wk. Sacrificed at day 0, week 1, 4, 8. Protocol 2: DE alone or DE+NAC 7h/day, 1-5 days.	**Airway Hyperresponsiveness:** Penh values increased in BALB/c mice compared to the control at day 0, but no significant changes occurred after this time. Penh values increased in C57BL/6 mice at 1 wk compared to the control but returned to control levels at 8 wk. **BALF:** Compared to the other strain, the total number of cells and macrophages increased significantly at 1 wk in C57BL/6 mice and at 8 wk in BALB/c mice. Neutrophils, lymphocytes, MCP-1, IL-12, IL-10, IL-4, IL-13 increased significantly for both strains. No eosinophils were found. IL-1β and IFN-γ increased significantly in BALB/c mice compared to C57BL/6 mice. **HO-1 mRNA and Protein:** HO-1 mRNA was more marked in BALB/c mice at 1 wk and C57BL/6 mice at 4 and 8 wk. HO-1 protein percentage changes from the control were greater in BALB/c mice at 1 wk and C57BL/c mice at 8 wk. **NAC:** NAC inhibited the increased Penh values, total number of cells and macrophages in C57BL/6 mice at 1 wk and neutrophils and lymphocytes in both strains.
Reference: Liu et al. (2008, 156709) **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 11 wk **Weight:** NR	DEP (5500-watt single-cylinder diesel engine generator (Yanmar, Model YDG 5500E), 406 cc displacement air-cooled engine, Number 2 Diesel Certification Fuel, 40 weight motor oil) **Particle Size:** ~0.1 µm (MMAD)	**Route:** Intranasal **Dose/Concentration:** Average particle concentration: 1.28 mg/m^3 **Time to Analysis:** Four groups: saline+air control, saline+DEP, A. fumigatus+air, A.fumigatus+DEP. A. fumigatus exposure every 4 day for 6 doses. DEP exposure 5 h/day for 3 wk concurrent with A. fumigatus exposure.	A.fumigatus+DEP increased IgE, the mean BAL eosinophil percentage, goblet cell hyperplasia, and eosinophilic and mononuclear cell inflammatory infiltrate around the airways and blood vessels compared to the A. fumigatus or DEP treatments. A.fumigatus+DEP also caused methylation at the IFN-γ promoter sites CpG-53, CpG-45, and CpG-205.
Reference: Lopes et al. (2009, 190430) **Species:** Mouse **Gender:** Male **Strain:** BALB/c **Age:** 6-8 wk **Weight:** NR	PM (high density traffic; winter 2004; São Paulo, Brazil) (NO_2, CO, SO_2) **Particle Size:** 10 µm (diameter)	**Route:** Open-Top Exposure Chamber **Dose/Concentration:** 33.86 ± 2.09 µg/m^3 **Time to Analysis:** Some rats pretreated with papain. Exposed to UAP or filtered air 24 h/day, 7 days/wk, 2 mo.	The papain+UAP treatment increased Lm values, collagen fibers, and decreased the density of elastin fibers over the papain+filtered air treatment. The papin+UAP treatment increased 8-isoprotane more than any other group.

Reference	Pollutant	Exposure	Effects
Reference: Mangum et al. (2004, 097326) **Species:** Rat **Gender:** Female **Strain:** CDF (F344)/CrlBR **Age:** 7 wk	TiO_2 (DuPont) **Particle Size:** NR	**Route:** Whole-body Inhalation **Dose/Concentration:** 10, 50 or 250 mg/m^3 **Time to Analysis:** 6 h/day, 5 days/wk, 13 wk. Parameters measured 0, 4, 13, 26, 52 wk post-exposure.	**OPN (osteopontin) Expression:** At 0 wk, OPN mRNA expression exhibited a dose-dependent increase. Low dose induced a 2-fold increase while the high dose induced an almost 100 -fold increase. At 4 wk, the mid-dose and high-dose elevated OPN mRNA levels. At 13 wk, the high dose elevated OPN mRNA levels. No significant elevation with mid dose level was observed. At 26 wk, the mid and high dose induced elevated OPN mRNA levels. At 52 wk, rats in the low, mid and high dose groups all indicated elevated levels of OPN mRNA. Specifically, the low, mid and high doses induced a 3-fold increase, 7-fold increase and 400-fold increase, respectively. **OPN Protein in BALF:** Data was not reported at 0 and 4 wk. At 13 wk, protein increased 9-fold (~800 pg/mL OPN) at mid dose and 100 -fold (~8000 pg/mL OPn) at high dose. At 26 wk, the mid and high dose groups remained elevated. At 52 wk, protein increased by 2.5 fold in low dose, 7-fold in mid dose and 166-fold in high dose group. **Histopathology:** At 52 wk, slight OPN immunoreactivity was observed in control and low dose group (immunostaining mostly limited to intraalveolar MACS).Trichrome-stained lung sections from control and low dose groups showed no increase in collagen. Rats exposed to mid or high dose groups showed areas of lesions.
Reference: Martin et al. (2007, 096366) **Species:** Mouse **Gender:** Male **Strain:** BALB/c **Age:** 1-2 mo	UAP-BA: Urban Air particles (Buenos Airs, Argentina) **Particle Size:** <2.5 µm	**Route:** Intranasal Installation **Dose/Concentration:** 0.17 mg/kg **Time to Analysis:** 3×day, 3 days/wk, 2 days apart (1, 4, 7 day). Parameters measured 1 h post-exposure.	**Particle Characteristics:** 3 types, ultrafines <0.2 um (inorganics ND), bunched agglomerates of ultrafines and <40 um with aluminum silicates, ions and trace metals. **BALF Cells:** Increased amount of phagocytes in alveolar area, reducing airspace percentage (control 52.9% ± 1.39, UAP-BA 24.7% ± 2.87). Increased number of PAS positive cells. **Morphometry:** Induced focal inflammatory lesions. Accumulation of refractile material in upper and lower respiratory tract. PM in phagocytes of bronchiolar lumen and alveolar space. No evidence of fibrosis and/or collagen changes.
Reference: Mauad et al. (2008, 156743) **Species:** Mouse **Gender:** Male, Female **Strain:** BALB/c **Age:** 10 day **Weight:** Parental: 21.4 ± 4.0 - 26.3 ± 2.8 g; 15 day-old offspring: 7.8 ± 1.1 - 9.0 ± 1.0 g; 90 day-old offspring: 20.3 ± 2.3 - 27.4 ± 1.8 g	PM (busy traffic street São Paulo, Brazil; Aug. 2005-April 2006) (NO_2, SO_2, CO) **Particle Size:** 2.5, 10 µm (diameter)	**Route:** Open-Top Chamber **Dose/Concentration:** $PM_{2.5}$: filtered chamber- 2.9 ± 3.0 µg/m^3, nonfiltered chamber- 16.9 ± 8.3 µg/m^3; Outdoor concentration: PM_{10}- 36.3 ± 15.8 µg/m^3, CO- 1.7 ± 0.7ppm, NO- 89.4 ± 31.9 µg/m^3, SO_2- 8.1 ± 4.8 µg/m^3 **Time to Analysis:** Nonfiltered exposure 24 h/day for 4 mo. Mated at 120 days exposure. After birth, 30 females and offspring transferred to filtered or nonfiltered chamber. Killed 15 or 90 day of age.	Mild foci of macrophage accumulations containing black dots of carbon pigment occurred in the alveolar areas on 90 day-old mice. Surface-to-volume ratio decreased from 15 to 90 days of age and was higher in mice exposed to air pollution. PM exposure reduced inspiratory and expiratory volumes at higher levels of transpulmonary pressure.
Reference: McDonald et al. (2004, 087459) **Species:** Mouse **Strain:** C57BL/6 **Age:** 8-10 wk	DEE: high load, No 2, No cat (620: 1 dilution) DEE-ER (Control): Emissions Reduced (high load, low sulfur ECD1) (same dilution) (Yanmar diesel generator, 406 cc, 5500 watt load) **Particle Size:** DEE: 110 nm; DEE-ER: NR	**Route:** Whole-body inhalation **Dose/Concentration:** DEE PM: 236 µg/m^3 DEE-ER PM: 7 µg/m^3 **Time to Analysis:** DEE: 6 h/day for 7 days. DEE-ER: 6 h/day for 7 days. RSV administered post-exposure for some: single, 4 days. Those not infected with RSV sacrificed immediately upon last exposure.	**Differences in Exposure Conditions:** CO, PM, EC, OC, nitrate, alkyne, c2-c212 alkenes, phenanthrenes, total particle PAHs, total Oxy-PAHs, benzene, pyrene, benzo(ayrene, zinc were reduced by 90-100% in the emissions reduction case. Most other components were reduced by around 60%. **DEE vs. DEE-ER Effects:** DEE increased viral retention and lung histopathology. DEE-ER increases were not statistically significant. **Cytokines:** DEE increased TNF-α, IL-6, IFN-γ and HO-1. DEE-ER responses were not statistically significant (significantly higher variability in DEE-ER controls vs. DEE controls).

Reference	Pollutant	Exposure	Effects
Reference: McQueen et al. (2007, 096266) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Weight:** 228-500 g	DEP: SRM 2975 (NIST) **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 0.5 mL/rat of 1 mg/mL; 1-2.2 mg/kg **Time to Analysis:** 6 h. Pre-exposure: Vagotomy (sectioning of vagus nerve) or atropine, 1 mg/kg i.p. administered 30 min prior, 2 and 4 h post.	**BALF Cells:** A 9-fold increase in neutrophils with high individual variability in response was observed. Bilateral vagotomy prior to DEP reduced neutrophil increase to 3 fold. Vagotomy with saline instillation had no effect. Atropine reduced neutrophils to levels similar to saline response. No differences were observed between DEP response in anesthetized when compared to conscious animals. Macrophages, eosinophils and lymphocytes remain unchanged. **Respiratory Response:** RMV increased post DEP. Vagatomy reduced response by one-third. Atropine pre-treatment did not have effect.
Reference: Medeiros et al. (2004, 096012) **Species:** Mouse **Gender:** Male **Strain:** BALB/c **Age:** 60 days **Weight:** 20-30 g	CP: Carbon particles PSA: ROFA (solid waste incinerator hospital Sao Paulo, Brazil) PSB: electric precipitator, steel plant, Brazil) PSA/PSB Characteristics: Generally, PSB had greater component concentrations than PSA: Br (100+x), Cr (3x), Fe (10+x), Mn (2x), Rb (60+x), Se (7x), Zn (4x). PMA>PMB: Ce (3x), Co (10+x), La (100x), Sb (15x), V (50x). **Particle Size:** CP: 1.7 ± 2.5 µm (78%<2.5 µm); PMA: 1.2 ± 2.2 µm(98 %<2.5 µm); PMB: 1.2 ± 2.2 µm (98%<2.5 µm)	**Reference:** Intranasal Instillation **Dose/Concentration:** CP: 10 µg/mouse; 0.5 mg/kg PSA: 0.1, 1 or 10 µg/mouse; 0.005, 0.05, 0.5 mg/kg PSB: 0.1, 1 or 10 µg/mouse; 0.005, 0.05, 0.5 mg/kg **Time to Analysis:** Single, 24 h	**BALF Cells:** No change in BAL cell count was seen. Quantitative cellular counts increased for perivascular area for both groups at all dose levels. Inflammatory cells in alveolar septum area only increased for PSA.
Reference: Mutlu et al. (2006, 155994) **Species:** Mouse **Strain:** C57BL/6 **Age:** 6-8 wk **Weight:** 20-25 g	PM_{10} Collected by baghouse from Dusseldorf, Germany **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 100 ng/mouse; 1 µg/mouse; 10 µg/mouse; 100 µg/mouse **Time to Analysis:** 1-7 days	**Alveolar Fluid Clearance:** At 100 µg/mouse, decreased clearance peaked at 24 h and recovered at 7 days. **Histology:** Evidence of mild lung injury at doses of 100 µg/mouse or more was seen. **BALF Cells:** Significant increase in total cell number was observed. Neutrophils increased but this was not statistically significant. **Wet/Dry Ratio:** Exposure did not induce any effects. **Na, K-ATPase:** At 100 µg/mouse, decreased activity of Na, K-ATPase in basolateral membranes was observed.
Reference: Nadziejko, et al. (2002, 087460) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 16 wk	CAPs: produced at Tuxedo, NY laboratory using centrifugal aerosol concentrator FA: Fine Particle Sulfuric Acid Aerosol UFA: Ultra-Fine Particle Sulfuric Acid Aerosol **Particle Size:** CAPs: $PM_{2.5}$; FA: 160 nm; UFA: 50-75 nm	**Route:** Nose-only Inhalation **Dose/Concentration:** CAPS 80, 66 µg/m^3; avg 73 µg/m^3 FA: 299, 280, 119, 203 µg/m^3; avg 225 µg/m^3 UFA: 140, 565, 416, 750 µg/m^3; avg 468 µg/m^3 **Time to Analysis:** 10 exposures of 4 h each, each exposure at least 1 wk apart. (2 exposures to CAPs, 4 to FA and 4 to UFA)	**Respiratory Rate:** CAPs decreased the respiratory rate as did FA at all dose levels. However, the FA-induced respiratory rate was not statistically significant unless the data was combined. UFA increased this rate significantly.
Reference: Nemmar et al. (2007, 156800) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 16 wk **Weight:** 424 ± 8g	DEP: SRM 2975 **Particle Size:** <1 µm	**Route:** Intravenous Injection **Dose/Concentration:** 0.02, 0.1 or 0.5 mg/kg **Time to Analysis:** single, 24 h	**BALF Cells:** Marked cellular influx at all dose levels Was observed. Macrophages increased at the high dose, but this was not statistically significant. PMN increased significantly at all dose levels. **Wet/Dry Ratio:** All dose levels induced increases.

Reference	Pollutant	Exposure	Effects
Reference: Nemmar et al. (2003, 087931) **Species:** Hamster **Gender:** Male and Female **Weight:** 100-110 g	PS: Polystyrene particles PSC: Polystyrene particles, Carboxylate modified PSA: Polystyrene particles, Amine modified **Particle Size:** PS, PSC, PSA-60: 60 nm; PSA-400: 400 nm	**Route:** IT Instillation **Dose/Concentration:** 5, 50 or 500 µg/animal; 0.05, 0.5, 5 mg/kg **Time to Analysis:** Single, 10 min post-exposure Rose Bengal administered to induce thrombosis, immediate study thereafter	**BALF Cells:** Both PSA-60 and PSA-400 (PSA-60>PSA-400) induced a massive influx of PMNs. PSA-60 effect may exhibit some dose-dependency. **BALF Inflammatory/Injury Markers:** Small increases in total protein were seen at 500 µg level for both PSA-60 and PSA-400. LDH was increased at all PSA-60 levels but not for 500 ug PSA-400. Histamine increased for all PSA-60 levels and PSA-400 but due to high variability only the effect at 500 µg PSA-60 was statistically significant.
Reference: Nemmar et al. (2003, 097487) **Species:** Hamster **Gender:** NR **Weight:** 100-110 g	DEP: SRM 1650 **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 50 µg/animal **Time to Analysis:** Single exposure, parameters measured 1, 3, 6 or 24 h post- exposure.	**BALF Cells:** DEP led to a significant PMN flux at 1 h (13% of total cell number), 6 h (22%) and 24 h (37%). **Histamine:** Concentrations in BALF were consistently elevated starting at 1 h. Plasma histamine did not increase until 6 h. **Pretreatment with Histamine Receptor Antagonist:** A major decrease in DEP induced PMN infiltration was seen. No effect on histamine in BALF or plasma was observed.
Reference: Pereira et al. (2007, 156019) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 3 m	Ambient Particles (Porto Allegre, Brazil) **Particle Size:** <10µm	**Route:** Whole-body Inhalation **Dose/Concentration:** P-6: 34, 22 or 225 µg/m^3 P-20: 139 or 112 µg/m^3 P-I: 99 µg/m^3 **Time to Analysis:** P-6: single/continuous for 6 h P-20: single/continuous for 20h P-I: intermittent (5 h) periods per day for 4 days consecutively Parameters measured 0 or 24 h post-exposure	**BAL Inflammatory/Injury Markers:** An increase in lipid peroxidation was statistically significant only for the 20 h continuously exposed group. Leukocytes also increased at P-20. No change at P-6. Total protein remained unaffected at all dose levels. **Wet to Dry Ratio (0h):** No effect was observed.
Reference: Pinkerton et al. (2004, 087465) **Species:** Rat **Gender:** Female (pregnant), Offspring- NR **Strain:** SD **Age:** 10 days (pups), Pregnant females- 10-14 days of gestation **Weight:** NR	PM (Fe and soot from combustion of acetylene and ethylene in a laminar diffusion flame system) **Particle Size:** Median diameter: 72-74 nm; size range: 10-50 nm	**Route:** Inhalation **Dose/Concentration:** Mean mass concentration: 243 ± 34 µg/m^3; Average Fe concentration: 96 µg/m^3 **Time to Analysis:** Exposed 10 days postnatal age, 6 h/day, 3 days (consecutive).	A significant reduction of cell proliferation occurred only within the proximal alveolar region of exposed animals compared to controls. There were no significant differences between the groups for alveolar formation and separation within the proximal alveolar region.
Reference: Pinkerton et al. (2002, 087645) **Species:** Rat **Gender:** Male, Female **Strain:** SD **Age:** 11-13 wk (adult male), 10-12 days (neonatal) **Weight:** NR	PM (Fe, Soot) (ethylene, iron pentacarbonyl, acetylene combined; Fe_2O_3; soot: 60% EC, 40% OC) (CO, NO_X) **Particle Size:** Fe (diameter) 40 nm; Soot (primary particles, diameter) 20-40 nm	**Route:** Whole-body Inhalation **Dose/Concentration:** Adult males: Fe- 57, 90 µg/m^3, Soot- 250 µg/m^3, Fe+Soot- Fe: 45 µg/m^3, Total PM: 250 µg/m^3; Neonates: Fe+Soot- Low: Fe- 30 µg/m^3, Total PM: 250 µg/m^3, High: Fe- 100 µg/m^3, Total PM: 250 µg/m^3 **Time to Analysis:** Adult males exposed to Fe, soot, Fe+Soot, or filtered air. Exposed 6 h/d, 3 days (consecutive). BAL, 2 h postexposure, lung tissue, 24 h postexposure. Neonatal rats exposed to Fe+Soot 10-12 day-old and 23-25 day-old.	**Fe:** Only the high dose had significant effects. This dose increased total protein in the lavage fluid, decreased total antioxidant power, induced GST activity, and induced a non-significant, increasing trend of GSH and GSSG. IL-1β, intracellular ferritin, and NF-κB increased. **Fe+Soot, Soot:** Fe+Soot significantly reduced the total antioxidant power in BALF and supernatant from lung tissue homogenate. Fe+Soot significantly increased GSSG, IL-1β, NF-κB, CYP1A1, and CYP2E1. CYP2B1 increased but was not significant. Soot alone was not significant for anything. **Neonates:** The high-dose significantly decreased cell viability, increased LDH activity, and increased IL-1β and ferritin. Both doses significantly increased GSSG, GRR, and GST, and decreased total antioxidant power.

Reference	Pollutant	Exposure	Effects
Reference: Pires-Neto et al. (2006, 096734) **Species:** Mouse **Gender:** Male **Strain:** Swiss **Age:** 6 days	Ambient Air: $PM_{2.5}$, NO_2 and CB (Sao Paulo, Brazil) **Particle Size:** $PM_{2.5}$	**Route:** Whole-body Inhalation **Dose/Concentration:** $PM_{2.5}$: 46.49 µg/m^3 Control: 18.62 µg/m^3 NO_2: 59.52 µg/m^3 Control: 37.08 µg/m^3 CB: 12.52 µg/m^3 Control: 0 µg/m^3 **Time to Analysis:** 24 h/day, 7 days/wk for 5 mo (weaned at 21 days into exposure, mothers removed)	**Nasal Cavity:** Increased total mucus and acidic mucus at proximal and medial areas of cavity. Nonsecretory epithelium declined. No significant changes in amount of neutral mucus, volume proportion of neutral mucus, volume proportion of total mucus, thickness of epithelium, volume proportion of nonsecretory epithelium or ratio between neutral and acidic mucus were observed. **Types of Acidic Mucus Cells:** Proximal and medium cells increased. Effects on distal cells were equivocal.
Reference: Pourazar et al. (2005, 088305) **Species:** Human **Gender:** Male and Female (nonatopic & nonsmokers) **Age:** 21-28 yr	DEP: generated from idling Volvo diesel engine DEP 300 µg/m^3 comprised of: NO_2 1.6 ppm NO 4.5 ppm CO 7.5 ppm Hydrocarbons 4.3 ppm Formaldehyde 0.26 mg/m^3 Suspended particulates 4.3×10^6/cm^3 **Particle Size:** <10 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** DEP 300 µg/m^3 **Time to Analysis:** Single exposure for 1 h. Parameters measured 6 h post exposure.	**Transcription Factors:** Exposure induced increased cytoplasmic and nuclear immunoreactivity of phosphorylated p38 MAPK in bronchial epithelium. Increased nuclear translocation of phosphorylated p38 and JNK, MAPK as well as increased nuclear phosphorylated tyrosine immunoreactivity were observed. No change in total or nuclear c-fos immunoreactivity was seen. Exposure induced increased nuclear translocation of phosphorylated JNK significantly associated with phosphorylation of nuclear c-jun and also resulted in an increase in nuclear p65. **Cytokines:** Expression of IL-8 was positively associated with nuclear phosphorylated p38 post-exposure.
Reference: Pradhan et al. (2005, 096128) **Species:** Rat **Gender:** Female **Strain:** Wistar Albino **Weight:** 120-180 g	RSPM: Respirable Suspended PM (Lucknow, India) Quartz dust (positive control) **Particle Size:** < 5 µm	**Route:** IT Instillation **Dose/Concentration:** 2.5, 5.0, or 10.0 mg/ 0.05 ml; 20, 42, 83 mg/kg **Time to Analysis:** 15 days.	**Relative Lung Weight:** A dose-dependent increase in total lung weight of RSPM-instilled animals was observed. **BALF Cells:** Exposure induced a dose-dependent increase in total cells dose-dependent with the low and mid dose levels. PMNs increased massively at all dose levels with RSPM inducing less of an increase than Quartz. Exposure at low dose levels resulted in an influx of inflammatory cells (predominantly macrophages into lumen of alveolar ducts and alveoli). Reaction at the high dose was more intense than that seen in mid dose-exposed lungs. **BAL Inflammatory/Injury Markers:** A significant dose-dependent increase in LDH and NO was observed, but the Quartz-induced increase was greater than the RSPM-induced increase. An increase in protein was significant at the mid dose level for RSPM and significant at the high dose level for both RSPM and Quartz. **Lung Biochemistry:** An increase in lipid peroxidation was dose-dependent. Superoxide dismutase (SOD) enzyme levels showed a dose-dependent decrease.
Reference: Ramos et al. (2009, 190116) **Species:** Guinea Pig **Gender:** NR **Strain:** NR **Age:** NR **Weight:** 330-370 g	WS (Pine wood) (CO(<80ppm), CO_2 (0.35%), O_2 (20.1%), $PM_{2.5}$, PM_{10}) **Particle Size:** $PM_{2.5}$, PM_{10}	**Route:** Whole-body Inhalation **Dose/Concentration:** WS: 60 g, $PM_{2.5}$: 363 ± 23 µg/m^3, PM_{10}: 502 ± 34 µg/m^3 **Time to Analysis:** Exposed 3 h, 5 days/wk for 1, 2, 3, 4, 6, 7 mo.	WS significantly decreased body weight between 4 and 7 m exposure. The concentration of blood carboxyhemoglobin increased. Recovered BALF cells were higher in WS-exposed pigs. Macrophages and neutrophils increased. Inflammation in the lungs was seen. Pulmonary arterial hypertension and emphysematous lesions were observed. Macrophage and lung tissue homogenate elastolysis increased. Collagenolysis increased. Generally, MMP-2, MMP-9, and MMP-1 increased. BAL macrophage apoptosis increased with time.

Reference	Pollutant	Exposure	Effects
Reference: Rao et al. (2005, 095756) **Species:** Rat **Strain:** SD **Weight:** 175 g	DEP: SRM 2975 **Particle Size:** 0.5 µm	**Route:** IT Instillation **Dose/Concentration:** 5, 35, 50 mg/kg bw **Time to Analysis:** Sacrificed 1, 7, 30 days post single exposure. Cytokines measured after 24 h incubation (in vitro).	**BALF Cells:** Macrophages unaffected. Increased PMNs at 1 day for all dose levels, sustained elevation at 7days for mid and high dose and at 30 days for all dose levels. **BAL Inflammatory/Injury Markers:** Increased albumin at 1 and 30 days at all dose levels. Increased LDH except at low dose at 7 days. **Cytokines:** The high dose induced a significant increase of mRNA expression for IL-1β, iNOS, MCP-1, and MIP-2 in BAL cells. MCP-1 mRNA sustained high levels at 7 days for mid and high dose and at 30 days for all dose levels. mRNA expression of IL-6, IL-10, TGF-β1, TNF-α were unaffected. However, IL-6 and MCP-1 proteins increased significantly in BALF at 1 day for mid and high dose, returning to basal levels at 7 days. MIP-2 increased for all dose levels at all time points. NO level unaffected.
Reference: Reed et al. (2006, 156043) **Species:** Rat, Mouse **Gender:** Male and Female **Strain:** CDF (F344)/CrlBR (rat), SH (rat), A/J (mouse), and C57BL/6 (mouse) **Age:** 6-12 wk	HWS (burned mix of hardwood in noncertified wood stove using a Pineridge model 27000, Heating and Energy Systems, Inc. Clackamas, OR) Measured Components: EC, OM, NO_3, SO_4, NH_4, metals **Particle Size:** ~0.25 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** Low: 30 µg/m^3 Mid-low: 100 µg/m^3 Mid-high: 300 µg/m^3 High: 1000 µg/m^3 **Time to Analysis:** 6 hr/day, 7 days/wk for 1wk or 6 mo. Immediate post-exposure analysis.	**Organ Weights:** Liver declined in rats of both genders at 1 wk and female rats at 6 m. Lung volume increased and lung weight decreased in female rats at 6 m. Spleen weight increased in female mice and rats at 1 wk. Thymus weight decreased in male rats at 1 wk. **Cells:** Eosinophils decreased and lymphocytes increased in males at 6m. Neutrophils decreased at 6m in both genders. Minimal increases in alveolar macrophages and sparse brown-appearing macrophages in all species. **Bacterial Clearance:** Mice instilled with bacteria were mostly unaffected by exposure, except for a decline in histopathology summary score after 6m. **Tumorigenesis:** No values for exposed groups differed significantly from controls. There was no evidence of progressive exposure related trend.
Reference: Reed et al. (2004, 055625) **Species:** Rat, Mouse **Gender:** Male and Female **Strain:** CDF (F344)/CrlBR (rat), A/J (mouse) **Age:** 12 wk	DE: generated from two 2000 model 5.9 L Cummins ISM turbo diesel engines Co-exposure to 8 gas and 8 solid exhaust components measured **Particle Size:** 0.10 - 0.15 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** Low: 30 µg/m^3 Mid-low: 100 µg/m^3 Mid-high: 300 µg/m^3 High: 1000 µg/m^3 **Time to Analysis:** 6 h/day, 7 days/wk for 1wk or 6 mo. Analyzed 1 day post-exposure.	**Organ Weights:** Kidney weight increased after 6m for both males and female rats at the high dose. Kidney and liver weight increased for female mice at all dose levels at 6 mo. Lung weight increased at high dose at 6m for female mice and male rats. Spleen weight decreased in male mice at the low and mid-high levels. **Cells:** Minimal increases in alveolar macrophages and PM within the macrophages were seen. **Cytokines:** TNF-α decreased in female rats after 6m. **Tumorigenesis:** No significant effect was observed.
Reference: Reed et al. (2008, 156903) **Species:** Mouse **Gender:** Male, Female **Strain:** C57BL/6, A/J, BALB/c **Age:** NR **Weight:** NR	GEE (2 1996 General Motors 4.3-L V-6 engines; unleaded gasoline) **Particle Size:** 150 nm (MMAD)	**Route:** Whole-body Inhalation **Dose/Concentration:** Control: 2.5 ± 2.9, Low-exposure: 6.6 ± 3.7, Mid-exposure: 30.3 ± 11.8, High-exposure; 59.1 ± 28.3, High filtered exposure: 2.3 ± 2.6 µg/m^3 **Time to Analysis:** Exposed 6 h/day, 7 days/wk, 3 days-6 mo.	**Body and Organ Weight and Histopathology in A/J:** Kidney weight decreased, but no effects pertaining to weight were significant. No visible inflammatory changes were seen. **Lung Damage in A/J:** No significant effect was seen, but hypomethylation was seen in females at 1wk, and methylation was reduced in all exposed female groups. **Bacteria in Lungs of C57BL/6:** Exposure did not affect the clearance of bacteria from the lung. **Respiratory Allergic Response in BALB/c:** Exposure had little effect, but serum total IgE increased significantly for the high-exposure group. Increasing trends were seen in OVA-specific serum IgE and IgG1, as well as neutrophils and eosinophils.

Reference	Pollutant	Exposure	Effects
Reference: Reed et al. (2008, 156903) **Species:** Mouse **Gender:** Male, Female (only BALB/c) **Strain:** C57BL/6, A/J, BALB/c **Age:** NR **Weight:** NR	GEE (two 1996 General Motors 4.3-L V-6 engines; regular, unleaded, non-oxygenated, non-reformulated gasoline blended to US average consumption for summer 2001 and winter 2001-2002- Chevron-Phillips) **Particle Size:** 150 nm (MMAD)	**Route:** Whole-body Inhalation **Dose/Concentration:** PM; Low- 6.6 ± 3.7 µg/m^3, Medium- 30.3 ± 11.8 µg/m^3, High- 59.1 ± 28.3 µg/m^3 **Time to Analysis:** A/J - exposed 6 h/days, 7 days/wk, 3 days-6 mo. C57BL/6- 1wk exposure. Instillation of P. aeruginosa. Killed 18 h postinstillation. BALB/c- Conditioned to exposure chambers and mated. Pregnant females exposed GD 1 and throughout gestation. Offspring exposures continued until 4 wk-old. Half of offspring sensitized to OVA. Tested for airway reactivity by methacholine challenge 48 h post-instillation and euthanized.	The kidney weight of female A/J mice decreased at 6m and was strongly related to PM by the removal of emission PM. PM-containing macrophages increased by 6 mo. Hypomethylation occurred in females at 1 wk. The clearance of P. aeruginosa was unaffected by exposure. Serum total IgE significantly and dose-dependently increased. OVA-specific IgE and IgG1 gave slight exposure-related evidence but were not significant.
Reference: Reed et al. (2008, 156903) **Species:** Rat **Gender:** Male, Female **Strain:** CDF (F344)/CrlBR, SHR **Age:** NR **Weight:** NR	GEE (two 1996 General Motors 4.3-L V-6 engines; regular, unleaded, non-oxygenated, non-reformulated Chevron-Phillips gasoline, U.S. average consumption for summer 2001 and winter 2001-2002) **Particle Size:** 150 nm (MMAD)	**Route:** Whole-body Inhalation **Dose/Concentration:** PM; Low- 6.6 ± 3.7 µg/m^3, Medium- 30.3 ± 11.8 µg/m^3, High- 59.1 ± 28.3 µg/m^3 **Time to Analysis:** 6 h/day, 7 days/wk, 3 days-6 mo.	**Organ Weight:** At 6 mo. exposure, the heart weights of male and female rats increased and male rats' seminal vesicle weight decreased. **Histopathology:** PM-containing macrophages increased by 6 mo. **Lung DNA Damage:** Hypermethylation occurred in medium- and high-exposure male rats at 6 mo. **BAL:** For both genders in the high-exposure group, LDH and MIP-2 significantly increased at 6 mo. ROS decreased at 1wk and 6 mo. Generally, the production of hydrogen peroxide and superoxide decreased in the high-exposure group and medium- and high-exposure groups, respectively. **Removal of Emission PM:** The removal of emission PM strongly linked PM to increased seminal vesicle weight, red blood cell counts, LDH, lipid peroxides, and methylation.
Reference: Rengasamy et al. (2003, 156907) **Species:** Rat **Gender:** Male **Strain:** SD **Weight:** ~200 g	DEP: SRM1650 CB Elftex-12 furnace black, Cabot, Boston, MA **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 5, 15, or 35 µg/kg **Time to Analysis:** Single; 1, 3, 5, 7 days post exposure	**CYP1A1:** DEP at all doses significantly increased CYP1A1 protein, was maximal at 1 day, and normalized at 5 days. CB had no effect. **CYP2B1:** DEP and CB at 15 and 35 mg/kg inhibited activity at 1 day. Protein level significantly decreased at 1 day with 5, 15 and 35 mg/kg DEP and at 15 and 35 mg/kg CB. A time dependent decrease was shown at 35 mg/kg for both DEP and CB.
Reference: Renwick et al. (2004, 056067) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Weight:** 370-470 g	FCB: Fine Carbon Black (Huber 990) UCB: Ultrafine Carbon Black (Printex 90, Degussa) FTO: Fine Titanium Dioxide (Tioxide) UTO: Ultrafine Titanium dioxide (Degussa) **Particle Size:** FCB: 260 nm; UCB: 14 nm; FTO: 250 nm; UTO: 29 nm	**Route:** IT Instillation **Dose/Concentration:** 125 or 500 µg/rat **Time to Analysis:** Single, 24 h	**BALF Cells:** UTO and UCB induced a large dose-dependent increase in percent neutrophils (only statistically significant at 500 µg for UTO). **BAL Inflammatory/Injury Markers:** UTO and UCB also increased total protein content only at the 500 µg dose. UCB induced LDH release at 125 and 500 µg, UTO and CB at 500 µg. UTO and UCB induced large dose-dependent increases in GGT activity (only statistically significant at 500 µg for UTO). **Phagocytosis:** All 4 particles decreased but only at the 500 µg level. **Chemotaxis:** Only UTO and UCB at 500 µg/l increased chemotactic migration.

Reference	Pollutant	Exposure	Effects
Reference: Rhoden et al. (2004, 087969) **Species:** Rat **Gender:** Male **Strain:** SD **Weight:** 250-300 g	CAPs (Boston, MA) **Particle Size:** CAPS: 0.1-2.5 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** 1060 ± 300 µg/m^3 **Time to Analysis:** Single exposure for 5 h. Analyzed 24 h post-exposure. (CAPS-NAC = CAPS with 50 mg/kg bw NAS (N-acetylcysteine) pretreatment)	**Particle Characteristics:** Major components did not appear to show any correlation to total particle mass. Included Na, Mg, Al, Si, S, Cl, K, Ca, Ti, V, Cr, Mn, Fe, Ni, Cu, Zn, Br, Ba, Pb. Metals Al, Si and Fe (somewhat less for Pb, Cu, K) correlated with TBARS. **BALF Cells:** CAPS increased PMN 4 fold. NAS treatment reduced this increase to control levels. **BAL Inflammatory/Injury Markers:** LDH and total protein not affected. Histology confirms slight inflammation with CAPS and no inflammation with CAPs-NAC. **Oxidative Stress:** CAPS increased TBARS and oxidized protein by 2+ fold. NAS fully prevented the increase in TBARS and partially prevented an increase in protein carbonyl. **Tissue Damage:** Wet/dry ratio increased with CAPS but significantly decreased with NAC.
Reference: Rhoden et al. (2008, 190475) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** NR **Weight:** 300 g	Urban Air Particles (UAP) (SRM 1649) **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 1mg in 100 µL saline **Time to Analysis:** Instilled with UAP. CL analysis:15 min post-exposure. BAL measurements: 4 h post-exposure. Some rats pre-treated with MnTBAP 2 h prior to UAP exposure.	UAP significantly increased the total cell number, PMN, MPO activity, and protein levels. MnTBAP prevented UAP-induced lung inflammation. UAP increased oxidants in lung CL, which was prevented by MnTBAP.
Reference: Rivero et al. (2005, 088653) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 3 mo. **Weight:** 250 g	Ambient air (Sao Paulo, Brazil) **Particle Size:** <2.5 µm	**Route:** IT Instillation **Dose/Concentration:** 100 or 500 µg/rat; 0.4 or 2 mg/kg **Time to Analysis:** Single, 24 h	**Histopathology:** At both doses, acute alveolar inflammation was observed and was more pronounced in the 500 µg group. **Lung Morphometry:** Lumen wall ratio values show a dose-dependent increase in peribronchial as well as intra-acinar pulmonary arterioles. No effect in myocardial arterioles were observed. **Tissue Damage:** Lung wet/dry ratios were unaffected.
Reference: Roberts et al. (2004, 198903) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** 60-90 days **Weight:** 300-350 g	ROFA: SRI (cyclone power plant) **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 0.5 mg/rat; 1.67 mg/kg **Time to Analysis:** Single, 6 and 24 h	**Technology:** Laser capture microdissection of airway cells were used to analyze results. **Protein: pERK1/2:** ERK1/2 ratio increased by 60% at 6 h and 80% at 24 h. NF-κB activity increased at 6 h but was not statistically significant.
Reference: Saber et al. (2005, 097865) **Species:** Mouse **Gender:** Female **Strain:** TNF(-/-) (B6, 129S-Tnftm1Gk1), C57/BL **Age:** 9-10 wk	DEP: SRM 2975 CB: Printex 90 (Degussa) **Particle Size:** DEP: 215 nm; CB: 90 nm	**Route:** Nose-only Inhalation **Dose/Concentration:** DEP: 20 mg/m^3; CB: 20 mg/m^3 **Time to Analysis:** 90 min/day for 4 days consecutively, 1 h	**BALF Cells:** Neutrophils increased significantly to 15% when compared to control (4%) with DEP exposure. No response difference was observed between TNF (+/+) and TNF(-/-). CB did not induce any changes in neutrophil numbers. **Cytokines:** IL-6 increased 2-3 fold in DEP and CB exposure in both normal and knockout mice. IL-1β was unaffected. **mRNA:** In TNF (+/+) mice, DEP and CB increased expression of TNF mRNA 2- fold. IL-6 mRNA expression was high in DEP-exposed knockout mice when compared to normal mice. **DNA:** DNA strand breaks increased in both strains. Knockout mice showed a higher response to CB and DEP exposure. For normal mice, only CB induced a statistically significant effect.

Reference	Pollutant	Exposure	Effects
Reference: Schins et al. (2004, 054173) **Species:** Rat **Gender:** Female **Strain:** Wistar Kyoto **Weight:** 350-550 g	Soluble fractions PMC: $PM_{10-2.5}$ PMF: $PM_{2.5}$ -B: Borken, Germany (rural) -D: Duisburg, Germany (industrialized) **Particle Size:** $PM_{10-2.5}$, $PM_{2.5}$	**Route:** IT Instillation **Dose/Concentration:** 0.32 ± 0.01 mg/rat; 0.91± 0.58 mg/kg **Time to Analysis:** Single, 18 h	**BALF cells:** Both PMC showed a massive increase in neutrophils. PMC-B induced the greatest increase followed by PMC-D. Both PMF did not induce a significant increase. **BAL Inflammatory/Injury Markers:** PMC from both sites induced markedly higher endotoxin concentration vs PMF as follows in decreasing order: PMC-B, PMC-D, PMF-B, PMF-D, control. Glutathione decreased only for PMC-B. LDH and total protein were unaffected. **Cytokines:** TNF-α and IL-8 increased with PMC from both sites. PMF induced a slight increase in IL-8 but did not induce an increase in TNF-α. **Radical Formation:** Formation of hydroxyl radicals increased with exposure. Relative intensity was: PMC-D, PMF-D, PMC-B, PMF-B, and control.
Reference: Seagrave et al. (2005, 088000) **Species:** Rat **Gender:** Male **Strain:** F344/DCrl BR **Age:** 11 ± 1 wk	PM from 3 sources: NT: New Technology bus, Detroit Diesel 50G, exhaust oxidation catalyst, 216 miles, 2002 model - in use NE: Normal emitter bus, Detroit Diesel 50G, no catalyst, 134259 miles, 1997 model - in use HE: High Emitter bus, Cummins L10G, no catalyst, >250, 000 miles, 1992, retired Fuel composition very similar for 3 vehicles: methane (96-96.8%), ethane (1.6-1.9%), carbon dioxide (0.9-1.1%), nitrogen (0.6-0.8%), traces of other gases **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 0.25-2.2 mg/rat in 0.5mL saline **Time to Analysis:** Single, 24 h	**Engine Specific Emission data:** HE had significantly higher PM and SVOC recovered emission rates than NE and NT. **Organic mass in PM:** The following PM sources are listed in decreasing order of percent of total mass: HE, NE, NT. **Total PAH:** The following PM sources are listed in decreasing order of total mass: HE, NT, Control, NE. **Nitro PAH:** The following PM sources are also listed in decreasing order of total mass: NE, HE, Control, NT. Authors note confounding technical issues (mostly technique related) with mostly mild effects. **BAL Inflammatory/Injury Markers:** LDH showed dose-dependent increases with HE inducing higher increases than NT and NE. Total protein exhibited dose-dependent increases with HE, NT and the positive control SRM2975 inducing higher levels than NE. **Potency Factors Cytotoxicity and Inflammation:** HE was significantly more potent than NT and NE, with NT also showing significant potency. **Lung Toxicity:** The results were highly variable but the general toxicity levels in increasing order is the following: NE, NT, HE, Normal gasoline, diesels, and high gasolines, though individual factors may differ greatly.
Reference: Seagrave et al. (2006, 091291) **Species:** Rat **Gender:** Male **Strain:** F344/Crl BR, **Age:** 11 ± 1 wk	$PM_{2.5}$ sources: BHM: Birmingham, Alabama; urban JST: Jefferson Street, Atlanta, Georgia; urban PNS: Pensacola, Florida; urban/residential CTR: Centreville, Alabama; rural "smoke" = downwind of forest fires/burns (NR) **Particle Size:** $PM_{2.5}$	**Route:** IT Instillation **Dose/Concentration:** 0.75, 1.5, 3 mg/rat **Time to Analysis:** Single, 24 h	**BALF PMN:** In general, the winter samples induced greater increases in potency than the summer samples except for PNS. For the winter samples, the samples that induced the greatest increases, in descending order, are: JST, BHM, CTR, PNS and Smoke. For the summer, the samples that induced increases, in descending order, are: BHM, JST, PNS, and CTR. **BALF Macrophages:** For the winter, the BHM and JST samples significantly increased potency whereas the PNS sample induced significantly negative potency. For the summer, only the BHM sample significantly induced potency. **BALF Lymphocytes:** Only the JST-W and BHM-W significantly increased potency. The BHM-S, CTR-S and PNS-S also significantly increased potency. **Histopathology:** All the winter and summer samples, excepting PNS, significantly induced inflammation. **Lung weight/body Weight Ratio:** In general, for all end points, JST-S was significantly less potent than JST-W. The summer samples of BHM and CTR were also generally more potent than their winter counterparts.

Reference	Pollutant	Exposure	Effects
Reference: Seagrave et al. (2005, 088000) **Species:** Rat **Gender:** Male, Female **Strain:** CDF(F-344)/CrlBR **Age:** 10-12 wk	DE: (Two 6 cyl Cummins ISB turb0) HWS = hardwood smoke (mixed black/white oak, uncertified conventional wood stove) DE: EC = 557 µg/m^3 OC = 269 µg/m^3 NO = 45 ppm NO_2 = 4 ppm CO = 30 ppm THV = 2 ppm HWS: EC = 43 µg/m^3 OC = 908 µg/m^3 NO or NO_2 = 0 ppm CO = 13 ppm THV = 3 ppm **Particle Size:** DE: 0.14 ± 1.8 µm; HWS: 0.36 ± 2.1 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** 30, 100, 300, 1000 µg/m^3 TPM **Time to Analysis:** 6 h/day, 7 days/wk for 6 mo. 1 day post-exposure	**Particle Characteristics:** Major differences K: HWS>>DE; Ca DE>>HWS; Zn: DE>>HWS. **BALF Cells:** No effects were observed except for an increase in macrophages at 30 µg/m^3 for HWS males exposed to HWS. **Cytokines:** IL-1β was unaffected by DE or HWS. MIP-2 decreased for both genders at 1000 HWS. TNF-α decreased in females with DE exposure. No TNF-α effects for HWS were observed. **BAL Inflammatory/Injury Markers:** LDH was unaffected by DE. Exposure to HWS induced an increase for males only at 100 and 300 but not at 1000 µg/m^3. Protein was unaffected by DE. HWS exposure showed male-only effects at 100 and 300 µg/m^3 but not at 1000. AP was unaffected by DE or HWS except for slight decline induced by HWS at 1000 µg/m^3 for both genders. **Other:** β-glucose was unaffected by DE. HWS-exposed females showed decreased β-glucose at 100 and 300 but not at 1000 µg/m^3. **BALF GSH to (GSH+GSSG):** No effects for DE were observed. HWS significantly decreased the ratio in both males and females at 1000 µg/m^3. The effect for females was greater than the male effect.
Reference: Seagrave et al. (2008, 191990) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** 10-12 wk **Weight:** 250-300 g	GEE (2 1996 General Motors 4.3-L V6 gasoline engines; conventional Chevron Phillips gasoline, U.S. average composition) (CO, NO, NO_2, SO_2, THC) ($PM_{2.5}$ composition-EC, OC, SO4, NH4, NO_3) Simulated downwind coal emission atmospheres (SDCAs) (fly ash, gas-phase pollutants, sulfate aerosols, NO, NO_2, SO_2) Paved Road Dust (RD) (Los Angeles, CA; New York City, NY; Atlanta, GA) **Particle Size:** GEE: MMAD- 150 nm, RD: 2.6 ± 1.7 µm, SDCA: 0.1-1.0 µm	**Route:** Nose-only Inhalation **Dose/Concentration:** GEE: 60 µg/m^3, SDCAs: 317-1072 µg/m^3, RD: 306-954 µg/m^3; GEE: CO-104 ppm, NO- 16.7 ppm, NO_2- 1.1 ppm, SO_2-1.0ppm, THC- 12 ppm; SDCAs: CO- <1 ppm, NO-0.19-0.62 ppm, NO_2- 0.10-0.37 ppm, SO_2- 0.07-0.24 ppm, THC- <1 ppm **Time to Analysis:** 6 h exposure, immediately post-exposure	GEE produced CL in the lungs, heart, and liver. RD produced a significant effect in the heart at the low dose. SDCAs had no effect on CL. GEE did not affect the amount of macrophages or PMN. SDCAs increased macrophages. The RD low dose increased macrophages and PMN. SDCAs increased Penh values and tidal volumes.
Reference: Singh et al. (2004, 087472) **Species:** Mouse **Gender:** Female **Strain:** CD-1 **Age:** 6-8 wk	A-DEP (4cyl light duty 2.7l Isuzu diesel at 6 kg/m) DEP: SRM 2975 **Particle Size:** A-DEP >50 µm	**Route:** Oropharyngeal Aspiration **Dose/Concentration:** 25 or 100 µg/mouse **Time to Analysis:** single, 4 h (18 h post-exposure measurements taken but NR due to similar results)	**Particle Characteristics:** DEP had 60% EC vs 9% in A-DEP. A-DEP had 50% OC vs 5% in DEP. Phenanthrene and Fluoranthene fractions were much more prevalent in PAH from DEP than A-DEP. **BALF Cells:** PMNs significantly increased dose-dependently with DEP and remained elevated at 18h. Endotoxin induced the greatest increases of PMNs. Macrophages increased with A-DEP and were unaffected by DEP. **Cytokines:** Endotoxin induced massive responses for IL-6, MIP-2 and TNF-α but no response from IL-5. A-DEP increased all 4 cytokines but only at the 100 µg dose level. Similarly, DEP only increased IL-6 at the 100 µg dose level. **BAL Inflammatory/Injury Markers:** Microalbumin increased for both pollutants except DEP induced increases only at 100 µg. Endotoxin increased microal-bumin. NAG increased with 100 µg A-DEP.

Reference	Pollutant	Exposure	Effects
Reference: Smith et al. (2003, 042107) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** 11-12 wk	CAPs (Fresno, CA) **Particle Size:** <2.5 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** 6 exp in 2 sets of 3: Fall1 = 847 µg/m^3 Fall2 = 260 µg/m^3 Fall3 = 369 µg/m^3 Winter1 = 815 µg/m^3 Winter2 = 190 µg/m^3 Winter3 = 371 µg/m^3 **Time to Analysis:** 4 h/days for 3 consecutive days. Parameters measured immediately following last exposure.	**Particle Characteristics:** Nitrate showed the highest variability near 10 fold, followed by Si, S and EC. OC concentration was relatively consistent. Metals otherwise appeared proportionate to the concentrations. **BALF Cells:** Total cells increased at wk1. Percent of macrophages reduced in wk2 with CAPs. Number of neutrophils increased with CAPs, but only achieved statistical significance during wk1 of the fall and winter. Lymphocytes increased but were not statistically significant. **BAL cell permeability**: Upon CAPs exposure, the proportion of nonviable cells were increased up to 242% when compared to controls. The fall of wk2 induced the highest significant increases followed by fall wk1, fall wk3, and winter wk3.
Reference: Smith et al. (2006, 110864) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** 8 wk **Weight:** 260-270 g	CFA: Coal Fly Ash (400 MW, Wasatch Plateau, Utah) (aerodynamic separation) **Particle Size:** 0.4-2.5 µm	**Route:** Nose-only Inhalation **Dose/Concentration:** 1400 µg/m^3 $PM_{2.5}$ including 600 µg/m^3 PM_1 **Time to Analysis:** 4 h/days for 3 consecutive days. Parameters measured 18 or 36 h post-exposure.	**BALF Cells:** Percent and total number of neutrophils in BALF and blood increased significantly at both 18 and 36 h. Percent of macrophages decreased slightly while number of macrophages increased in bronchiole-alveolar duct regions at both time periods. **Cytokines:** MIP-2 and transferrin increased at 18 h. IL-1β increased at 36 h. **Other:** Gamma glutamyl transferase decreased at 36 h. Lung antioxidant increased at 18 h.
Reference: Song et al. (2008, 156093) **Species:** Mouse, **Gender:** Female **Strain:** BALB/c **Age:** 5-6 wk	DEP collected from a 4JB1-type, light-duty (2740 cc), four-cylinder diesel engine operated using standard diesel fuel at speeds of 1500 rpm under a load of 10 torque. **Particle Size:** 0.4 µm (mean diameter)	**Route:** Intranasal Instillation (days 1-5), Whole-body Inhalation (days 6-8) **Dose/Concentration:** 0.6 mg/mL in 50 µL of saline (days 1-5), 6mg/m^3 for 1 h/day for 3 days (days 6-8). **Time to Analysis:** Enhanced Pause (Penh), measured on day 9. BAL and lung tissues collected on day 10.	**Airway Hyperresponsiveness:** Intranasal exposure plus aerosolized DEP caused a significant increase in methacholine-induced Penh over the control. **BAL Analysis:** There was no significant increase in IFN-γ in the BAL fluid following DEP treatment but there was a significant increase in IL-4 levels compared to the control. (IL-4 increase could indicate that DEP modulates Th-2 cytokines in the mouse model). DEP also induced an increase in total neutrophils and lymphocytes in the BAL when compared to the control. The nitrite concentration in BAL (indicating NO generation) was significantly greater in the DEP exposed group than the control. **Histology:** Peribronchial and perivascular infiltrates were more common in the group exposed to DEP than the control. **Ym1 and Ym2 Expression:** (see explanation in comments section) Ym1 and Ym2 transcripts were upregulated in response to DEP exposure in mice.
Reference: Steerenberg et al. (2006, 088249) **Species:** Rat **Strain:** Crl/WKY **Age:** 6-8 wk	Ambient air samples PMC, PMF: -I: Rome, Italy -N: Oslo, Norway -PL: Lodz, Poland -NL: Amsterdam, Netherlands Measured Components: Li, Be, B, Na, Mg, Al, K, Ca, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Se, Sr, Mo, Cd, Sn, Sb, Ba, Ce, Nd, Sm, Au, Hg, Tl, Pb, Bi, U, Si, Endotoxins, Cl, NO-, SO4 **Particle Size:** PMC: 2.35-8.5 µm; PMF: 0.12-2.35 µm	**Route:** IT Instillation **Dose/Concentration:** 1 and 2.5 mg/animal **Time to Analysis:** Single, 24 h	**Particle Characteristics:** Concentrations of metals were highest in Rome. Amsterdam was noted for high Mg and V. Lodz was noted for high Pb, Zn, PAH. More of PMC was composed of Fe, Mn, Al, Cr, Cu. More of PMF, on the other hand, was composed of Zn, Pb, Ni, V. **BALF Cells:** PMNs increased. **Cytokines:** MIP-2 increased dose-dependently. TNF-α also increased. **BAL Inflammatory/Injury Markers:** CC16 decreased substantially. Crustal material (endotoxin, Na, Cl and metals but not Ti, As, Cd, Zn, V, Ni, Se) was positively associated with short term CC16. Albumin increased.

Reference	Pollutant	Exposure	Effects
Reference: Stinn et al. (2005, 088307) **Species:** Rat **Gender:** Male and Female **Strain:** Crl: (WIU BR **Age:** 40 days	DE (generated from 1.6 L VW diesel under USFTP 72) CO: 10, 37 ppm CO_2: 2170, 6540 ppm NO: 7.0, 22.8 ppm NO_X: 8.6, 28.3 ppm SO_2: 0.83, 3.09 ppm NH_4: ND Measured Major Components: NO, SO_2, 1-nitropyrene, Zi. 50% by DE weight is EC. **Particle Size:** 0.19-0.21 µm (MMAD)	**Route:** Nose-only Inhalation **Dose/Concentration:** 3 and 10 mg/m^3 **Time to Analysis:** 6 h/day, 7 days/wk for 24 mo; 6 mo. post-exposure	**Body Weight:** Mean weight increased substantially during the first few weeks in all groups. Food consumption decreased in 1-24 mo but was recovered in 24-30 mo. Body weight decreased at 23 mo in all categories, but recovered except in high dose males at 30 mo. **Organ Weight:** Absolute weight of lungs, larynx and trachea increased from 0 to 12 to 24 mo and stayed elevated at 30 mo: Low<Hi, male ~ female. **Pulmonary Parameters:** Respiratory frequency, tidal volume, and minute volume were unaffected in any group measured between 3 and 24 mo. EC increased dose-dependently in exposure groups. No male/female difference was observed, but increases were greater at 24 mo than at 18 mo. **BALF Cells:** PMNs and lymphocytes showed dose and time-dependent effects at 18 and 24 mo (no data at 30 mo). Lymphocytes increased 50 fold in high dose males at 24 mo. Peripheral monocytes and neutrophils increased 3 fold in DE groups at the end of the study. Particle-filled macrophages in alveolar lumen and interstitium increased at 12, 24, 30 mo in both genders at all dose levels. **BAL Inflammatory/Injury Markers:** LDH increased in dose and time-dependent manner. **Nasal Cavity Histopathology:** All effects were resolved at 30 mo. Nasal cavity hyperplasia increased at the high dose at 12 and 24 mo in both genders. Squamous metaplasia of respiratory epithelium increased in high dose females (12, 24 mo). **Larynx Histopathology:** No effects were observed. **Lung Histopathology:** Alveolar region hyperplasia of alveolar epithelium increased at 12, 24, 30 mo in both genders at all dose levels except for 12 mo low dose males and females. Above lung histopathology was not time-dependent, though perhaps some small dose-dependence was observed. The following histopathology findings showed strong dose- and time-dependent increases that occurred in both genders (24-30 mo): goblet cell hyperplasia of bronchial epithelia, cuboidal/columnar hyperplasia of alveolar epithelium, chronic active inflammation and septal fibrosis. **Tumorigenicity:** Lung tumors were more prevalent in females than males and appeared to be dose-dependent. The major 3 types of tumors are the following:: bronchio-alveolar adenoma, bronchiolo-alveolar adenoma and benign keratinizing cystic cell tumors. Enhanced effects in females versus males may be the result of enhanced metabolism (body volume versus body weight) and increased respiratory volume/bw for females.

Reference	Pollutant	Exposure	Effects
Reference: Sureshkumar et al. (2005, 088306) **Species:** Mouse **Gender:** Male **Strain:** Swiss **Age:** 10-12 wk **Weight:** 20-25 g	GE: Gasoline Exhaust (Honda generator EBK 1200, four stroke one cyl) Including: SO_2 = 0.11 mg/m^3 NO_X = 0.49 mg/m^3 CO = 18.7 ppm **Particle Size:** GE >4 µm = 34.1% 3-4 µm = 15.8% 2-3 µm = 15.8% 1.5-2 µm = 10.6% 0.5-1.5 µm = 5.3% <0.5 µm = 18.4%	**Route:** Nose-only Inhalation **Dose/Concentration:** 0.635 mg/m^3 **Time to Analysis:** 15 min/day 7, 14 or 21 days; ; <1 h post-exposure	**BALF Cells:** Neutrophils (%) increased at 7, 14 and 21 days (stable). Total cell count, macrophages and eosinophils were unaffected. Leukocytes and lymphocytes increased, though not significantly. **Cytokines:** GE caused time-dependent increases in TNF-α and IL-6. IL-10 and IL-1β were unaffected. **BAL Inflammatory/Injury Markers:** γ-GGT, ALP and LDH increased after 2 wk of GE exposure and stayed stable at 21 days. Total protein slightly increased on 14 and 21 days, though these increases were not statistically significant. **Histopathology:** Minor changes at 7 days, mild edema in alveolar region at 14 days and sloughing of epithelial cells in bronchiolar region and focal accumulation of inflammatory cells in alveolar region at 21 days were observed in a time-dependent manner.
Reference: Tesfaigzi et al. (2002, 025575) **Species:** Rat **Gender:** NR **Strain:** Brown-Norway **Age:** 7-8 wk **Weight:** 310-330 g	WS (wood stove- Vogelzang Boxwood Stove, Model BX-42E, wood- Pinus edulis) (CO, NO, NO_X, total hydrocarbon) **Particle Size:** Smaller size fraction: 0.405-0.496 µm, larger size fraction: 6.7-11.7 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** Target concentration (low, high exposure): 1, 10 mg/m^3; CO- 15-106.4 ppm, NO- 2.2-18.9 ppm, NO_X- 2.4-19.7 ppm, total hydrocarbon- 3.5-13.8 ppm **Time to Analysis:** 3 h/day, 5 days/wk, 4 or 12 wk.	**Respiratory Function:** Total pulmonary resistance increased for exposure groups and was significant for the low-exposure group. In exposed groups, forced expiratory flows and quasistatic compliance were lower and dynamic lung compliance higher, the latter being significant for the high-exposure group. For the high-exposure group, vital capacity slightly decreased, residual volume slightly increased, and CO-diffusing capacity had a slight, significant decrease. **BALF Cells:** Macrophages decreased significantly in the high-exposure group. Particle-laden macrophages increased with concentration. Lymphocytes and neutrophils slightly increased in the high-exposure group. **Cytokines:** LDH increased slightly and protein levels decreased slightly in the high-exposure group. Cytokines were below detectable levels. **Histopathology:** WS caused minimal to mild chronic inflammation in the epiglottis of the larynx. PAS-positive cells increased in the 30 day high-exposure group. AMs increased with time and concentration. Particle-laden macrophages were seen after 90 days. AB- and PAS-positive epithelial cells increased for the 90 day low exposure group.
Reference: Tin-Tin-Win-Shwe et al. (2006, 088415) **Species:** Mouse **Gender:** Male **Strain:** BALB/c **Age:** 7wk	CB14: Printex 90 (Degussa) CB90: Flammruss 101 (Degussa) **Particle Size:** CB14: 14 nm CB95: 95 nm	**Route:** IT Instillation **Dose/Concentration:** 25, 125, 625 µg/mouse; approx. 1, 5, 25 mg/kg **Time to Analysis:** 1/wk for 4wk. 4 h post-exposure	**Body Weight, Thymus, Spleen, Splenic Cell Count:** No effects were observed. **BALF Cells:** Increased total cell numbers were observed for 125, 625 µg CB14 (dose-dependent) and 625 µg CB95. Total cell count was twice as high for CB14 at 125 and 625 µg compared to CB95. AM numbers exhibited a dose-dependent response for both CB14 and CB95 for all doses except 125 µg. Lymphocyte numbers increased at 125 and 625 µg for CB14 and 625 µg for CB95. PMN numbers increased at 125 and 625 µg for CB14 and CB95, but the response was greater with CB14. PMN numbers were proportional to dose surface area for both PM sizes. **BAL Cytokines:** CB14 and CB95 induced dose-dependent increases in IL-1β. TNF-α increased at 125 and 625 µg dose in CB14 with the 125 dose inducing a slightly greater increase. CB14 and CB95 induced CCL-3 increases 125 and 625 µg. **Chemokine mRNA in lung and lymph nodes:** CCL-3 mRNA increased for CB14 but not CB95 4 h following the last exposure. CCL-2 was unchanged. **Mediastinal lymph nodes:** The number of CB-laden phagocytes increased in a dose-dependent manner for CB14 and CB95. CB14 had higher numbers at all doses compared to CB95.

Reference	Pollutant	Exposure	Effects
Reference: Tong et al. (2006, 097699) **Species:** Mouse **Gender:** Male **Strain:** KP600 CD-1 **Weight:** 22-26 g	$PM_{2.5}$ (collected from stacked filter air sampler in Shanghai, China) Fe: $FeSO_4$ Zn: $ZnSO_4$ PMF: $PM_{2.5}$ + $FeSO_4$ PMFZ: $PM_{2.5}$ + $FeSO_4$ + $ZnSO_4$ Major Measured Components: Fe 26 ppm, Zn 9 ppm, S 61 ppm **Particle Size:** $PM_{2.5}$	**Route:** IT Instillation **Dose/Concentration:** PM: 25 mg/mL, 1mg/mouse Fe: 15mg/mL, 0.6 mg/mouse Zn: 15mg/mL, 0.6 mg/mouse PMF: PM 25 mg/mL + Fe 15 mg/mL, 1.6 mg/mouse PMFZ: PM 25 mg/mL + Fe 15 mg/mL, 1.6 mg/mouse **Time to Analysis:** Instilled twice at 0 and 24 h. Parameters measured 24 h following last exposure (at 48 h).	**Synchrotron X-ray imaging:** PMFZ showed the greatest increase in alveolar changes. Fe induced more hemorrhagic changes, whereas Zn induced more nonuniformity of lung texture. This suggests that Zn induces PBMC in a dose-dependent manner which releases IL-1, IL-6, TNF-α, and IFN-γ. **Histopathology:** PMFZ induced the most severe changes including serious inflammation/pus in bronchia and bronchial epidermal cell hyperplasia. For Fe or PMF hemorrhagic changes predominated but were less severe than PMFZ.
Reference: Upadhyay et al. (2008, 159345) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 6 mo. **Weight:** NR	Ultrafine Carbon Particles (UFCP) **Particle Size:** Size- 31 ± 0.3 nm, MMAD- 46 nm, Surface area concentration- 0.139 m^2 particles/m^3, Mass specific surface area- 807 m^2/g	**Route:** Whole-body Inhalation **Dose/Concentration:** 172 µg/m^3 **Time to Analysis:** 24 h exposure. 4 days recovery. Sacrificed 1st or 3rd day of recovery.	**Pulmonary Inflammation:** UFCP did not cause pulmonary inflammation. **Pulmonary and Cardiac Tissue:** HO-1, ET-1, ETA, ETB, TF, PAI-1 significantly increased in the lung on the 3rd recovery day. HO-1 was repressed in the heart, but the other markers had slight, nonsignificant increases.
Reference: Wallenborn et al. (2007, 156144) **Species:** Rat **Gender:** Male **Strain:** WKY, SH,, and stroke-prone SH (SHRSP) **Age:** 12-15 wk	PM: precipitator unit power plant residual oil combustion **Particle Size:** PM: 3.76 µm (bulk) ± 2.15	**Route:** IT Instillation **Dose/Concentration:** WKY vs SHRSP: 1.11, 3.33, 8.33 mg/kg SH vs SHRSP: 3.33, 8.33 mg/kg **Time to Analysis:** Single, 24 h Note: 4 h post-exposure study done on WKY vs SHRSP but not published.	**BALF Cells:** A dose-dependent increase in total cells and neutrophils was observed. Equal response for all 3 strains except for SH, for both concentrations was observed. **BAL inflammation/Injury Markers:** LDH exhibited a dose-dependent increase in equal response for all 3 strains. WKY had higher baseline levels of NAG activity but, upon PM exposure, SHRSP induced higher increases than WKY. GGT exhibited a dose-dependent response for all 3 strains. SHRSP showed the highest increase followed by WKY and SH. Protein levels increased at the high dose level with SHRSP exhibiting the highest increases followed by SH and WKY. Albumin levels were inconsistent between experiments. **Oxidative Stress - Lung:** (WKY vs SHRSP only): SOD decreased following increased exposure levels with SHRSP levels generally higher than WKY. Ferritin levels declined only in SHRSP. **GPx:** No action but SHRSP levels were similar to SHR and, in the WKY vs SHRSP experiment, SHRSP exhibited higher activity level than WKY. **Ferritin:** Equivocal results were observed. Levels decreased at the high dose for WKY and SHRSP but increased at medium doses for SH and SHRSP. **ICDH:** Levels increased for WKY and decreased for SHRSP.
Reference: Wallenborn et al. (2008, 191171) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 13 wk **Weight:** NR	Zinc Sulfate ($ZnSO_4$, aerosolized) **Particle Size:** NR	**Route:** Nose-only Inhalation **Dose/Concentration:** 9.0 ± 2.1 µg/m^3, 35 ± 8.1 µg/m^3, 123.2 ± 29.6 µg/m^3 **Time to Analysis:** Exposed 5 h/days, 3 days/wk, 16 wk. Half of the rats used for plasma/serum analysis, other half for isolation of cardiac mitochondria.	A trend toward increased BALF protein was seen. No pulmonary-related effects were seen.

Reference	Pollutant	Exposure	Effects
Reference: Wegesser and Last (2008, 190506) **Species:** Mouse **Gender:** Male **Strain:** BALB/c **Age:** 8-10 wk	Ambient $PM_{2.5-10}$ Collected from San Joaquin Valley, CA **Particle Size:** $PM_{10-2.5}$	**Route:** IT Instillation **Dose/Concentration:** 25-50 µg/mouse **Time to Analysis:** 3, 6, 18, 24, 48, 72 h post IT instillation.	**BALF Cells:** Increased amount of viable cells found in PM-exposed mice with dose-response relationship between dose of PM and number of total cells recovered in BALF. At 6 h, increased numbers of macrophages at both 25 and 50 µg/mouse. Increased percentage of neutrophils observed with 50 µg/mouse PM only. Furthermore, both macrophages and neutrophils increased with longer time period from instillation, peaking at 24 h. At 50 µg/mouse, MIP-2 concentrations increased, peaking at 3 h, though not statistically significant and returned to basal levels by 6 h. Positive correlation observed between MIP-2 concentration and increased neutrophil counts. No correlation found between MIP-2 and macrophages.
Reference: Whitekus et al. (2002, 157142) **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 6-8 wk **Weight:** NR	DEP (light-duty, four-cylinder engine- 4JB1 type, Isuzu Automobile, Japan; standard diesel fuel) (extracts) **Particle Size:** 0.5-4 µm	**Route:** Inhalation **Dose/Concentration:** 200, 600, 2000 µg/m^3 **Time to Analysis:** Exposed 1 h/day,10 days. Animals receiving OVA had 20 min OVA exposure after DEP exposure.	DEP+OVA dose-dependently increased IgE and IgG1, being more effective than the OVA-alone treatment. This effect was significantly suppressed by thiol antioxidants NAC or BUC. DEP+OVA increased carbonyl protein and lipid peroxide over OVA. NAC or BUC suppressed lipid peroxide and protein oxidation. No general markers for inflammation were observed.
Reference: Wichers et al. (2004, 055636) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 75 days	PM (HP-12): inside wall of stack of Boston, MA power plant burning # 6 oil. **Particle Size:** PM: 3.76 µm ± 2.15	**Route:** IT Instillation **Dose/Concentration:** 0.83, 3.33 or 8.33 mg/kg **Time to Analysis:** single, 6 h for Whole-body plethysmographs (WBP) and repeated daily for 4-7 days, 96 or 192 h post-exposure non-WBP animals: single, 24, 96, 192 h post-exposure	**Tidal Volume:** A dose-dependent decrease in tidal volume (45 % at high dose) was sustained for 1 day with very slow recovery over 7 days. **Breathing Frequency:** Dose-dependent increase (100 % at high dose) with recovery at 7 days was observed. **Minute Ventilation:** Small dose-dependent increases were observed with a return to normal ventilation in 2 days. **Penh (enhanced pause):** Equivocal results in all groups were observed (due to major control variation). **BALF Cells:** Dose-dependent increases in total cells at 24 h, with declined, but still elevated, levels at 192 h. Neutrophils increased significantly (10 fold) at 24 h in the mid and high dose groups and showed declined, but still elevated, levels at 192 h. Macrophages slowly increased in a dose-dependent manner at 192 h. **BAL Inflammatory/Injury Markers:** Protein and albumin increased at 24 h, returned to relative basal level at 192 h at the mid and high dose levels. NAG exhibited dose-dependent increases at 24 h and sustained these levels through 192 h.
Reference: Wichers et al. (2006, 103806) **Species:** Rat **Gender:** Male **Strain:** SH **Age:** 71-73 days **Weight:** 255-278 g	PM (HP-12): inside wall of stack of Boston, MA power plant burning # 6 oil. **Particle Size:** 1.95 µm ± 3.49	**Route:** Whole-body Inhalation **Dose/Concentration:** 13 mg/m^3 **Time to Analysis:** Phase I: 1st day, filtered air, 2nd day, 6 h of PM Phase II: 1st day filtered air, 4 days of 6 h PM each Immediate post-exposure	**Body/ Lung Weight:** No effects on Phase I rats were observed. HP-12 exposure increased body weight, left lung, right intercostal, and right diaphragmatic lobes in Phase II rats. However, results appeared due to normal growth in juvenile rats over 4 days. **Lung lobe to Body Weight Ratio:** No effects at 1 or 4 days were observed. **Deposition calculations:** V and Co were used to estimate deposition rates (good correlation between two metals at R_2 = 0.94). Total HP-12 deposition using Co was 26 and 99 µg (for 1 day and 4 day experiments) and using V was 31 and 116 µg. Modeling information estimated HP-12 deposition at 43% in conducting airways and 57% in alveolar region. **Breathing parameters:** No changes were observed for 1 or 4 days studies except for a possible decrease in frequency for the 1 day study.

Reference	Pollutant	Exposure	Effects
Reference: Witten et al. (2005, 087485) **Species:** Rat **Gender:** Female **Strain:** F344 **Age:** 8 wk **Weight:** ~175 g	DEP (heavy-duty Cummins N14 research engine operated at 75% throttle) **Particle Size:** 7.234-294.27 nm	**Route:** Nose-only Inhalation **Dose/Concentration:** Low- 35.3 ± 4.9 µg/m^3, High- 632.9 ± 47.61 µg/m^3 **Time to Analysis:** Exposed 4 h/day, 5 days/wk, 3 wk. Pretreated with saline or capsaicin.	There were no differences for substance P. The low-exposure group had significantly less NK1. DEP reduced NEP activity. Plasma extraversion dose-dependently increased and was greatest in capsaicin animals. Respiratory permeability dose-dependently increased. IL-1β was significantly higher for the low-exposure group. IL-12 was significantly lower in the capsaicin high-exposure group. TNF-α increased in the high-exposure group and capsaicin low-exposure group. High exposure induced particle-laden AMs in the lungs, perivascular cuffing consisting of mononuclear cells, alveolar edema and increased mast cell number. Neutrophil and eosinophil influx was not seen.
Reference: Wong et al. (2003, 097707) **Species:** Rat **Gender:** Female **Strain:** F344/NH **Age:** ~4 wk **Weight:** ~175 g	DEP (Cummins N14 research engine at 75% throttle) (EC-34.93-601.67 µg/m^3, OC- 1.90-11.25 µg/m^3, Sulfates 0.94-17.96 µg/m^3, Na- 4.07-4.78 ng/m^3, Mg-0.60-0.86 ng/m^3, Ca- 5.05-10.66 ng/m^3, Fe- 3.17-6.44, Cr- 0.68-1.31 ng/m^3, Mn- 0.11-0.22 ng/m^3, Pb- 0.97-1.24 ng/m^3) **Particle Size:** 7.5-294.3 nm	**Route:** Nose-only Inhalation **Dose/Concentration:** Low- 35.3 ± 4.9 µg/m^3, High- 669.3 ± 47.6 µg/m^3 **Time to Analysis:** Exposed 4 h/day, 5 days/wk, 3 wk. Pretreated with saline or capsaicin.	DEP dose-dependently increased plasma extraversion, which was further increased by capsaicin. In the high-exposure group, particle-laden AMs (which were reduced by capsaicin), inflammatory cell margination, perivascular cuffing with subsequent mononuclear cell migration and dispersal, increased mast cells, and decreased substance P were all seen. NK-1R was downregulated in the low-exposure group and upregulated in the capsaicin-pretreated high-exposure group. NEP decreased significantly for both groups.
Reference: Wu et al. (2003, 199749) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** 60 days	Zn^{2+} **Particle Size:** NA	**Route:** IT Instillation **Dose/Concentration:** 50 µm/rat **Time to Analysis:** Single, 24 h	**Cells:** Decreased number of airway epithelial cells shown with PTEN protein immunostaining. Macrophages were unaffected.
Reference: Yamamoto et al. (2006, 096671) **Species:** Mouse **Gender:** Male **Strain:** BALB/c **Age:** 7 wk **Weight:** 23 g	CB14: Printex 90 (Degussa) CB95: Flammruss 101 (Degussa) LTA: Lipoteichoic acid 14CL: CB14 + LTA 95CL: CB95 + LTA CB14 measured Components: C 96.79%, HR 0.19%, N0.13%, S 0.11%, Ash 0.05%, O 2.74% CB95 measured Components: C 97.98%, HR 0.15%, N 0.28%, S 0.46%, Ash 0%, O 1.14% **Particle Size:** CB14: 14 nm; CB95: 90 nm	**Route:** IT Instillation **Dose/Concentration:** CB14: 0, 25, 125, 625 µg/mouse CB95: 0, 25, 125, 625 µg/mouse LTA: 10 or 50 µg/mouse 14CL: 125 µg CB14 + 10 or 50 µg LTA 95CL: 125 µg CB95 + 10 or 50 µg LTA **Time to Analysis:** Single, 4 and 24 h	**BALF Cells:** CB95 induced dose-dependent increases of PMN. CB14 induced an increase in PMNs but the increases were not dose-dependent. LTA massively increased PMN. LTA induced dose-dependent increases in total cells, especially at high dose at 24 h. LTA had massive synergistic effect with CB14 and CB95 for total cells and PMNs. Total cell count and PMN levels were highest in 14CL with levels at 24 h higher than at 4 h. Macrophage data were inconsistent. **Cytokines:** CB95 induced dose-dependent increases in IL-6, TNF-α, CCL2 and CCL3. CB14 induced dose-dependent increase in CCL2 and CCL3. Exposure induced increases of IL-6 at the high dose only. Slight effect on TNF-α was observed. LTA induced dose-dependent increases of IL-6, TNF-α and CCL3. 14CL massively induced IL-6 and CCL2. No combination of CB and LTA affected TNF-α or CCL3. **mRNA Expression:** LTA, 14CL and 95CL increased TLR_2 mRNA expression with 95CL and 14CL inducing higher increases than LTA. No effect on TLR4 mRNA expression was observed.

Reference	Pollutant	Exposure	Effects
Reference: Yanagisawa et al. (2003, 087487) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6 wk **Weight:** 29-33 g	DEP: (4JB1 light duty 4cyc 2, 74 liter Isuzu engine) LPS DEP-OC: organic compounds DL: DEP + LPS DOL: DEP-OC + LPS **Particle Size:** 0.4 µm	**Route:** IT Instillation **Dose/Concentration:** DEP/DEP-OC: 125 µg/mouse LPS: 75 µg/mouse **Time to Analysis:** Single, 24 h	**BALF Cells:** DEP and DEP-OC increased neutrophils but the increases were not statistically significant. LPS increased neutrophils significantly. DL and DOL massively increased neutrophils at greater levels than LPS alone. Macrophages were unaffected. **Cytokines:** LPS increased IL-1β, MIP-1α, MCP-1 and KC. DEP and DEP-OC had no effect. DL induced further increases. DOL decreased cytokines compared to LPS alone. DEP-OC increased IL-1β and MIP-1α mRNA expression slightly. DEP had no effect. LPS significantly increased IL-1β and MIP-1α mRNA expression. DL increased expressions while DOL did not. **Pulmonary Edema:** LPS, DEP and DEP-OC increased edema. DL further increased this effect. DOL had no effect compared to LPS alone. **Histology:** DL elevated neutrophil inflammation interstitial edema and alveolar hemorrhages. DOL induced neutrophilic inflammation without the alveolar hemorrhages. **mRNA Expression of TLRs:** DEP-OC, DL, DOL and LPS increased TLR_2. DEP had no effect. All particles increased TLR4 mRNA expression.
Reference: Yokohira et al. (2007, 097976) **Species:** Rat **Gender:** Male **Strain:** F344/DuCrj **Age:** 10 wk	DQ-12: Quartz dust (Douche Montan) HT: Hydrotalcite (Kyoward 500, PL-1686, KYOWA) POF: Potassium Octatitanate fiber (TISMO, Otsuka) PdO: Palladium Oxide CB: Carbon Black (Mitsubishi Kasei) **Particle Size:** DQ12 <7 µm HT: 7.8 ± 1.5 µm POF: <50 um length; <2 µm width PdO: 0.54 ± 1.11 µm CB: 28 nm	**Route:** IT Instillation **Dose/Concentration:** 4 mg/rat in 0.2 ml saline **Time to Analysis:** Single, 1 and 28 days	**Lung Weight/Body Weight Ratio:** DQ-12, HT and POF induced increases after 1 day. After 28 days, all samples induced increases in lung weight. **BALF Cells:** Neutrophils increased significantly in walls and alveolar spaces in all groups on 1 day except at HT. At 28 days, this increase was maintained only in walls with severe and moderate elevations, except for DQ-12. **Histopathology:** DQ-12 caused pulmonary edema both at 1 and 28 days. PdO and CB induced edema at 28 days. Fibrosis was observed after 28 days with the most significant increase, in decreasing order, induced by DQ-12,PdO, POF, HT, CB, and the control. Histiocyte infiltration was observed after 1 day for DQ-12, POF and PdO. At 28 days, infiltration was observed for DQ-12, HT, POF and PdO. Restructuring of alveolar walls and microgranulation was observed for all 5 particles but only at 28 days with DQ 12, PdO, HT, POF, CB and control. **Immunohistochemistry:** BrdU: At 1 day all 5 particles elevated in both area and number. Activity declined after 28 days but was still higher than the control. **iNOS:** At 1day DQ-12, POF and PdO induced increases. At 28 days, DQ-12 and HT induced increases. **MMP-3:** DQ-12 induced increases at both 1 and 28 days and PdO at 28 days. **Toxicity scoring:** The levels of toxicity are, in decreasing order, as follows: DQ-12, HT/PdO/POF, and CB.

Reference	Pollutant	Exposure	Effects
Reference: Zhao et al. (2006, 100996) **Species:** Rat **Strain:** SD **Age:** NR **Weight:** 200 g	DEP: SRM 2975 DEPE: SRM 1975 **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 35 mg/kg **Time to Analysis:** Single, 1 day AG group coexposed 30 pre and 3, 6, 9 h post DEP/DEPE	**iNOS Expression in AMs:** Both DEP and DEPE increased 12 and 6 fold respectively. NO and peroxynitrite levels increased accordingly. AG had no effect on iNOS expression but AG attenuated NO for both DEP and DEPE but peroxynitrite only for DEPE. DEP induced much higher levels of oxidants than DEPE. Unlike DEPE, DEP was unaffected by AG. **Role of iNOS in Lung Injury:** DEP and DEPE induced inflammation (PMN), cellular toxicity (LDH) and lung injury (protein). AG significantly attenuated the DEPE response but no effect was observed on the DEP responses. **Cytokines:** IL-12 levels were induced by both DEPE and DEP, with DEPE inducing higher increases than DEP, and both were significantly attenuated by AG. DEP and DEPE induced similar increases in IL-10 levels. AG increased DEP effect 3 fold and attenuated DEPE to control. **CYP Enzymes:** DEP and DEPE induced increases in CYP1A1 level and activity. AG attenuated CYP1A1 activity for both DEP and DEPE. CYP2B1 level and activity were slightly decreased by DEP and DEPE. AG had no effect. **Cytosol Phase II Enzymes:** DEPE had no effect; AG treatment increased catalase activity. DEP reduced catalase and GST activities. AG had no effect. Neither DEP, DEPE nor AG affected QR quinone reductase.
Reference: Zhou et al. (2003, 087940) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** 10-12 wk	UFe: Ultrafine Fe particles **Particle Size:** 72 nm	**Route:** Whole-body Inhalation **Dose/Concentration:** 57 or 90 μg/m^3 **Time to Analysis:** 6 h/days for 3 days, parameters measured within 2 h post-exposure.	**BALF Cells:** No significant changes observed in total cell number, cell viability or cell differentials. **Cytokines:** Only at the high dose was an increase in IL-1β observed. No effect on TNF-α or NF-κB-DNA binding activity was observed. **BAL Inflammatory/Injury Markers:** At the high dose, total protein increased. No significant changes were observed in LDH. **Intracellular Ferritin:** The high dose induced increases. No significant differences were observed between the low dose and control. **Oxidative stress:** Antioxidant level by FRAP value decreased at the high dose. GST (glutathione-S-tranferase) activity increased at the high dose. No effect on intracellular GSH and GSSG (glutathione disulfide) was observed.

Table D-4. Effects related to immunity and allergy.

Study	Pollutant	Exposure	Effects
Reference: Apicella et al. (2006, 096586) **Species:** Mouse **Strain:** BALB/c **Cell Line:** 112D5 hybridoma Primary Macrophages: Peritoneal	Poly OVA (Ovalbumin on polystyrene beads) Soluble OVA **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** PolyOVA and Soluble OVA: 0.2,1.0 or 5.0 µg/mL **Time to Analysis:** 48 h	**IL-6:** Stimulation with PolyOVA higher than stimulation with soluble OVA **TNF-α:** Stimulation with PolyOVA higher than stimulation with soluble OVA. **IL-10:** No modifications in levels after PolyOVA or soluble OVA stimulation. **Viability of Peritoneal Macrophages:** Stimulation with PolyOVA led to 33% decrease in viability. Stimulation with soluble OVA led to 24% in viability. **Effects of PolyOVA Stimulated Macrophages:** Culture supernatants from PolyOVA stimulated macrophages had a percentage increase of asymmetric IgG; however, the addition of rmIL-6 at identical concentrations did not induce a significant increase. It also decreased the proliferation of 112D5 hybridoma.
Reference: Arantes-Costa et al. (2008, 187137) **Species:** Mouse **Gender:** Male **Strain:** BALB/c **Age:** 6 wk **Weight:** NR	ROFA (solid waste incinerator powered by combustible oil; São Paulo, Brazil) **Particle Size:** NR	**Route:** Intranasal Instillation **Dose/Concentration:** 60 µg ROFA in 50 µL saline **Time to Analysis:** OVA sensitized days 1 and 14. OVA-challenged days 22, 24, 26, and 28. ROFA exposed 1-3 h after OVA challenge or saline. Pulmonary responsiveness measured day 30 then sacrificed. Lungs removed, fixed for 48 h.	ROFA increased pulmonary responsiveness and decreased ciliated cells in nonsensitized mice, which were both further amplified in the presence of OVA. ROFA did not affect eosinophils, macrophages, chronic inflammation, or neutral or acidic mucus.
Reference: Archer et al. (2004, 088097) **Species:** Mouse **Strain:** BALB/c DO11.10+/+ transgenic - ova specific receptor for OVA peptide 323-339 **Age:** 4 wk	PM = SRM 1648 (NIST) TiO_2 **Particle Size:** SRM1648: avg 1.4 µm TiO_2: avg 0.3 µg (sic)	**Route:** Intranasal instillation **Dose/Concentration:** 500 µg/30 µl sterile saline, initial 0-750 µg range finding **Time to Analysis:** Ova challenge at 68 h, Methacholine aerosolization/AR at 72 h	**Airway responsiveness (WBP):** AR induced by Ova/Mch challenge was significantly and dose-dependently increased at doses of SRM1648 ≥500 µg . TiO_2/Ova exposure was not significantly different from saline. PM associated endotoxin did not contribute to enhanced AR. **Lung inflammation/pathology:** No increases in BAL macrophages or eosinophils and no histological alterations after PM exposure. Both TiO_2 and PM increased pulmonary neutrophils, indicating particles alone were responsible for this increase and that the inflammatory response could occur independently of AR.
Reference: Barrett et al. (2006, 155677) **Species:** Mouse **Gender:** Male **Strain:** BALB/c **Age:** 8-10 wk	HWS (black/white oak) CO Total Vapor Hydrocarbon (TVH) **Particle Size:** 0.25 ± 3.3, 0.35 ± 2.5, 0.35 ± 2.0, 0.36 ± 2.1 µm (MMAD±GSD)	**Route:** Whole-body Inhalation **Dose/Concentration:** HWS: 30, 100 300, 1000 µg/m^3 CO: 0.7, 1.6, 4.0, 13 ppm TVH: 0.3, 0.6, 1.3, 3.1 ppm **Time to Analysis:** Pretreatment: ip 10 µg OVA and 2 mg aluminum hydroxide post-OVA. OVA aerosol challenge on day 14, followed by 3 days of HWS. Pre-OVA received aerosol OVA challenge on day 14, then 3 days of HWS on days 26-28 and an immediate (second) OVA challenge HWS 6 h/day for 3 days. Sacrificed 18 h post-exposure.	**Allergic Inflammation:** A statistically significant increase in eosinophils was observed at 300 µg/m^3 HWS following OVA challenge as compared to OVA alone. No changes in macrophages, neurophils and lymphocytes were observed. Post-OVA HWS did not significantly alter BAL cytokine or serum antibody levels, but linear trend analyses indicated decreases in IL-2, IL-4, and IFN-γ in the absence of OVA, as well as a statistically significant upward trend in OVA-specific IgE when HWS exposure followed OVA challenge. HWS exposure pre-OVA (prior to second OVA challenge) resulted in a decrease in IL-13 (statistically significant at the high dose but no evidence of an exposure-dependent response), an increase in OVA IgG1 (trend significant) and no change in IL-2, IL-4, IL-5, IFN-γ, OVA IgE, total IgE or OVA IgG2a.

Study	Pollutant	Exposure	Effects
Reference: Burchiel et al. (2005, 088090) **Species:** Mouse **Gender:** Female **Strain:** A/J **Age:** 12-14 wk	HWS (black/white oak) HWS particle Mass BC OC CO Total Vapor Hydrocarbon 29 other minor components PAH and metals **Particle Size:** 0.3 ± 3, 0.4 ± 2, 0.4 ± 2, 0.4 ± 2 µm (MMAD ± GSD)	**Route:** Inhalation **Dose/Concentration: HWS:** 30, 100, 300, 1000 µg/m^3 BC: 3, 12, 25, 43 µg/m^3 OC: 40, 107, 281, 908 µg/m^3 CO: 1, 2, 4, 13 ppm TVH: ND, 1, 1, 3 ppm **Time to Analysis:** 6 h/day for 6 mo.	**Proliferative Responses:** HWS increased splenic T cell proliferation at 100 µg/m^3 with a dose dependent decrease at 300 and 1000 µg/m^3 exposures ($p<0.05$) HWS exposure did not affect T (CD3), helper T cell (Th, CD4), cytotoxic T cell (CTL, CD8), macrophage (Mac-1), natural killer cell (NK, CD16) cell markers or B cell proliferative response to LPS.
Reference: Burchiel et al. (2004, 055557) **Species:** Mouse **Strain:** AJ **Age:** 10-12 wk	DE generated alternatively from two 2000 Cummins ISB Turbo Diesel 5.9 L engines using no 2 (chevron) oil and 15w/40 oil (Rotella T, Shell) run according to USEPA Dynamometer Schedule for Heavy-Duty Diesel Engines 18 PAHs quantified at exposure levels (text mentions 65) **Particle Size:** NR	**Route:** Inhalation **Dose/Concentration:** 30, 100, 300, 1000 mg/m^3 diesel PM **Time to Analysis:** 6 h/day, 7 days/wk for 6 mo.	**Proliferative Responses:** DE depressed splenic T cell proliferation at all exposure levels but was not dose-dependent and most pronounced at the 30 µg/m^3 level. ($p<0.05$ at all levels) Splenic B cell proliferation was increased at the 30 µg/m^3 level, but not at the other exposure levels. Little, if any, PAH was found in DE, and the majority of PAH tested in vitro enhanced T cell proliferation (below), so PAH is likely not responsible for the immunosuppressive effect of DE on murine spleen cell responses.
Reference: Chan et al. (2006, 097468) **Species:** Mouse **Strain:** DO11.10, BALB/c, Nrf 2$^{-/-}$ **Cell Types:** Primary bone marrow dendritic cells and dendritic cell line (BC1), T cells (BMDC)	DEP: DE particles DEP methanol extract: **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** DEP: 10 µg/mL LPS: 5 ng/mL **Time to Analysis:** 24 h	**Dendritic Cell Maturation:** Organic DEP chemicals interfered in the expression of several DC maturation markers. Both DEP and DEP extracts were found to inhibit CD86 expression and IL-12 production in LPS-exposed DCs, and intact particles were not as effective as DEP extract. DEP extract treatment of BC1 cells reduced their ability to stimulate co-cultured antigen-specific T cells, leading to decreased IFN- y and increased IL-10 without affecting IL-4 or IL-13. DEP extract also induced oxidative stress and interfered with DC activation by several other Toll-like receptor agonists as well as the NF-kB cascade. Inhibition of IL-12 production by DEP extract was shown to be mediated by pro-oxidative chemicals that engage the Nrf2 pathway. Taken together the inhibition of both IL-12 and IFN- y indicates a suppression of the Th1 pathway and provides a novel explanation for the adjuvant effect of DEPs on allergic inflammation.

Study	Pollutant	Exposure	Effects
Reference: Ciencewicki et al. (2007, 096557) **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 10-12 wk **Weight:** 17-20 g	DE: generated from a 30-kW (40 hp), 4-cylinder Deutz BF4M1008 diesel engine Influenza A/Bangkok/1/79 (H3N2 serotype) from Dr. Melinda Beck of the University of North Carolina, Chapel Hill O_2, CO, NO_2, NO, SO_2 O_2: 20.9- 20.5% (Lo, Hi) CO: 0.9-5.4 ppm NO_2: 0.25-1.13 ppm NO: 2.5-10.8 ppm SO_2: 0.06-0.32 ppm H_3N_2: NR **Particle Size:** NR	**Route:** Inhalation; Oropharyngeal aspiration (virus) **Dose/Concentration:** DE: 529 or 2070 µg/m^3 **Time to Analysis:** 4 h/day for 5 days. Virus exposure immediately after last DE exposure. Analyzed 18 h post infection.	**DE exposure on susceptibility to Influenza Infection:** Mice exposed to 0.5 mg/m^3 had significantly greater levels of HA mRNA compared to air-exposed mice. HA levels not significantly altered in mice exposed to 2.0 mg/m^3. **DE Exposure on the Influenza-induced Inflammatory Response:** f IL-6 mRNA levels were significantly greater when exposed to 0.5 mg/m^3 of DE prior to infection compared to air exposure. Significantly increased amount of IL-6 protein observed in exposed mice. Exposure to DE in absence of influenza infection had no significant effect on IL-6 mRNA or protein levels. **DE Exposure on Pulmonary Injury:** Infection with the influenza virus increases levels of PMN in BAL fluid. Exposure to either dose of DE prior to infection showed no significant effect on PMN levels Exposure to DE alone had no effect on PMNs in BAL fluid. Neither exposure to DE nor infection with influenza significantly increased BAL fluid protein levels when compared to non-infected, air-exposed. **Other Markers of Injury,** NAG and MIA were not statistically affected by DE or influenza exposure. **DE Exposure on the Influenza Induced Interferon Response:** No significant change in TFN-α mRNA levels at either dose of DE, although mice exposed to 0.5 mg/m^3 of DE prior to infection had significantly greater levels of IFN-B MRNA compared to air controls. No effect on any of the IFNs observed in uninfected mice exposed to DE. **DE Exposure on Surfactant Protein Expression:** Influenza virus infection alone significantly increased expression of SP-A in air-exposed. Exposure to 0.5 mg/m^3 of DE prior to infection had significant decreases in levels of SP-A mRNA in the lungs, this effect was not observed in 2.0 mg/m^3 DE exposed. Decrease seen in expression of SP-A protein in lungs of mice exposed to 0.5 mg/m^3 DE prior to infection. Levels of SP-D mRNA and protein were significantly decreased in lungs of mice exposed to 0.5 mg/m^3 of DE prior to infection compared with mice exposed to air or 2.0 mg/m^3 DE prior to infection. Exposure to 0.5 mg/m^3 of DE prior to infection with influenza decreased levels of SP-D, especially in airways. Mice exposed to 2.0 mg/m^3 DE prior to infection showed no significant difference.
Reference: Day et al. (2008, 190204) **Species:** Mouse **Gender:** Male **Strain:** BALB/c **Age:** 8-10 wk **Weight:** NR	GEE (General Motors 1996 model 4.3-L V6 engine; regular unleaded fuel) (CO, NO, NO_2, SO_2, NH_3) **Particle Size:** NR	**Route:** Whole-body Inhalation **Dose/Concentration:** Low(L)- 6.6 ± 3.7 PM/m^3, Medium(M)- 30.3 ± 11.8 PM/m^3, High(H)- 59.1 ± 28.3 PM/m^3, High-Filtered(HF) **Time to Analysis:** Pre-OVA protocol: OVA or saline sensitized 7 days. OVA challenge day 14. GEE or air exposed 6 h/day on days 26-28. Immediately after exposure on day 28 challenged with OVA. Tested for MCh-induced changes 24 h post-exposure then sacrificed. Post-OVA protocol: OVA or saline sensitized 7 days. OVA challenge day 14. GEE or air exposed days 15-17. Tested for MCh-induced changes 24 h post-exposure then sacrificed.	**Pre-OVA:** In nonsensitized mice, neutrophils and IgE decreased in the H group. IL-2 increased in the HF group and was dose-dependent. Eosinophils dose-dependently decreased. OVA-specific IgE increased in the H group, and OVA-specific IgG2a dose-dependently increased. In OVA-sensitized mice, OVA-specific IgG1 increased in the M group. Airway hyperresponsiveness was lower in the M and HF groups. **Post-OVA:** In nonsensitized mice, neutrophils dose-dependently decreased, IL-4 decreased in the M group, IL-5 decreased in the HF group, and IFN-γ decreased at all exposures. In OVA-sensitized mice, IL-13 dose-dependently decreased.

Study	Pollutant	Exposure	Effects
Reference: de Haar et al. (2005, 097872) **Species:** Mouse **Gender:** Female **Strain:** BALB/cANNCrl **Age:** 6-8 wk **Weight:** NR	CBP: Carbon black particles in phosphate buffered saline, 1: 10 & 1: 100 dilutions (Brunschwich Chemicals, Amsterdam, The Netherlands) OVA: Ovalbumin **Particle Size:** CBP: 30-50 nm	**Route:** Intranasal Droplet **Dose/Concentration:** CBP± OVA 200, 20, 2 µg (3.3, 0.33, 0.033 mg/ml) OVA only: 20 µg (0.5 mg/ml) **Time to Analysis:** Droplet applied on days 0, 1, 2. Sacrificed on day 4 or challenged with OVA droplet on days 25, 26, & 27. Sacrificed on day 28	**Acute Airway Damage and Inflammation:** Only day 4 had LDH increased in the 200 µg CBP+OVA group. The 200 µg CBP+OVA group induced significantly higher numbers of BAL cells compared to OVA control. Total protein and TNF-a levels were increased only in 200 µg CBP+OVA group. RAS, parameter for phagocytosis, 200 µg and 20 µg CBP+OVA had higher levels than OVA controls. **Adjuvant Activity on PBLN:** Total lymphocytes in PBLN significantly increased 4-5 fold in the 200 µg CBP+OVA exposed. 20 µg and 2 µg exposures did not increase the number of PBLN cells compared to OVA control. All CBP+OVA concentrations induced higher levels of IL-4, IL-5, IL-10, and IL-13, with 200 µg concentration having 10-200 times higher levels. IFN-y cytokine was increased in the 200 µg dose. **IgE Production:** In CBP+OVA, IgE were significantly increased. **PBLN and Lung Lymphocytes after OVA Challenge:** PBLN cell numbers increased in OVA and CBP+OVA sensitized mice. CD4 and CD8 populations increased in both groups. PBLN levels in CBP+OVA and challenged with PBS were higher than mice treated with OVA and challenged with PBS, both groups cytokine production was low, only IL-5 levels were significant in the CBP+OVA/PBS group. Higher lung lymphocyte numbers were caused by higher numbers of CD4 and CD19. Production of IL-5 and IL-10 was four to five times higher than in OVA treated mice. **OVA Challenge Induces Asthma like Airway Inflammation in CBP+OVA Sensitized Mice:** Total number of cells in BAL increased 10 fold in CBP+OVA mice challenged with OVA. Eosinophils exhibited highest increase in CBP+ OVA/OVA group. Perivascular and peribronchial infiltrates and goblet cell hyperplasia in CBP+OVA/OVA was confirmed by histological examination. Antigen specific inflammation induced in CBP+OVA mice.

Study	Pollutant	Exposure	Effects
Reference: de Haar (2006, 144746) **Species:** Mouse **Gender:** Female **Strain:** BALB/cANNCr **Age:** 6-8 wk **Weight:** NR	CBP: fine (F) and ultrafine (UF) carbon black particles (Ken Donaldson Group) TiO_2: fine and ultrafine OVA: Ovalbumin **Particle Size:** F CBP: 260.0 nm UF CBP: 14.0 nm F TiO_2: 250.0 nm UF TiO_2: 29.0 nm	**Route:** Intranasal Droplet **Dose/Concentration:** CBP: 200 µg (3.3 mg/mL) TiO_2: 200 µg (3.3 mg/mL) OVA: 10 µg CBP+OVA: 200 +10 µg **Time to Analysis:** Days 0,1,2: Exposed to OVA or CBP+OVA. Sacrificed on day 8 & analyzed after 2 h, or continued to second group. Second group: days 25, 26, 27 given OVA challenge day 28: sacrificed , analyzed 24 h post sacrifice	**Ultrafine Particles Induce Lung Inflammation:** UF TiO_2 and CBP induced a local inflammatory response in the airways and showed higher levels of LDH and total protein as compared to mice exposed to the F particles. Cytokine levels were much higher in groups exposed to ultrafine particles. Histologic analysis of the airways showed that exposure to ultrafine TiO_2 or CBP leads to peribronchial and perivascular inflammatory infiltrates (mostly neutrophils). Exposure to OVA alone, or combined with fine TiO_2 and fine CBP had no effects on lung histology. **Ultrafine Stimulate Local Immune Responses:** TiO_2 and CBP particles stimulated the local immune response against co administered OVA antigen. Fine TiO_2 particles induced a low but significant increase in PBLN cell number. Both types of ultrafine particles elicited higher levels of Th-2 associated cytokines, with UF CBP stimulating a greater response. IFN-y production was low, but significantly higher than OVA exposures. **Ultrafine TiO_2 Increase OVA-specific IgE and IgG1 Levels:** Levels of OVA specific IgE were significantly increased in animals exposed to the UF TiO_2+ OVA compared to F TiO_2 or OVA-only. Average IgE level in mice exposed to ultrafine CBP+OVA was not a significant increase. OVA-specific IgG2a not detected in any groups. **Ultrafine Particles Stimulate Allergic Airway Sensitization Against OVA:** At day 28, the PBLN cell numbers were significantly higher in both ultrafine and combination with OVA. Production of OVA specific IL-4, IL-5, IL-10 and IL-13 by PBLN cells was significantly increased in both ultrafine TiO_2 and CBP. IFN-y levels were significantly increased in ultrafine CBP+OVA treated animals. F TiO_2 had low, but significant, increases in IL-4 and IFN-y compared to OVA only. Allergic airway inflammation and Influxes of eosinophils, neutrophils and lymphocytes were only found in both groups exposed to ultrafine particles.
Reference: de Haar (2008, 187128) **Species:** Mouse **Gender:** Female **Strain:** BALB/c, CD80/CD86-deficient, DO11.10 **Age:** 6-8 wk **Weight:** NR	Ultrafine Carbon Black (UFCB) (Brunschwich Chemicals; Amsterdam, The Netherlands) **Particle Size:** Diameter: 30-50 nm	**Route:** Intranasal Exposure **Dose/Concentration:** 20 µg/mL **Time to Analysis:** Exposed days 1, 2, 3. OVA challenge days 25, 26, 27. Spleens and lymph nodes from DO11.10 mice pooled and CD4+ T-cells isolated. Solution injected into tail veins of BALB/c mice day 0. CTLA4-Ig ip injected days 0, 2. PBLN cell suspensions plated, restimulated with OVA 4 day.	UFCB+OVA induced proliferation of CD4+ T-cells, increased cytokine production. UFCB+OVA did not induce any effects in CD80/CD86-deficient mice. UFCB-induced airway inflammation is dose-dependent.
Reference: de Haar et al. (2008, 187128) **Species:** Mouse **Cell Line:** Myeloid dendritic cells (mDCs)	Ultrafine Carbon Black (UFCB) (Brunschwich Chemicals; Amsterdam, The Netherlands) **Particle Size:** Diameter: 30-50 nm	**Route:** Cell Culture **Dose/Concentration:** 25 µg/mL **Time to Analysis:** 18 h	UFCB+OVA increased mDCs in the peribronchial lymph nodes, and their expressions of CD80, CD86, and MHC-11.

Study	Pollutant	Exposure	Effects
Reference: Dong et al. (2005, 088079) **Species:** Rat **Gender:** Male **Strain:** Brown-Norway (BN/CrlBR) **Age:** NR **Weight:** 200-225 g	DEP: SRM 2975 (NIST, Gaithersburg, MD) OVA: Ovalbumin **Particle Size:** 0.5 µm (MMAD)	**Route:** Inhalation **Dose/Concentration:** DEP: 20.6 ± 2.7 mg/m^3 OVA 40.5 ± 6.3 mg/m^3 **Time to Analysis:** 4 h/dayfor 5 days + OVA 30 min/day1 x wk on days 8,15 & 29. Sacrificed on days 9 or 30.	**Lung Inflammation/Injury:** Both the BAL proteins and inflammatory cell counts for DEP exposure alone were not different from those of the air exposed control, suggesting that DEP exposure did not cause lung injury at 9 or 30 days post-exposure. OVA exposure caused significant increases in neutrophils, lymphocytes, eosinophils, albumin and LDH activity in the lung after two exposures. DEP did show a strong effect on OVA-induced inflammatory responses. **Alveolar Macrophage (AM) function:** OVA exposure resulted in an increase in NO levels in the acellular BAL fluid and AM conditioned media. This increase was significantly attenuated in rats exposed to DEP. DEP exposure had no significant effect on the production of IL-10 or IL-12 by AM recovered from rats 9 and 30 days post exposure. In contrast, OVA sensitization elevated both IL-10 and IL-12 secretion by AM at both time points. **Lymphocyte population and cytokine production:** DEP exposure was found to increase the numbers of total lymphocytes, T cells and their CD4+ and CD8+ subsets in LDLN. OVA exposure also significantly increased these cell counts on days 9 and 30. DEP+OVA exposure showed a significant reduction in total lymphocytes, T cells, CD4+ and CD8+ subsets on day 30. Levels of IL-4 and IFN-y in lymphocyte conditioned media were below detection limit of the ELISA kits. **Intracellular GSH levels in AM and Lymphocytes:** DEP exposure alone slightly decrease GSH levels in AM, but markedly reduced GSH concentration in lymphocytes on days 9 and 30. OVA exposure significantly decreased intracellular GSH in both cell types. Combined exposure showed AM and lymphocytes to have depleted intracellular GSH. **OVA specific IgE and IgG levels in serum:** In all samples collected on day 9, both serum IgG and IgE levels were under the detection limits. On day 30, no measureable IgE levels were found. The OVA exposure, however, resulted in elevated IgE levels, and was enhanced in rats preexposed to DEP. IgE and IgG levels for DEP+OVA was tw0 times higher than OVA alone indicating that DEP has an adjuvant effect on the production of IgG and IgE. **Effects of DEP and OVA on Lung iNOS expression**: AM from various exposure groups did not stain for iNOS. 1 rat at day 9 from the combined DEP+OVA group showed a slightly positive iNOS staining. On day 30, 2 of 5 rats from combined exposure group and 1 from the OVA group showed a positive airway staining.

Study	Pollutant	Exposure	Effects
Reference: Dong et al. (2005, 088083) **Species:** Rat **Gender:** Male **Strain:** Brown-Norway (BN/CrlBR) **Age:** NR **Weight:** 200-225 g	DEP: SRM 2975 Diesel Exhaust Particles (NIST) OVA: Ovalbumin **Particle Size:** 0.5 µm (MMAD)	**Route:** Nose-only Inhalation **Dose/Concentration:** DEP 22.7 ± 2.5 mg/m^3 OVA 42.3 ± 5.7 mg/m^3 **Time to Analysis:** Day 1, 8, 15: OVA exposure 30 min/day Days 24-28: DEP exposure 4 h/day Day 29: OVA challenge Day 30: Whole-body plethysmography Day 31: Sacrifice	**Effect of DEP on OVA Induced Allergic Responses:** DEP exposure had a synergistic effect with OVA on inducing airway hyper-responsiveness (AHR) in rats. DEP alone had no effect on IgG production. Levels of OVA-specific IgG and IgE increased in OVA+DEP exposure. This indicates that DEP pre-exposure augments the immune response of rats to OVA in the production of allergen specific IgG and IgE. **Effect of DEP on OVA Induced Cell Differentiation:** Neither DEP, OVA nor the combination induced elevated levels of LDH activity or albumin content, indicating that the exposure protocols did not cause significant lung injury. DEP alone induced moderate but significant increase of neutrophil numbers. OVA exposure induced a greater infiltration of neutrophils than DEP, and infiltration of eosinophils and lymphocytes. OVA-induced eosinophil count markedly increased with DEP exposure. Total lymphocytes, T cells, and their CD4+ and CD8+ subsets in LDLN from rats sensitized and challenged by OVA were significantly higher than those of air-exposed non sensitized rats. DEP+OVA exposure resulted in substantial increase in T cells compared to OVA alone. **Effect of DEP on OVA-induced Oxidant Generation and GSH Depletion:** Exposure to DEP or OVA alone had no effect on ROS production by AM. Substantial elevation seen in ROS for the DEP+OVA exposed group. Both OVA and DEP exposures resulted in an increased presence of NO in the acellular BAL fluid and in AM conditioned media; OVA+DEP exposure further increased these levels. The ATII cells from OVA exposed rats exhibited a higher percentage of cells that produce NO and superoxide than air exposed, non sensitized rats. DEP and OVA exposure resulted in a significant increase in the percentage of cells that produce NO and superoxide over the control. **iNOS Expression:** Immunohistological analysis in lung tissues showed no AM staining in any group. Airway epithelium was found to be positive in all 5 rats from the DEP+OVA group and 3 of 5 rats from single exposure of DEP or OVA and 2 of 5 in air only exposed rats. iNOS expression was significantly higher in ATII cells isolated from rats exposed to combined DEP and OVA . **GSH levels in AM and lymphocytes:** Levels were slightly lowered by DEP or OVA exposure, though not statistically significant. DEP+OVA showed a significant reduction in GSH levels.

Study	Pollutant	Exposure	Effects
Reference: Drela et al. (2006, 096352) **Species:** Mouse **Gender:** Male **Strain:** BALB/c **Age:** 6 wk **Weight:** NR	ASM: Air suspended PM from Upper Silesia (Poland) 1µg of ASM: Pb (1.136 ng) Cu (0.004 µg) Co (0.072 ng) Mn (0.406 ng) Fe (0.016 µg) Cd (0.154 ng) Cr (0.418 ng) Ni (0.238 ng) **Particle Size:** 0.3-10 µm	**Route:** Intraperitoneal Injection **Dose/Concentration:** 170 mg/kg **Time to Analysis:** Single, 72 h	**CD28 Expression on Thymocytes at Different Stages of Development:** ASM exposure accelerated thymocyte maturation but did not alter the expression of CD28 on peripheral CD4 and CD8 T cells isolated from lymph nodes. A slight but not statistically significant decrease in the expression of CD28 on spleen T cells from ASM animals was observed. **Distribution of CD28(low) and CD28(high):** Acute exposure to ASM resulted in the increase of CD28(low) and decrease of CD28 (high) thymocyte percentages in the total thymocyte population. The percentages of CD28 low and high thymocytes did not differ between intact and PBS controls. Acute ASM exposure resulted in the increase of the percentage of CD28(low) and the decrease of CD28(high) thymocytes in the CD3 low subset. The percentage of CD28 low and high positive thymocytes did not differ in CD3 high thymocyte subset. **Natural Regulatory CD4+ CD25+ T Cells in the Thymus:** The development of thymic natural regulatory cells was unaffected by ASM. **Proliferation of Splenocytes and Lymph Node Lymphocytes:** Decreased proliferative responses were evident in splenocytes from ASM-exposed animals when cells were stimulated with low but not high levels of anti-CD3 mAb. In contrast, lymph node lymphocytes from ASM treated mice had increased proliferative responses independent of anti-CD3 concentration. Both CD4+ and CD8+ T cells from ASM treated mice proliferated more vigorously than from controls. Almost all CD8+ T cells from ASM mice were induced to proliferate.
Reference: Dybing et al. (2004, 097545) **Species:** Mouse **Gender:** NR **Strain:** BALB/cA **Age:** NR **Weight:** NR	UP: Urban ambient particles collected in 5 different sites (Amsterdam, Lodz, Oslo, Rome, Dutch seaside) during four-wk periods in spring, summer, winter seasons from March 2001 to March 2004. DEP as reference std: SRM 1650 (NIST) OVA: Ovalbumin (Sigma Chemical, St. Louis, MO) **Particle Size:** UP: PM_{10} and $PM_{2.5}$	**Route:** Injection in hind foot pad **Dose/Concentration:** UP: 100- 200 µg DEP: 50 µg OVA: 50 µg **Time to Analysis:** Day 0: 1 exposure to OVA alone, OVA w/particles, particles alone. Day 6: Lymph nodes harvested Day 21: 1 OVA w/o particles exposure Day 26: Antibody assay	**Allergy Screening:** All samples were immunostimulatory in the popliteal lymph node assay; activity was weak in the absence of OVA but statistically significant when injected with OVA, indicating an adjuvant effect. Particle adjuvancy was further demonstrated via significant enhancement of OVA-specific antibody responses. All ambient particle fractions from all seasons increased IgG1. Except for a few coarse samples, all fractions significantly increased IgE. All fine fractions and some coarse fractions significantly increased IgG2a, indicating that most particles could exert both Th1 and Th2 adjuvancy. In general, fine particles demonstrated stronger adjuvant activity than coarse in a pair-wise comparison of coarse and fine particles from the same location.
Reference: Dybing, et al. (2004, 097545) **Species** Rat **Cell Lines:** Type 2 cells, AM	UP: Urban ambient particles collected in 5 different sites (Amsterdam, Lodz, Oslo, Rome, Dutch seaside) during four-wk periods in spring, summer, winter seasons from March 2001 to March 2004. DEP: SRM 2975 (NIST) OVA: Ovalbumin (Sigma Chemical, St. Louis, MO) **Particle Size:** PM_{10} and $PM_{2.5}$	**Route:** Cell Culture **Dose/Concentration:** 0-50 µg/ml **Time to Analysis:** 20 h	**Inflammation:** The coarse fractions were more potent than the fine fractions. Among the samples, the overall effects of the coarse fractions on the cells were dependent on the site of collection. High MIP-2 levels were found using particles from some spring collections. Coarse particles collected in summer demonstrated the highest potency, and samples collected during winter proved to be less potent but seasonal variation was not obvious for all sites. Only minor responses were observed using fine fractions from urban sites.

Study	Pollutant	Exposure	Effects
Reference: Farraj et al. (2006, 141730) **Species:** Mouse **Gender:** Male **Strain:** BALB/c **Age:** 6 wk **Weight:** NR	DEP: SRM 2975 NIST OVA: Ovalbumin Anti-p75: Rabbit anti-mouse p75 neurotrophin receptor polyclonal antibody (Chemicon, Temecula, CA) Anti-trkA: anti-mouse trkA NGF receptor antibody (Santa Cruz, Santa Cruz, CA) **Particle Size:** DEP: 1.47 µm (MMAD), 2.75 GSD	**Route:** Nose-only Inhalation **Dose/Concentration:** DEP: 1.78 to 2.18 mg/m^3 Anti-p75: 50 µl Anti-trkA: 50 µl OVA injection: 20 µg MCH: 0, 16, 32, 64 mg/ml **Time to Analysis:** On day 0: ip injection of 20 µg OVA Day 14: intranasal instillation of 50 µl anti-p75 or anti-trkA, 1 h after 1st exposure challenged with OVA aerosol for 1 h followed by a h exposure to DEP 24 h after DEP exposure: MCH challenge	**Airways Responsiveness:** No significant differences in avg baseline Penh values of any treatment groups. Vehicle sensitized mice: exposure to DEP, anti-p75 or anti-trkA had no effect on MCH-induced Penh values. OVA-sensitized DEP-exposed: seen increase of Penh values**.** Administration of anti-p75 or anti-trkA to OVA sensitized mice reversed DEP induced Penh increases. **Lung Function in Ventilated Mice:** Compared to vehicle sensitized mice, central airway resistance (Rn) increased 62% in OVA sensitized mice was not a significant increase. OVA-sensitized DEP-exposed mice, anti-p75 decreased central airway resistance (Rn) and anti-trkA did not significantly alter Rn. though Rn response for anti-p75 was significantly less than anti-trkA response, Constant phase model parameter of tissue elastance not significantly affected by any treatments or by increasing MCH dose, indicating development of significant regional ventilation inhomogeneity during bronchoconstriction. **Airway Pathology:** OVA-sensitized mice had small increases in intraepithelial mucus compared to vehicle-sensitized mice. DEP exposure did not enhance severity of OVA-induced airway pathology. Anti-p75 or anti-trkA administration did not influence airway morphology. **BAL Cells:** Vehicle-sensitized DEP-exposed mice had significantly enhanced macrophage numbers by 92% compared to air-exposed, vehicle-sensitized mice. Anti-p75 or Anti-trkA administration significantly suppressed DEP-induced macrophage increase to levels similar to air-exposed, vehicle-sensitized group. DEP co exposure significantly decreased number of macrophages in OVA-sensitized mice to control levels. Anti-trkA or anti-p75 had no effect in OVA-sensitized, DEP-exposed. Eosinophil number greater in OVA-sensitized DEP-exposed mice than in vehicle-sensitized air-exposed mice. No significant effects of DEP exposure on neutrophils from vehicle- or OVA-sensitized mice. **Cytokines:** IL4: OVA-sensitized DEP-exposed had five-fold increase over vehicle-sensitized, air-exposed mice and anti-trkA or anti-p75 significantly inhibited the DEP-induced increase. IL5, IL13: OVA-sensitized DEP-exposed had no significant change. Anti-p75 or anti-trkA administration had no significant effect. **Serum IgE**: OVA sensitized mice had a 10 fold increase in IgE levels for air and DEP exposed mice. Anti-p75, anti-trkA treatment did not cause significant effects on IgE levels.

Study	Pollutant	Exposure	Effects
Reference: Farraj et al. (2006, 088469) **Species:** Mouse **Gender:** Male **Strains:** C57/Bl6 **Age:** 6 wk	DEP: SRM 2975 collected from diesel-powered industrial forklift filter (NIST) OVA: Ovalbumin Anti-p75: Rabbit anti-mouse p75 neurotrophin receptor polyclonal antibody **Particle Size:** 1.47 (MMAD), 2.75 (GSD)	**Route:** Nose-only Inhalation **Dose/Concentration:** DEP: 0.87 mg/m^3 MCH: 0, 16, 32, 64 mg/ml OVA: 20 µg ip Anti-p75: 50 µl **Time to Analysis:** Day 0: OVA in gel vehicle, ip Day 14: anti-p75 exposure, intranasal instillation 1 h post anti-p75 exposure, OVA aerosol challenge for1 h 1 h post OVA challenge: DEP exposure for 5 h 48 h post DEP exposure: MCH challenge	**Airway Responsiveness:** No significant differences in average Penh values among any vehicle control groups. No significant differences in treatment groups in OVA-sensitized mice at baseline 0, 16, or 32 mg/mL of MCH. At 64 mg/mL MCH, OVA-sensitized, DEP-exposed mice had a 22% increase in Penh compared to vehicle mice, and a 68% increase compared to vehicle-sensitized, air-exposed mice. Instillation of anti-p75 inhibited the DEP induced increased Penh. **BALF Cells:** DEP exposure in vehicle-sensitized mice significantly increased macrophages by 161% compared to air-exposed, vehicle-sensitized mice, while OVA-sensitized mice had 69% increase. Anti-p75 administration significantly suppressed DEP-induced macrophage increase in vehicle-sensitized mice. No significant effects of DEP exposure or anti-p75 treatment in OVA-allergic mice. OVA-sensitized air-exposed mice had a several hundred fold increase in the number of eosinophils. No significant effects of DEP exposure or anti-p75 treatment on eosinophils from OVA-sensitized mice. OVA-exposure or DEP-exposure had no significant effects on neutrophil or lymphocyte number . **Cytokines:** No significant effects of DEP alone or with OVA on IL-4, IL-5, or IL-13. **Serum IgE:** OVA sensitization in the presence or absence of DEP or anti-p75 caused at least a 3 fold increase in IgE levels. No significant effects of DEP or anti-p75 treatment on IgE levels.
Reference: Finkelman et al. (2004, 096572) **Species:** Mouse **Gender:** Female **Strains:** BALB/c, C57BL/6 **Age:** 2-4 mo	DEP: 4JB1 type; Isuzu Automobile, Tokyo, Japan **Particle Size**: 2 µm (MMAD)	**Route:** Group1: 1 ip injection of 2 mg of DEP. Group 2: daily ip injections of 2 mg of DEP **Dose/Concentration:** 2 mg **Time to Analysis:** 2-96 h	**Serum Cytokines:** Mice in group 1 demonstrated an increase in serum IL-6 production but no increase in IL-4 or IL-2 production. IFN-γ levels were decreased in group 2. TNF production was not affected. **Spleen Cytokines:** When injected before LPS, DEP had little effect on the LPS-induced TNF-α and IL-6 response, but resulted in a minor suppression of INF-γ and IL-10. DEP LPS-induced increase in INF-γ mRNA responses in spleen cells. DEP caused a dose related suppression of LPS stimulated INF-γ. DEP had little or no effect on the percentage of NK or NKT cells in the spleen and inhibited LPS-induced IFN-γ production by NK and NKT. DEP failed to inhibit the IFN-γ response by anti-CD3 mAb-activated NKT cells. Oxidant activity was not responsible for DEP inhibition of LPS-induced IFN-γ production.
Reference: Fujimaki and Kurokawa (2004, 096575) **Species:** Mouse **Gender:** Male **Strains:** BALB/c **Age:** 4 wk **Cell Types:** Cervical lymph-node (CLN) cells	DE ± particles: Comparison of exposure to DE including particles and exposure to particle-filtered DE DE: 12.09 ± 0.15 NO_X, 1.99 ± 0.02 NO_2, 10.02 ± 0.12 NO, 0.18 ± 0.002 SO_2 and 1769.2 ± 13.2 CO_2 (all in ppm). DE gas: 11.93 ± 0.13 NO_X, 2.93 ± 0.06 NO_2, 8.91 ± 0.09 NO, 0.11 ± 0.003 SO_2 and 1838.8 ± 15.3 CO_2 (all in ppm) **Particle Size:** 0.4 µm (MMAD)	**Route:** Whole-body Inhalation **Dose/Concentration:** Exposure to; 0, 1.0 mg/m^3 or 1.0 mg/m^3 DE gas only (0.04 mg/m^3 PM) **Time to Analysis:** Exposure for 12 h daily for 5 wk. Days 14 and 35 challenge with sugi basic protein (SBP), a cedar pollen allergen, intranasally. Evaluation is 24 and 48 h after final SBP injection.	**CLN Response:** Exposure to DE or DE gas did not affect B1 lymphocyte subpopulations of CLN. Culture supernatants of CLN cells from DE exposed/SBP immunized mice showed significant increase in MCP-1 at 24 and 48 h. Exposure to DE or DE gas significantly increased the amount of TARC and MIP-1α in CLN cells from SBP-immunized mice at 48 h.

Study	Pollutant	Exposure	Effects
Reference: Fujimaki et al. (2005, 156456) **Species:** Mouse **Gender:** Male **Strains:** C57BL/6 **Age:** 4 wk	DE generated by 4 cyl 2.74 l Isuzu diesel DE gas = DE filtered to remove particles Composition of Diesel Exhaust**:** DE DEP: 1.01 mg/m^3 1796 ppm CO_2 12.09 ppm NO_X 0.18 ppm SO_2 Composition of filtered DE Gas: DEP: 0.04 mg/m^3 1839ppm CO_2 11.93ppm NO_X 0.11 ppm SO_2 Sugi Basic Protein (SBP)- allergen **Particle Size:** 0.4 µm (average diameter)	**Route:** Whole-body Inhalation **Dose/Concentration:** 1.0 mg DEP/m^3 or 1.0 mg DEP/m^3 DE gas **Time to Analysis:** 12 h daily, 5 wk. All mice were injected IP with 100 µg SBP before exposure to gas or DE and again received 50 µg SBP intranasally on days 14 and 35. Evaluation is 1 day after final SBP-immunization (mice are euthanized and CLN and blood samples are collected)	**CLN:** Exposure to DE and gas led to a decrease in total number of CLN cells and percentage of CD4+ and TCR-B levels. Cell proliferation response to SBP was higher in gas-exposed mice than in the control group. The production of MCP-1 increased in CLN cells when stimulated with SBP (in vitro) but the difference was not significant at 24 and 48 h. SBP-stimulated cells in gas-exposed mice showed greatly enhanced MIP-1α production at 24 and 48 h. Exposure to gas increased the amount of TARC in the culture supernatants of CLN cells. **Plasma:** Exposure to DE or gas significantly decreased the anti-SBP IgG1 antibody titers and increased the anti-SBP IgG2a antibody titers in mouse plasma.
Reference: Fujimoto et al. (2005, 096556) **Species:** Mouse **Gender:** Female 1st day of pregnancy) **Strains:** Slc: IRC	DEP: generated by a 2369-cc diesel engine operated at 1050 rpm and 80% load with commercial light oil **Particle Size:** 0.4 µm (MMAD)	**Route:** Whole-body Inhalation **Dose/Concentration:** 0.3, 1.0 and 3.0 mg DEP/m^3 (Groups 1,2,3) **Time to Analysis:** Exposure began at 2 days postcoitum and was continued until 13 days postcoitum. Exposure time was 12 h daily for 7 days/wk. Pregnant females were sacrificed 14 days postcoitum.	**mRNA Expression in Placentas**: In groups exposed to DE, the expression of CYP1A1 mRNA decreased to undetectable levels during placental absorption and INF-γ was increased. Levels of CYP1A1 mRNA in normal placentas from DE-exposed mice were unchanged. mRNA levels of inflammatory cytokines IL-2, IL-5, IL-12α, IL-12B and GM-CSF increased in placentas of mice exposed to DE.
Reference: Gao et al. (2004, 087950) **Species:** Human **Cell Line:** Lung fibroblasts infected with Mycoplasma fermentans	ROFA: collected near a power plant in FL burning low sulfur # 6 oil. (PM from Dusseldorf, volcanic ash for Mt. St. Helens, PM from Utah used to compare against ROFA in one experiment) $NiSO_4$, $CuSO_4$, $VOSO_4$, Na_3VO_4 **Particle Size:** NR	**Route:** Cell Culture; seeded into 6-well plates (3-4.5×10^5 cells/3 mL/well) or 24-well plates (0.6-1×10^5 cells/1.0 mL/well) **Dose/Concentration:** PM: 3, 10, 20, 40, 50 µg/ml Metallic salts: 2, 20, 200 µM **Time to Analysis:** 24, 48h	**Cytokines:** ROFA exposure in combination with Mycoplasma fermentans infection synergistically amplifies the induction of IL-6 production in human lung fibroblasts (HLF). PM from the other sources has little synergistic effect on IL-6 release. Exposing HLF cells to,M. fermentans derived macrophage activating lipopeptide-2 (MALP-2) and ROFA has the same synergistic effect as M. fermentans infection and ROFA. MALP-2 and ROFA extract have a similar synergistic effect that requires more time to appear. ROFA contains high levels of V, Ni, Fe and Cu. Exposure of HLF to $NiSO_4$ alone and $NiSO_4$ with MALP-2 produced 10 and 50 fold increases, respectively, in IL-6 production. Exposure of HLF to $CuSO_4$, $VOSO_4$ and Na_3VO_4, with and without the presence of MALP-2, did not produce as dramatic results as seen with Ni. The action of $NiSO_4$ and MALP-2 on IL-6 production was found to be dose dependent.

Study	Pollutant	Exposure	Effects
Reference: Gavett et al. (2003, 053153) **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 7wk	$PM_{2.5}$ from the German cities of Hettstedt or Zerbst PM Composition: samples from Hettstedt have several-fold higher levels of Zn, Mg, Pb, Cu and Cd than samples from Zerbst. **Particle Size:** $PM_{2.5}$	**Route:** Oropharyngeal Aspirations **Dose/Concentration:** 50-100 µg **Time to Analysis:** Single, 18 h. Sensitization Model: Mice were exposed to 50 µg PM 2 h before being sensitized with 10 µg OVA, repeated two days later. On day 14 all mice were challenged with 20 µg OVA. Parameters measured on days 2 and 7 after final exposure to OVA. Challenge Model: Mice were sensitized IP with 20 µg OVA or adjuvant only. 14 days later mice were exposed to 100 µg $PM_{2.5}$ followed 2 h later by 20 µg OVA. Parameters measured on days 2 and 7 after final exposure to OVA.	**BAL Analysis**: Hettstedt PM significantly increased BAL protein and NAG levels. Zerbst PM did not. Mice exposed to Zerbst had lower levels of LDH than control groups. Hettstedt exposed mice had increased levels of IL-1B, IL-6 and MIP-2 in comparison to control and to mice exposed to Zerbst PM. $PM_{2.5}$ at a dose of 100 µg was not found to be toxic, therefore used for subsequent studies. **Airway Responsiveness (PenH)**: In allergic mice tested immediately after exposure, Hettstedt PM increased PenH 190% compared to baseline, Zerbst increased PenH by 120% and the Control increased by 44%.:.: Two days after OVA challenge, no differences in non-allergic mice from either group. In allergic mice, Hettstedt PM still caused a significant response to Mch responsiveness, Zerbst none. No effects on day seven. **IgE Levels**: Serum collected on day 2 showed antigen-specific IgE was increased by Hettstedt $PM_{2.5}$ in both the sensitization and challenge phases when compared to the control and exposure to Zerbst. Day 7 serum indicated no effect. **BALF Cells**: In non-allergic mice both Hettstedt and Zerbst PM increased neutrophil numbers (3-fold; not statistically significant) and in allergic mice, only Hettstedt PM significantly increased neutrophil count. Eosinophil numbers were increased only in allergic mice exposed to Hettstedt PM. Lymphocyte numbers were not different among groups. **BAL Injury Markers:** At 2 days after both Hettstedt and Zerbst PM administered in allergic mice caused significant increases in protein, LDH and NAG compared to the non-allergic groups. Both PMs caused an increase in LDH in allergic mice compared to the allergic control, but only Hettstedt caused an increase NAG in allergic mice compared to control. At 7 days no effect. **BAL Cytokines**: Allergic mice had increased levels of IL-4, IL-5 and IL-13 compared to non-allergic mice (at 2 days after). IL-5 was significantly increased by exposure to either PM in allergic mice compared to non-allergic mice. Exposure to either PM caused an increase in TNF-α and IFN-γ (by 6-8 fold) in allergic mice, there was also an increase in these inflammatory cytokines in the non-allergic group but was not statistically significant. No significant effects were observed in animals that underwent the sensitization protocol alone for any measurement or endpoint.
Reference: Gowdy et al. (2008, 097226) **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** ~12-14 wk **Weight:** 17-20 g	DEP (30kW (40hp) 4-cylinder Deutz BF4M1008 diesel engine, steady state, 20% full load) (Low dose: 21% O_2, 0.4wt ratio OC/EC; High dose: 20.7% O_2, 0.4wt ratio OC/EC) (CO, NO_X, SO_2) **Particle Size:** Diameter: ~240 nm	**Route:** Inhalation **Dose/Concentration:** Low- 514 ± 3 µg/m^3, High-2026 ± 38 µg/m^3 **Time to Analysis:** 4 h/day, 1 or 5 days (consecutive). Necropsied immediately or 18 h postexposure.	**BAL Analysis:** Neutrophils and lung injury dose-dependently increased. ICAM-1 increased immediately after both exposures and after 18h postexposure in the low dose. **Cytokines:** After 1 day exposure, IFN-γ and TNF-α increased immediately at both doses and the high dose, respectively. Immediately after 5 days exposure TNF-α and IFN-γ increased at both concentrations and IL-6 increased at the low dose. At 18 h postexposure IL-6 and IFN-γ increased at both doses, TNF-α and IL-13 increased at the low dose, and MIP-2 dose-dependently increased. **CCSP, Surfactants:** CCSP decreased. SP-A and SP-D decreases were only significant after 5 days exposure, 18 h post-exposure.

Study	Pollutant	Exposure	Effects
Reference: Hamada et al. (2007, 091235) **Species:** Mouse **Gender:** Female (Pregnant close to partruition) **Strain:** BALB/c	ROFA (obtained from a precipitator until of a local power plant) Composition of ROFA (in µg/mL): 341.2 Ni, 323.4 V, 232.2 Zn, 18.3 Co, 15.8 Mn, 8.4 Ca, 6.7 Cu, 6.1 Sr, 5.0 mg, 0.9 Sb, and 0.6 Cd. **Particle Size:** NR	**Route:** Nebulized ROFA leachate **Dose/Concentration:** 50 mg/mL dilution **Time to Analysis:** Pregnant mice exposed to nebulized ROFA leachate for 30 min/day at days 14, 16 and 18 of pregnancy. Newborns received a single injection (ip) of OVA (5 µg)+ alum (1mg) at day 0 followed by exposure to: 1. aerosolized OVA days 12, 13 and 14 (2-wk old protocol) OR 2. aerosolized OVA days 32, 33 and 34 (5 wk old protocol) Analysis 48 h after final allergen exposure	**Susceptibility to Asthma**: Exposure of mother to PBS aerosols during pregnancy did not result in prominent asthma features in young. The offspring of the ROFA mothers revealed increasing AHR and elevated numbers of eosinophils in the BAL fluid. Similar results were seen in both the 2-wk and 5-wk old groups. **IgE Levels**: Histopathology revealed prominent inflammation in the lungs of the ROFA neonates and increased allergen-specific IgE and IgG1 levels in the 5-wk group. **Maternal Influence**: Breast milk was not shown to be responsible for the increased susceptibility to allergy seen in offspring. **IL-4 and IFN-γ**: IL-4 and IFN-γ levels in maternal mice showed no difference between PBS exposed or ROFA exposed mice. Cultured spleen cells from mice born of ROFA-exposed mothers showed either increased or similar levels of IL-4 and decreased production of IFN-γ causing an increase in the ratio of IL-4/IFN-γ indicating greater susceptibility to develop Th2-allergic response. **Eosinophils:** Exposure of mothers to Ni levels similar to those found in ROFA had no appreciable effect on BAL eosinophil.
Reference: Hao et al. (2003, 096565) **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 6-7 wk	DEP (4-cylinder diesel engine under a 10-torque load) **Particle Size:** NR	**Route:** Nebulization **Dose/Concentration:** 2 mg DEP m^3 **Time to Analysis:** Mild Sensitization- Mice receive IP OVA alum and are challenge with aerosolized OVA with and without DEPs. Mice sacrificed d19. Postchallenge Model- DEPs are delivered to mice sensitized by IP OVA and alum. Mice sacrificed d23. Transgenic Mice: Mice exposed to nebulized saline or DEPs for 1 h daily for 3 days. Mice sacrificed day 5.	**Mild Sensitization:** Exposure of previously OVA sensitized mice to aerosolized DEP and OVA did not affect OVA-specific IgE production, BAL eosinophilia or methacholine-induced AHR. Aerosolized particles induced inflammation and increased MBP deposition and MBP positive eosinophils in the mucosa. **IL-5 Transgenic:** Exposure to aerosolized DEP did not change BAL cytokine levels, but did increase AHR and BAL cell count. **Classic Sensitization, Post-Challenge:** Did not lead to a discernable increase in OVA-induced AHR. DEP treatment was associated with increased airway inflammation and mucin production in larger and intermediary airways.
Reference: Harkema et al. (2004, 056842) **Species:** Rat **Gender:** Male **Strain:** F344, BN **Age:** 10-12 wk **Weight:** NR	CAPs (Detroit; July-Sept. 2000; Harvard Ambient Fine Particle Concentrator) **Particle Size:** 2.5 µm (diameter)	**Route:** Inhalation; IT Instillation. **Dose/Concentration:** 4 day concentration: 676 ± 288 µg/m^3, 5 day concentration: 313 ± 119 µg/m^3, July concentration: 16-185 µg/m^3, September concentration: 81-755 µg/m^3; IT Instillation- 200 µL (soluble and insoluble) **Time to Analysis:** 10 h/day 1, 4, 5 day (consecutive); F344 rats sensitized to endotoxin, BN rats to OVA. Both groups killed 24 h post-exposure.	The retention of PM in the airways was enhanced by allergic sensitization. Recovery of anthropogenic trace elements was greatest for CAPs-exposed rats. Temporal increases in these elements were associated with eosinophil influx, BAL protein content and increased airway mucosubstances. A mild pulmonary neutrophilic inflammation was observed in rats instilled with the insoluble fraction but instillation of total, soluble or insoluble $PM_{2.5}$ in allergic rats did not result in differential effects.

Study	Pollutant	Exposure	Effects
Reference: Harrod et al. (2003, 097046) **Species:** Mouse **Gender:** NR **Strains:** C57BL/6 **Age:** 8-10 wk	DEE: Diesel Engine Emissions generated from a 5.9-liter turbo diesel engine fueled by Number 2 fuel. DEE Composition: NO_X: 2.0-43.3 ppm CO: 0.94-29.0 ppm SO_2: 8.3-364.9 ppb **Particle Size:** 0.1-0.2 µm (MMAD)	**Route:** Whole-body Inhalation RSV: IT administration **Dose/Concentration:** DEE: 38.8 µg/m^3 (low level) or 10027 µg/m^3 (high level) RSV: 100 µl **Time to Analysis:** 6 h/day, 7 days After the final 6 h exposure period mice were infected with RSV. Parameters measured 4 days post infection	**Viral Gene Expression:** For air+RSV, RSV-F gene expression was not apparent but RSV-G gene expression was detectable at very low levels. In DEE+RSV (for high and low levels), RSV-F and -G were markedly elevated. ß-Actin mRNA levels not changed in DEE-exposed compared to air-treated. DEE+RSV for high and low levels show 10- to 20- fold induction of RSV-G mRNA levels as compared to air+RSV. **BALF Cells:** Uninfected low-level DEE did not induce statistically significant increase in cell numbers as compared to air+RSV. High level DEE+RSV caused increase as compared to air+RSV. Uninfected high-level DEE had increase as compared to uninfected air group. For all groups, alveolar macrophages were predominant cell type and no substantial changes in infiltrating cell populations by exposure to DEE were noted. **Lung Inflammation & Airway Epithelial Morphology**: Lung sections from air- or DEE-exposed, uninfected did not exhibit any observable change. Low level DEE + RSV had increased inflammatory cell infiltration in peribronchial regions and loss of normal cuboidal appearance of Clara cells as compared to air+RSV. High level DEE+RSV had more apparent lung-inflammation, especially surrounding bronchi and bronchioles, and increased appearance of pseudo-stratified, columnar epithelial cell morphology and apparent airway epithelial cell sloughing as compared to low level DEE+RSV, indicating dose-related increase in lung histopathology to RSV infection by prior DEE exposure. **Cytokines:** TNF-α and IFN-γ were significantly increased in RSV-infected mice exposed to low or high level DEE and not increased in RSV-infected mice exposed to air. TNF-α levels elevated to similar levels for low and high level DEE+RSV. IFN-γ exhibited more dose-related increase with higher levels in high level DEE+RSV versus low level DEE+RSV. **Mucous Cell Metaplasia:** DEE exposure in uninfected was not altered. Mucous metaplasia was increased in epithelium of RSV-infected mice when exposed to DEE in a dose-dependent manner. Following high level DEE+RSV, mucous staining of airway epithelial cells in more distal airways was occasionally observed. **CCSP Production in Airway Epithelium:** DEE alone did not have an effect CCSP-producing cells, or Clara cells, decreased in Low DEE + RSV and further decreased in high level DEE+RSV in large and terminal airways. **Surfactant Protein B:** proSP-B staining post RSV alone shows now discernible decrease when compared to uninfected. Staining levels in alveolar lung regions decreased when exposed to low level DEE+RSV, and further decreased in high level DEE+ RSV. Staining in airway epithelium following high level DEE+RSV diminished when compared to RSV alone or low level DEE+RSV. **SP-A:** In alveolar type II cells and airway epithelial cells for untreated and air +RSV, no discernible changes in levels. Prior exposure to low or high level DEE decreased SP-A staining in alveolar type II cells and airways epithelial cells during RSV infection.

Study	Pollutant	Exposure	Effects
Reference: Harrod et al. (2005, 088144) **Species:** Mouse **Gender:** Male **Strain:** C57B1/6 **Age:** 10-12 wk **Weight:** NR	DEE (2 2000 model 5.9-1 Cummins ISB turbo diesel engines, No. 2 certification diesel fuel) **Particle Size:** NR	**Route:** Inhalation **Dose/Concentration:** Low- 30 µg/m^3 PM, Mid-Low- 100 µg/m^3 PM, Mid-High- 300 µg/m^3 PM, High- 1000 µg/m^3 PM **Time to Analysis:** 6 h/d, 7 days/wk, 1 wk or 6 mo. 1 wk exposure repeated on separate occasion. Immediately after exposure, mice anesthetized, IT instilled with Pseudomonas aeruginosa.	**Bacterial Clearance:** Lung bacterial clearance was decreased at all levels after 1wk exposure and was concentration-dependent 18h postinfection. Bacterial clearance was not affected at 6m and bacterial counts were higher. **Inflammation, Particle Deposition:** Lung inflammation and histopathology were increased in all exposure groups postinfection. All exposure groups possessed particle-laden macrophages. Higher doses had a concentration-dependent increase. **Ciliated, Clara Cells, TTF-1:** Generally, ciliated cells decreased with exposure dose, were more discernible in inflamed airways, and higher doses caused effects in small distal airways. Clara cells decreased equally at all exposures and were most notable in the distal airway epithelium. TTF-1 decreased postinfection.
Reference: Heidenfelder et al. (2009, 190026) **Species:** Rat **Gender:** Male **Strain:** Brown-Norway **Age:** 10-12 wk **Weight:** NR	CAPs (Grand Rapids, MI; July) **Particle Size:** Diameter: 0.1-2.5 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** CAPs: 493 ± 391 µg/m^3; OC: 244 ± 144 µg/m^3, EC: 10 ± 4 µg/m^3, Sulfate: 79 ± 131 µg/m^3, Nitrate: 39 ± 67 µg/m^3, Ammonium: 39 ± 59 µg/m^3; Urban dust (Fe, Al, Ca, Si): 18 ± 6 µg/m^3 **Time to Analysis:** Sensitized to OVA 3 day. Challenged with OVA or saline 2wk later for 3 day. Exposed to CAPs 8h/d, 13d. OVA or saline challenge 9 day after first challenge. Sacrificed 24 h after last CAPs exposure.	CAPs enhanced the effects of OVA by causing differential expression in genes primarily involved in inflammation and airway remodeling. CAPs exposure alone had no effect on gene expression. CAPs+OVA also increased IgE, mucin glycoprotein, and BALF total protein, and caused a more severe bronchopneumonia, increased mucus cell metaplasia/hyperplasia and mucosubstances.
Reference: Hiramatsu et al. (2003, 155846) **Species:** Mouse **Gender:** Female **Strains:** BALB/c and C57BL/6 **Age:** 8 wk **Weight:** 17-22 g	DE -DE (generated by diesel engine and diluted with filtered clean air) **Particle Size:** NR	**Route:** Inhalation **Dose/Concentration:** Low -0.1 mg/m^3 High - 3 mg/m^3 **Time to Analysis:** 7 h/day, 5 days/wk, 1 or 3 mo	**Lung Histopathology:** DEP-laden macrophages accumulated in the alveoli and peribronchial tissues in a dose- and duration-dependent manner in both strains. Lymphocytes and neutrophils increased in both strains, but were greatest in the BALB/c mice. **BALF and Mac-1 Positive Cells:** BALT formation in DEP-laden AMs was seen at the high dose group and was greater in the BALB/c mice. Mac-1 positive cells, a marker for phagocytic activation of the AMs, was observed in the high dose groups of both strains at 1 and 3 mo, and in the low dose group at 1 mo. in BALB/c mice. **Cytokine and iNOS mRNA expression:**1 month of exposure increased TNF-α, IL-12p40, IL-4 and IL-10 mRNA in a dose-dependent manner. IL-1B and iNOS decreased in a dose-dependent manner. IFN-γ mRNA expression increased in BALB/c mice and decreased in C57BL/6 mice. Similar results were seen at 3 mo, except IL-4 and IFN-γ mRNA expression decreased in the BALB/c mice. In C57BL/6 mice, IL-4 and IL-10 mRNA increased at the low dose but decreased at the high dose. NF-κB activation occurred after 1 wk and 1 month DE exposure and was more prevalent in BALB/c mice.

Study	Pollutant	Exposure	Effects
Reference: Hiramatsu, (2005, 088285) **Species:** Mouse **Gender:** Female **Strains:** BALB/c **Age:** 8 wk **Weight:** 17-22 g	DE (generated by diesel engine and diluted with filtered clean air.) Mycobacterial Infection -M.tuberculosis (ATCC35812) Kurono strain **Particle Size:** NR	**Route:** Inhalation **Dose/Concentration:** Low - 0.1 mg/m^3 High - 3 mg/m^3 Mycobaterial infection: 5 mL (nebulized) of a 106 colony-forming units (CFU) suspension **Time to Analysis:** 7 h/day, 5 day/wk, 1, 2 or 6 mo. Subset infected on last day of DE exposure. CFU evaluation 7 wk postinfection.	**Histopathological Observations:** DEP-laden AMs and DEPs in the alveoli and peribronchial tissues increased in a time-dependent manner. DE-exposed mice had a greater number of mycobacterial lesions, which were disseminated. Lesions in the control mice had clear borders and consisted of epithelial cells and lymphocytes. Tubercle bacilli and DEPs coexisted in AMs. BALT was seen around DEPs in the 2 and 6-month exposure groups. Inflammation cells increased in a time-dependent manner with respect to DE exposure. **Granulomatous Lesions in Lungs:** 6-month DE-exposed mice had a significantly higher amount of gross lesions than the 6-month control mice. **Mycobacterial Burden:** CFU in lungs were increased in DE-exposed animals but only the 6 month exposure resulted in statistically significant increases (a ~4-fold increase over control). CFU in spleen were not significantly altered by DE exposure. **Cytokines and iNOS mRNA Expression:** Infected DE-exposed mice had time-dependent increases of TNF-α, IL-1B, IL-12p40, IFN-γ and iNOS mRNAs compared to the infected control mice. IL-12 mRNA expression decreased in infected 6-month DE-exposed mice.
Reference: Ichinose, T. et al. (2003, 041525) **Species:** Mouse **Gender:** NR **Strains:** BALB/cAnN, ICR, C3H/HeN **Age:** 6 wk **Weight:** NR	DE: DE generated by 3059cc 4-cylinder diesel engine Der f: Crude extract of D. farinae **Particle Size:** 0.4 µm (MMAD)	**Route:** Inhalation **Dose/Concentration:** 1. Air 2. DE only: 3.0 mg/m^3 3. Air + Der f: 1 mg Der f 4. DE 3.0 mg/m^3 + 1 mg Der f **Time to Analysis:** DE: 12 h/day, 7 days/wk, 8 wk Der f: 2 wk intervals, 6 wk Analyzed 3 days after last instillation	**Light Microscopic Observations:** DE exposure caused the proliferation of nonciliated cells and epithelial cell hypertrophy. Soot-containing macrophages were found in the alveolar tissue spaces. Accumulated lymphocytes were present in the peribronchiolar lymphoid tissue. Inflammatory cells and soot-containing macrophages were found in the submucosal layer and the vessel interstitium of mice treated with DE+Der f in all strains. DE+Der f treated C3H/He mice had desquamated goblet cells. **Eosinophil Infiltration:** DE treated C3H/He mice had a slight eosinophil infiltration in the submucosal layer. DE+Der f treated mice in all strains had a slight to moderate eosinophil infiltration. **Lymphocyte Accumulation:** Lymphocytes significantly increased in all strains under the DE treatment as compared to the air+saline treatment, and further increased under the DE+Der f treatment. **Goblet Cell Proliferation:** Little proliferation was seen in all strains under the DE treatment. DE+Der f caused a significant increase in proliferation compared to air+Der f in ICR mice, but a significant decrease in C3H/He mice. **Local Cytokine and Chemokine Expression in Lung Tissue Supernatant:** DE+saline significantly increased MIP-1α in all strains. MCP-1 also increased but not significantly. DE+Der f increased IL-5, RANTES, eotaxin, MCP-1 and MIP-1α in all strains as compared with air+saline and air+Der f. IL-5 decreased in C3H/He mice treated with DE+Der f compared to air+Der f. IL-3 decreased in ICR and C3H/He mice compared to air+saline. **Der f-specific Immunoglobulin Production in Plasma:** Increased production of IgG1 was statistically significant in ICR and C3H/He mice treated with DE+Der f as compared to air+Der f. IgE was low in all strains.

Study	Pollutant	Exposure	Effects
Reference: Ichinose et al. (2004, 180367) **Species:** Mouse **Gender:** NR **Strains:** BALB/c, ICR and C3H/He **Age:** 5 wk **Weight:** NR	DEP: 2740cc 4-cylinder engine D. farinae: crude extract **Particle Size:** 0.4 µm (MMAD)	**Route:** IT Instillation **Dose/Concentration:** 1. D. farinae: 1 µm in PBS 2. D. farinae + DEP: 1 µg in PBS + 50 µg mg DEP **Time to Analysis:** 4 times at 2 wk intervals. Mice examined 3 wk after last instillation	**Histological Changes:** Mice in all three strains treated with DEP+D. farinae had a significant recruitment of eosinophils, more proliferation of goblet cells, and more eotaxin positive macrophages in the alveoli than mice treated with D. farinae alone. **Local Cytokine Expression in Lung Tissue Supernatant:** DEP+D. farinae induced significant elevation of IL-5 in ICR and C3H/He mice as compared to D. farinae alone. Production levels of IL-4 and RANTES did not correlate with the manifestations of allergic airway inflammation induced by the D. farinae treatment with or without DEP. **Cytokine Expression in Plasma:** IL-5 in C3H/He mice treated with DEP+D. farinae was significantly higher than D. farinae alone. RANTES was unaffected by the DEP treatment in all strains. **D. farinae-specific Immunoglobulin Production in Plasma:** The adjuvant effect of DEP on IgG1 production was observed in all three strains, with C3H/H3 being statistically significant. The production levels of IgG1 correlated with the manifestations of eosinophilic airway inflammation by both treatments. No adjuvant effect on IgE production was observed.
Reference: Inoue et al. (2007, 096724) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6 wk **Weight:** 29-33 g	PM-OC: Urban PM, collected for 1 month during early summer, 2001 in Urawa city Saitama, Japan LPS **Particle Size:** <2.0 µm	**Route:** IT Instillation **Dose/Concentration:** Vehicle group: PBS PM-OC group: 4 mg/kg of PM-OC LPS group: 2.5 mg/kg of LPS PM-OC+LPS group: combined administration of PM-OC +LPS **Time to Analysis:** Single, 24 h	**Effects of PM-OC on LPS Related Lung Inflammation**: PM-OC alone did not significantly increase the infiltration of neutrophils, but LPS challenge showed a marked increase in the number of neutrophils compared with vehicle. Administration of LPS combined with PM-OC significantly increased the infiltration of neutrophils compared with LPS administration alone. **Effects of PM-OC on Histological Changes in the Lung:** Combined treatment with PM-OC and LPS resulted in enhanced neutrophilic inflammation. **Effects of PM-OC on Pulmonary Edema Related to LPS**: LPS group compared with vehicle group had a significant increase in lung water. The combined administration of PM-OC and LPS resulted in further increase in the lung water compared with LPS administration alone, however it was not statistically significant. **Effects of PM-OC on Protein Expression IL-1B, MIP-1α, MCP-1 and KC:** The concentrations of these molecules were below the detection limits in the PM-OC group. LPS treatment significantly increased the protein levels of these molecules compared with the vehicle treatment. In the PM-OC + LPS group all concentrations, particularly KC, were smaller than in the LPS group.

Study	Pollutant	Exposure	Effects
Reference: Inoue et al. (2006, 090951) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6 wk **Weight:** 29-33 g	Carbon black (14 nm PrinteX 90; PrinteX 25; Degussa, Dusseldorf, Germany) **Particle Size:** 14 nm - 300 m^2/g 56 nm - 45 m^2/g	**Route:** IT Instillation **Dose/Concentration:** Vehicle group: PBS at pH7.4 LPS group: 2.5 mg/kg of LPS in vehicle Nanoparticle groups: 4 mg/kg carbon black nanoparticles (14 nm or 56 nm) in vehicle LPS + nanoparticle group: combined administration of carbon black and LPS in vehicle **Time to Analysis:** Single, 24 h	**Effects of Nanoparticles**: Nanoparticles alone increased number of total cells and neutrophils, but not statistically significant. LPS exposure significantly increased numbers for both groups. Nanoparticles and/or LPS enhance pulmonary edema. **Histology**: Treatment with LPS+14 nm nanoparticles markedly enhanced neutrophil sequestration into the lung parenchyma compared to LPS alone. LPS+56 nm nanoparticles did not. **Cytokines**: IL-1B level significantly greater for both LPS+ nanoparticles groups. TNF-α was not significantly altered among the experimental groups. **Chemokines**: Challenge with 14 nm nanoparticles alone elevated the levels of all chemokines without significance except for KC. LPS alone and with both nanoparticle groups caused significant increases in all chemokines. . **Formations of 8-OHdG in Lung:** LPS plus nanoparticles resulted in intensive expression 8-OHdG, strongest in LPS+14 nm nanoparticle **Plasma Coagulatory Changes**: PT - no change for any group. APTT - some change with LPS and LPS + nanoparticle groups, fibrinogen level significantly elevated after LPS and for LPS+14 nm nanoparticle. APC decrease with LPS (significant) and LPS + nanoparticle groups. vWF increase with LPS (significant) and LPS+14 nm (significant).
Reference: Inoue et al. (2004, 087984) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6 wk **Weight:** 29-33 g	DEPs [4JB-1 type light-duty, four-cylinder, 2.74 liter Isuzu diesel engine (Isuzu Automobile Co., Tokyo Japan)] Washed DEP and DEP-OC - extracted with dichloromethane **Particle Size:** NR	**Route:** IT instillation **Dose/Concentration:** Vehicle group: PBS; Washed DEP group: 4mg/kg of DEP; DEP-OC group: 4mg/kg of DEP-OC;LPS group: 2.5mg/kg of LPS; Washed DEP+LPS group: combined administration of washed DEP +LPS; DEP-OC+ LPS group: combined administration of DEP-OC + LPS **Time to Analysis:** 4 h	**COX-1 mRNA:** Slightly elevated in both washed DEP and DEP-OC groups, but slightly decreased in other groups compared to vehicle group. **COX-2 mRNA:** Slightly increased with DEP-OC, increased with LPS, washed DEP + LPS and DEP-OC + LPS groups compared to vehicle. COX-2 in the DEP-OC + LPS decreased when compared to the LPS only group. **Pulmonary Edema:** Washed DEP + LPS group showed a synergistic enhancement of pulmonary edema and local expression of proinflammatory chemokines (MCP-1, MIP-1α, KC, IL-1B).
Reference: Inoue et al. (2006, 096720) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6-7 wk **Weight:** 29-33 g	Carbon black (PrinteX 90; PrinteX 25; Degussa, Dusseldorf, Germany) **Particle Size:** 14 nm - 300 m^2/g 56 nm - 45 m^2/g	**Route:** IT instillation **Dose/Concentration:** Vehicle group: PBS Ovalbumin (OVA) group: 1mg OVA; Nanoparticle groups: 50 mg carbon black nanoparticles (14 nm or 56 nm);;OVA + nanoparticle group: combined administration of nanoparticles and OVA **Time to Analysis:** Vehicle group - weekly for 6wk OVA group - biweekly for 6 wk Nanoparticle groups - weekly for 6 wk OVA+Nanoparticle group (same protocol as OVA and Nanoparticle) studied 24 h after last administration	**Nanoparticles:** Exposure to carbon nanoparticles resulted in the lung expression of TARC, GM-CSF and MIP-1α. The levels were higher in the 14 nm group compared to the 56 nm group. **OVA:** In the presence of OVA, nanoparticles enhanced levels of TARC, GM-CSF, MIP-1α, IL-2 and IL-10, with the effects seen more prominently in the 14 nm particles + OVA group.

Study	Pollutant	Exposure	Effects
Reference: Inoue et al. (2005, 088625) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6-7wk **Weight:** 29-33 g	Carbon black (PrinteX 90; PrinteX 25; Degussa, Dusseldorf, Germany) **Particle Size:** 14 nm - 300 m^2/g 56 nm - 45 m^2/g	**Route:** IT Instillation **Dose/Concentration:** Vehicle group: PBS; Ovalbumin (OVA) group: 1mg OVA; Nanoparticle groups: 50mg carbon black nanoparticles (14nm or 56 nm); OVA + nanoparticle group: combined administration of nanoparticles and OVA **Time to Analysis:** Vehicle group - weekly for 6 wk OVA group - biweekly for 6 wk Nanoparticle groups - weekly for 6 wk OVA+Nanoparticle group: same protocol as OVA and Nanoparticle studied 24 h after last administration	**Nanoparticles + OVA:** Nanoparticles given with OVA enhanced airway inflammation, characterized by increased eosinophils, neutrophils, mononuclear cells and goblet cells. In addition, nanoparticles + OVA significantly increased local expression of IL-4, IL-5, eotaxin, IL-13, RANTES, MCP-1 and IL-6. The formation of 8-OHdG was enhanced by nanoparticles + OVA. **14 nm Nanoparticles:** All these effects were more prominent when 14 nm nanoparticles were used. The 14 nm nanoparticle + OVA group significantly raised levels of total IgE and antigen specific production of IgG1 and IgE.
Reference: Inoue et al. (2006, 190142) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6 wk **Weight:** 29-33 g	Whole DE (generated by 4-cylinder, 3.059l, Isuzu diesel engine, Isuzu automobile, Tokyo, Japan) LPS **Particle Size:** 110 nm (peak particle size)	**Route:** Whole-body Inhalation **Dose/Concentration:** 0.3 mgsoot/m^3 1.0 mgsoot/m^3 3.0 mg soot/m^3 LPS: 125 mg/kg **Time to Analysis:** LPS prior to 12 h exposure to exhaust	BAL fluid, total cells, neutrophils, protein and gene levels (MCP-1 and KC) decreased compared to control with LPS, but were smaller with LPS + DE. Results are suggestive that short-term exposure to DE does not exacerbate LPS-related lung inflammation.
Reference: Inoue et al. (2007, 096702) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6 wk **Weight:** 29-33 g **Cell Type** Splenocytes	DEPs [4JB-1 type light-duty, four-cylinder, 2.74 liter Isuzu diesel engine (Isuzu Automobile Co., Tokyo Japan)] LPS **Particle Size:** $PM_{2.5}$	**Route:** Cell Culture (Splenocytes resuspended to cell density of 1×10^6/mL and 1000 mL applied into each of 12-well plate) **Dose/Concentration:** DEP: 100 mg/mL; LPS: 1 mg/mL; LPS(1mg/mL) + DEP (1, 10 or 100 mg/mL) **Time to Analysis:** 72 h	**Cell viability:** No effect. **Mononuclear cell response:** Incubation with DEP alone inhibited basal cytokine production. LPS significantly increased protein levels of IFN-γ, IL-2, and IL-10 compared to control. DEP suppressed the LPS-enhanced protein levels in a dose-dependent manner and moderately elevated the IL-13 level.
Reference: Inoue et al. (2007, 198885) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6-7 wk **Weight:** 20-30 g	Carbon nanoparticles (PrinteX 90, PrinteX 25; Dusseldorf, Germany) OVA **Particle Size:** CB14 = 14 nm, CB56 = 56 nm	**Route:** IT Instillation **Dose/Concentration:** 50 µg and/or 1 µg OVA in PBS **Time to Analysis:** 1×/wk for 6 wk; sacrifice 24 h after last exposure	**Lung Responsiveness:** Respiratory system resistance, Newtonian resistance and tissue dampening were significantly higher in the nanoparticle + OVA groups. Elastance and tissue elastance were higher in these groups but not significantly so. Compliance was significantly lower in the nanoparticle + OVA groups compared to the control. **Lung mRNA Level for Muc5ac**: Levels were significantly higher in nanoparticle + OVA groups compared to the control.
Reference: Inoue et. al. (2007, 096692) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 6-7 wk **Weight:** 29-34 g	DEP-OC collected from 4JB1 type, light duty, 4 cylinder, 2.74 liter Isuzu diesel engine, Isuzu Automobile Company, Tokyo, Japan) OVA **Particle Size:** 0.4 µm	**Route:** IT Instillation **Dose/Concentration:** 50 µg and/or 1 µg OVA in PBS **Time to Analysis:** DEP or DEP-OC w/ or w/o OVA initially; OVA or vehicle every 2 wk for 6 wk; DEP components or vehicle 1×/wk for 6 wk; sacrifice 24 h after last instillation	Total respiratory system resistance, elastance, Newtonian resistance, tissue damping, tissue elastance displayed general positive trends and were significantly higher in OVA and OVA + DEP-OC groups. Compliance displayed a general negative trend and was significantly lower in the washed DEP + OVA group.

Study	Pollutant	Exposure	Effects
Reference: Ito et al. (2006, 088391) **Species:** Rat **Cell Line:** L2 cells of alveolar epithelial cell type II origin	DEP - generated from 2982-cc common rail direct injection diesel engine with oxidation catalyst and exhaust gas recirculation system. **Particle Size:** $PM_{2.5}$	**Route:** Cell Culture **Dose/Concentration:** 1×10^6 1,10 or 30 mg/mL **Time to Analysis:** 3 h	**ICAM-1 and LDL Receptor mRNA**: Up-regulation in a dose-dependent manner. Statistically significant at 30 mg/mL compared to control. **HO-1 and PAF Receptor mRNA**: Up-regulation in dose-dependent manner and statistically significant at all doses compared to control. **Correlation Between HO-1 and ICAM-1, LDL, and PAF:** Significant correlation between HO-1 and each of these.
Reference: Jang et al. (2005, 155313) **Species:** Mouse **Gender:** Female **Strains:** BALB/c **Age:** 5-6 wk	DEP -generated from 4JB1 type, light duty, four-cylinder diesel engine (Isuzu Automobile, Co, Tokyo, Japan) O_3 - (generated with Sander Model 50 ozonizers, Sander, Eltze Germany) OVA **Particle Size:** NR	**Route:** Whole-body Inhalation **Dose/Concentration:** DEP: 2,000 µg/µL (sic) O_3: 2 ppm (avg 1.98 ± 0.08 ppm) OVA sensitization: 10 mg **Time to Analysis:** OVA sensitization, DEP, O_3 and OVA Challenge on d21- 23 Exposed to O_3 for 3 h and DEP for 1 h AH and BAL measured 1 day after last challenge	**Airway Responsiveness**: OVA + O_3 + DEP exposure group had significantly higher methacholine-induce Penh than sham group or OVA group. **Total cells, proportion of eosinophils and neutrophils**: The OVA + O_3 + DEP group was significantly higher than OVA group and OVA+ O_3 group. **IL-4:** OVA + O_3, OVA + DEP and OVA + O_3 + DEP IL-4 level increased compare to OVA group. **IFN-γ:** Levels significantly decreased in OVA + DEP and OVA + O_3 + DEP compared to OVA + O_3.
Reference: Jaspers et al. (2005, 088115) **Species:** Human **Cell Lines:** A549 cells, primary human bronchial and nasal epithelial cells	DEas: aqueous-trapped solution of DE (emissions from Caterpillar diesel engine, model 3304) Influenza: A/Bangkok/1/79 (H3N2 serotype) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** Influenza: 3×10^5 cells infected with 320 hemagglutination units (HAU) DEas**:** For A549 cells: 6.25, 12.5, 25 µg/cm^2. For bronchial and nasal cells: 22 or 44 µg/cm^2. **Time to Analysis:** 2 h incubation with DEas then virus added. HA RNA levels analyzed at 0, 15, 30, 60 or 120 min post infection. IFN and MxA responses: analyzed 24 h post infection. Fluorescence: some cells treated with GSH-ET 30 min before DEas exposure. Measured 2 h post-influenza infection.	**A549 Cells Increased Susceptibility:** DEas enhances HA RNA levels in A549 cells in a dose-dependent manner. 25 µg/cm^2 significantly enhanced levels in A549 cells compared to the influenza-infected controls. Viral protein levels were increased in A549 cells. Exposure to DEas increased the number of influenza-infected epithelial cells in A549 cells. **Human Nasal and Bronchial Cells Susceptibility:** Exposure to DEas increased HA RNA levels in the nasal and bronchial cells. Statistically significant at 22 µg/cm^2 for nasal cells and approaching significance at 44 µg/cm^2 for bronchial cells. Exposure of both types to 44 µg/cm^2 enhanced viral protein levels. **Influenza Induced IFN Response in A549:** Exposure to DEas does not suppress but enhances IFN-ß mRNA levels. Treatment enhanced influenza-induced nuclear levels of both phospho-STAT-1 and ISFG3g. ISRE-promoter activity was enhanced, but not significantly. Treatment enhanced myxovirus resistance protein (MxA) mRNA levels. This data suggest that DEas exposure enhances influenza virus replication without suppressing production of IFN-ß or IFN-ß-inducible genes. **Influenza Induced IFN Response in Human Nasal and Bronchial Cells:** Exposure to DEas increased IFN-ß and MxA levels. **Oxidative Stress in A549:** DEas exposure dose-dependently increases oxidative stress in A549 cells within 2-h post-exposure. Add the antioxidant GSH-ET and it reverses the effect. Pretreatment with GSH-ET A549 cells reversed the effects of DEas on the number of influenza-infected cells, and reduced HA RNA levels. **Oxidative Stress in Human Bronchial Cells:** The results were the same as A549 cells pretreated with GSH-ET. Or Pretreatment with GSH-ET also reversed effects of DEas on HA RNA levels.

Study	Pollutant	Exposure	Effects
Reference: Kaan and Hegele (2003, 095753) **Species:** Guinea pig **Gender:** Female **Strain:** Cam Hartley **Age:** 22-29 days **Weight:** 250-300 g **Cell Types:** AM	PM_{10} - EHC-93 obtained (Environmental Health Canada, Ottawa, ON, Canada) RSV - Human RSV (long strain/lot18D) (American Tissue Culture Collection, Bethesda, MD) **Particle Size:** PM_{10} (0.35 µm MMAD)	**Route:** Cell Culture **Dose/Concentration:** PM_{10}: 500 µl/well (100 µg/ml MEM) RSV exposure:: 1 ml/well (6×10^6 pfu/ml MEM) Groups: PM_{10}+RSV RSV+PM_{10} RSV only PM_{10} only negative control **Time to Analysis:** PM_{10} - 60 min; RSV - 90 min Parameters measured 24 h post treatment	**Interaction on Phagocytic Ability of AM:** Not affected by sequential exposure to RSV and PM_{10}. More than 95% of AM exposed to PM_{10} engulfed PM. AM exposed to PM_{10} showed significant increase in mean side scatter in comparison to negative control and RSV-infected AM. No significant difference between AM exposed only to PM_{10} and AM exposed to both agents. No significant side mean side scatter difference between AM exposed to PM only and to both agents. **Interaction on RSV Immunopositivity:** PM_{10} exposure inhibits. All RSV-treated groups showed significantly greater proportion of RSV-immunopositive cells compared with negative control. PM_{10}+RSV showed significantly smaller proportion of RSV-immunopositive cells compared with RSV group. RSV+PM_{10} group similar to RSV group. Proportion of RSV-immunopositive AM was influenced by the sequence of exposure to RSV and PM_{10}. **Interaction on RSV Replication:** PM exposure suppressed RSV replication. AM exposed to both agents produced 3 to 9 fold less RSV progeny compared with RSV alone group. Quantity of RSV progency was not significantly affected by the sequence of exposure RSV and PM_{10}. Negative control and PM_{10} only did not propagate progeny. **Interaction of RSV Yield:** RSV alone group produced the highest RSV yield, those exposed to both agents, independent of sequence, showed a 5-fold decrease. **Cytokine production:** RSV infection stimulated all three cytokines measure (IL-6, IL-8 and TNF-α) compared to negative control. IL-6: PM_{10} significantly reduced RSV-induced IL-6 production. IL-6 was affected by the sequence of exposure to PM_{10} and RSV (PM_{10}+RSV vs. RSV+ PM_{10}). IL-8: PM_{10} significantly decreases RSV-induced IL-8 production and baseline. No affect on sequence of exposure. TNF-α: production was increased when exposed to RSV, PM_{10} or a combination of both agents. No differences among treatments.
Reference: Kleinman et al. (2005, 087880) **Species:** Mouse **Gender:** Male **Strains:** BALB/c **Age:** 8-19 wk **Weight:** NR	CAPS: fine (F) and ultrafine (UF) using VACES system; performed a 2 sites in Los Angeles, CA, one 50-m downwind and another 150-m downwind from a complex of three roadways, State Road CA60, Interstate 10, and Interstate 5 F CAPS in 2001 and 2002, UF CAPS in 2002 only OVA: Ovalbumin **Particle Size:** UF: dp ≤ 150 nm F: dp ≤ 2.5 µm	**Route:** Whole-body Inhalation OVA sensitization: nasal instillation OVA challenge: inhalation **Dose/Concentration:** UF at 50 m: 433 µg/m^3 -UF at 150 m: 283 µg/m^3 F at 50 m or 150 m: average 400 µg /m^3 OVA sensitization: 50 µg/5 µl OVA challenge: 30 mg/m^3 **Time to Analysis:** CAPS: 4 h/day, 5 days/wk for 2 wk Sensitization: On morning of each exposure 1st Challenge: week after 10 days of treatment 2nd Challenge: one week following 1st challenge Sacrificed: 24 h after 2nd challenge	There were significantly higher concentrations of IL-5, IgE, IgG1 and eosinophils in mice exposed to either CAPS compared to air. Mice exposed to CAPS at 50-m downwind showed higher levels of IL-5, IgG1, and eosinophils than those exposed to CAPS 150-m downwind.

Study	Pollutant	Exposure	Effects
Reference: Kleinman et al. (2007, 097082) **Species:** Mouse **Gender:** NR **Strains:** BALB/c **Age:** 6-8 wk	CAPS - concentrated fine (F) and ultrafine (UF) using VACES system - performed a 2 sites in Los Angeles, CA, on 50-m downwind and another 150-m downwind from State Road CA60 and Interstate 5. Fall 2001-summer 2004 OVA **Particle Size:** F: $PM_{2.5}$; UF: PM0.15	**Route:** Whole-body Chamber **Dose/Concentration:** 50 m - F: 394 ± 94 µg/m^3 50 m - UF: 297 ± 189 µg/m^3 150 m - F: 387 ± 68 µg/m^3 150 m - UF: 213 ± 95 µg/m^3 OVA - 50 mg in 5 mL saline **Time to Analysis:** 3, 4 h/day, 5 days/wk, 2wk OVA the morning of each exposure	**50m Site**: higher levels and statistically significant concentration curves of IL-5 and IgG1 in F-CAP mice at the 50 m site. **150m Site:** in no cases were responses greater than the 50m or control groups. **F vs. UF:** The study was not able to differentiate between the effects of F PM and UF PM exposures.
Reference: Klein-Patel et al. (2006, 097092) **Species:** Cattle and Human **Cell Types** Bovine tracheal epithelial cells (BTE) and A549	ROFA V_2O_5, $VOSO_4$, SiO_2 TiO_2, $Fe_2(SO_4)_3$, $NiSO_4$, LPS **Particle Size:** 1.95 µm (MMAD)	**Route:** Cell Culture **Dose/Concentration:** ROFA: 0, 2.5, 5, 10, 15, 20 µg/cm^2 LPS: 100 ng/mL V_2O_5: 0, 0.15, 0.3, 0.61, 1.25, 2.5, 5, 10, 20 µg/cm^2 $NiSO_4$, $Fe_2(SO_4)_3$, TiO_2, SiO_2: 0, 1.23, 2.5, 5, 10, 20 µg/cm^2 $VOSO_4$: 0, 0.145, 0.29, 0.58, 1.16, 2.32 µg/cm^2 **Time to Analysis:** LPS: 0, 6, or 18 h ROFA: 0, 2,4,6 h V_2O_5: 0, 0.25, 0.5, 1, 2, 4, 6, 8h $NiSO_4$, $Fe_2(SO_4)_3$, TiO_2, SiO_2, $VOSO_4$: 6 h	**ROFA in BTE:** ROFA and ROFA leachate inhibition of LPS-induced TAP gene expression increases with exposure time and dose. Washed particles of ROFA at doses 2.5 to 10 mg/cm^2 significantly increased inducible TAP expression. **Soluble Metals in BTE:** V_2O_5 inhibition of LPS and IL-1β induced TAP gene expression increases with exposure time and dose. $NiSO_4$ exhibits non-significant dose dependent suppression of inducible TAP gene expression. $Fe_2(SO_4)_3$, TiO_2 and SiO_2 were found to have no effect. **A549:** Results with ROFA and V_2O_5 in BTE were replicated using the A549 cell line and IL-1β to induce hBD2 gene expression. **Cellular Viability:** Was not significantly affected in ROFA doses below 20 µg/cm^2 and V_2O_5/$VOSO_4$ doses below 2.5 µg/cm^2.
Reference: Koike and Kobayashi (2005, 088303) **Species:** Rat **Gender:** Male **Strains:** Wistar Kyoto **Age:** 8-10 wk **Weight:** 280-350 g **Cell Types:** AM, PBM (peripheral blood monocytes), T-cells (antigen sensitized)	Whole DEP: Diesel Exhaust Particles collected in the dilution tunnel of a diesel inhalation facility. (Ratio of organic extract to residual particles in the whole DEP was 3: 1.) Organic extract of DEP Residual particles of DEP OVA: Ovalbumin **Particle Size:** NR	**Route:** Cell Culture (1×10^6 cells/ml) **Dose/Concentration:** Whole DEP: 10, 30, 100 µg/mL Organic extract of DEP: 7.5, 22.5, 75 µg/mL Residual particles: 2.5, 7.5, 25 µg/mL **Time to Analysis:** 24 h post exposure	**Ia Antigen and Costimulatory Molecules:** Most control AM did not express these molecules. Whole DEP did not cause any increase in expression level. 20% of control PBM expressed Ia and 10% B7; expression of these molecules was significantly increased by whole DEP. Organic extract significantly increased the expression of Ia and B7 molecules on PBM similar to whole DEP. Residuals caused no effect. Organic extract-induced expression of Ia antigen in PBM was reduced by treatment with NAC. **AP Activity:** After exposure to organic extract, T cell proliferation was significantly increased by the addition of control PBM in a cell number-dependent manner. AP activity of PBM was increased over control by exposure to 3 µg/mL organic extract, although higher concentrations suppressed the activity of PBM. **Cytokine Production:** Organic extract treatment of PBM decrease IFN-γ production from T-cells stimulated by PBM. No significant effect on IL-4 observed. **HO-1 Protein Level:** Levels in PBM were significantly increased by exposure to whole DEP or organic extract. Levels induced by organic extract was diminished by NAC treatment.

Study	Pollutant	Exposure	Effects
Reference: Last et al. (2004, 097334) **Species:** Mouse **Gender:** NR **Strains:** BALB/c **Age:** 6 wk **Weight:** 16-20 g	PM - aerosol of soot and iron oxide OVA **Particle Size:** $PM_{0.1}$ - $PM_{2.5}$	**Route:** Inhalation OVA - Intraperitoneal Injections; Aerosol Exposure **Dose/Concentration:** PM - 235-256 µg/m^3 OVA - 10 µg/0.1 mL injection OVA aerosol - 10 mL of 10 mg/mL (1%) solution **Time to Analysis:** PM: 4 h/day, 3 days/wk; OVA: 2 ip injections days 1 and 15. Aerosol on day 28 after first ip; 60 min 3x/wk	**2 Wk PM Exposure/4 Wk OVA Aerosol Treatment:** The OVA alone group had significantly more airway collagen than the PM alone group. Histology showed significantly more collagen in the treatment than the air alone group. There was a significantly greater amount of goblet cells than the OVA alone group. **4 Wk OVA Aerosol/ 2 Wk PM Treatment:** The OVA treatment had significantly more goblet cells than the PM alone group. **6 Wk Concurrent PM and OVA Treatment:** Significantly more cells were observed in the OVA alone group over the treatment. The treatment had significantly more lymphocytes and significantly less macrophages than groups exposed to PM before or after OVA. Histology showed significantly more collagen in the treatment than the air or PM alone groups. The treatment had significantly more goblet cells than the OVA alone group.
Reference: Li et al. (2007, 093156) **Species:** Mouse **Gender:** Female **Strain:** BALB/c, C57BL/6 **Age:** 9 wk **Weight:** NR	DEP (2369-cc diesel engine manufactured by Isuzu Motor, operated at 1050 rpm, 80% load, commercial light oil) **Particle Size:** NR	**Route:** Inhalation **Dose/Concentration:** DEP: 103.1 ± 9.2 µg/m^3, CO: 3.5 ± 0.1 ppm, NO_2: 2.2 ± 0.3 ppm, SO_2: <0.01 ppm **Time to Analysis:** Protocol 1: Exposed 7h/day, 5days/wk. Sacrificed at day 0, week 1, 4, 8. Protocol 2: DE alone or DE+NAC 7h/d, 1-5 days.	**Airway Hyperresponsiveness:** Penh values increased in BALB/c mice compared to the control at day 0, but no significant changes occurred after this time. Penh values increased in C57BL/6 mice at 1wk compared to the control but returned to control levels at 8 wk. **BALF:** Compared to the other strain, the total number of cells and macrophages increased significantly at 1wk in C57BL/6 mice and at 8wk in BALB/c mice. Neutrophils, lymphocytes, MCP-1, IL-12, IL-10, IL-4, IL-13 increased significantly for both strains. No eosinophils were found. IL-1B and IFN-γ increased significantly in BALB/c mice compared to C57BL/6 mice. **HO-1 mRNA and Protein:** HO-1 mRNA was more marked in BALB/c mice at 1wk and C57BL/6 mice at 4 and 8 wk. HO-1 protein percentage changes from the control were greater in BALB/c mice at 1wk and C57BL/c mice at 8 wk. **NAC:** NAC inhibited the increased Penh values, total number of cells and macrophages in C57BL/6 mice at 1 wk and neutrophils and lymphocytes in both strains.
Reference: Li et al. (2009, 190457) **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 6-8 wk **Weight:** NR	CAPs (downtown Los Angeles, CA from major freeway, traffic mainly passenger cars and diesel trucks; Jan. 2007 or Sept. 2006) Ultrafine carbon black (UFCB; used as control) **Particle Size:** Fine- <2.5 µm (diameter), UF- <0.15 µm (diameter)	**Route:** Intranasal Instillation **Dose/Concentration:** 0.5 µg PM in 50 µL suspension **Time to Analysis:** Day 1 exposed to PM or saline. Day 2 exposed to PM+OVA or OVA or saline alone. Repeated on days 4, 7, 9. Different experiment: NAC ip injected 4 h pre-instillation on days 1, 2, 4, 7, 9. All animals rested and OVA aerosol challenged 30 min on days 21, 22. Sacrificed day 23.	UFP alone had no effect on the lung. UFP+OVA significantly increased eosinophils, and OVA-specific IgG1 and IgE. The induction of eosinophils and IgG1 were inhibited by NAC. Generally, UFP+OVA mice had greater signs of inflammation than the other groups as determined by pulmonary histopathology and airway morphometry. UFP had a greater PAH content than fine particles. UFP significantly increased IL-5, IL-13, TNF-α, IL-6, KC, MCP-1, and MIP-1α.
Reference: Li et al. (2009, 190457) **Species:** Mouse **Cell Line:** RAW 264.7	CAPs (downtown Los Angeles, CA from major freeway, traffic mainly passenger cars and diesel trucks; Jan. 2007 or Sept. 2006) Ultrafine carbon black (UFCB) **Particle Size:** Fine- <2.5 µm (diameter), UF- <0.15 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** 1, 5, 8.3, 10 µg/mL **Time to Analysis:** NR	UFP induced greater HO-1 expression than fine particles. The higher PAH content of UFP correlated with HO-1 expression.

Study	Pollutant	Exposure	Effects
Reference: Liu et al. (2008, 156709) **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 11wk **Weight:** NR	DEP (5500-watt single-cylinder diesel engine generator (Yanmar, Model YDG 5500E), 406 cc displacement air-cooled engine, Number 2 Diesel Certification Fuel, 40 weight motor oil) **Particle Size:** ~0.1 µm (MMAD)	**Route:** Intranasal Exposure **Dose/Concentration:** Average particle concentration: 1.28 mg/m^3 **Time to Analysis:** Four groups: saline+air control, saline+DEP, A. fumigatus+air, A.fumigatus+DEP. A. fumigatus exposure every 4 days for 6 doses. DEP exposure 5 h/dayfor 3 wk concurrent with A. fumigatus exposure.	A.fumigatus+DEP increased IgE, the mean BAL eosinophil percentage, goblet cell hyperplasia, and eosinophilic and mononuclear cell inflammatory infiltrate around the airways and blood vessels compared to the A. fumigatus or DEP treatments. A.fumigatus+DEP also caused methylation at the IFN-γ promoter sites CpG-53, CpG-45, and CpG-205.
Reference: Liu et al. (2007, 093093) **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 11wk	DEP: 5500-watt single-cylinder diesel engine. **Particle Size:** NR	**Route:** Inhalation **Dose/Concentration:** Average particle concentration 1.28 mg/m^3. **Time to Analysis:** 1. Aerosol vehicle (saline) + air 2. Aerosol vehicle (saline) + DEP 3. A. fumigatus + air 4. A. fumigatus + DEP A. fumigatus: 62.5 µg aerosolized protein extract in 50 µL PBS; 6 total doses, every 4 d. DEP exposure 5 h/day 3wk concurrent with A. fumigatus.	**IgE Production:** IgE production increased with the A.fumigatus treatment and increased further with the A.fumigatus and DEP treatment. **Histopathology:** A. fumigatus with DEP caused an increase in goblet cell hyperplasia and eosinophil and mononuclear cell infiltrate around the airways and blood vessels as compared to the control and DEP treatments. **Gene Methylation:** Greater methylation at the CpG-53 site of the IFN-γ promoter occurred under the A. fumigatus + DEP treatment compared to the A. fumigatus or DEP treatments. The DEP treatment did not induce methylation. Methylation correlated with increased IgE and hypomethylation with decreased IgE. Hypomethylation occurred in the IL-4 promoter under the A. fumigatus + DEP treatment.
Reference: Lundborg et al. (2007, 096040) **Species:** Rat **Gender:** Male **Strains:** SD **Age:** NR **Weight:** 300-400 g **Cell Line:** AM	Carbon-Black Particles (93% C) DEPs (97% C) - toluene-extracted 10-fold Cr, Mn, N; 50-100 fold Al, Cd, Cu, Fe, Mg, Pb, Zn more in DEP aggregates **Particle Size:** Carbon aggregates: 0.17 ± 0.08 µm (mean diameter) Diesel Particles: 0.69 ± 0.46 µm (mean diameter) Primary particles: 0.044 ± 0.01 µm (mean diameter)	**Route:** Cell Culture (0.5×10^6 AM/well) **Dose/Concentration:** 20 µg/mL surface area: 159 ± 4m^2/g **Time to Analysis:** 6 different experiments. AM pre-exposed to carbon or washed DEP. Loaded with particles. Incubated with S. pneumoniae, ATCC strain or clinical isolates.	**Effect of Time on Survival of S. Pneumoniae when Incubated with Carbon Loaded AM:** Loading AM with carbon significantly increased the bacterial survival. Bacteria opsonization decreased bacterial survival. **Effect of Carbon Load in AM on Survival of S. Pneumoniae:** Bacterial survival increased in a dose-dependent manner as the carbon particle load of AM increased. **Survival of S. Pneumoniae after Incubation with Carbon or Washed Diesel Loaded AM:** Bacterial survival increased in carbon loaded AM compared to the control. No difference existed with the washed diesel particles. **Survival of the ATCC Strain and Clinical Isolates of S. Pneumoniae when Incubated with Carbon Loaded AM or Control AM:** Carbon significantly increased the CFU of opsonized and unopsonized bacteria for the ATCC strain and clinical isolates. **Ability of carbon or washed diesel loaded AM, incubated with the ATCC strain of S. pneumoniae, to induce LPO of lung surfactant:** A 97% increase in the surfactant LPO occurred after incubation with washed diesel loaded AM compared to control AM. The effect of washed diesel particles was significantly greater than that of carbon particles. **LPO by carbon loaded AM incubated with the ATCC strain or clinical isolates in the presence of absence of surfactant:** LPO induced by AM increased when incubated with carbon loaded AM compared to control AM.

Study	Pollutant	Exposure	Effects
Reference: Matsumoto et al. (2006, 098017) **Species:** Mouse **Gender:** Female **Strains:** BALB/c **Age:** 6 wk **Weight:** 15-20 g	DE (collected from a 2369 cm^3 diesel engine operated at 1050 rpm and 80% load with commercial light oil; engine exhaust passed through a particulate air filter and charcoal filer) Diluted DE introduced into the exposure chamber. Composition of the DE: 3.5 ± 0.1 ppm CO, 2.2 ± 0.3 ppm NO_2, <0.01 ppm SO_2 and 103.1 ± 9.2 µg/m^3 DEP. **Particle Size:** NR	**Route:** Whole-body Inhalation **Dose/Concentration:** 100 µg/m^3 DE **Time to Analysis:** Mice were initially sensitized w/ OVA (20ug absorbed to 2 mg alum diluted with 0.5 mL saline) via ip injection on day 0, 6 and 7. Two wks later the mice were challenged with OVA (0.1mg in 0.1mL saline) intranasally on day 21. DE for 1d or 1,2, 3, 4 or 8 wk (at 7 h/day for 5 days/wk).	**Airway Hyperresponsiveness:** Exposure to DE significantly increased airway reactivity to methacholine after 1 wk in both 24 and 48 mg/mL Mch and after 4 wk in the 48 mg/mL. DE exposure caused an increase in airway sensitivity after 1 wk of exposure, 4 wk and 8 wk of exposure did not result in a significant increase. **BAL Cells:** The total cell count was increased after 1 wk of DE exposure. This increase was mostly due to an increase in eosinophils. After 1 wk the total cell count dropped drastically even after continuous exposure to DE. DE did not effect the number of CD3, CD4, CD8 or NK1 cells at any point in time. **Cytokine/Chemokine mRNA Levels:** DE exposure on day 1 caused an increase in mRNA levels of IL-4, IL-5 and IL-13 when compared to the control mice but longer periods of DE exposure failed to cause an increase. Protein levels of IL-4 were significantly elevated at compared to control at day 1, but did not persist with time. mRNA levels of MDC were increased at 1 wk of exposure (compared to control) but also decreased at time periods after. mRNA levels of RANTES were increased at 2 and 3 wk after exposure and remained elevated at 4 wk but not significantly. The level of RANTES protein increased as the weeks went along, but increased significantly only at 8 wk. **Histopathology:** OVA sensitization caused an increase peribronchial and perivascular infiltration of inflammatory cells which peaked at 1 wk after exposure and decreased afterward. DE exposure did not cause/show any additional signs of inflammation.
Reference: Morishita et al. (2004, 087979) **Species:** Rat **Gender:** Male **Strain:** Brown-Norway **Age:** 10-12 wk	CAPs (generated from ambient air in an urban Detroit community). **Particle Size:** 0.1-2.5 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** July 676 µg/$m^{3;}$ September 313 µg/m^3 **Time to Analysis:** First rats were sensitized (days 1-3) and challenged (days 14-16) with saline (control) or OVA by intranasal instillation (5% in saline, 150 µL/nasal passage). 4 days after the last intranasal challenge, rats began exposure in the chambers. Exposures were 10 h long. The July exposure was for 4 consecutive days. The September exposure was for 5 consecutive days.	**Recovery of Trace Elements in Animal Lung Tissues:** July Exposure- Anthropogenic trace elements were below limit of detection in pulmonary tissue of animals exposed to July CAPs. September Exposure- Several elements were recovered from pulmonary tissue during the Sept. exposure. La concentrations were increased in both control/CAPs exposure and in the OVA/CAPs exposure groups. V concentration was increased in OVA/CAPs exposed animals but not in rats exposed to just CAPs. S content was only significant in animals exposed to OVA/CAPs compared to the non-exposed control. **Particle Characterization:** July PM had an average mass concentration twice as high as the September mass concentration. S concentration was four-folds higher in July PM. In the September PM- the concentration of La was 12.5 fold higher than in July PM, V was 2.7 fold higher than in July PM and Mn was 1.5 fold higher than in July PM. **BALF Analysis:** Eosinophil concentration was not significantly different when comparing rats exposed to CAPs only in either July or September (this was explained by the elapsed time between exposure and BALF collection). However OVA and CAP exposure in the September group led to elevated eosinophil levels. Similarly, the protein content was only significantly increased in the September OVA/CAP exposed rats, compared to the control group.

Study	Pollutant	Exposure	Effects
Reference: Nygaard et al. (2005, 088655) **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 6-7 wk	Coarse and fine ambient air particles collected in Rome (spring), Oslo (1-summer, fine only, 2- following spring, fine and coarse), Lodz (summer) and Amsterdam (spring). These represent areas with high population and dominance of traffic. DEP (Standard reference material 1650a) **Particle Size:** Fine PM 0.1-2.5 µm; Coarse PM 2.5-10 µm	**Route:** Subcutaneous Injection into mouse footpads. **Dose/Concentration:** 100 µg of particle **Time to Analysis:** Animals were in eight groups: 1. Control- Hank's Balanced Salt Solution 2. OVA- 50 ug 3. OVA (50 µg)+ Amsterdam Coarse PM (100 µg) 4. OVA (50 µg)+ Amsterdam Fine PM (100 µg) 5. OVA (50 µg)+ Lodz Coarse PM (100 µg) 6. OVA (50 µg)+ Lodz Fine PM (100 µg) 7. 5. OVA (50 µg)+ Oslo Coarse PM (100 µg) 8. OVA (50 µg)+ Oslo Fine PM (100 µg) Analysis 5 days after injection.	**Cell Numbers and Cell Phenotypes in the Lymph Node**: The overall number of B lymphocytes, lymph node cells, PLN cells, and the expression of MHC class II, CD86 and CD23 on B lymphocytes were increased by coexposure of OVA+ the particles compared to the OVA or particle groups alone. The OVA + particle groups displayed a significant decrease in T lymphocytes. Particles only significantly increased the number of lymph node cells and MHC Class II expression. There were no differences observed between coarse and fine PM fractions. **Cytokine Production by Lymph Node (ex vivo culture of popliteal lymph node cells):** The OVA + particle (DEP and Oslo1 only) significantly increased IL-4 and IL-10 levels. No change was observed in IFN-γ. The particle groups only increased IL-4 and IL-10. All coarse and fine particle fractions co-exposed with OVA significantly increased IL-4 and IL-10 compared to OVA alone. There was no significant difference between coarse and fine particles. IFN-γ levels were not significantly affected by most of the groups, but the fine fractions of PM consistently produced higher levels of IFN-γ. **Lymph Node Histology:** OVA + particle groups resulted in significantly enlarged lymph nodes and the formation of germinal centers.
Reference: Nygaard et al. (2005, 087980) **Species:** Mouse **Gender:** Female **Strains:** BALB/c **Age:** 6-8 wk	Polysterene Particles (PSP) **Particle Size:** 0.1 µm (diameter)	**Route:** Subcutaneous Injection into footpads. **Dose/Concentration:** 40 µg PSP (5.94×10^{10} particles) per injection suspended in HBSS. One injection per footpad **Time to Analysis:** 1. HBSS 2. OVA (10 µg per injection) 3. PSP (40 µg per injection) 4. OVA (10 µg per injection) + PSP (40 µg per injection). Antibody experiments: reinjected with 10 µg OVA on day 21. Killed on day 26. Popliteal lymph node cell experiments-- animals injected. Killed 1 to 21 days post-injection.	**OVA-specific IgE, IgG1 and IgG2a Antibodies:** Analysis at day 26 indicated IgE, IgG1 levels were significantly higher in mice exposed to OVA+PSP compared to mice injected with HBSS, OVA or PSP. No significant difference was observed for IgG2a levels. **Number of Particle Containing Cells:** There was no significant difference between PSP alone and OVA+PSP. Throughout days 0 -21 the number of particle-containing cells in the PSP or OVA+ PSP groups were significantly greater than the HBSS group. **Total Cell Numbers, B and T Lymphocytes and MHC class II Expression:** The total cell number and B lymphocytes significantly increased by coexposure to OVA+ PSP when compared to the other groups. Both OVA and OVA+PSP increased T lymphocytes on Days 1, 3 and 5. MCH class II expression was significantly higher in the OVA+PSP group on days 5, 7 and 21 than other groups. **Cell Types and Surface Markers:** The number of CD40+ B Lymphocytes showed a slight but significant decrease with OVA+PSP and OVA compared to HBSS and PSP. CD86+, CD23+ and CD69+ B lymphocytes were significantly higher in OVA+PSP group than other groups. PSP alone did not affect CD86+ or CD23+ levels. **Cytokine Production:** IL-4 and IL-10 were significantly higher in the OVA+PSP group when compared to the other groups. OVA alone caused a slight increase compared to PSP. PSP did not alter IL-4 or IL-10 levels.

Study	Pollutant	Exposure	Effects
Reference: Nygaard et al. (2004, 058558) **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 6-7 wk **Weight:** NR	CB (carbon black/DEP) Polystrene Particles (PSP) **Particle Size:** PSP diameter: 0.0588, 0.202, 1.053, 4.64 or 11.14 µm	**Route:** Single subcutaneous injection into footpad **Dose/Concentration:** 10 µg OVA + 40 µg (low dose) or 200 µg (high dose) of particles **Time to Analysis:** 5 days after OVA injection	**OVA Specific IgE and Ig2a:** OVA with CB, DEP or PSP of diameters 0.0588 and 0.202 µm increased IgE compared to OVA alone, as well as the 1.053, 4.64 and 11.14 µm PSP. OVA with 0.0588 µm PSP or CB significantly increased IgG2a compared to OVA alone. **Primary Cellular Response:** All OVA and PSP groups (except the low dose of 11.14 µm PSP) had more total lymph node cell numbers than the OVA alone group. The low and high does groups of 0.202 µm PSP had the greatest amount of cell proliferation and lymphoblasts. The OVA and 0.202 PSP treatment produced the greatest amounts of B lymphocytes, IL-4, IL-10 and IFN-γ. IL-2 in the PLN cells was significantly lower in both dosage groups of OVA and 0.202 PSP than the OVA control. **Particle Mass, Size, Number and Surface Area:** Total particle surface area explained 64% of the variance in the IgE levels. 60-80% variance of the PLN cellular parameters (except CD23) were explained by total particle surface area, number and diameter.
Reference: Reed et al. (2008, 156903) **Species:** Mouse **Gender:** Male, Female (only BALB/c) **Strain:** C57BL/6, A/J, BALB/c **Age:** NR **Weight:** NR	GEE (two 1996 General Motors 4.3-L V-6 engines; regular, unleaded, non-oxygenated, non-reformulated gasoline blended to US average consumption for summer 2001 and winter 2001-2002-Chevron-Phillips) **Particle Size:** 150 nm (MMAD)	**Route:** Whole-body Inhalation **Dose/Concentration:** PM; Low- 6.6 ± 3.7 µg/m^3, Medium- 30.3 ± 11.8 µg/m^3, High- 59.1 ± 28.3 µg/m^3 **Time to Analysis:** A/J- 6 h/day, 7days/wk, 3 days-6 mo. C57BL/6- 1wk exposure. Instillation of P. aeruginosa. Killed 18 h postinstillation. BALB/c- Pregnant females exposed GD 1 and throughout gestation. Offspring exposures continued until 4wk-old. Half of offspring sensitized to OVA. Tested for airway reactivity by methacholine challenge 48 h post-instillation and euthanized.	The kidney weight of female A/J mice decreased at 6 mo. and was strongly related to PM by the removal of emission PM. PM-containing macrophages increased by 6 mo. Hypomethylation occurred in females at 1 wk. The clearance of P. aeruginosa was unaffected by exposure. Serum total IgE significantly and dose-dependently increased. OVA-specific IgE and IgG1 gave slight exposure-related evidence but were not significant.
Reference: Roberts et al. (2007, 097623) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** 10 wk **Weight:** 250-300 g	R-Total = ROFA (Residual oily fish ash) R-Soluble = Soluble fraction of ROFA R-Chelex = R-Soluble+Chelex (insoluble resin) **Particle Size:** 2.2 µm (mean diameter)	**Route:** IT Instillation **Dose/Concentration:** 10 mg/kg (2.5-3 mg) **Time to Analysis:** Pre-exposure to ROFA samples on Day 0. Inoculation with 5×10^4 L. Monocytogenes or saline on day 3. Sacrifice on days 6, 8, 10.	**Uninfected Groups:** Compared to the controls, the R-total and R-soluble groups had increased LDH, PMNs, lymphocytes and AMs. The R-total group had a slight, but significant increase in IL-6 and the R-soluble group had a decrease in IL-2. **Infected Groups:** The R-soluble group had increased levels of LDH (which also increased for the R-total group), albumin, BALF cells, NK cells, PMA-stimulated and zyomason-stimulated CL compared to all other groups at various time points. NOX was significantly elevated in the R-soluble group at early time points, but in later time points R-soluble and R-total AMs produced less NOX than the controls. IL-10 and IL-6 increased in the R-soluble group, while IL-12, IL-4 and IL-2 decreased. IL-12 also decreased in the R-total group.
Reference: Saxena et al. (2003, 054395) **Species:** Mouse **Gender:** Female **Strain:** C57B1/6J **Age:** 18-30 wk **Weight:** NR	DEPs (standard) **Particle Size:** NR	**Route:** Intrapulmonary Instillation **Dose/Concentration:** 100 µg/mouse **Time to Analysis:** Pre-exposure to 2.5×10^4 bacillus Calmette-Guerin bacteria (BC G) with or without coadministration of DEP. Sacrifice 5 wk later.	The BC G + DEP group had four times the BC G lung load than BC G alone. The load was significantly greater in other organs in the BC G + DEP group. Interstitial lymphocytes, T, B and NK cells were increased in the BC G + DEP group over the DEP-alone group. DEP caused no release of NO by AMs, but inhibited the release of NO in response to IFN-γ. Except for CD8 cells, no increase in IFN-γ was seen in the BC G + DEP group.

Study	Pollutant	Exposure	Effects
Reference: Schneider et al. (2005, 088368) **Species:** Mouse **Strain:** BALB/c **Cell Line:** RAW 264.7	SRM 1648 (greater than 63% inOC; 4-7% OC; Si, S, Fe, Al, K greater than 1% by weight; Mg, Pb, Na, Zn, Cl, Ti, Cu, As, Cr, Ba, Br, Mn less than 1%) TiO_2 **Particle Size:** TiO_2 = 0.3 µm average, 1.0 µm max SRM 1648 = 0.4 µm (mean diameter)	**Route:** Cell Culture (625,000 cells/cm^2 in 96 well plate) **Dose/Concentration:** 0, 7.8, 15.6, 31.2, and 62.5 µg/cm^2 **Time to Analysis:** 1, 3, 6, and 12 h	No significant toxicity was exhibited by SRM 1648. The rate of dye oxidation was significantly higher in SRM 1648-exposed cells. SRM 1648 significantly increased reduced glutathione compared to the control at the 12-h time point. SRM 1648 increased GSH and concurrently caused significant PGE2 production compared to the no ester control at the 6-h and 12-h time points.
Reference: Schober et al. (2006, 097321) **Species:** Human **Gender:** Male and Female **Age:** 21-39 yr treatment group; 23-32 yr control group **Tissue Type:** Whole blood samples	PM - organic extracts of airborne sample AERex1d - urban aerosol 1 day sample (total air volume - 1270m^3) AERex5d - urban aerosol 5 day sample (total air volume - 6230m^3) rBet v 1 (birch pollen allergen 1a, Biomay, Vienna, Austria) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 100 µL heparinized whole blood **Time to Analysis:** Blood stimulated with PBS/IL-3 for 10 min. Incubated with rBet v 1 alone or with AERex for 20 min. Ice bath 5 min. Incubated with antibody reagent 20 min.	Nine organic compound classes were identified in AERex1d and AERex5d, with AERex1d having 20 times more PAHs. Basophil activation increased in all treatment groups up to 90%, with AERex1d being the most pronounced. 5-50 fold lower concentrations of AERex1d were needed to achieve the maximal effect on basophil activation. AERex-induced enhancement of CD63 upregulation of rBet v 1 in sensitized basophils occurred in a dose-dependent manner. The AERex-alone treatment did not affect CD63 expression.
Reference: Shwe et al. (2005, 111553) **Species:** Mouse **Gender:** Male **Strains:** BALB/c **Age:** 8 wk **Weight:** NR	CB = carbon black particles (Degussa, Germany) CB14: C: 96.79% H: 0.19% N: 0.13% S: 0.11% Ash: 0.05% Others including O: 2.74% CB95: C: 97.98% H: 0.15% N: 0.28% S: 0.46% Others including O: 1.14% **Particle Size:** CB14 = 14 nm (primary particle size); CB95 = 95 nm (primary particle size)	**Route:** IT instillation **Dose/Concentration:** 25, 125, or 625 µg in 1 mL saline solution **Time to Analysis:** 1/wk for 4 wk; 4 or 24 h after last instillation	**BALF Cells**: In CB14, the total number of BAL cells increased significantly and dose-dependently. In CB95, only the 625µg dose showed a significant increase. **Cytokine and Chemokine:** For CB14 and CB95, 125 or 625 µg showed a significant IL-1B increase in a dose-dependent manner. For CB14, only the 625 µg dose showed a significant IL-6 increase. No difference was observed in the CB95 group. For CB14, only larger doses showed a significant TNF-α increase. For CB95, no significant differences were observed. **In BAL Fluid:** CCL-2 production was significantly increased for the 625µg dose in both the CB14 and CB95 groups. CCL-3 production was significantly increased for the larger doses in both the CB14 and CB95 groups. **Splenic Lymphocytes:** No significant differences were detected among the CB14 dosages, except for CD8+. No significant differences were observed among the various groups for CB95. **Deposition in Lymph Nodes:** For all dosages, greater deposition of CB14 than CB95 was observed. **Chemokine mRNA Expression in Lungs and Lymph Nodes:** At 125 µg, significant increases of CLL-3 mRNA expression was observed for CB14; for CB95, no differences were detected.

Study	Pollutant	Exposure	Effects
Reference: Sigaud et al. (2007, 096100) **Species:** Mouse **Gender:** Male **Strains:** BALB/c **Age:** 8-10 wk **Weight:** NR	CAPs: Concentrated Ambient Particles (Collected from ambient Boston air on Teflon filters.) TiO_2 IFN-γ S. pneumoniae (ATCC 6303, American Type Culture Collection, Manassas, VA) **Particle Size:** CAPs: <2.5 µm	**Route:** IFN-γ priming: aerosol Particle exposure and infection: Intranasal Instillation **Dose/Concentration:** CAPS or TiO_2: 50 µg/50 µL PBS S. pneumoniae: 105CFU/25 µl saline **Time to Analysis:** Primed for 15 min One time particle exposure 3 h post priming with lung RNA analyzed 3, 6, 24 h after exposure Sacrificed 24 h after exposure or one time infection	**Inflammation:** Saline-primed and unprimed mice exposed to CAPs produced a significant increase in PMNs in the lung (100% more than mice exposed to TiO_2.) Groups primed with IFN-γ then exposed to CAPs produced a strong inflammatory response, a 2.5 increase in PMNs when compared to the increase caused by PBS+ CAPs exposure. **Cytokine Levels:** IFN-γ primed and CAPs exposed groups **Inflammation+ S. Pneumo Infection:** Saline-primed and unprimed mice exposed to CAPs produced a significant increase in PMNs in the lung (100% more than mice exposed to TiO_2.) Groups primed with IFN-y then exposed to CAPs produced a strong inflammatory response, a 2.5 increase in PMNs when compared to the increase caused by PBS+CAPs exposure. **Cytokine Levels:** IFN-y primed and CAPs exposed groups showed a 1.5-fold increase over the control. **PMNs:** Treatment with CAPs enhanced inflammation, causing a 2-fold increase in PMN numbers as compared to the infected control. IFN-y+CAPs+S. pneumo produced a 3.5 fold increase compared to the infected control and a 1.6-fold increase compared to PBS+CAPs+S.pneumo. Despite increased numbers of PMNs in the IFN-y+CAPs groups, the lungs were unable to clear the S. pneumo infection. **Bacterial Load:** Control groups showed efficient clearance of bacteria after infection. Unprimed, CAPs-treated, infected groups did not show a decrease in bacterial numbers. IFN-y+CAPs showed a 2.5-fold increase in bacterial numbers. **Histopathology:** Indicated moderate pneumonia in PBS+CAPs and severe pneumonia in IFN-y+CAPs. The other groups did not indicate areas of pneumonia. **Bacterial Uptake AM and PMN Cells:** In all the treated groups, the bacterial content in AMs showed a decrease, with a more marked decrease in the IFN-y+CAPs group, but these decreases were not statistically significant. Groups exposed to CAPs showed a statistically significant decrease in bacterial uptake by PMNs. **ROS Levels in AM and PMN Cells:** Intracellular ROS significantly increased in AM cells in the IFN-y+CAPs group, approximately 50% greater than controls. In PMNs, iROS increased 100% in the IFN-y+CAPs groups as compared to the controls.

Study	Pollutant	Exposure	Effects
Reference: Steerenberg et al. (2004, 087474) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** 6-8 wk	DEP:SRM1650a (NIST, Gaithersburg, MD EHC-93: ambient PM (Ottawa, Canada) O_3 (positive control) L. mono: Listeria monocytogenes (strain L242/73 type 4B) **Particle Size:** DEP, EHC-93: NR	**Route:** DEP/EHC-93: intranasal droplet; O_3: Whole-body inhalation **Dose/Concentration:** DEP/EHC-93: 50 µg (1.0 mg/ml) O_3: 2mg/m^3 L. mono: 0.2 or 0.3 ml (5x106 PFU/ml) *I have emailed author regarding correct dose **Time to Analysis:** DEP/EHC-93: 1/day for 7 days (-7 days to -1 days) O_3 24 h/day for 7 days (-7 days to -1 daysR All rats infected on day 0. Sacrificed on days 3, 4, or 5.	**Body weight:** Growth declined for O_3 exposed group while DEP or EHC-93 groups grew progressively. Exposure to L. mono caused all groups to decline in weight. **Bacterial Count in the Lung:** The number of bacteria in the lung of those rats exposed to O_3 was significantly greater than those exposed to saline. No differences in bacteria number were found for rats exposed to saline, EHC-93 or DEP at any time. **Bacterial Count in the Spleen:** The O_3 exposed group exhibited statistically significant increases in bacteria numbers when compared to the saline-treated group. No differences in bacteria number were found for rats exposed to saline, EHC-93 or DEP at any time. Exposure to O_3 decreases the defense of the respiratory tract against L. mono infection; however, DEP and EHC-93 did not appear to affect the host defense system in regards to clearing/fighting L. mono.
Reference: Steerenberg et al. (2005, 088649) **Species:** Mouse **Gender:** Male **Strain:** BALB/cByJ.ico **Age:** 6-8 wk	PM: collected from Rome, Oslo, Lodz, Amsterdam and De Zilk during the spring, summer and winter. Rome, Oslo, Lodz and Amsterdam represent areas with high population and dominance of traffic. De Zilk, selected as a negative control site, has low traffic emissions and natural allergens. EHC-93: used as a positive control OVA: Ovalbumin **Particle Size:** Coarse PM: 2.5 - 10.0 µm (MMAD); Fine PM: 0.1 - 2.5 µm (MMAD); Ultrafine: <0.1 µm (MMAD); EHC-93: NR	**Route:** Intranasal Exposure OVA challenge: aerosol **Dose/Concentration:** PM: 450 µg PM (at 0, 3, or 9 mg/ml) OVA sensitization: 50 µg (0.4 mg/ml) . OVA challenge: 20 µg (0.4 mg/ml) EHC-93 was administered at 0 - 900 µg to evaluate any dose-response relationship. **Time to Analysis:** Sensitization and PM exposure on days 0, 14 Challenged on days 35, 38, 41 for 20 min/day Sacrificed on day 42	**Effects of Coarse and Fine Particles:** Immunoglobulins: 6/13 of the coarse and 9/13 fine PM samples induced an increase in IgE and IgG1when compared to the control. IgG2a levels were increased in 3/13 of the coarse and 5/13 of the fine PM. Particles from De Zilk induced all three immunoglobulins, except the fine PM did not induce IgG2a. De Zilk was intended as a negative control (see Table 3). Analysis among the sites comparing the subclasses of antibodies indicated a rank as follows: Lodz >Rome ≥ Oslo. **Histopathology:** 9/13 of the coarse PM samples and 5/13 of the fine PM samples induced an inflammatory response. **BALF Cells:** Lodz (spring/ summer) coarse and fine PM induced a significant increase in eosinophils, neutrophils and monocytes. The coarse and fine PM from Rome (spring) induced an increase in neutrophils and the coarse PM induced an increase in eosinophils. Also both Lodz and Rome from the coarse PM from the spring induced an increase in macrophages. Other PM samples did not have an effect on BAL cell counts. **Cytokine Production:** None of the samples produced a significant effect on IL-4 levels. IFN-γ levels were significantly decreased in mice exposed to the fine PM fraction (in 8/13 of the samples) when compared to control. Coarse particle exposure did not appear to affect IFN-γ levels. TNF-α levels were significantly increased (in 2 of the 13 samples) when exposed to coarse PM; fine PM showed similar responses compared to the OVA only group. IL-5 was significantly increased in 4/13 of the coarse and fine PM samples. **Analysis of PM Components:** Samples from Lodz, Oslo and Rome (all spring) were evaluated and the water-soluble coarse PM fraction showed increased immunoglobulin and pathological responses and the water-insoluble fine PM fraction from Lodz (Spring) showed increased reactivity. Leukocytes and cytokines showed no major differences.

Study	Pollutant	Exposure	Effects
Reference: Steerenberg et al. (2004, 087981) **Species:** Mouse **Gender:** Male **Strain:** BALB/cByJ.ico **Age:** 6-8 wk **Treatment:** 1. C.D2-Vil6: Nramp1S and Nramp1R deficient 2. B6.129P2: Nos2tmLau: iNOS deficient 3. BALB/clL4 (tm2Nnt): deficient in IL-4 4. BALB/c (wild type) pretreated with N-Acetylcysteine (NAC)	EHC-93 OVA **Particle Size:** NR	**Route:** Sensitization, Challenge: Intranasal NAC: IP injection **Dose/Concentration:** OVA: 200 µg (0.4 mg/ml) EHC-93: 150 µg (3 mg/ml) NAC: 320 mg/kg **Time to Analysis:** OVA-only or OVA+EHC-93 sensitization on days 0 and 14. Some mice received NAC before intranasal exposure on days 0 and 14 OVA challenge on days 35, 38 and 41 Sacrificed on day 42	**Natural-Resistance-Associated Macrophage Protein 1 (Nramp1):** When exposed to only OVA, Nramp1S evoked less of an antibody responses (IgE, IgG1 and IgG2a) compared to Nramp1RHowever when coexposed to OVA and EHC-93, the level of increased production of antibodies was similar in both groups. After coexposure, the wild-type showed increased histopathological lesions, whereas the macrophage-stimulation-deficient types showed only a slight increase (not significant). IL-4, IFN-γ, TNF-α and IL-5 levels were similar in wild-type and the Nramp1 strains. **Pretreatment with NAC:** IgG2a concentration was increased further in the group pretreated with NAC. The wild-type mice and the NAC pretreated mice showed similar histopathological lesion patterns. IL-4 levels were similar in wild-type and the NAC pretreated mice. (IFN-γ, TNF-α and IL-5 levels not reported) **Inducible Nitric Oxide Synthase (iNOS):** The wild-type and the iNOS-deficient mice had similar levels of increased IgE antibody production. The IgG1 and IgG2a antibody response was twice as great in the iNOS-deficient mice compared to the wild type. The wild-type and the iNOS-deficient mice showed similar histopathological lesions. No differences in BAL cells or cytokines were observed between the wild-type and iNOS-deficient mice. **IL-4:** The IL-4-deficient mice did not produce an increase in IgE or IgG1 antibodies, as was seen in the wild-type mice. The IgG2a antibody response in the IL-4-deficient mice was similar to the wild type response resulting in adjuvant activity for the IgG2a antibodies. Overall the histological response of the wild-type mice was greater compared to the IL-4 deficient mice. There was no real difference between the two strains observed in the BAL cells, except IL-5 was significantly lower in the IL-4-deficient mice.

Study	Pollutant	Exposure	Effects
Reference: Stevens et al. (2008, 155363) **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 10-12 wk **Weight:** 17-20 g	DE: generated using a 30 kW 4-cylinder Deutz BF4M1008 diesel engine connected to a 22.3 kW Saylor Bell air compressor. The engine was operated on diesel fuel purchased from a service station in Research Triangle Park, NC. The engine was operated at a steady-state, approx. 20% of engine's full load. High composition: O_2: 4.3 ± 0.07 ppm NO: 9.2 ± 0.30 ppm NO_2: 1.1 ± 0.05 ppm SO_2: 0.2 ± 0.10 ppm Low composition: O_2, NO, NO_2, SO_2 below detection limits **Particle Size:** NR	**Route:** Whole-body Inhalation OVA immunization and challenge: intranasal **Dose/Concentration:** High = 2000 µg/m^3 Low = 500 µg/m^3 **Time to Analysis:** DE exposure for 4 h/day on days 0-4. OVA immunization 40 min after DE exposure on days 0-2 Challenged on days 18 and 28. Sacrificed 4 h after last exposure of day 4 for gene set analysis or 18, 48, or 96 h after the last challenge	**IgE Antibody Production:** In the absence OVA, IgE antibodies were not detected. 18, 48 and 96 h following OVA, mice exposed to low and high doses of DE had an increase in antibodies over time. Mice exposed to high dose had an increase (non-significant) to the OVA exposed control at the 48 h time mark **BAL Cells:** Cell counts at 18 and 96 h after OVA treatment did not differ among treatment groups. At 48 h the number of eosinophils, neutrophils and lymphocytes were significantly increased in mice exposed to both high and low concentrations of DE. With DE exposure alone, only neutrophils were statistically increased in the high DE concentration. This indicates the combination exposure of DE and an antigen is essential to promote the development of allergic lung disease. **BAL Cytokines:** IL-6 production showed a dose-dependent and time-dependent increase, but was significantly increase in the high dose group at 96 h. The high dose group saw a non significant increase in IL-10 levels over time. The greatest increase in IL-10 for the low dose group occurred18 h after OVA stimulation. **Pulmonary Inflammation and Lung Injury:** No differences among the groups were observed for macrophage, lymphocyte, neutrophil and eosinophil counts. Protein and LDH levels were not found to be increased in the BALF of any group. **Gene Analysis:** Pair wise comparisons revealed significant gene set difference between the high DE and control groups. Comparison of the high DE/OVA versus air/OVA showed significant changes in 23 gene sets, including genes involved in oxidative stress responses. The high DE/saline versus the air/saline showed significantly altered pathways. Altered pathways include those for cell adhesion, cell cycle control, apoptosis, growth and differentiation, and cytokine signaling. The results show that relatively short exposures to DE cause mild increases in immunologic sensitization to allergen.

Study	Pollutant	Exposure	Effects
Reference: Takizawa et al. (2003, 157039) **Species:** Human **Cell Lines:** Normal Small Airway Epithelial Cells and Bronchial Epithelial Cells (BET-1A)	Suspended DEP: collected using a 2,300-cc Isuzu diesel engine using standard diesel fuel at 1,050 rpm under a load of 6 torque. DE exposure in vitro (air exposure): collected using a 2,300-ml Isuzu diesel engine at 1,050 rpm. Composition: Fine particles: 1 mg/m^3 CO: 10.6 ppm NO_2: 7.3 ppm SO_2: 3.3 ppm **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** Suspended DEP: varying doses from 0-50 µg/ml IL-13: varying doses from 0-25 ng/ml DE exposure in vitro (air exposure): 100 µg/m^3 **Time to Analysis:** Cells were exposed to varying concentrations of suspended DEP for up to 24 h. NF-κB: analyzed at 6 h after suspended DEP exposure Air exposure at 0, 2, 4, 8 or 14 h	Preliminary experiments indicated that DEP at 0.1- 50 µg/mL had no significant cytotoxicity to BET-1A cells and human bronchial epithelial cells (as analyzed by LDH levels). **Eotaxin Production:** (Eotaxin is a cc chemokine that plays a role in eosinophil accumulation in a variety of allergic disorders) Epithelial and BET-1A cells treated with suspended DEP or IL- showed a dose-dependent stimulatory effect on eotaxin release or production. Simultaneous exposure to 25 ng/mL IL-13 and DEP depicted an additive effect for both cell types. **Eotaxin mRNA:** At 25 µg/mL, suspended DEP showed a time-dependent effect on eotaxin mRNA levels up to 12 h in both cell types. Extracted RNA from human bronchial epithelial cells exposed to varying doses of DEP showed a dose-dependent effect for both cell types (up to 25 µg/mL DEP) on eotaxin mRNA levels after 12 h of exposure. IL-13 also induced a dose-dependent increase on eotaxin mRNA levels in cells in both cell types. Combination of IL-13 and DEP showed an additive effect on mRNA levels in BET-1A cells. DE exposure in vitro also showed a time-dependent stimulatory effect on eotaxin production in BET-1A cells. **NF-κB / STAT6 Activation:** (it has been suggested that NF-κB plays a role in the trans-criptional regulation of eotaxin gene expression) Cells exposed to 1-25 µg/mL DEP for 6 h increased NF-κB. BET-1A cells treated with suspended DEP failed to activate STAT6. **Effect of NAC and PDTC on Eotaxin mRNA Levels:** (NAC and PDTC are antioxidant reagents with inhibitory effects on NF-κB activation) in BET-1A, both NAC and PDTC showed a dose-dependent inhibitory effect on DEP-induced eotaxin production. Both reagents also blocked DEP-induced eotaxin mRNA levels in BET-1A cells. NAC and PDTC did not suppress eotaxin production or eotaxin mRNA levels in IL-13 stimulated BET-1A cells. In addition pre-treatment with NAC attenuated NF-κB activation induced by DEP but had no effect on STAT6 induction by IL-13. These findings suggest that DEP stimulated eotaxin gene expression via NF-κB dependent, but STAT6-independent, pathways.

Study	Pollutant	Exposure	Effects
Reference: Tesfaigzi et al. (2005, 156116) **Species:** Rat **Gender:** Male **Strain:** Brown-Norway **Age:** 6 wk	PM: Wood smoke generated from a conventional wood stove that has a 0.5m^3 firebox and a sliding gate air intake damper. The stove was operated over a 3-phase burn cycle that spanned 6 h. Fire was started (initiated exposure) with unprinted / unbleached newspaper and a mix of black and white oak. Wood smoke components: organic material, small amounts of EC and metals and associated analytes. **Particle Size:** 0.36 µm (MMAD)	**Route:** Whole-body Inhalation **Dose/Concentration:** PM: 1000 µg/m^3 **Time to Analysis:** Exposed to wood smoke or filtered air 6 h/day for 70 consecutive days OVA IP injection immunization on days 2, 9 OVA aerosol exposure 2 h/day on days 67-70 following daily exposure to wood smoke or filtered air Sacrificed day 70	**Body Weight and Respiratory Function:** No difference in clinical signs or body weight was observed when comparing the two rat groups. The wood smoke exposed group had a 45% lower dynamic lung compliance when compared to those exposed to the filtered air group before the methacholine challenge. Challenging the rats with methacholine caused a decrease in dynamic lung compliance in both groups, but the decrease was greater in the air-exposed group. At the highest dose of methacholine, the dynamic lung compliance in controls was similar to the baseline value of the smoke-exposed group. No significant differences in total pulmonary resistance were observed. Wood smoke exposed rats had a 10% increase in functional residual capacity than the air-exposed group. **BAL Cells and Cytokines:** There was no difference in lymphocyte, eosinophil or neutrophils in the BALF of either group. There was an increase, though not statistically significant, in macrophages the wood smoke exposed group when compared to the filtered air group. In the BALF, IFN-γ and IL-1ß levels were significantly decreased, IL-4 and GRO-α levels were increased in rats exposed to wood smoke compared to filtered air. Serum IgE levels experienced a reduction trend in the wood smoke group, but it did not reach significance. Both groups showed mild signs of inflammation. The average eosinophils present in stained tissue was 21% higher in the wood smoke exposed group compared to the air exposed.
Reference: Tomita et al. (2006, 097827) **Species:** Mouse **Gender:** Female **Strain:** C57BL/6J; AHR-deficient; mEH-deficient; ARNT floxed (loxP sequences inserted in Arnt gene); Tcell-specific ARNT-deficient **Age:** 7 wk **Weight:** 20 g	DEP: two independent preparations fractionated into 13 different fractions based on acidic and basic functionality (one from light-duty, 4-cylinder diesel engine using standard diesel fueled and other generated from A4JB-type, Isuzu automobile, Japan) Individual PAH tested (Osaka, Japan): BbF = benzo[b]fluoranthene BeP = Benzo[e]pyrene IDP = Indeno[1,2,3-cd]pyrene BpPe = Benzo[ghi]perylene BaP = Benzo[a]pyrene BkF = Benzo[k]fluoranthene Per = Perylene DBA = Dibenzo[a,h]anthracene **Particle Size:** NR	**Route:** Intraperitoneal Injection **Dose/Concentration:** DEP, fractionated DEP or PAH compounds: 0.5 µg - 10 mg/kg bw in 50 µl of olive oil **Time to Analysis:** Single, sacrificed 3 days post-exposure.	**Effect on Thymus:** DEP treatment (10 mg/kg of body weight) caused severe atrophy of the thymus while the spleen and lymph nodes appeared normal. Three days following DEP treatment showed a marked reduction in thymus size. The total number of thymocytes was reduced by more than 70% mostly due to a massive reduction in DP cells (CD4+CD8+). DEP induced no significant alterations in the cell numbers of CD4/CD8 ratios in the spleen and lymph nodes. **DEP Extracts:** Only the WAC (carbonic acid fraction) and BE (weak basic fraction) did not produce a significant reduction in thymocyte numbers in vivo. Among the active fractions, 7 produced a marked selective loss of immature DP thymocytes, similar to the crude extract of DEP. **PAH Effects:** Thymic involution was severely induced by the N and various other fractions. 7 out of the 8 PAH compounds were significantly effective in decreasing the number of thymocytes upon in vivo exposure. Only BpPe did not have an effect. **AHR/ARNT and mEH Deficient Mice (BaP and DEP only):** In the absence of AHR, BaP treatment did not result in a loss of thymocytes. Like DEP, BaP produced severe thymic involution in mEH-deficient mice. DEP-mediated thymic involution was significantly enhanced in mEH-deficient mice.

Study	Pollutant	Exposure	Effects
Reference: Verstraelen et al. (2005, 096872) **Species:** Human **Tissue/Cell Types:** Monocyte-derived dendritic cells (Mo-DC) Cord blood samples of seven women were collected from umbilical vessels of placentas of normal, full-term infants.	DEP- SRM 2975 **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** DEP in varying concentrations: 0.2, 2, 20, 200, 2000 ng/mL LPS 100 ng/mL **Time to Analysis:** 24 h	**Biological Markers**: Exposure to DEP alone did not alter expression levels of HLA-DR, CD86 or CD83. Treatment with LPS alone caused a non-significant increase in all three markers when compared to the control. Treatment with DEP+LPS caused a significant increase in the expression of CD83 and a non-significant increased expression of HLA-DR and CD86. DEP+ LPS induced a bell-shape dose-response curve on the expression of all three markers, with a dose of 20 ng/mL DEP + 100 ng/mL LPS causing the largest increase in upregulation. When only the results of the LPS-responsive donors (5 out of 7 blood cord samples) were included, the effects described above become more pronounced.
Reference: Walczak-Drzewiecka et al. (2003, 188803) **Species:** Mouse **Cell Line:** C1.MC/C57.1 (C57) Mast Cells	Metal and Transition Metal Ions: Sr^{2+}, Ni^{2+}, Cd^{2+}, Al^{3+}, Pb^{2+} **Particle Size:** NR	**Route:** Cell culture, **Dose/Concentration:** 0.1- 5 µmol **Time to Analysis:** 10 min - 4 h	**B-Hex Mediator Release in Mast Cells:** Incubation with $SrCl_2$, $NiSO_4$, $CdCl_2$ or $AlCl_3$ resulted in a 2-5% release of B-hexoaminidase in mast cells. Incubation with a mixture of all these compounds induced a greater (11%) release in B-hexoaminidase, indicating there might be a additive effect. **Cell Viability:** Incubation of cells at concentrations and incubation time employed did not result in decrease in cell viability. **Antigen-Mediated Mediator Release in Mast Cells**: Al^{3+} and Ni^{2+} enhanced antigen-mediated release. 10-7 M $AlCl_3$ released 23% of B-hexoaminidase compared to antigen alone, which induced 11% release of B-hexoaminidase. Cd^{2+}, Sr^{2+} and Pb^{2+} enhanced antigen-mediated release to a lesser extent. Ni^{2+}, Al^{3+}, Sr^{2+} and Cd^{2+} depicted a dose-dependent relationship with antigen-mediated B-hexoaminidase release. **Antigen-Induced Protein Phosphorylation**: Addition of the antigen induced the anticipated phosphorylation of multiple proteins in C57 mast cells The presence of Ni^{2+} and Pb^{2+} mediated an increase in phosphorylation of several of the proteins and Al^{3+} mediated a decrease in phosphorylation of multiple proteins (specifically the 56 and 37 kD bands). **Antigen-Mediated Cytokine Secretion (IL-4):** At certain concentrations all tested metal and transition metal ions were able to induce IL-4 secretion or enhance antigen-induced IL-4 secretion in mast cells, but no dose-dependent relationship was established.
Reference: Wan and Yu (2006, 157104) **Species:** Human **Cell Lines:** Human, B cell lymphocytes PMBC (>98.5% B cells-CD19+CD20+; <1 % T cells (CD3+)) Human lymphocyte cell lines -- DG75 NQO1 wild type	DEP from 4 cyl Isuzu diesel methanol extracts **Particle Size:** NR	**Route:** Cell Culture, PMBC = 1×10^6 cell DG 75 = 3×10^6 cells IgE PMBC 1×10^6/mL B-cells 0.5×10^6/mL **Dose /Concentration:** 2.5, 5, 10, 20 µg DEPX/ plate (20 µg/mL) IgE DEPX 100 ng/mL sulfurophane at 0 - 30 µmol **Time to Analysis:** 6 h mRNA; 16 h protein assay. IgE 14 days.	**Induction of NQO1 by DEPX**: In PBMCs and DG75DEPX dose-dependently induced NQO1 mRNA expression NQO1 ARE was increased NAC inhibited NQO1 gene expression dose dependently. p38 MAPK and P13K inhibition partially blocked NQO1 mRNA and ARE induction by DEPX. **Induction of phase II enzymes:** DEPX induced IgE potentiation was reduced dose dependently by induced phase II enzymes.

Study	Pollutant	Exposure	Effects
Reference: Whitekus et al. (2002, 157142) **Species:** Mouse **Cell Line:** RAW 264.7	DEP (light-duty, four-cylinder engine-4JB1 type, Isuzu Automobile, Japan; standard diesel fuel) (extracts) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 50 µg/mL **Time to Analysis:** Exposed to antioxidants 5 h. HO-1 western blot, determination of cellular GSH:GSSG ratios, carbonyl protein content, lipid hydroperoxides performed.	DEP significantly reduced the GSH:GSSG ratio. This effect was prevented by adding thiol antioxidants NAC or BUC. DEP increased lipid peroxide levels, but the addition of all antioxidants decreased these levels. DEP increased carbonyl groups. NAC, BUC, and luteolin reduced HO-1 expression.
Reference: Whitekus et al. (2002, 157142) **Species:** Mouse **Gender:** Female **Strain:** BALB/c **Age:** 6-8 wk **Weight:** NR	DEP (light-duty, four-cylinder engine-4JB1 type, Isuzu Automobile, Japan; standard diesel fuel) (extracts) **Particle Size:** 0.5-4 µm	**Route:** Inhalation **Dose/Concentration:** 200, 600, 2000 µg/m^3 **Time to Analysis:** Exposed 1 h/day, 10 days. Animals receiving OVA had 20 min OVA exposure after DEP exposure.	DEP+OVA dose-dependently increased IgE and IgG1, being more effective than the OVA-alone treatment. This effect was significantly suppressed by thiol antioxidants NAC or BUC. DEP+OVA increased carbonyl protein and lipid peroxide over OVA. NAC or BUC suppressed lipid peroxide and protein oxidation. No general markers for inflammation were observed.
Reference: Witten et al. (2005, 087485) **Species:** Rat **Gender:** Female **Strain:** F344 **Age:** 8 wk **Weight:** ~175 g	DEP (heavy-duty Cummins N14 research engine operated at 75% throttle) **Particle Size:** 7.234-294.27 nm	**Route:** Nose-only Inhalation **Dose/Concentration:** Low- 35.3 ± 4.9 µg/m^3, High-632.9 ± 47.61 µg/m^3 **Time to Analysis:** Exposed 4 h/day, 5 days/wk, 3 wk. Pretreated with saline or capsaicin.	There were no differences for substance P. The low-exposure group had significantly less NK1. DEP reduced NEP activity. Plasma extraversion dose-dependently increased and was greatest in capsaicin animals. Respiratory permeability dose-dependently increased. IL-1β was significantly higher for the low-exposure group. IL-12 was significantly lower in the capsaicin high-exposure group. TNF-α increased in the high-exposure group and capsaicin low-exposure group. High exposure induced particle-laden AMs in the lungs, perivascular cuffing consisting of mononuclear cells, alveolar edema and increased mast cell number. Neutrophil and eosinophil influx was not seen.
Reference: Wong et al. (2003, 097707) **Species:** Rat **Gender:** Female **Strain:** F344/NH **Age:** ~4 wk **Weight:** ~175 g	DEP (Cummins N14 research engine at 75% throttle) (EC- 34.93-601.67 µg/m^3, OC- 1.90-11.25 µg/m^3, Sulfates 0.94-17.96 µg/m^3, Na- 4.07-4.78 ng/m^3, Mg-0.60-0.86 ng/m^3, Ca- 5.05-10.66 ng/m^3, Fe- 3.17-6.44, Cr- 0.68-1.31 ng/m^3, Mn-0.11-0.22 ng/m^3, Pb- 0.97-1.24 ng/m^3) **Particle Size:** 7.5-294.3 nm	**Route:** Nose-only Inhalation **Dose/Concentration:** Low- 35.3 ± 4.9 µg/m^3, High-669.3 ± 47.6 µg/m^3 **Time to Analysis:** Exposed 4 h/day, 5 days/wk, 3 wk. Pretreated with saline or capsaicin.	DEP dose-dependently increased plasma extraversion, which was further increased by capsaicin. In the high-exposure group, particle-laden AMs (which were reduced by capsaicin), inflammatory cell margination, perivascular cuffing with subsequent mononuclear cell migration and dispersal, increased mast cells, and decreased substance P were all seen. NK-1R was downregulated in the low-exposure group and upregulated in the capsaicin-pretreated high-exposure group. NEP decreased significantly for both groups.

Study	Pollutant	Exposure	Effects
Reference: Yanagisawa et al. (2006, 096458) **Species:** Mouse **Gender:** Male **Strain:** ICR **Age:** 5 wk **Weight:** 25-28 g	Washed DEP (carbonaceous core), DEP-OC(extracted organic chemicals) and Whole DEP Particles collected from: 4JB1-Type, four-cylinder, 2.74 L, Isuzu diesel engine, while operated on standard diesel fuel at 200 g under a load of 10 torques. **Particle Size:** 0.4 µm (MMAD)	**Route:** IT Instillation **Dose/Concentration:** 50 µg/0.1L 1. Control- 0.1mL PBS 2. DEP-OC- 50 µg 3. Washed DEP- 50 ug 4. Whole DEP- 50 ug DEP-OC + 50 ug Washed DEP5. OVA- 1 µg = 6. DEP-OC- 1 µg + OVA 7. Washed DEP- 50 µg + OVA 8. Whole DEP- 50 µg DEP-OC + 50 µg Washed DEP + OVA **Time to Analysis:** All groups received OVA or PBS every 2 wk for 6 wk and the PM component or PBS once a week for 6 wk.	**BALF Cells**: DEP-OC + OVA caused a significant increase in PMN infiltration in the BALF compared to the control. Exposure to Whole DEP+ OVA caused PMN count to rise further. OVA alone DEP-OC +OVA, Washed DEP + OVA and Whole DEP + OVA all caused a significant increase in macrophages compared to the control. **Lung Histology**: Exposure to OVA, Washed DEP, DEP-OC and Whole DEP caused a slight increase in PMNs, mononuclear cells and goblet cell proliferation. Treatment with all three DEP groups + OVA caused a significant increase in mononuclear cells, PMNs and goblet cell proliferation. Whole DEP + OVA had the greatest impact. **Th1 and Th2 Cytokine Expression**: Washed DEP+OVA caused a significant increase in IFN-γ compared to control, whereas Whole DEP+OVA caused a significant decrease compared to control. No significant differences in IL-2 and IL-4 levels were seen among groups. DEP-OC+ OVA and Whole DEP+ OVA caused significant increases in IL-5 compared to control and compared to OVA Whole DEP+OVA caused significant increase in IL-13 compared to control **Eotaxin and MIP-1α Expression**: OVA increased eotaxin levels and DEP-OC+OVA caused a more significant increase in eotaxin. Whole DEP alone caused a significant increase in MIP-1α and Whole DEP+OVA caused an even greater increase in MIP-1α. **IgG1 Levels:** Exposure to DEP-OC+OVA caused an increase in IgG1 and exposure to Whole DEP+OVA caused greater elevation in IgG1 levels.
Reference: Yang et al. (2003, 087886) **Species:** Mouse **Gender:** Female **Strain:** B6C3F1 **Age:** 6-8 wk	DEP- SRM 1650 **Particle Size:** 0.5 µm (MMAD)	**Route:** IT Aspiration **Dose/Concentration:** 1, 5, or 15 mg /kg **Time to Analysis:** 3 times in 2 wk or 6 times in 4 wk.	**Toxicity of DEP Exposure**: DEP did not have a significant effect on body, liver or spleen weight. The highest dose of DEP caused an increase in lung weight and lung weight relative to body weight. None of the hematological parameters were significantly different in the mice exposed for 2 wk; in the 4 wk group there was a significant decrease in platelet counts in mice exposed to 15 mg/kg. **Exposure on Spleen IgM AFC:** DEP exposure for 2 wk induced a dose-dependent decrease in spleen AFC in response to sRBC immunization. Mice exposed to 15 µg/kg depicted a 35% reduction in total spleen activity. In the group exposed to DEP for 4 wk, the decrease in AFC was not significantly different than the control. **DEP Exposure on Spleen Cell Number/Lymphocyte Counts:** Exposure for 2 or 4 wk did not affect total number of nucleated splenocytes. DEP caused a 30% reduction in total T cells. The number of B cells were not significantly affected. **DEP Exposure on Spleen T-Cell Function:** (evaluated in 2 wk exposure group only) DEP induced a dose-dependent decrease in spleen cell proliferation to ConA. DEP did not affect spleen cell proliferation in response to anti-CD3 mAb. Production of IL-2 in response to ConA was reduced in a dose-dependent manner by DEP exposure. IFN-γ production was decreased by exposure to DEP. IL-4 production was not measured.

Study	Pollutant	Exposure	Effects
Reference: Yin et al. (2005, 088133) **Species:** Rat **Gender:** Male **Strain:** Brown-Norway (BN/CrlBR) **Age:** NR **Weight:** 200-250 g	DEP = SRM 2975 (NIST) Listeria **Particle Size:** NR	**Route:** Nose-only inhalation (DEP), IT instillation (Listeria) **Dose/Concentration:** 100,000 CFU (Listeria); 21.2 ± 2.3 mg/m^3 (DEP) **Time to Analysis:** DEP exposure for 4 h/day for 5 days; infection with Listeria 7 days post-exposure; sacrifice 3 and 7 days postinfection	**Lung Deposit:** Estimated mean lung deposit of DEP = 406 ± 29 µg/rat DEP prolonged growth of bacteria in lung **Alveolar Macrophage (AM) Response:** DEP significantly inhibited Listeria-induced IL-1β secretion at day 7 and TNF-α and IL-12 at both day 3 and day 7 IL-10 production was enhanced at day 7. **T-Lymphocyte Response:** DEP significantly reduced the development of T cells in response to Listeria infection. These lymphocytes displayed increased production of IL-6 at day 7, but significantly diminished levels of IL-10, IL-2 and IFN-γ.
Reference: Yin et al. (2004, 097685) **Species:** Rat **Gender:** Male **Strain:** Brown-Norway (BN/CrlBR) **Age:** NR **Weight:** 200-250 g	DEP = SRM 2975 (NIST) Listeria **Particle Size:** NR	**Route:** Inhalation (DEP), IT instillation (Listeria) **Dose/Concentration:** 20.62 ± 1.31 mg/m^3 (DEP). 100,000 CFU Listeria **Time to Analysis:** DEP exposure for 4 h/day for 5 days; inoculation with bacteria 2 h postexposure; sacrifice 3, 7, 10 days postinfection	**Lung Deposit:** Estimated mean lung deposit of DEP = 389 ± 25 µg/rat **Pulmonary Responses and Bacterial Clearance:** DEP significantly augmented Listeria-induced PMN infiltration, lung CFU and recoverable AM at all times post-infection. LDH activity was increased 3 days post-infection. Bacterial count in DEP exposed rats remained significantly higher through day 7. **Cytokine Production by AM:** DEP exposure significantly lowered Listeria-induced production of IL-1β, TNF-α and IL-12. Production of IL-10 was strongly augmented. **T-lymphocyte Responses:** DEP moderately but not significantly lowered the total number of lymphocytes, CD4+ cells and lymphocyte IL-10 production. Listeria-induced T-cell development was strongly inhibited, as were the development of CD8+ cells, IL-12 production and IFN-γ secretion. DEP and Listeria exposure showed and increased production of IL-6 at day 3 and day 7 post-exposure.
Reference: Yin et al. (2007, 198980) **Species:** Rat **Gender:** Male **Strain:** Brown-Norway (BN/CrlBR) **Age:** NR **Weight:** 225-250 g **Cell Line:** AM	DEP = SRM 2975 eDEP = organic DEP extract wDEP = washed DEP CB = carbon black **Particle Size:** DEP: median diameter- 19.4 µm, surface area- 91 m^2/g; CB: 0.1-0.6 µm	**Route:** IT Instillation of Listeria; Cell Culture (2.5×10^5 cells/well) **Dose/Concentration:** DEP: 10, 50, 100 µg/mL; CB: 50 µg/mL **Time to Analysis:** Sacrifice 7 days postinfection or no infection. Cell culture: 1, 4, 16, 24 h.	**AM Phagocytosis:** None of the DEP or CB treatments were cytotoxic or affected the number of adherent cells. 10-100 µg/mL. DEP significantly decreased AM phagocytosis in a concentration- and time-dependent manner, with increased concentration and time decreasing activity. **Bacterial Activity:** The inhibition of AM bactericidal activity by DEP was time- and concentration-dependent. eDEP and wDEP inhibited the AM bactericidal activity but were less effective than DEP. The CB treatment was not significant. **Cytokine Secretion by AM:** DEP and eDEP concentration-dependently decreased TNF-α, IL-1B and IL-12, but increased IL-10. wDEP and CB did not show a significant effect. **Cytokine Secretion by Lymphocytes:** DEP and cDEP concentration-dependently decreased IL-2 and IFN-γ. wDEP and CB had little effect, except high concentrations of wDEP decreased IFN-γ.

Study	Pollutant	Exposure	Effects
Reference: Yin et al. (2004, 087983) **Species:** Rat **Gender:** Male **Strain:** Brown-Norway (BN/CrlBR) **Age:** NR **Weight:** 225-250 g **Cell Line:** AM	DEP = SRM2975 eDEP = organic DEP extract wDEP = washed DEP CB = carbon black **Particle Size:** DEP- NR, CB- 0.1-0.6 µm	**Route:** IT Instillation of Listeria; Cell Culture **Dose/Concentration:** 50 µg/mL (DEP or CB) **Time to Analysis:** Killed 7 days postinstillation. AM isolated then incubated. DEP treatments for up to 24 h.	**DEP-Induced ROS Production:** ROS was induced by DEP or eDEP and inhibited by eDEP with ANF or NAC. eDEP induction of ROS was time-dependent. wDEP or CB did not induce ROS. **DEP-Induced HO-1 Expression:** DEP- or eDEP-induced HO-1 expression was inhibited by ANF, NAC or SB203580. wDEP or CB did not induce ROS. DEP or eDEP exposure resulted in a 2.5- to 3-fold induction of HO-1 expression in uninfected AM. **eDEP-Modulated Cytokine Production:** eDEP exposure resulted in a time-dependent increase in LPS-stimulated IL-10 or TNF-α production, and both were inhibited by ANF or NAC. wDEP did not affect either. SOD pretreatment attenuated eDEP-upregulated HO-1 expression, inhibited IL-10, and reversed eDEP inhibition of IL-12. Znpp decreased IL-10.
Reference: Yin et al. (2003, 096127) **Species:** Rat **Gender:** Male **Strain:** Brown-Norway (BN/CrlBR) **Age:** NR **Weight:** 200-250 g	DEP = SRM 1650a L. monocytogenes **Particle Size:** NR	**Route:** Nose-only Inhalation (DEP); IT Instillation (Listeria) **Dose/Concentration:** 50 or 100 mg/m^3 (DEP); 100,000 bacteria per 500 µL sterile saline (Listeria) **Time to Analysis:** DEP exposure for 4 h. Bacterial inoculation. Sacrificed 3, 7 days post-exposure.	**Lymphocyte Population:** DEP-alone exposure increased total lymphocytes, T cells and T-cell subsets. Elevated cell counts in the combined exposure were DEP dose-dependent, with the 100 mg/m^3 treatment having significant increases in the cell number and CD8+/CD4+ ratio. **IL-2:** DEP exposure in noninfected rats at both doses increased IL-2 in the 24 h culture and decreased IL-2 in the 48 h culture. The increase in IL-2 at 3 days postinfection was not significant. DEP exposure increased IL-2Rα in response to ConA stimulation. DEP-treated infected rats had increases in ConA-inducible CD4+/IL-2Rα+ and CD8+/ IL-2Rα+. **IL-6:** IL-6 production was dose-dependent in DEP-treated uninfected rats and infected rats. The combined exposure produced less IL-6 than the DEP-alone or Listeria-alone treatments. **IFN-γ:** DEP decreased IFN-γ at 3 days post-exposure, but increased at 7 days post-exposure in a dose-dependent manner. Uninfected DEP-treated rats did not substantially respond to HKLM. HKLM-induced IFN-γ production is strongly inhibited at all tested DEP doses.
Reference: Zelikoff et al. (2003, 039009) **Species:** Rat **Gender:** Male **Strain:** F344 **Age:** 7-8 mo **Weight:** NR	CAPS (concentrated ambient $PM_{2.5}$ from New York City) S.pneumoniae **Particle Size:** 0.4 µm (MMAD)	**Route:** Nose-only Inhalation (CAPS); IT Instillation (S.pneumoniae) **Dose/Concentration:** CAPS: Study 1- Mean- 345 µg/m^3; 60-600 µg/m^3. ,Study 2- Mean-107 µg/m^3; 65-150 µg/m^3 (S.pneumoniae 2-4×10^7) **Time to Analysis:** Study 1: Uninfected rats exposed to air or CAPS for 3 h. Sacrificed 3, 24, or 72 h post-exposure or IT instilled 4, 24, 72, 120 h and sacrificed 4, 24, 72 h postinfection Study 2: Infection with bacteria. Exposed 48 h later to CAPS or filtered air for 5 h. Sacrifice 9, 18, 24, 72, 120 h post-exposure.	**Study 1:** CAPS did not effect cell numbers, viability, profiles, lavageable LDH activity, total protein, or total circulating WBC counts. Exposure to CAPs prior to infection significantly increased PMN and decreased lymphocytes. WBC levels returned to control levels by 4 h postinfection. CAPS had no effect on circulating monocyte values. CAPS significantly increased bacterial burdens at 24 h, but thereafter the burden decreased to below control levels. **Study 2:** In CAPS exposed rats, PMN decreased, Pam increased, and the cytokines TNF-α, IL-1β and IL-6 decreased. Lymphocytes and monocytes were unaffected. Bacterial burdens in CAP-exposed rats were about 10% greater than air controls at 9 h and >300% greater at 18 h. CAPS significantly increased the percent of affected lung area and severity of infection.

Study	Pollutant	Exposure	Effects
Reference: Zelikoff et al. (2002, 037797) **Species:** Rat **Gender:** Male **Strain:** Fischer 344 **Age:** 7-9 mo. **Weight:** NR	Ambient NYC PM Single transition metals of Fe, Mn, Ni Streptococcus pneumoniae **Particle Size:** NYC PM: $PM_{2.5}$ $Fe^{2+,}$ Mn^{2+}, Ni^{2+}: 0.4 µm (MMAD)	**Route:** Nose-only Inhalation, IT instillation (S. pneumoniae) **Dose/Concentration:** Single metals/NYC PM: 65-90 µg/m^3; 15-20×10^6 (S.pneumoniae) **Time to Analysis:** Infection/no infection followed by 5 h exposure to NYC PM or single transition metal. Sacrifice 4, 5, 9, 18, 24, and 120 h after exposure.	CAPs exposure to infected rats significantly increased pulmonary bacterial burdens of S. pneumo in a time-dependent manner. At 9 h, 18 h, 24 h, and 5 days after CAPs exposure, bacterial burdens were 10%, 300%, 70% and 30% above controls. Uninfected rats exposed to the single transition metals showed significant alterations in PMNs and lymphocytes values at 1 h post-exposure. Exposure to Fe of uninfected rats significantly increased superoxide anion production by pulmonary macrophages. Uninfected rats exposed to inhaled Fe significantly reduced B-lymphocyte proliferation at 48 h, but did not affect T-lymphocyte production. Inhaled Ni, for the uninfected, significantly decreased T-lymphocyte production at 18 h, and did not affect B-lymphocyte production. Inhalation of Fe by infected rats facilitated an increase in bacterial numbers while Ni inhibited bacterial clearance. Inhaled Fe by infected also significantly decreased PMNs and lymphocyte numbers by 35% and increased pulmonary macrophage numbers by 29% when compared to the air exposed group. Results demonstrated that inhalation of Fe altered innate and adaptive immunity in uninfected hosts, and both Fe and Ni reduced pulmonary bacterial clearance in previously infected rats.
Reference: Zhong et al. (2006, 093264) **Species:** Mouse **Gender:** Male **Strain:** BALB/c **Age:** 6-8 wk **Weight:** NR **Cell Line:** J774A.1, IFN-y-primed AMs, unprimed AMs	CAPs: Concentrated Air Particles (Boston, MA) Urban air particles (UAP) SRM1649 (Washington, DC) TiO_2 Carbon Black (CB) (Sigma, St. Louis, MO) Streptococcus pneumoniae: strain ATCC6303 **Particle Size:** UAP = NR; TiO_2/CB = NR; CAPs: ≤$PM_{2.5}$	**Route:** Cell Culture **Dose/Concentration:** NR, 100 µg/mL **Time to Analysis:** CAPs for 1 h; bacteria for 1 h. Binding measured 15 h after bacteria exposure. Ingestion measured 2 h after bacteria exposure. Rate and number of killed bacteria measured 2 h after bacteria exposure.	**Binding, Internalization and Killing of Bacteria:** CAPS significantly increased binding of bacteria by IFN-y-primed AMs, normal AMs and J774A.1. CAPS decreased internalization and absolute number of bacteria killed by macrophages of all types. The rate of killing of internalized bacteria was similar in the presence or absence of CAPs; however, CAPs did cause a decrease in the absolute number of bacteria killed by all three types of macrophages, due to the decrease in internalization. **Effects of other particles:** TiO_2 and CB had no effect on J774 binding or internalization of S. pneumo. TiO_2 and CB's effects on primed and unprimed AMs were not reported. Testing with UAPs, however, showed effects similar to those observed with CAPs. **Soluble components:** The soluble fraction of CAPs, especially iron, is responsible for decreased internalization.

Table D-5. Effects of the central nervous system.

Reference	Pollutant	Exposure	Results
Reference: Calderón-Garcidueñas et al. (2003, 156316) **Species:** Dog **Gender:** Male, Female **Strain:** Mixed breed **Age:** 7d-10 yr **Weight:** 349 ± 116g - 20 kg	Urban Air (Mexico City-high PM region, Tlaxcala- low PM region) (PM, Pb, volatile organic compounds, formaldehyde, acetaldehyde, mutagenic PM, alkane hydrocarbons, Ni, V, Mn, Cr, peroxyacetyl NO_4^{2-}, LPS, endotoxins) **Particle Size:** PM: 2.5, 10 µm	**Route:** Ambient Air Exposure **Dose/Concentration:** Mexico City: PM_{10}: 78 µg/m^3, $PM_{2.5}$: 21.6 µg/m^3, Pb in TSP: <0.4 µg/m^3 **Time to Analysis:** Dogs raised in house or outdoor-indoor kennel. Lifetime exposure.	Mexico City dogs had significantly greater apurinic and apyrimidic sites in the olfactory bulb and hippocampus. Histopathological changes in the respiratory and olfactory epithelium were greatest in Mexico City dogs. Mexico City dogs also had greater immunoreactivity than the controls for NF-κB, iNOS, cyclooxygenase-2, glial fibrillatory acidic protein, ApoE, amyloid precursor product and B-amyloid.

Reference	Pollutant	Exposure	Results
Reference: Campbell et al. (2005, 087217) **Species:** Mouse **Strain:** BALB/c **Age:** 7 wk	CAPs from Los Angeles, lacking reactive organic and H_2O soluble gases, O_3, NO_X, SO_X **Particle Size:** F+UF: <2.5 µm; UF: <0.18 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** 20-fold concentration of near highway ambient air, avg UF concentration: 282.5 µg/m^3, avg F concentration: 441.7 µg/m^3 **Time to Analysis:** 4 h/day, 5 days/wk for 2 wk	Mice were challenged with OVA prior to exposure and 1 and 2 wk following exposure, and then brains were assayed. F+UF and UF exposure increased NF-κB DNA binding in brain. TNF-α increased with F+UF. IL-1α increased with UF and F+UF. This suggests a possible link between PM exposure and neurodegenerative disease processes.
Reference: Che et al. (2007, 096460) **Species:** Rat **Strain:** SD **Gender:** Male and Female **Age:** 9 wk **Weight:** 190-220 g	Gasoline exhaust (collected from 1996 Guangzhou passenger car with Dongfeng Gasoline Series 155 kw engine and no exhaust catalytic converter fuelled with 90-octane Pb-free gasoline from China Petroleum). **Particle Size:** NR	**Route:** IT Instillation **Dose/Concentration:** 5.6, 16.7, or 50.0 L/kg, final volume 0.3 mL/rat **Time to Analysis:** 1/wk for 4 wk; 24 h post-instillation.	A dose-dependent increase was observed in brain DNA damage starting at 5.6 L/kg. Increase in lipid peroxidation and carbonyl protein was also observed at 50 L/kg. Decrease in brain SOD occurred at all exposures. GPx activity was unchanged with exposure. This suggests an association between gasoline exhaust and oxidative damage to the brain.
Reference: Kleinman et al. (2008, 190074) **Species:** Mouse **Gender:** Male **Strain:** ApoE$^{-/-}$ **Age:** 6 wk **Weight:** NR	CAPs (Los Angeles, CA) (OC, EC = ~50%; sulfate, nitrate ~11%) **Particle Size:** NR	**Route:** Whole-body Inhalation **Dose/Concentration:** High dose: Mass concentration- 114.2 µg/m^3, Low dose: Mass concentration: 30.4 µg/m^3 **Time to Analysis:** 5 h/day, 3days/wk, 6 wk; 24 h postexposure.	Activated AP-1 dose-dependently increased. Activated NF-κB significantly increased with the high CAPs dose. GFAP (which represented activated astrocytes) and activated JNK significantly increased with the low CAPs dose.
Reference: Liu et al. (2005, 088650) **Species:** Rat **Strain:** Wistar **Gender:** Male **Age:** 8 wk	CAPs from Taiyuan, China **Particle Size:** <2.5 µm	**Route:** IT Instillation **Dose/Concentration:** 0, 1.5, 7.5, or 37.5 mg/kg, final volume 0.2 mL/rat **Time to Analysis:** 24 h	In the brain, SOD and CAT activity were significantly decreased at the 2 highest doses; GSH levels were significantly decreased at the highest dose. This suggests an association between PM exposure and oxidative damage mediated by prooxidant/antioxidant imbalance or high levels of free radicals.
Reference: Sirivelu et al. (2006, 111151) **Species:** Rat **Gender:** Male **Strain:** Brown Norway **Age:** 12-13 wk	CAPs from Grand Rapids, MI **Particle Size:** <2.5 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** 500 µg/m^3 **Time to Analysis:** 8h; assayed at 24-h PE	**PVN:** CAPs alone or with OVA increased NE. **MPA:** CAPs increased Da when treated with OVA while no changes in NE, 5-HIAA and DOPAC were observed. **Arcuate nucleus:** OVA sensitization increased NE levels. **OB:** CAPs and OVA increased NE levels, but no changes in Da, DOPAC, or 5-HIAA were observed. **Other areas:** No differences in other areas of hypothalamus, substantia nigra, or cortex were observed. CAPs alone or with OVA increased serum corticosterone. These results suggest that CAPs can cause region-specific modulation of neurotransmitters in brain and that the stress axis may be activated causing aggravation of allergic airway disease.
Reference: Veronesi et al. (2005, 087481) **Species:** Mouse **Strain:** ApoE$^{-/-}$ or C57Bl/6 **Age:** Young adults	CAPs from Tuxedo, NY **Particle Size:** <2.5 µm	**Route:** Whole-body Inhalation **Dose/Concentration:** Average daily concentration 113 µg/m^3 **Time to Analysis:** 6 h/day, 5days/wk for 4 mo	CAPs-exposed ApoE$^{-/-}$ mice had an 29% reduction in TH-stained neurons and a 8% increase in GFAP staining compared to air-exposed ApoE$^{-/-}$. No differences were see in C57 mice. The results suggest that ApoE$^{-/-}$ mice, characterized by increased brain oxidative stress, are susceptible to PM-induced neurodegeneration.

Reference	Pollutant	Exposure	Results
Reference: Win-Shwe et al. (2008, 190146) **Species:** Mouse **Gender:** Male **Strain:** BALB/c **Age:** 7 wk **Weight:** NR	DEP (Nanoparticle-rich - NPDE; 81-diesel engine, steady-state condition, 5 h/d, 2000rpm, 0 Nm) (CO, CO_2, NO, NO_2, SO_2) **Particle Size:** 26.21 ± 1.50 nm (diameter)	**Route:** Whole-body Inhalation **Dose/Concentration:** 148.86 ± 8.44 μg/m^3 **Time to Analysis:** 5 h/day, 5 days/wk, 4 wk. Some mice ip injected with lipoteichoic acid (LTA) 1×/wk, 4 wk. Morris water maze behavioral test: 3 days acquisition, 2 day probe trial.	Mice in the LTA+NPDE group had significantly longer mean escape latencies, indicating impaired acquisition of spatial learning. NPDE directly increased NR1 and TNF-α. LTA+NPDE increased NR2A, NR2B, and IL-1β, however LTA was primarily responsible for the increases.
Reference: Zanchi et al. (2008, 157173) **Species:** Rat **Gender:** Male **Strain:** Wistar **Age:** 45 days	ROFA from Universidade de São Paulo, Brazil **Particle Size:** 1.2 ± 2.24 μm (MMAD)	**Route:** Intranasal Instillation **Dose/Concentration:** 20 μg/10 μl saline **Time to Analysis:** 30 days	Exposed rats had increased lipid peroxidation in striatum and cerebellum. This could be reversed with N-acetylcysteine treatment. ROFA treatment altered motor activity shown by decreased general exploration and peripheral walking, and was not prevented by NAC. Results suggests that chronic ROFA induces behavioral changes and brain oxidative stress.

Table D-6. Reproductive and developmental effects.

Reference	Pollutant	Exposure	Effects
Reference: Fedulov et al. (2008, 097482) **Species:** Mouse **Gender:** Female (pregnant), Offspring: NR **Strain:** BALB/c **Age:** NR **Weight:** NR	DEP Carbon black (CB) TiO_2 **Particle Size:** NR	**Route:** Intranasal Instillation **Dose/Concentration:** DEP, TiO_2: 50 μg in 50 μL, 50 μg/mouse; CB: 250 μg in 50 μL **Time to Analysis:** Particle samples baked 3 h. Protocol 1a: Pregnant mice treated with DEP or TiO_2. Analyzed 19 or 48 h later. Protocol 1b: Pregnant mice DEP, TiO_2 or CB treated day 14 of pregnancy. 4 day-old offspring i.p. injected with OVA+alum. 12-14 days-old exposed aerosolized OVA.	DEP increased BAL PMN counts in normal and pregnant mice. In pregnant mice, DEP and TiO_2 increased IL-1β, TNF-α, IL-6 and KC compared to nonpregnant controls. Offspring of DEP, CB or TiO_2 exposed mice had increased AHR and airway inflammation. TiO_2 exclusively altered the expression of 80 genes in pregnant mice.
Reference: Fujimoto et al. (2005, 096556) **Species:** Mouse **Strain:** Slc:ICR **Gender:** Females (pregnant mice and fetuses) **Age:** NR (pregnant females), 14 days of gestation (fetuses)	DE: generated by 2369 cc diesel engine at 1050 rpm at 80% load with commercial light oil **Particle Size:** 0.4 μm (MMAD)	**Route:** Inhalation **Dose/Concentration:** 0.3, 1.0 or 3.0 mg DEP/m^3 **Time to Analysis:** 12 h/day, 7 days/wk from 2 day post coitum to 13 dpc. Sacrificed 14 dpc. mRNA expression examined in female fetuses.	Significant increase in absorbed placentas were observed in the 0.3 and 3.0 concentration. A decrease in absorbed placentas was observed for the 1.0 concentration. Increased inflammatory cytokine mRNA in placentas from exposed offspring were observed. An increased number of absorbed placentas in DE-exposed offspring were seen.
Reference: Hougaard et al. (2008, 156570) **Species:** Mouse **Strain:** C57Bl/6 **Gender:** Pregnant females, male and female offspring **Age:** 12 ,16 wk (female offspring), 13, 17 wk (male offspring)	DEP(SRM2975) **Particle Size:** 90 m^2/g (SA)	**Route:** Whole-body Inhalation **Dose/Concentration:** 20 mg DEP/m^3 **Time to Analysis:** Exposed 1 h/dayfrom gestation days 7-19. Mice separated for behavioral testing on PND 22 (day of delivery is PND 0). Behavioral testing at 12, 16 wk for female offspring and 13, 17 wk for male offspring.	Body weight of exposed unchanged at birth. Body weight decreased at weaning. Unchanged dams & pups at weaning. At 2 mo, exposed female pups required less time to locate platform in spatial Reversal task of Morris Water maze.

Reference	Pollutant	Exposure	Effects
Reference: Hougaard et al. (2008, 156570) **Species:** Mouse **Gender:** Female (pregnant), Offspring- male, female **Strain:** C57BL/6 **Age:** NR **Weight:** NR	DEP (SRM 2975) **Particle Size:** 240 nm (MMAD); surface area 90 mg^2/g, density 2.1 g/cm^3	**Route:** Inhalation **Dose/Concentration:** 19.1 ± 1.13 mg DEP/m^3 **Time to Analysis:** Pregnant dams exposed GD 7-19, 1 h/day. GD 20 named PND 0 for pups. Weights recorded, 1 pup from each group sacrificed PND 2. Weights recorded PND 9. PND 22 1 male and female removed from each group for behavioral testing. Dams and remaining offspring sacrificed PND 23 or 24.	DEP females gained more weight during gestation. Generally, DEP pups weighed less. No significant DNA damage was measured, but DEP caused slightly higher IL-6, MCP-1, and MIP-2. Plasma thyroxin levels as well as learning and memory were similar amongst the groups.
Reference: Huang et al. (2008, 156574) **Species:** Rat **Gender:** Male (adults), male and female (fetuses) **Strain:** Wistar **Age:** 8 wk (male adults), 20 days of gestation (fetuses)	ME: Motorcycle Exhaust (generated from 1992 Yamaha cabin motorcycle with two-stroke 50 cc engine). **Particle Size:** NR	**Route:** Nose-only Inhalation **Dose/Concentration:** 1: 10 and 1: 50 dilutions **Time to Analysis:** 2 h/day (1 h in morning and 1 h in afternoon), for 5 consecutive days/wk, for 4 wk (1:50, 1:10 dilutions) and 2 wk (1:10 dilution). Male mated with untreated females. Pregnant females sacrificed on 20 days of gestation. Male and female fetuses observed.	After exposure, decreased body weight and testicular spermatid number were observed. 1: 10 ME exposure for 4 wk (no recovery) decreased testicular weight and increased the inflammatory cytokine mRNA. Glutathione system and lipid peroxidation were not affected.
Reference: Lichtenfels et al. (2007, 097041) **Species:** Mouse **Gender:** Male and Female **Strain:** Swiss **Age:** NR	Ambient air in São Paulo, Brazil **Particle Size:** NR	**Route:** Ambient Air Exposure **Dose/Concentration:** NA **Time to Analysis:** Males housed in open-top chambers for 24 h/day, everyday for 4 mo, beginning 10 days after birth. Males mated to non-exposed females immediately following exposure. Males sacrificed immediately following mating. Pregnant females remain in chamber and sacrificed on 19 days of pregnancy.	Decreased testicular, epididymal sperm counts, decreased number of germ cells, and decreased elongated spermatids were observed. Decreased SSR, and a sex ratio shift (fewer males) also occurred after exposure.
Reference: Mauad et al. (2008, 156743) **Species:** Mouse **Gender:** Male, Female **Strain:** BALB/c **Age:** 10 days **Weight:** Parental: 21.4 ± 4.0 - 26.3 ± 2.8 g; 15 day-old offspring: 7.8 ± 1.1 - 9.0 ± 1.0 g; 90 days-old offspring: 20.3 ± 2.3 - 27.4 ± 1.8 g	PM (busy traffic street São Paulo, Brazil; Aug. 2005-April 2006) (NO_2, SO_2, CO) **Particle Size:** 2.5, 10 µm (diameter)	**Route:** Ambient Air Exposure **Dose/Concentration:** $PM_{2.5}$: filtered chamber- 2.9 ± 3.0 $µg/m^3$, nonfiltered chamber- 16.9 ± 8.3 $µg/m^3$; Outdoor concentration: PM_{10}- 36.3 ± 15.8 $µg/m^3$, CO- 1.7 ± 0.7 ppm, NO- 89.4 ± 31.9 $µg/m^3$, SO_2- 8.1 ± 4.8 $µg/m^3$ **Time to Analysis:** Nonfiltered exposure 24 h/day for 4 mo. Mated at 120 days exposure. After birth, 30 females and offspring transferred to filtered or nonfiltered chamber. Killed 15 or 90 days of age.	Mild foci of macrophage accumulations containing black dots of carbon pigment occurred in the alveolar areas on 90 day-old mice. Surface-to-volume ratio decreased from 15 to 90 days of age and was higher in mice exposed to air pollution. PM exposure reduced inspiratory and expiratory volumes at higher levels of transpulmonary pressure.
Reference: Mohallem et al. (2005, 088657) **Species:** Mouse **Strain:** BALB/c **Gender:** Female **Age:** 10 wk, 10 days	Filtered or ambient air in downtown Sao Paulo situated at crossroads with high traffic density (predominant source of air pollution is automotive). **Particle Size:** NR	**Route:** Whole-body Inhalation **Dose/Concentration:** PM_{10}: 35.5 ± 12.8 $µg/m^3$; CO: 2.2 ± 1.0 ppm; NO_2: 107.8 ± 42.3 $µg/m^3$; SO_2: 11.2 ± 5.3 $µg/m^3$ **Time to Analysis:** Exposed for 24 h/7days/wk for 4 mo. Newborns mated after reaching reproductive age of 12 wk. All pregnant females sacrificed between 19th and 20th day of pregnancy.	No effects in adult exposed animals. Increased implantation failure of neonatal exposed-dams. Sex ratio, # of pregnancies, resorbtions, fetal deaths, and fetal placenta Weights unchanged after neonatal ambient air exposure.

Reference	Pollutant	Exposure	Effects
Reference: Mori et al. (2007, 096564) **Species:** Mouse **Strain:** C57/BL **Gender:** Male **Age:** 6 wk	DEP: generated by 4-cylinder diesel engine **Particle Size:** NR	**Route:** Dorsal Subcutaneous Instillation **Dose/Concentration:** 0.2 ml (of 1.1mg/ml or 0.37 mg/ml) **Time to Analysis:** 2×/wk for 10 wk; 1 wk post last instillation.	cDNA library screen after sub-cutaneous injection identified activated clones related to prostanoids and arachadonic acid (Platg2c2c, Acsl6) and sperm production (Stk35). However, the route of exposure was unconventional.
Reference: Ono et al. (Ono et al., 2007, 156007) **Species:** Mouse **Strain:** ICR **Gender:** Pregnant females, male offspring **Age:** NR (pregnant females), 12 wk (offspring)	DE: generated from 4-cyl diesel Isuzu engine at 1500 rpm using standard diesel fuel. **Particle Size:** NR	**Route:** Inhalation **Dose/Concentration:** NR **Time to Analysis:** Exposed from 2 day post coitum to 16 dpc. Parameters for male offspring measured on days 8, 16, 21, 35, 84 and sacrificed at 84 days.	PND 8 and 16 male reproductive accessory gland weight decreased. PND 21 decreased serum testosterone (T); PND 84 increased serum T. FSHr, sTAR mRNA decreased PND 35 and 84. Relative testis and epididymal weight unchanged. Sertoli cell degeneration observed.
Reference: Ono et al. (Ono et al., 2007, 156007) **Species:** Mouse **Strain:** ICR **Gender:** Male offspring, Pregnant females **Age:** 12 wk (male offspring)	DE: generated from 4JB-2type, light duty 3060 cc 4-cyl Isuzu diesel engine under 1500 rpm **Particle Size:** NR	**Route:** Whole-body Inhalation **Dose/Concentration:** 1.0 mg DEP/m^3 **Time to Analysis:** Pregnant females exposed from 2 day postcoitum- 16 dpc. Without undergoing further exposure, male offspring sacrificed at 12 wk.	Dose-dependent increase in seminiferous tubule degeneration and decreased DSP. After 1 mo recovery, DSP recovered at the lowest dose.
Reference: Pinkerton et al. (2004, 087465) **Species:** Rat **Gender:** Female (pregnant), Offspring- NR **Strain:** SD **Age:** 10 days (pups), Pregnant females- 10-14 days of gestation **Weight:** NR	PM (Fe and soot from combustion of acetylene and ethylene in a laminar diffusion flame system) **Particle Size:** Median diameter: 72-74 nm; size range: 10-50 nm	**Route:** Inhalation **Dose/Concentration:** Mean mass concentration: 243 ± 34 µg/m^3; Average Fe concentration: 96 µg/m^3 **Time to Analysis:** Exposed 10 days postnatal age, 6 h/day, 3 days (consecutive). Bromodeoxyuridine injected 2 h before necropsy. .	A significant reduction of cell proliferation occurred only within the proximal alveolar region of exposed animals compared to controls. There were no significant differences between the groups for alveolar formation and separation within the proximal alveolar region
Reference: Silva et al. **(Silva et al., 2008, 156981)** **Species:** Mouse **Strain:** Swiss **Gender:** Females (pregnant mice) **Age:** 1st, 2nd, 3rd wk of pregnancy (females), GD19 (fetuses)	Ambient air: Sao Paulo, Brazil **Particle Size:** NR	**Route:** Ambient Air Exposure **Dose/Concentration:** NR **Time to Analysis:** 1st wk, 2nd wk, 3rd wk or combo of exposure during pregnancy.	Decreased fetal weight with exposure in 1st wk of pregnancy. Decreased placental weight with exposure in any of the 3 wk of pregnancy.

Reference	Pollutant	Exposure	Effects
Reference: Somers et al. (2002, 078100) **Species:** Mouse **Strain:** Swiss Webster **Gender:** Male and Female **Age:** 6-8 wk (adult male and females), 5 days (pups)	Ambient air: 2 sites in Canada (polluted industrial area 1km downwind from two integrated steel mills & rural location 30 km away) **Particle Size:** NR	**Route:** Ambient Air Exposure **Dose/Concentration:** NR **Time to Analysis:** Exposed 24 h/day, 7 days/wk for 10 wk from September 10, 1999- November 21, 1999. Exposed to clean air for 6 wk post-treatment. Paired with mice within exposure group. 5d old pups measured.	ESTR germ line mutations following exposure. Heritable mutation rate increased 1.5 to 2 fold in urban vs. rural site. Increased frequency is paternal line dependent.
Reference: Somers et al. (2004, 078098) **Species:** Mouse **Gender:** NR **Strain:** Sentinal Lab **Age:** NR **Weight:** NR	PM (rural or urban-industrial) **Particle Size:** >0.1 µm	**Route:** Ambient Air Exposure **Dose/Concentration:** Mean TSP: Rural- 16.2 ± 8.3 - 31.7 ± 13.2 µg/m^3, Urban-Industrial- 38.9 ± 10.5 - 115.3 ± 25.3 µg/m^3 **Time to Analysis:** Exposed 10 wk. Bred 9 wk postexposure.	The offspring of urban-industrial mice inherited paternal ESTR mutations 1.9-2.1 times more than rural or HEPA-filtered offspring. Maternal ESTR mutations were not significant.
Reference: Sugamata et al. (2006, 157025) **Species:** Mouse **Strain:** ICR **Gender:** Pregnant Females, male and female offspring **Age:** 11 wk (offspring), NR (pregnant females)	DE **Particle Size:** NR	**Route:** Inhalation **Dose/Concentration:** 0.3 mg DEP/m^3 **Time to Analysis:** Pregnant females exposed from 2 day post coitum to 16 dpc. Offspring sacrificed 11 wk after birth.	Exposed pups had increased caspase 3 positive cells and decreased purkinjie cell number (cerebellum), similar to human Autism brain phenotype.
Reference: Tozuka et al. (2004, 090864) **Species:** Rat **Strain:** F344 **Gender:** Pregnant females, male and female fetuses **Age:** Gestation day 20 (fetuses), NR (pregnant females)	DE: generated by diesel engine (309 cc Model NFAD-50) **Particle Size:** NR	**Route:** Whole-body Inhalation **Dose/Concentration:** 1.73mg/m^3 **Time to Analysis:** Exposed 6 h/day from GD 7-20 with no exposure on Saturdays or Sundays (4 non-exposure days total). Fetuses and maternal blood collected on GD20. PAHs: Exposed 6 h/day from GD 7-14 with no exposure on Saturdays or Sundays. Breast milk collected PND14.	Gestational and lactational exposure to DE's And PAHs. 7 milk PAHs increased in DE-exposed dams. DE exposure can lead to PAH pup exposure through breast milk.
Reference: Tsukue et al. (2004, 096643) **Species:** Mouse **Strain:** Slc: ICR **Gender:** Pregnant females, female fetuses **Age:** Gestation day 14 (fetuses)	DE: generated by 2369 cc Isuzu diesel engine operating at 1050 rpm with 80% load and using commercial light oil. **Particle Size:** NR	**Route:** Whole-body Inhalation **Dose/Concentration:** 0.1 mg DEP/m^3 (at 1:8 dilution with clean air) **Time to Analysis:** Exposed for 8h/day from 2 day postcoitum to 13 dpc (with no exposure on days 4, 5, 11, 12). Sacrificed 14 dpc. Only female fetuses studied.	SF-1 & MIS mRNA did not change. Other steroidogenic genes were also unchanged. BMP-15 and oocyte differentiation mRNA decreased.

Reference	Pollutant	Exposure	Effects
Reference: Tsukue et al. (2002, 030593) **Species:** Mouse **Strain:** C57/BL **Gender:** Females, male and female offspring **Age:** 6 wk, 70 days post natal (offspring)	DE: generated by light-duty, 4-cyl Isuzu diesel engine at 1500 rpm. **Particle Size:** NR	**Route:** Whole-body Inhalation **Dose/Concentration:** 0.3, 1.0 or 3.0 mg DEP/m^3 **Time to Analysis:** Exposed 12 h/day, 7 days/wk for 4 mo. Some females sacrificed immediately following exposure. Remainder mated with unexposed males. Parameters measured in offspring at postnatal day 70.	DE-exposed females had decreased uterine weight at 4 mo. Offspring had decreased body weight at 6 and 8 wk of age. Decreased rate of good nesting construction (3 mg/m^3). AGD decreased In males (30 and 70 days old). Organ weight decreased in females and female crown to rump length decreased.
Reference: Ueng et al. (2004, 096199) **Species:** Mouse **Gender:** Female **Strain:** Wistar **Age:** 21days **Cell Line:** MCF-7	ME: generated from a Yamaha Cabin motorcycle 2-stroke 50-cc engine and variable venture carburetor **Particle Size:** NR	**Route:** Intraperitoneal Instillation. Cell Culture. **Dose/Concentration:** IP: 1, 10, 50 µg/ml Cell Culture: 0.01, 0.1, 1, 10, 50, 100 µg/ml **Time to Analysis:** IP: 1/day for 3 days and sacrificed on 24 day. Cell Culture: 3, 24, 30, 48 h and 2 days.	10 mg/kg +E2 induced anti-estrogenic uterine effects and antiestrogenic with in vitro (MCF-7 cells) E2 screen.
Reference: Veras et al. (2008, 190493) **Species:** Mouse **Gender:** Male, Female **Strain:** BALB/c **Age:** 20 days, newborns **Weight:** NR	PM (downtown São Paulo, Brazil near crossroads with high traffic density, 67% $PM_{2.5}$ comprises air pollution) **Particle Size:** 2.5 µm (diameter)	**Route:** Open-Top Chamber **Dose/Concentration:** $PM_{2.5}$- 27.5 µg/m^3; NO_2- 101 µg/m^3; CO- 1.81 µg/m^3; SO_2- 7.66 ppm **Time to Analysis:** 20 days-old mice maintained in filtered or nonfiltered chamber until 60 days-old. Offspring maintained in respective chambers until 21 days-old. Offspring mate at 60 days-old. Females euthanized 18th GD.	Fetal weight and maternal blood space volume and surfaces declined in the groups exposed to nonfiltered air. Fetal capillary surfaces were greater in nonfiltered air groups. There was a significant gestational effect on maternal:fetal surface ratios with values declining significantly in groups exposed during pregnancy to nonfiltered air. The total oxygen diffusive conductance of the intervascular barrier increased significantly during pregestational exposure to nonfiltered air. Mass-specific conductance increased during pregestational and gestational periods of exposure to nonfiltered air.
Reference: Veras et al. (2009, 190496) **Species:** Mouse **Gender:** Male, Female **Strain:** BALB/c **Age:** 20 days **Weight:** NR	PM (São Paulo, Brazil; near crossroads with high traffic density) (Al, Ca, Cu, Fe, K, Na, Ni, P, Pb, S, Si, Ti, V, Zn, C) **Particle Size:** 2.5 µm (diameter)	**Route:** Open-Top Chamber **Dose/Concentration:** Mean: Non-filtered- 27.5 µg/m^3, Filtered- 6.5 µg/m^3 **Time to Analysis:** 20 days-old mice maintained in filtered or non-filtered chamber. Allowed to mate at 60 days. 2 generation model.	Ambient air pollution extended the estrus cycle, which reduced the number of cycles. Antral follicles decreased. Mating time increased and fertility and pregnancy indices decreased. The mean post-implantation loss rate increased, which was influenced by both pre- and post-gestational exposure. Fetal weight decreased and was also influenced by pre- and post-gestational exposure, which exhibited a significant interaction.
Reference: Watanabe (2005, 087985) **Species:** Rat **Gender:** Female (pregnant), Offspring- male **Strain:** F344/DuCrj **Age:** 7 days of gestation - parturition (females), 96 days (offspring) **Weight:** 240-262 g (offspring)	DE (309cc engine, Model NFAD50, Yanmar Diesel Co., Osaka, Japan, 1800rpm, 45% load) (PM, NO_2) **Particle Size:** 90% <0.5 µm	**Route:** Inhalation **Dose/Concentration:** High dose total group: PM- 1.71 µg/m^3, NO_2- 0.79 ppm; Low dose total group: PM- 0.17 µg/m^3, NO_2- 0.10 ppm **Time to Analysis:** Pregnant rats exposed gestational day 7 to delivery 6 h/day. 5 groups: high dose total DE, high dose PM, NO_2 filtered, low dose total DE, low dose PM, NO_2 filtered, clean air control. Offspring sacrificed day 96 after birth.	All groups had significantly less daily sperm production than the control. PM and NO_2 in DE decreased spermatogenia but was not significant, however the high dose PM filtered group achieved significance. Pachytene cells, spermatids, and Sertoli cells were lower in all groups compared to the control.

Reference	Pollutant	Exposure	Effects
Reference: Yauk et al. (2008, 157164) **Species:** Mouse **Strain:** C57BL/6 x CBA F1 hybrid **Gender:** Male **Age:** 7-9 wk	HEPA-Filtered air (PM removed) and ambient air at 2 sites: -2 km from two integrated steel mills -1 km from major highway on Hamilton Harbor Components: Metals 3.6 ± 0.7 µg/m^3 TSP 9.4+17 µg/m^3 **Particle Size:** NR	**Route:** Ambient Air Exposure **Dose/Concentration:** NR **Time to Analysis:** Parameters measured 3, 10 wk, or 10 + 6 wk recovery following exposure.	10+6 wk exposure induced increased ESTR mutations in sperm DNA of exposed v filtered. No testicular DNA adducts seen in exposed males. At 3 wk DNA increased adducts seen in lungs of exposed males, not in filtered males. Mutations were PM dependent, and gas-phase independent.
Reference: Yokota et al. (2009, 190518) **Species:** Mouse **Gender:** Female (pregnant), Male (offspring) **Strain:** ICR **Age:** NR **Weight:** NR	DE (2369-cc diesel engine, Isuzu Motors, Ltd., Tokyo, Japan; 1050 rpm, 80% load, commercial light oil) **Particle Size:** NR	**Route:** Inhalation. Pre-natal Exposure **Dose/Concentration:** DE: 1.0 mg/m^3; CO: 2.67 ppm, NO_2: 0.23 ppm, SO_2: <0.01 ppm **Time to Analysis:** Pregnant mice exposed 8 h for 5 days from GD 2-17. Mothers and pups kept in clean room. Pups weaned on PND 21 then transported to Tokyo University of Science. 2wk acclimation. Exposed 12 h light/dark cycle. Activity monitor with infrared ray sensor measured spontaneous motor activity (SMA), 10 min intervals 2 days. After behavioral test, mice decapitated.	Prenatal DE exposure decreased SMA in the male offspring. DE decreased locomotor activity during the light phase. Dopamine levels in the striatum and nucleus accumbens did not change, but HVA concentrations decreased in DE-exposed mice.
Reference: Yoshida et al. (2006, 156170) **Species:** Mouse **Strain:** ICR, C57Bl/6J or DDY **Gender:** Pregnant Females, Male fetuses **Age:** 14 days of gestation (fetuses), 2-13 days of gestation (pregnant females)	DE(generated from a 4-cyl., 2300 cc diesel Isuzu engine at 1050 rpm and 80% load). **Particle Size:** NR	**Route:** Whole-body Inhalation **Dose/Concentration:** 0.1 mg DEP/m^3 **Time to Analysis:** Exposure on 2-13 days of gestation. Parameters measured on 14 days of gestation.	Responses to exposure showed strain-related variations with ICR as the most sensitive followed by C57 and ddY as the least sensitive. MIS mRNA expression, a factor in male gonadal differentiation, was significantly decreased in the ICR and C57 strains. Ad4BP/SF-1 expression was significantly decreased in the ICR strain only.
Reference: Yoshida et al. (2006, 097015) **Species:** Mouse **Strain:** ICR **Gender:** Pregnant females and male offspring **Age:** 2-16 days postcoitum (pregnant females), 28 days (male offspring)	DE: generated by 4Jb1-type, light duty 4-cylinder Isuzu diesel engine using standard diesel fuel at 1500 rpm. **Particle Size:** NR	**Route:** Whole-body Inhalation **Dose/Concentration:** 0.3, 1.0 or 3.0 mg DEP/m^3 **Time to Analysis:** Pregnant females exposed 12 h/days, 7 days/wk from 2-16 days postcoitum. Offspring sacrificed on postnatal day 28.	NOAEL 0.3 mg DEP/m^3. DE exposure induced increased reproductive gland weight (two higher doses) in male mice. mRNA decreases in aromatase and 3 µ-hD (3.0 mg DEP/m^3). No change in sex ratio. Two higher doses induced significant increased reproductive organ weights. Male pup weight Increased at PND 28. Increased serum T was observed in pups exposed to 1.0mg DEP/m^3. Serum T positively correlated with DSP, testis weight, steroid enzyme mRNA.
Reference: Yoshida et al. 2004 (2004, 097760) **Species:** Mouse **Gender:** Female (pregnant), Offspring- male **Strain:** ICR **Age:** 4, 6 wk **Weight:** NR	DE **Particle Size:** NR	**Route:** Inhalation **Dose/Concentration:** 6wk-old males, embryos: 0.3, 1.0, 3.0 mg DEP/m^3, Pregnant mice: 0.1, 3.0 mg DEP/m^3 **Time to Analysis:** 6 wk-old males: Exposed 12 h/day, 6 mo. 1 mo clean air exposure. Pregnant mice: Exposed 2-13 p.c. 8 h/day. Male embryos: Exposed 2-16 p.c. Examined at 4 wk-old.	**6wk-old Males:** In the seminiferous tubules, DE dose-dependently caused degenerative and necrotic changes, desquamation of the seminiferous epithelium, and loss of spermatozoa. Spermatogenesis was still inhibited after a 1m clean air exposure. **Pregnant Mice:** Ad4BP/5F-1 and MIS mRNA significantly and dose-dependently decreased in male fetuses exposed to DE. **4wk-old Male Newborns:** Tissue weight of the testis and accessory reproductive glands were significantly greater in DE-exposed mice. Blood testosterone concentration was 8X higher than the control at 1.0 mg DEP/m^3. No significant differences occurred for testosterone synthetase mRNA.

Table D-7. Mutagenic/genotoxic effects in bacterial cultures.

Reference	Pollutant	Exposure	Effects
Reference: Binkova et al. (2007, 156273) **Species:** Salmonella (±S9 (rat liver)) **Cell Line:** Calf thymus DNA	PM (Prague, Košice, Sofia, Czech Republic; summer, winter) (organic extracts) **Particle Size:** Diameter: <10 µm	**Route:** Cell Culture **Dose/Concentration:** 100 µg EOM/mL **Time to Analysis:** PM collected 24 h daily 3 mo, extracted. 24 h incubation BaP, c-PAH, EOM, with or without S9. 32P-Postlabeling 4 h. Autoradiography 1-24 h.	DNA adducts in EOM treatments were greater with S9 than without. Positive correlations were found between the amount of DNA adducts and the PAH content (notably BaP) in the EOM treatment.
Reference: Brits et al. (2004, 087397) **Species:** S. typhimuriam **Strain:** TA98 ± S9 (Ames); TA104 recN2-4 and TA104pr1 (Vitotox) **Cell Line:** Human whole blood (Comet, MN assays)	PM (Flanders, Belgium; urban, rural, industrial sites) (organic extracts) **Particle Size:** 10 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** 2.5, 5, 10, 20m^3 air equivalents/mL **Time to Analysis:** Air samples extracted. Ames assay 48 h. Vivotox test. Comet assay 24 h. MN assay.	**Ames:** S9 induced mutagenicity of all extracts from all areas in a dose-dependent manner. Without S9, only extracts from the urban and industrial areas were mutagenic at the highest dose. **Vitotox:** Extracts were toxic at the highest dose. **Comet:** Significant DNA damage in the extracts was seen and enhanced by S9. **MN:** A dose-response relationship was seen in the urban extracts for increased micronucleated binuclear cells.
Reference: Brown et al. (2005, 095919) **Species:** S. typhimuriam **Strain:**TA98 **Cell Line:** Rat hepatoma H4IIE	PM (New Zealand, summer, winter) (extracts) **Particle Size:** 10 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** 9.7-20.8 µg/m^3 (summer), 21.8-61 µg/m^3 (winter) **Time to Analysis:** Air samples collected 15 days, extracted. Ames test: Bacteria growth 12 h, incubated 24 h. Hepatoma bioassay: 24 h incubation 2x. EROD assay.	Generally, the mutagenic rate was positively correlated to PM_{10}, as well as PAH and BaP. PM_{10} levels were higher and more mutagenic in winter than summer.
Reference: Bunger et al. (2006, 156303) **Species:** Salmonella typhimuriam **Strain:** TA98, TA 100	DEP (diesel fuel (DF), low-sulfur diesel fuel (LSDF), rapeseed oil methyl ester (RME), and soybean oil methyl ester (SME)) (SOF-soluble organic fractions) **Particle Size:** Total particulate matter (no OCC) (gh-1): Mean DF- 4.0 ± 0.2; 2.8 ± 0.5; 1.8 ± 0.0; 3.4 ± 0.2; 1.2 ± 0.1	**Route:** Cell Culture **Dose/Concentration:** Log 2 dilutions of extracts: 1.0, 0.5, 0.25, 0.125 **Time to Analysis:** SOF extracted 12 h. Plates incubated 48 h.	**No OCC:** Without oxidation catalytic converter (OCC), DF extract produced the highest number of revertant colonies at all load modes in both TA98 and TA100 ± S9. RME, SME, and LSDF extracts caused lower or no mutagenic effects, seen especially at partial load modes and idle motion. **OCC:** With OCC, all extracts reduced the number of revertant colonies in TA98 and TA100 ±S9 at partial load modes B, C, and D. At load mode A (rated power), there was an increase of the number of revertant colonies in all assays -S9, significant for extracts from RME (TA98, TA100) and SME (TA98). S9 lowered frequency of mutations. At load mode E (idling), number of revertant colonies of DF extracts increased ±S9.
Reference: Bunger et al. (2007, 156305) **Species:** Salmonella typhimuriam **Strain:** TA98, TA 100	Diesel engine emissions (DEE)—rapeseed oil (RSO) and rapeseed methyl ester (RME, biodiesel), natural gas derived synthetic fuel (GTL), and diesel fuel (DF) (SOF- soluble organic fractions) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** Log 2 dilutions of extracts: 1.0, 0.5, 0.25, 0.125 **Time to Analysis:** SOF extracted 12 h. Plates incubated 48 h.	Compared to DF, RSO significantly increased mutagenic effects of particle extracts (i.e., revertants) by 9.7-59 in TA98 and by 5.4-22.3 in TA100. (mRSO, RSO with lowered viscosity and fuel preheating in tank, produced highest number of revertant colonies in both strains ±S9.) RSO fuels condensates had 13.5 times stronger mutagenicity than DF. RME extracts had moderate but significantly higher mutagenic response in TA98 +S9 and TA100 -S9. Effects of GTL did not differ significantly from DF.

Reference	Pollutant	Exposure	Effects
Reference: de Kok et al. (2005, 088656) **Species:** S. typhimurium **Strain:** TA98 (with and without rat liver S9) **Cell Line:** Salmon testis DNA	TSP (Total suspended particulate , Maastricht, The Netherlands; PM_{10} and $PM_{2.5}$ from 6 urban locations with different traffic intensities.) (organic extracts) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** Mutagenicity assay: 2.5, 9, or 18m^3 sampled air in 100 µL DMSO; DNA adduct assay: 5 µL DMSO containing PM_{10} or TSP from equivalent 50m^3 sampled air. $PM_{2.5}$ concentration equivalent to 35m^3 sampled air. **Time to Analysis:** Mutagenicity assay: Cells incubated 1 h with extracts. DNA adduct assay: DNA incubated 4 h with extracts.	Overall, the direct mutagenicity and DNA reactivity of $PM_{2.5}$ extracts were higher compared to PM_{10} and TSP. S9 generally reduced mutagenic activity in TA98 but increased reactivity to Salmon testis DNA. Total PAH and total carcinogenic PAH levels correlated with the mutagenicity of TSP and the S9-mediated mutagenicity of $PM_{2.5}$. Neither transition metal composition nor radical generating capacity of PM correlated with mutagenic potential. Total PAH and carcinogenic PAH levels from PM_{10} and $PM_{2.5}$ correlated with direct and S9-mediated DNA adducts; for TSP these levels correlated with direct DNA reactivity only.
Reference: DeMarini et al (2004, 066329) **Species:** Salmonella **Strain:** TA98, TA98NR, TA98/1, 8-DNP6, YG1021, YG1024, TA100	A-DEP and forklift DEP (SRM 2975) DEP (EOM) **Particle Size:** 0.4 µm (mean diameter)	**Route:** Cell Culture **Dose/Concentration:** 0, 0.25, 0.5, 1.0, 2.0 EOM µg/plate **Time to Analysis:** DEPs sonicated 20min. Centrifuged 10 min. Organic material extracted and concentrated. Ames assay. Incubated 3 days.	A-DEPs were more mutagenic in both TA98 and TA100 than SRM 2975. There was 22× more PAH-related and 8-45× more nitroarene-related activity.
Reference: El Assouli et al. (2007, 186914) **Species:** S. typhimuriam **Strain:** TA98 (±S9)	PM (Jeddah, Saudi Arabia; 11 sites, urban, winter) (organic extracts) **Particle Size:** 10 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** 2.5, 50, 100 µg/plate; EOM range: 6-40 µg/m^3 **Time to Analysis:** 24 h air samples, extracted. Refluxed 18-24 h. GC-MS. Comet assay. 48 h incubation. Ames assay.	PAHs varied from 0.83 to 0.18 ng/m^3. Only 2 locations of heavy petrol driven cars showed strong genotoxic responses. A correlation existed between DNA damage and the amount of pollutants and PAHs. Toxicity and mutagenicity occurred only in the presence of S9. Only 3 of the 11 sites exhibited moderate mutagenic activities.
Reference: Endo et al. (2003, 097260) **Species:** S. typhimuriam **Strain:** YG1024 (±S9)	PM (Tokyo, Japan; winter) (organic extracts) **Particle Size:** Diameter: >12.1 - 0.06> µm; Bimodal mass concentration: 1-2 µm	**Route:** Cell Culture **Dose/Concentration:** 2.5, 5, 10 µL; 0.30 - 22.76 µg/m^3 **Time to Analysis:** Air samples collected, extracted. 90 min pre-incubation. 48 h incubation.	Mutagenicity tests showed dose-response relationships that were higher without S9 and increased with decreasing size.
Reference: Erdinger et al. (2005, 156423) **Species:** S. typhimurium **Strain:** TA98. TA100, TA98NR	PM (Baden-Württemberg, Germany; urban, 8 locations, glass fiber filters) (organic extracts) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 0.25, 2.5, 5, 12.5, 25 m^3/plate **Time to Analysis:** Standard Ames test protocol followed.	Extracts were mutagenic in all strains evaluated. No significant difference in response with or without metabolic activation. Activity in TA98NR suggests that the mutagenicity correlates with concentrations of air pollutants such as NO_X.
Reference: Iba et al. (2006, 156582) **Species:** S. typhimuriam **Strain:** TA98, TA100 (±S9 (rat liver))	PM (wood smoke (WS) (New Jersey) and cigarette smoke (CS) (Tobacco Research and Health Institute, University of Kentucky) (organic extracts) **Particle Size:** 10 µl aliquots of organic extracts	**Route:** Cell Culture **Dose/Concentration:** 62.5, 12.5 µg TPM equivalent/plate **Time to Analysis:** Incubation, shaking 25 min. Agar added. 48 h incubation. Rat lung explants incubated 18 h. 12 h incubation with treatments.	WS and CS were equally mutagenetic to TA98, but CS was 3-fold more mutagenetic to TA100 than WS. CS induced CYP1A1 in the explants, but WS did not.
Reference: Liu et al. (2005, 097019) **Species:** S. typhimurium **Strain:** YG1024, YG1029 **Cell Line:** Chinese hamster lung V79 cells	DEP extract (DP), gasoline engine exhaust particulate extract (GP), diesel exhaust SVOC extract (DSVOC), gasoline engine SVOC extract (GSVOC), NIST SRM 1650a **Particle Size:** Gasoline PM: 0.554 mg extract (mg PM)-1; Diesel PM: 0.363 mg extract (mg PM)-1	**Route:** Cell Culture **Dose/Concentration:** 1.48, 4.44, 13.3, 40, 120, 360, 1080 µg/plate **Time to Analysis:** 30 min preincubation. 48 h (YG1029). 66 h (YG1024). Overnight preincubation 20 h.	**Mutations:** All samples induced mutations in both strains. The increase was highly significant and dose-dependent. Response with S9 was generally greater than without S9. PM extract was more mutagenic than SVOC extract. **DP, GP, and GSVOC:** Dose-response was seen for DNA damage and micronuclei induction. GP, GSVOC and SRM 1650a were stronger inducers of micronuclei than DP.

Reference	Pollutant	Exposure	Effects
Reference: Matsumoto et al. (2007, 187020) **Species:** S. typhimuriam **Strain:** TA98, TA100 (±S9)	APM (airborne particulate matter) APE (airborne particulate extracts) (Hokkaido, Japan; residential) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** Crude APE: 979mg/m^3 air (CALUX BaP Equivalent (BaPEq)), 21 mg/m^3 air (CALUX TCDD Equivalent (TCDDEq)); Cleaned APE: 7.87 mg/m^3 air (CALUX BaPEq), 0.614 mg/m^3 air (CALUX TCDDEq) **Time to Analysis:** Air samples collected, extracted. Preincubation with S. typhimuriam. 3, 24 h exposure in CALUX assay. RNA extracted from mice 6 days after last application.	Most of the CALUX BaPEq for crude APE was derived from PAH-like compounds, as suggested by the CALUX BaPEq of cleaned APE accounting for 0.80% of CALUX BaPEq for crude APE. CALUX TCDDEq showed TCDD and similar compounds to have a low contribution. The TA100 strain was more mutagenic to APE, with and without S9. S9 increased mutagenicity in both strains.
Reference: Pastorkova et al. (2004, 087431) **Species:** S. typhimuriam **Strain:** TA98, YG1041 (±S9)	PM (EOM) (Plzeň, Prague, Ústí, Zďár - Czech Republic) **Particle Size:** 10 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** TA98 (4 doses): 20-200 µg/plate, YG1041 (4 doses): 4-20 µg/plate **Time to Analysis:** Collected 24 h every 18th day, Oct-Mar, 1999-2003. Extracted. Ames assay. 70 h incubation.	Significant dose-response effects in mutagenic potency of EOM occurred. Prague, one of the most polluted cities, had the highest mutagenicity values. Increasing time-trends were observed in the TA98 ± S9 mutagenicity and PAH concentrations.
Reference: Rivedal et al. (2003, 097684) **Species:** S. typhimurim **Strain:** TA100, TA98, TA100NR, TA98NR, TA98/1,8-DNP6	DEP (SRM 1650)(organic extracts) (fractionated into PAH, nitro-PAH, dinitro-PAH, aliphatics, polar fraction) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** Ames: 300, 600 DEP/plate; Gap junction: 100, 200 µg/mL DEP **Time to Analysis:** Extracted 16 h. Fractionated. Ames assay. Gap junction intracellular communication: exposed 1-6 h. Western blot.	TA100 was the most mutagenic without S9 activation. GJIC was dose- and time-dependently inhibited. The polar fraction was the most potent inhibitor. Nitro-PAH and dinitro-PAH were the most responsive fractions in the Ames assay.
Reference: Seagrave et al. (2003, 054979) **Species:** Salmonella **Strain:** TA98, TA100	Compressed natural gas (CNG) emissions (heavy-duty vehicles): High emitter (HE), Normal emitter (NE), New technology (NT) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** PM (mg/mi)- NE- 7.0, NT- 5.0, HE- 406; Recovered PM (mg/mi)- NE-1.26, NT- 0.71, HE- 57.1; Recovered SVOC- NE- 58, NT- 26.4, HE- 227.5 **Time to Analysis:** Samples collected in filters 7x/day over several days. Recovered PM, recovered SVOC extracts combined. Ames assay.	All three CNG emissions were mutagenic in both strains. Mutagenicity was reduced by S9 in TA100 but not in TA98. Activity ranking in both strains was HE>NE>NT.
Reference: Sharma et al. (2007, 156975) **Species:** S typhimurium **Strain:** TA98, YG1041, YG5161 **Cell Line:** Human A549 lung epithelial cells	PM (airborne, 4 sites: an oven hall and receiving hall in a waste incineration plant; heavy-traffic street; background; Mar-June 2005) **Particle Size:** 2.5 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** 0.25 mg/ml **Time to Analysis:** Samples taken over 7-16 days. A549 cells incubated 24 h. Comet and microsuspension assays performed.	**DNA damage:** Samples from all four sites induced DNA damage in the comet assay with the street samples more damaging than the oven hall sample. **Mutations:** Microsuspension assay was used to assess mutagenic activity. No mutagenic activity was observed for any of the non-polar fractions from any sample sites. The moderately polar fractions were all mutagenic, except for the oven hall sample, only when S9 was added. Comparatively, the polar and crude fractions were mutagenic without metabolic activation, suggesting a direct mutagenic effect.
Reference: Song et al. (2007, 155306) **Species:** S. typhimurium **Strain:** TA98, TA100 **Cell Line:** Rat fibrocytes L-929 cells	PM (soluble organic fraction (SOF) extracts from diesel engines using fuels blended with ethanol by volume: E0 - base diesel fuel; E5 - 5%; E10 - 10%; E15 - 15%; E20 - 20%) **Particle Size:** Density (g/cm^3): E0- 0.8379; E5- 0.8349; E10- 0.8324; E15- 0.8301; E20- 0.8279	**Route:** Cell Culture **Dose/Concentration:** Ames Assay: 0.025, 0.05, 0.1 mg/plate; Comet Assay: 0.125, 0.25, 0.5, 1.0 mg/mL **Time to Analysis:** Samples extracted 24 h. Ames and comet assays performed	All PM extracts induced higher mutational response in TA98 (3- to 5-fold increase over spontaneous) than in TA100 (2-to 3-fold increase). The highest brake specific revertants (BSR) ±S9 in both strains occurred with E20 and lowest BSR was in E5 (except in TA98 -S9). E0 and E20 caused more significant DNA damage (similar in effect) than the other extracts. Damage was dose-dependent but variable with increasing ethanol volume.

Reference	Pollutant	Exposure	Effects
Reference: Zhang et al. (2007, 157186) **Species:** S. typhimurium **Strain:** TA98, TA100 **Cell Line:** A549	Gasoline engine exhaust (GEE) Methanol engine exhaust (MEE) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** MTT Assay- 0.05-0.8 GEE or MEE L/ml; MN Assay- 0.025, 0.05, 0.1, 0.2 GEE or MEE L/ml; Comet Assay- 0.025, 0.05, 0.1, 0.2, 0.4 GEE or MEE L/ml; Ames Assay- GEE: 0.625, 1.25, 2.5, 5.0, 10, 20 L/plate; MEE: 0.3125, 0.625, 1.25, 2.5, 5.0, 10, 20 L/plate **Time to Analysis:** Organic extracts from GEE and MEE. MTT assay- 24 h incubation, followed by 2 or 24 h incubation, followed by 4 h incubation. MN assay- 24 h incubation. Comet assay. Ames assay- 72 h incubation.	**Mutagenicity:** GEE was mutagenic in TA98 but not TA100, -S9 at 10 and 20 L/plate and +S9 at ≥1.25 L/plate. Mutagenicity was higher with S9 than without at 0.625-10 L/plate and a dose-response was reported. MEE had no effect in either strain. **MN:** GEE significantly and dose-dependently induced MN. MEE had no significant effect at any dose. **DNA damage:** GEE significantly induced DNA damage at all doses compared to controls. MEE had no effect at any dose.
Reference: Zhao et al. (2004, 100972) **Species:** Rat **Gender:** Male **Strain:** SD **Age:** NR **Weight:** ~200 g **Cell Line:** S. typhimurium YG1024 (±S9)	DEP (SRM 2975) DEPE (SRM 1975) Carbon black (CB) (Elftex-12 furnace black, Cabot, Boston, MA) **Particle Size:** NR	**Route:** IT Instilled. Cell Culture. **Dose/Concentration:** DEP or CB: 35mg/kg; S9: 25, 50, 100, 200 µg/plate; Cytosolic protein: 20, 40, 80, 160 µg/plate; Microsomal protein: 5, 10, 20, 40 µg/plate **Time to Analysis:** Rats instilled. Sacrificed 1, 3, 7 days post-exposure. S9, cytosolic, microsomal fractions prepared from lung homogenates. Ames assay: 72 h incubation.	DEP and CB-exposed lung S9 time-dependently decreased 2-aminoanthracene (2-AA) mutagenicity. Metyrapone and α-napthoflavone inhibited the S9-activation of 2-AA in DEP and CB exposed rats. Lung S9 increased the mutagenicity of DEPE but not of DEP or CB. Liver S9 reduced DEPE dose-dependently. CYP2B1 and CYP1A1 activated DEPE, with CYP2B1 being more effective.
Reference: Zhao et al. (2006, 100996) **Species:** S. typhimuriam **Strain:** YGL024 (±S9)	DEP (SRM 2975) DEPE (SRM 1975) Aminoguanidine (AG) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** NR **Time to Analysis:** Lung S9 obtained from rats used in in vivo experiment. Ames test. Modified microsuspension assay. All assays in duplicate plates. Repeated 3x.	AG significantly lowered 2-aminoanthracene mutagenic activity of DEP or DEPE-exposed lung samples, with DEP being lowered the most.

Table D-8. Mutagenicity and genotoxicity data summary: In vitro and in vivo.

Reference	Particle	Exposure	Effects
Reference: Abou Chakra et al. (2007, 098819) **Species:** Human **Gender:** Male, Female **Age:** 6-13 yr and Adults **Participant Characteristics:** Non-smokers **Cell Line:** HeLa S3 cells	PM (3 French metropolitan cities: Urban $PM_{2.5}$ and PM_{10} from "Residential Sector," "Proximity Sector," "Industrial Sector") (organic extracts) **Particle Size:** 2.5, 10 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** 200 µL organic extract; 20 µL aphidicoline **Time to Analysis:** 24 h	Seasonal variation was observed with genotoxic effects being greater in winter. $PM_{2.5}$ was more active than PM_{10} extracts. Samples from the "Proximity Sector" (downtown area with heavy traffic) exhibited the strongest genotoxic responses.
Reference: Arrieta et al. (2003, 096210) **Species:** Rat **Cell Line:** Hepatoma (H4IIE) **Species:** Mouse **Cell Line:** Hepatoma H1l1.1c2	PM (El Paso, Texas; Juarez, Chihuahua, Mexico; Sunland Park, New Mexico) (organic extracts) **Particle Size:** 10 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** EROD test: 0.03, 0.17, 0.34, 0.50, 0.68, 4.96, 9.93 extract equivalents (m^3 air); Luciferase: 0.17, 0.51, 1.26, 5.01 extract equivalents (m^3 air) **Time to Analysis:** 24 h	EROD activity declined at higher extract amounts, but luciferase activity was not inhibited. Cytotoxicity occurred only at extract equivalents to 0.47 m^3 air. PAH concentration increased with PM mass.

Reference	Particle	Exposure	Effects
Reference: Bao et al. (2007, 097258) **Cell Line:** Human-hamster hybrid (AL)	DEP (organic extracts) (SRM 2975) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 10, 20, 50, 100 µg/mL **Time to Analysis:** Phagocytosis inhibitors: Exposed 24 h with or without cytochalasin B or ammonium chloride. Cytotoxicity: 24, 48 h incubation. Mutations: Exposed 24 h. 5-7 days culture. Incubated additional 7-8 days.	The nucleus of DEP-treated cells was condensed and shrunken compared to controls. DEPs accumulated in cells, disrupting the mitochondrial cristae, and were lodged in large cytoplasmic vacuoles. DEP produced minimal toxicity. CD59 locus mutations dose-dependently increased but decreased when simultaneously treated with cytochalasin B or ammonium chloride.
Reference: Carvalho-Oliveria et al. (2005, 077898) **Species:** T. pallida; A. cepa	PM (Sao Paulo, Brazil; spring, bus strike and non-strike days) (organic extracts) **Particle Size:** 2.5 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** Strike day: 47.32 µg/m^3; Non-strike day: 43.01 µg/m^3 **Time to Analysis:** 8 h. 24 h recovery. A. cepa roots induced 5 days. Exposed 30 h. Fixed 24 h.	Element concentrations, sulfur and BTEX decreased on the strike day. Micronuclei decreased in T. pallida during the strike. Toxicity measured in A. cepa was not significant, but higher on strike days.
Reference: Dybdahl et al. (2004, 089013) **Species:** Human **Cell Line:** A549	DEP (SRM 1650) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 10, 50, 100, 500 µg DEP/mL **Time to Analysis:** 2, 5, 24 h incubation.	DEP induced dose-dependent increases of IL-1α, IL-6, IL-8, TNF-α. The cytokines increased 4-18-fold at the highest dose. Cell viability did not decrease. Comet tail length increased at 100 and 500 µg/mL for 2, 5, 24 h.
Reference: Gabelova et al. (2007, 156458) **Species:** Human **Cell Line:** Hepatoma Hep G2	PM (PRG-SM, PRG-LB, Košice, Sofia; winter, summer) (organic extracts) **Particle Size:** 10 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** 5-150 µg/mL **Time to Analysis:** 2, 24, 48 h	Cell viability significantly decreased in the 24, 48 h exposure groups compared to the 2 h exposure group. DNA migration significantly dose-dependently increased at most concentrations. In general, oxidative DNA damage did not significantly increase.
Reference: Gabelova et al. (2007, 156457) **Species:** Human **Cell Line:** Hepatoma Hep G2 cell line	PM_{10} (Prague (Czech Republic), Ko˘sice (Slovak Republic) and Sofia (Bulgaria); urban, winter, summer) (organic extracts) **Particle Size:** 10 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** 5 -150 µg/ml **Time to Analysis:** 24 h DNA adduct formation. 2 h Comet assay. Oxidative DNA damage measured by Fpg-sensitive sites.	Total DNA adducts ranged from ~60 to 200 adducts per 108 nucleotides. Extracts also produced approximately the same levels of strand breaks. Results suggested that the genotoxic potential of ambient air was at least 6-fold greater in the winter compared to summer. No substantial difference was reported for oxidative DNA damage induced by summer vs. winter samples.
Reference: Gong et al. (2007, 091155) **Species:** Human **Cell Line:** Microvascular endothelial (HMEC)	DEP (aggregates, exhaust 4JB1-type LD,274 1,4-cylinder Isuzu diesel engine, 10 torque load, cyclone impactor, dilution tunnel constant volume sampler) **Particle Size:** <1 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** 5, 15, 25 µg/mL **Time to Analysis:** Cells treated with DEP, ox-PAPC (oxidized 1-palmitoyl-2-arachidonyl-sn-glycero-3-phosphorylchlorine), DEP+ox-PAPC	HO-1 expression was dose-dependent and greatest with the DEP+ox-PAPC treatment. DEP significantly dose-dependently upregulated or downregulated a number of genes and was shown to have a synergistic effect with co-treatment of ox-PAPC. The most varying genes were significantly enriched for EpRE, inflammatory response, UPR, immune response, cell adhesion, lipid metabolism, apoptosis and protein folding genes.
Reference: Greenwell et al. (2003, 097478) **Species:** Rat **Cell Line:** Epithelial fluid; icosahedral bacteriophage φX174-RF DNA	PM (South Wales, UK) (urban, industrial) **Particle Size:** Coarse diameter: 10-2.5 µm, Fine diameter: 2.5-0.1 µm	**Route:** Cell Culture **Dose/Concentration:** Urban mean: 18.7 ± 4.7 mg/day; Industrial mean: 22.6 ± 2.5 mg/day **Time to Analysis:** 24 h air samples 4-11 days. Substrates vortexed 1 h, suspended 4 h, centrifuged 1 h. Oxidation assay.	Industrial PM was more bioreactive than urban PM. Coarse fractions had greater oxidative potential and bioreactivity than fine fractions.
Reference: Gu et al. (2005, 195923) **Species:** Hamster **Strain:** Chinese **Cell Line:** Lung fibroblast (V79)	DPM (1980 model General Motors 5.7-L V-8 engine) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 25, 50, 100, 150 µg/mL; 10 µg DPM in 10 µg in DPPC/mL; 10 µg DPM in 10 µg DMSO/mL **Time to Analysis:** Chromosomal aberration: 24 h incubation. Treated 24 h. Incubated again 24 h. MN assay: 24 h treatment. Gene mutation: 24 h treatment. Cells replated. 7 days expression times. Staining at 8, 10 days.	DPM significantly and dose-dependently increased aberrant cells at 25-100 µg/mL. DPM increased MN formation dose-dependently. Mutant frequencies were not significant and showed no dose-dependent trends. DPM was toxic to cells at the highest concentration.

Reference	Particle	Exposure	Effects
Reference: Gualtieri et al. (2005, 097841) **Species:** Human **Cell Line:** A549	TD (Tire debris, generated by rotating new vehicle wheel against a steel brush, significant component of PM_{10}) (organic extracts) **Particle Size:** 10-80 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** 50, 60, 75 µg/mL **Time to Analysis:** Particles extracted 6 h. Cells subcultured every 3-4 days. After 24 h, TD treatments 24, 48, 72 h.	A time- and dose-dependent inhibitory effect on the reduction of MTT was seen. Mortality increased dose-dependently and was significantly greater than the controls. DNA strand breaks increased significantly in a dose-dependent manner. A significant cell cycle block in the G1 phase with a consequent decrease in the cell number in the S and G2/M phases was seen. Exposed cells had a modified morphology.
Reference: Gutierrez-Castillo et al. (2006, 089030) **Species:** Human **Cell Line:** A549	$PM_{2.5}$ and PM_{10} (4 monitoring stations in Mexico City: (1) downtown high auto traffic, (2) two industrial areas with high levels of auto traffic and low vegetation, (3) medium-traffic residential area) (winter, spring , 4 sampling days in each period) (aqueous and organic extracts) **Particle Size:** 2.5 or 10 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** 0.05, 0.07, 0.1m^3/ml equivalents $PM_{2.5}$; 0.82, 1.25, 1.63m^3/ml equivalents PM_{10} **Time to Analysis:** 48 h	Higher amounts of water-soluble metals were found in samples collected during winter. Water-soluble extracts increased DNA damage 1.7-fold over the background. Similar results were observed with organic extracts. In general, $PM_{2.5}$ extracts had greater genotoxic potential than PM_{10} extracts, and water soluble fractions form both particle sizes were more genotoxic than the corresponding organic extracts.
Reference: Izawa H et al. (2007, 190387) **Cell Line:** NA	DEPE (4JB-1 Isuzu 4-cylinder direct-injection 2740cc diesel engine; 1500 rpm, 10 kg/m load) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** DEP: Ah-1 experiment- 111, 55.5, 27.8, 13.9, 6.9, 3.5, 1.7 µg/mL; Foods, polyphenols experiment- 27.8 µg/mL **Time to Analysis:** DEPE incubated 2 h for dioxin toxicity measurement. Absorbance at 405 nm measured. Food, polyphenol inhibitory effects: food extract or polyphenol solution added to cytosol solution, shaken 5 min. DEPE added, shaken 5 min. 2 h incubation. Absorbance at 405 nm measured.	The dioxin toxicity equivalent was 6,479 ± 58 ng DEQ/g of DEP. The absorbance showed a sigmoid curve and dose-dependently increased from 6.9 to 27.8 µg DEP/mL. The Ginkgo biloba extract significantly inhibited AhR activation significantly more than the other foods, and was followed by green tea, onions, and garlic. Quercetin and myricetin dose-dependently inhibited AhR activation. Ginkgolides A and B had weak inhibitory effects and resveratol was the weakest.
Reference: Jacobsen et al. (2008, 156597) **Species:** Mouse **Cell Line:** FE1-MutaTM lung epithelial cells	DEP (SRM 1650b) Carbon black (CB) (Printex 90) **Particle Size:** DEP: 18-30 nm; CB: 14 nm; Agglomerates in suspensions: DEP Peaks- 249 nm, CB Peaks- 476 nm	**Route:** Cell Culture **Dose/Concentration:** 37.5, 75 µg/mL **Time to Analysis:** 8 repeated 72 h incubations.	**Mutagenicity:** The 75 µg/mL dose was significantly increased compared to the 37.5 µg/mL dose. Linear regression showed a significant increasing trend by increasing exposure. There was no change in the total cell numbers. **ROS:** ROS production increased in DEP-treated cells after 3 h of exposure. CB-treated cells showed a dose-dependent increase.
Reference: Karlsson et al. (2004, 198976) **Species:** Human **Cell Line:** Fibroblasts; calf thymus DNA with human liver microsomes or rat liver S9	PM (urban dust particles, SRM 1649) (extracted with DCM, acetone, DMSO, water) (Fe 3% w/w, Ti 0.32% w/w, V 0.04% w/w, Mn 0.03% w/w, Cu 0.025% w/w) **Particle Size:** <10 µm (mean diameter)	**Route:** Cell Culture **Dose/Concentration:** 0.1, 1.0, 10, 100 µg/cm^2 **Time to Analysis:** Fibroblasts exposed 24 h. Comet assay. Calf thymus incubated 2 h with microsomes or S9. 32P-labelled.	DNA damage increased dose-dependently, and a significant amount of DNA-damaged cells had particle interactions. DNA damage induced by the insoluble particle core significantly increased after each extraction. Native particles were more genotoxic than those extracted with DMSO, DCM and water, but not with acetone or hexane. DMSO extracts had the most adduct-forming PACs, and water extracts had the most oxidizing substances.
Reference: Karlsson et al. (2005, 086392) **Species:** Human **Cell Line:** A549	PM (subway station, urban street) Subway particles: O_2, Fe (Fe from Fe_3O_4) Street particles: Fe from Fe_2O_3 **Particle Size:** 10 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** Comet: 5, 10, 20, 40 µg/cm^2; 8-oxodG: 10 µg/cm^2 **Time to Analysis:** 4 h.	Both PM types induced concentration-dependent DNA damage, but subway particles were more potent. Subway particles caused more 8-oxodG formation and oxidation of dG, the latter of which was inhibited by deferoxaminemesylate. Oxidation from subway particles was due to nonsoluble, redox active substances, and soluble substances from street particles.
Reference: Karlsson et al. (2006, 156625) **Species:** Human **Cell Line:** A549; monocytes from heparinized whole blood	PM (wood- old, modern boiler; pellets-pellets burner, electrical ignition; tire-road simulator studded, friction tires; Street- busy street, Stockholm; Subway-platform near street) **Particle Size:** 2.5, 10 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** 40 µg/cm^2 **Time to Analysis:** Cells grown 24 h. Comet assay. Monocytes incubated 10 days. Macrophages incubated 18 h.	All particles tested caused DNA damage, but there was no significant difference between the size fractions. Subway particles were the most genotoxic. The urban street particles were the most potent inducers of the cytokines. On the Teflon filters, PM_{10} was somewhat more potent than $PM_{2.5}$.

Reference	Particle	Exposure	Effects
Reference: Kubátová et al. (2004, 087986) **Species:** Monkey **Cell Line:** African green kidney COS-1 (CV-1 cells with origin-defective SV40 mutants) (±S9)	PM (DE from diesel bus, wood smoke (WS) from chimney, hardwood smoke) (organic extracts) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 25, 50, 100, 200 µg/mL; 50mg of each material used for all experiments **Time to Analysis:** 24 h cytotoxicity. 2 h SOS chromotest.	WS had significantly increased cytotoxicity in fractions of 25-250°C, and DE in nonpolar fractions of 250 and 300°C and polar fractions of 50°C. The cytotoxicity of DE PM nonpolar fractions corresponded to increased concentrations of PAHs. WS was not genotoxic and DE was genotoxic in midpolarity fractions (50-250°C). Genotoxic response was not increased after S9 activation.
Reference: Landvik et al. (2007, 096722) **Species:** Mouse **Cell Line:** Hepatoma Hepa1c1c7 cells	DEP extracts (DEPE in the paper) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 10, 20, 30, 50, 70 µg/mL **Time to Analysis:** 24 h	50 and 70 µg/mL DEPE did not induce DNA fragmentation but did cleave caspase 3 to a minor extent.
Reference: Mehta et al. (2008, 190440) **Species:** Human **Cell Line:** A549	PM (SRM 1949a) **Particle Size:** ≤ 0.18 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** 0, 50, 100, 200, 400 µg/mL **Time to Analysis:** Cell culture and cell viability assay: PM treatment 24 h. 10 days incubation. Host cell reactivation assay: pGL3-luciferase plasmid UV irradiated 20 min. PM treatment 24 h. 16 h transfection. 24 h PM incubation. DNA repair synthesis assay: PM treatment 24 h. Proteinase K treatment 30 min. supf mutagenesis assay: PM treatment 24 h. PM culture 60 h. DNA extracted. Overnight incubation of transformed bacteria.	PM reduced colony-forming ability and repair synthesis capacity was proportional to the PM concentration. PM dose-dependently decreased HCR capacity and decreased more than TSP. PM induced cyclobutane dimmers and pyrimidine<6-4>pyrimidones mutations in UV-irradiated supf.
Reference: Meng and Zhang (2007, 198963) **Species:** Rat **Gender:** Male **Strain:** Wistar Kyoto **Age:** NR **Weight:** Mean: 230g; Range: 200-250g **Cell Line:** AMs from treated rats	PM (Baotou, Wuwei, China) (normal weather, dust storms, Mar 1-31) (organic extracts, water soluble fractions) **Particle Size:** 2.5 µm	**Route:** Cell Culture **Dose/Concentration:** AM: 0, 33.3, 100, 300 µg/mL; Water-soluble: 0, 75, 150, 300 µg/mL; Organic extracts: 0, 25, 50, 100 µg/mL; Mass concentration normal day: 68.49 ± 28.83 µg/m^3; Mass concentration dust storm day: 221.83 ± 69.89 µg/m^3 **Time to Analysis:** 24 h; cultures 4 h.	OC, NH_4^+, NO_3^- were higher in normal weather $PM_{2.5}$. SO_4^{2-}, Ca^{2+} were higher in dust storm $PM_{2.5}$. Fe, Al, Ca, Mg were 5x higher in dust storm $PM_{2.5}$. Cell viability reduced in a concentration-dependent manner, with normal weather being slightly more cytotoxic. DNA damage was dose-dependently induced, with normal weather and organic extracts showing the greatest damage.
Reference: Motta et al. (2004, 198953) **Species:** Hamster **Strain:** Chinese **Cell Line:** Epithelial liver, ovary	PM (Catania, Sicily; spring) (organic extracts) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 0.60, 1.21, 2.42, 4.85, 9.70, 19.40 µg/mL; 0.78, 1.56, 2.12, 6.25, 12.50, 25.00 µg/mL **Time to Analysis:** 24 h	The treatment was only slightly cytotoxic at the highest dose. DNA damage and aberrant cells generally increased with dose. No effect was seen in the Chinese hamster ovary cells without metabolic activation.
Reference: Oh and Chung (2006, 088296) **Cell Line:** A549 (Comet), CHO-K1 (CBMN), H4IIE (EROD-microbiassay)	Crude extract (CE) DEP and fractions of CE of DEP (organic extracts: F1 - organic bases, F2 - organic acids, F3 - aliphatic, F4 - aromatic, F5 - slightly polar, F6 --moderately polar, F7 - high polar) **Particle Size:** Diameter: <2.5 µm, 87.71%, 2.5-10 µm, 3.87%, >10 µm, 8.42%	**Route:** Cell Culture **Dose/Concentration:** 100 µg/mL **Time to Analysis:** DEP generated, extracted. Comet assay- 24 h incubation, CE, DEP exposed 24 h. MN assay- cultured 24 h, 4 h treatment, growth medium incubation 20 h. EROD-microbioassay- 48 h.	**DNA damage:** CE significantly increased the amount of DNA damage in A549 cells with and without SKF-525A, a CYP450 inhibitor, and in CHO-K1 cells. It significantly increased MN formation ±S9 compared to controls. **Organic Extracts:** Organic base (F1) and neutral (F3-F7) fractions of CE of DEP significantly induced DNA damage without SKF-525A compared to controls. Adding SKF-525A completely inhibited damage caused by F3, F4, F6 and F7 but kept the effect of F1 similar to that without SKF and only partially inhibited that of F5. F2 did not induce DNA damage with or without SKF. All fractions except F6 induced MN formation ±S9.

Reference	Particle	Exposure	Effects
Reference: Poma et al. (2006, 096903) **Species:** Mouse **Cell Line:** RAW 264.7	PM (L'Aquila, Italy; urban); air samples collected weekly basis Jan-Mar 2004. Carbon black (CB) **Particle Size:** 2.1-0.43 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** 1, 3, 10 µg/cm^2 **Time to Analysis:** Cells cultured 48 h. Treatment 48 h. MN assay: 44 h incubation, 28 h incubation.	PM and CB dose-dependently reduced cell proliferation and induced micronuclei. PM and CB also reduced cellular metabolism of the macrophages and induced significant amounts of apoptosis. PM produced more micronuclei than equally-weighted CB.
Reference: Roubicek et al. (2007, 156929) **Species:** Human **Cell Line:** A549	PM (Mexico City from an industrial area with high-traffic and a medium-traffic residential area) (aqueous or organic extracts) **Particle Size:** 10 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** 1.25, 1.63, 2.5 m^3/ml equivalents of PM_{10} **Time to Analysis:** Cells treated 24 h followed by 48 h incubation with cytochalasin B. Micronuclei frequency determined.	Water and organic extracts induced a significant dose-dependent increase in the micronuclei frequency. After doses of PM from different regions were normalized for mass differences, the genotoxic potency was higher for samples from the industrial area.
Reference: Salonen et al. (2004, 187053) **Species:** Mouse **Cell Line:** RAW 264.7	PM (Vallila, Finland; busy traffic site; spring, winter) **Particle Size:** <10 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** 15, 50, 150, 500, 1000 µg/mL of RPMI **Time to Analysis:** 24 h	PAHs decreased from winter to spring. TNF-α dose-dependently increased and was higher in spring samples. IL-6 generally increased in spring but not in winter. NO dose-dependently increased and was higher in winter. Cell viability generally decreased but there were no consistent potency differences between the samples. Generally, proinflammatory activity, cytotoxicity and IL-6 were associated with the insoluble PM fractions. Polymyxin B inhibited IL-6 and TNF-α. ·OH and 8-hydroxy-2'-deoxyguanosine dose-dependently increased and were higher in the spring and winter, respectively.
Reference: Seaton et al. (2005, 198904) **Species:** Human **Cell Line:** A549	PM (3 busy London underground (LU) stations and cabs) (LU dust in $PM_{2.5}$ samples: iron oxide 64-71%, chromium 0.1-0.2%, manganese 0.5-1%, copper <0.1-0.9%; respirable dust samples: 1-2%) **Particle Size:** Diameter: <2.5 µm, 10 µm, Median diameter: 0.4 µm	**Route:** Cell Culture **Dose/Concentration:** Assays: 1, 10, 50, 100 µg/mL **Time to Analysis:** 8, 24 h.	PM_{10} caused less LDH release, IL-8 stimulation and free radical activity than LU dust particles that contained $PM_{2.5}$. Chelation had little effect on PM_{10} soluble components.
Reference: Sevastyanova et al. (2007, 156969) **Species:** Human **Cell Line:** HepG2 cell line, embryonic lung diploid fibroblasts (HEL), or acute monocytic leukemia cells (THP-1)	PM_{10} (Prague, Czech Republic; Ko˘sice; Slovak Republic; Sofia, Bulgaria) (urban, summer, winter) (organic extracts) **Particle Size:** 10 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** 10-100 µg/ml **Time to Analysis:** 24 h	DNA adducts were observed in all cell types evaluated. Highest adduct levels were observed in HepG2 cells, followed by HEL and THP-1 cells. A correlation between DNA adduct levels and carcinogenic PAH content was observed in HepG2 cells at 50 µg/ml.
Reference: Shi et al. (2003, 088248) **Species:** Human **Cell Line:** A549	PM (Düsseldorf, Germany, July-Dec.) Weekly samplings July-Dec 1999. **Particle Size:** Fine diameter: <2.5 µm; Coarse diameter: 10-2.5 µm	**Route:** Cell Culture **Dose/Concentration:** Fine: 0.57-2.49 mg; Coarse: 0.66-1.89 mg; Concentration: 0.57 mg/mL **Time to Analysis:** NR	Coarse and fine particles generated ·OH, but coarse particles had significantly higher ·OH formation as well as 8-hydroxy-2'-deoxyguanosine formation. 8-hydroxy-2'-deoxyguanosine and ·OH had a significant correlation.
Reference: Skarek et al. (2007, 096814) **Species:** Rat **Cell Line:** Modified hepatoma H4IIE.luc; SOS: E. coli PQ37 (±S9)	PM (urban: Ústí and Laben, Karviná; background: Červenohorské sedlo, Košetice - Czech Republic; July) (organic extracts, TSP); GP (gas phase). 24 h samples July 2002 **Particle Size:** <2.5 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** SOS: 8, 4, 2, 1 m^3/ml; Dioxin: TSP+GP- 8, 1.33, 0.22, 0.04 m^3/ml, $PM_{2.5}$+GP: 4, 0.66, 0.11, 0.02 m^3 ml-1 **Time to Analysis:**. SOS chromotest: 22 h incubation. Dioxin toxicity test: 24 h exposure.	The urban areas had a much greater level of carcinogenic PAHs and overall number of PAHs than the background areas. Significant genotoxic activity was only detected at TSP+GP without S9 from urban areas. $PM_{2.5}$+GP had lower dioxin activity at the urban areas, but similar levels of toxicity were seen for both treatments in the background areas.
Reference: Song et al. (2007, 155306) **Species:** S. typhimurium **Strain:** TA98, TA100 **Cell Line:** Rat fibrocytes L-929 cells	PM (soluble organic fraction (SOF) extracts from diesel engines using fuels blended with ethanol by volume: E0 - base diesel fuel; E5 - 5%; E10 - 10%; E15 - 15%; E20 - 20%) **Particle Size:** Density (g/cm^3): E0- 0.8379; E5- 0.8349; E10- 0.8324; E15- 0.8301; E20- 0.8279	**Route:** Cell Culture **Dose/Concentration:** Ames Assay: 0.025, 0.05, 0.1 mg/plate; Comet Assay: 0.125, 0.25, 0.5, 1.0 mg/mL **Time to Analysis:** 24 h	All PM extracts induced higher mutational response in TA98 (3- to 5-fold increase over spontaneous) than in TA100 (2-to 3-fold increase). The highest brake specific revertants (BSR) ±S9 in both strains occurred with E20 and lowest BSR was in E5 (except in TA98 -S9). E0 and E20 caused more significant DNA damage (similar in effect) than the other extracts. Damage was dose-dependent but variable with increasing ethanol volume.

Reference	Particle	Exposure	Effects
Reference: Ueng et al. (2005, 097054) **Species:** Human **Cell Line:** Lung epithelium CL5 (cancerous), BEAS-2B, WI-38 normal lung fibroblast	MEP (Yamaha cabin motorcycle 2-strok 50-cc engine) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 1, 10, 100, 200 µg/mL **Time to Analysis:** microarray analysis. RT-PCR: 2 h. ELISA: 12 h incubation. Centrifuged 24 h post-treatment. Bioactivity: 12 h incubation. Centrifuged 24 h post-treatment. Medium replaced 48 h post-incubation. Fibroblasts determined 96 h post-incubation. Time response studies: 3-48 h treatment. Concentration response studies: 6 h treatment.	**Drug Metabolism Array Study:** MEP increased CYP1A1, CYP3A7 and UGT2B. **Cytokine Array Study:** MEP increased fibroblast growth factor (FGF)-6, FGF-9, IL-1α, IL-22 and vascular endothelial growth factor (VEGF)-D mRNA. **Oncogene, Tumor Suppressor, Estrogen Signaling Pathway:** MEP increased fra-1, c-src, SHC, p21, COX7RP, and decreased p53 and Rb expression. **RT-PCR:** MEP increased CYP1A1, CYP1B1, IL-6, IL-11, IL-1α, FGF-6, FGF-9, VEGF-D, fra-1 and p21. **Concentration and Time Responses:** Concentration and time-dependent increases occurred for FGF-9, IL-1α, IL-6, IL-11, but decreased time-dependently after 6 h exposure. **BEAS-2B Cells:** MEP had concentration-dependent increases on CYP1A1 and CYP1B1 but did not affect anything else. **Peroxide, MEP+NAC, WI-38 Cells:** MEP increased peroxide production. The MEP+NAC treatment reduced MEP-elevated levels of IL-1α, IL-6, FGF-9, VEGF-D to control levels. Fibroblasts increased in WI-38 cells.
Reference: Umbuzeiro et al. (2008, 190491) **Species:** Salmonella typhimurium **Strain:** TA98, YG1041 (+/- S9)	PM (urban; São Paulo, Brazil- Cerqueira César street station, Ibirapuera park station) (winter- June 17, 18; average temperature: 16ºC) (EOM) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** Cerqueira César: UPM- 156 µg/m^3, EOM- 57.7 mg/total UPM; Ibirapuera Park: UPM- 32 µg/m^3, EOM- 41.7 mg/total UPM; Salmonella assay- 0.5, 1, 5, 10, 50, 100 UPM equiv/plate (µg) **Time to Analysis:** Organic extraction 20 h. PAH fractionation.	The TSP and EOM were similar for both sites. The PAH fraction had very low mutagenicity for the Cerqueira César sample in the YG1041 strain and no mutagenicity for the Ibirapuera sample. Nitro-PAH and oxy-PAH had similar mutagenetic activities from both samples. S9 decreased mutagenicity in nitro-PAH but was increased in oxy-PAH. DNA adduct levels were dose-dependent and not different between the two sites.
Reference: Upadhyay et al. (2003, 097370) **Species:** Human **Cell Line** A549	PM (Dusseldorf, Germany) (Particles contain carbon (19.70%), hydrogen(1.4%),nitrogen (<.05%), oxygen(14.12%), sulfur (2.09%), ash (63.24%)) (Ionizable metals concentrations (ppm): Co(103), Cu(48),Cr(104),Fe(14,521), Mn(21.3), Ni(1,519),Ti(131), V(2,767) **Particle Size:** NR	**Route:** Cell Culture **Dose/Concentration:** 1, 5, 25, 100 µg/cm^2; 10, 25, 50, 100 µg/cm^2 **Time to Analysis:** 1, 4, 8, 12, 24 h.	PM induced dose- and time-dependent reductions in ds-DNA due to the formation of DNA-SB. The soluble component caused higher DNA damage. Apoptosis and DNA fragmentation increased dose-dependently. ΔΨm decreased dose-dependently in control cells, but not in cells with Bcl-xl overexpression. PM caused activation of caspase 9. Pretreatment with iron chelators or a free radical scavenger reduced PM-induced DNA-SB formation, DNA fragmentation, caspase 9 activation, and weakened ΔΨm reductions.
Reference: Valavanidis et al. (2005, 096432) **Cell Line:** NR	PM (TSP: high volume pumps, Athens; DEP: 2.0L engine GM Astra; GEP: 1.6L passenger vehicle Ford; Wood smoke soot: domestic fireplace exhaust chimney; PM_{10}: high volume sampling system, Athens; $PM_{2.5}$: high volume cascade impactor (Anderson) system **Particle Size:** >10.2 - <0.41 µm (diameter)	**Route:** Incubation **Dose/Concentration:** 20, 40 mg/5mL **Time to Analysis:** PM incubated with H_2O_2 and 2'-deoxyguanosine (dG). Stored 3-7 days at -20°C.	PM generated ·OH by a Fenton reaction, which is increased by the addition of EDTA but inhibited by deferoxamine. PM dose-dependently induced dG hydroxylation and 8-hydroxy-2'-deoxyguanosine formation. Transition metals Ni, V, Co, Cr that are capable of redox cycling electron producing ROS were found in the PM samples.
Reference: Xu and Zhang (2004, 097231) **Species:** Human **Cell Line:** A549	PM (Taiyuan, Beijing; Nov-Feb) (Taiyuan: coal-fume pollution; Beijing: coal-fume and vehicle exhaust) **Particle Size:** 2.5 µm (diameter)	**Route:** Cell Culture **Dose/Concentration:** 5, 50, 200 µg/mL **Time to Analysis:** 12-24 h	Taiyuan had a significantly higher daily $PM_{2.5}$ average than Beijing. It was shown that the smaller the particulate diameter, the higher the concentration of BaP and Pb. A dose- and time-response relationship was seen in DNA fragmentation.

Annex D References

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Annex E. Epidemiologic Studies

E.1. Short-Term Exposure and Cardiovascular Outcomes

E.1.1. Cardiovascular Morbidity Studies

Table E-1 Short-term exposure – cardiovascular morbidity outcomes: PM_{10}

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Baccarelli et al. (2007, 091310) **Period of Study:** Jan 1995-Aug 2005 **Location:** Lombardia region, Italy	**Outcome:** Fasting and postmethionine-load total homocysteine (tHcy) **Age Groups:** 11-84 yr **Study Design:** Cross-sectional / Panel **N:** 1,213 participants **Statistical Analyses:** Generalized additive models **Covariates:** Age, sex, BMI, smoking, alcohol, hormone use, temperature, day of the yr, and long-term trends **Season:** Adjusted for long-term trends to account for season **Dose-response Investigated?** No **Statistical Package:** R v2.2.1 **Lags Considered:** 1-day, 7-day ma.	**Pollutant:** PM_{10} (some TSP measures used to predict PM_{10}) **Averaging Time:** 24 h **Mean (SD):** NR **Percentiles:** 25th: 20.1 50th: 34.1 75th: 52.6 **Max:** 390.0 **Monitoring Stations:** 53 **Copollutant:** CO, NO_2, SO_2, O_3	**PM Increment:** IQR **Percent Change: [Lower CI, Upper CI]:** Homocysteine, fasting: 0.4 (-2.4, 3.3) Homocysteine, postmethionine-load: 1.1 (-1.5, 3.7) **Percent Change: per 25.7m3 increase in 7-day ma of PM_{10}** Homocysteine, fasting: 1.0 (-1.9, 3.9) Homocysteine, postmethionine-load: 2.0 (-0.6, 4.7) **Percent Change: on fasting homocysteine per IQR increase in 24-h PM_{10} levels** Among smokers: 6.2 (0.0, 12.7) Among non-smokers: -1.6 (-5.5, 2.5) **Percent Change: on postmethionine-load homocysteine per IQR increase in 24-h PM_{10} levels:** Among smokers: 6.0 (0.5, 11.8) Among non-smokers: -0.1 (-3.6, 3.5)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Baccarelli et al. (2007, 090733) **Period of Study:** Jan 1995-Aug 2005 **Location:** Lombardia region, Italy	**Outcome:** Prothrombin time (PT) Activated partial thromboplastin time (APTT) Fibrinogen Functional antithrombin Functional protein C Protein C, antigen Functional protein S Free protein S **Age Groups:** 11-84 yr **Study Design:** Cross-sectional / Panel **N:** 1,218 participants **Statistical Analyses:** Generalized additive models **Covariates:** Age, sex, BMI, smoking, alcohol, hormone use, temperature, day of the yr, and long-term trends **Season:** Adjusted for long-term trends to account for season **Dose-response Investigated?** No **Statistical Package:** R software v2.2.1	**Pollutant:** PM_{10} (some TSP measures used to predict PM_{10}) **Averaging Time:** Hourly concentrations used to calculate lags of same day, 7-day, 30-day, and h 0-6 **Mean (SD):** NR **Percentiles:** Sep-Nov: 5th: 33.1 50th: 51.2 75th: 76.5 Max: 148.9 Dec-Feb: 25th: 47.9 50th: 68.5 75th: 95.3 Max: 238.3 Mar-May: 25th: 30.0 50th: 64.1 75th: 64.8 Max: 158.5 Jun-Aug: 25th: 28.0 50th: 44.3 75th: 61.3 Max: 94.7 **Monitoring Stations:** 53 sites **Copollutant:** CO, NO_2 , SO_2, O_3	**PM Increment:** SD **Effect Estimate [Lower CI, Upper CI]:** Estimated changes in endpoint **PT (international normalized ratio):** At time of blood sample: -0.06 (-0.12, 0.00) Avg levels 7 days prior: -0.03 (-0.10, 0.04) Avg levels 30 days prior: -0.08 (-0.14, -0.01) (Hourly ma presented in Fig 2) **APTT (ratio to reference plasma):** At time of blood sample: 0.02 (-0.04, 0.08) Avg levels 7 days prior: 0.00 (-0.07, 0.06) Avg levels 30 days prior: 0.01 (-0.06, 0.08) **Fibrinogen:** At time of blood sample: 0.01 (-0.05, 0.07) Avg levels 7 days prior: -0.03 (-0.09, 0.04) Avg levels 30 days prior: -0.02 (-0.09, 0.05) **Functional antithrombin:** At time of blood sample: -0.02 (-0.09, 0.04) Avg levels 7 days prior: -0.06 (-0.13, 0.01) Avg levels 30 days prior: -0.06 (-0.13, 0.02) **Functional protein C:** At time of blood sample: 0.00 (-0.06, 6.1) Avg levels 7 days prior: -0.06 (-0.12, 0.01) Avg levels 30 days prior: -0.06 (-0.14, 0.01) **Protein C, antigen:** At time of blood sample: 0.00 (-0.06, 6.0) Avg levels 7 days prior: -0.04 (-0.10, 0.03) Avg levels 30 days prior: -0.06 (-0.14, 0.01) **Functional protein S:** At time of blood sample: 0.04 (-0.03, 0.10) Avg levels 7 days prior: -0.03 (-0.11, 0.06) Avg levels 30 days prior: -0.14 (-0.23, -0.05) **Free protein S:** At time of blood sample: 0.05 (-0.01, 0.10) Avg levels 7 days prior: 0.01 (-0.05, 0.07) Avg levels 30 days prior: -0.01 (-0.08, 0.06)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Barclay et al. (2009, 179935) **Period of Study:** Jan 2003-May 2005 **Location:** Aberdeen, Scotland	**Outcome:** Haematological outcomes, Heart Rhythm outcomes, & Heart Rate Variability outcomes **Age Groups:** 70.4 (8.9) **Study Design:** Panel **N:** 132 patients w/ chronic heart failure **Statistical Analyses:** Linear & Mixed Effects Regression Model **Covariates:** Age, temperature, humidity, pressure **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** Lags 0-2 day	**Pollutant:** PM_{10} **Averaging Time:** daily **Mean (SD):** 20.25 **Min:** 7.375 **Max:** 68.3 **Monitoring Stations:** 1 **Copollutant:** $PM_{2.5}$, PNC, NO_2 **Co-pollutant Correlation:** NO_2 city: 0.294 NO city: 0.112 NO_2 personal: 0.055 PNC DEOM: 0.241 $PM_{2.5}$ total: 0.476* $PM_{2.5}$ traffic: 0.882* PNC total: 0.125 PNC traffic: 0.190 *Correlations based on 3-day avg concentrations	**PM Increment:** NR **Beta (Lower CI, Upper CI):** Haemoglobin: 0.136 (-0.274, 0.546) Mean corpuscular haemoglobin: 0.030 (-0.232, 0.291) Platelets: 0.096 (-0.923, 1.115) Haematocrit: 0.131 (-0.289, 0.551) White blood cells: 0.034 (-1.175, 1.244) C reactive protein: -4.872 (-12.094, 2.351) IL-6: 2.207 (-4.995, 9.410) von Willebrand factor: 0.660 (-2.651, 3.970) E-selectin: -0.536 (-2.528, 1.457) Fibrinogen: -0.432 (-2.470, 1.607) Factor VII: 0.990 (-1.265, 3.245) day-dimer: -1.225 (-4.505, 2.055) All arrhythmias: -3.447 (-11.521, 4.627) Ventricular ectopic beats: -2.110 (-12.135, 7.915) Ventricular couplets: -1.561 (-10.811, 7.689) Ventricular runs: -0.709 (-6.677, 5.259) Supraventricular ectopic beats: 0.033 (-9.242, 9.308) Supraventricular couplets: 0.006 (-8.618, 8.629) Supraventricular runs: 3.710 (-2.847, 10.266) Avg HR: 0.321 (-0.197, 0.838) 24 h SDNN: 1.040 (-0.415, 2.494) 24 h SDANN: 1.195 (-0.473, 2.863) 24 h RMSSD: 0.321 (-0.197, 0.838) 24 h PNN: 2.837 (-3.791, 9.465) 24 h LF power: 0583 (-3.622, 4.787) 24 h LF normalized: -3.137 (-5.540, -0.733)* 24 h HF power: 0.872 (-4.649, 6.392) 24 h HF normalized: -2.223 (-4.952, 0.505) 24 h LF/HF ratio: -0.296 (-3.832, 3.240) *p < 0.05 **Notes:** LF= low frequency HF= high frequency
Reference: Briet et al. (2007, 093049) **Period of Study:** NR **Location:** Paris, France	**Outcome:** Endothelial Function **Age Groups:** 20-40 yr **Study Design:** Panel **N:** 40 white male nonsmokers **Statistical Analyses:** Multiple Robust Regrssion **Covariates:** R53R/R53H genotype, diet, subject factor, visit, temperature **Dose-response Investigated?** No **Statistical Package:** NCSS **Lags Considered:** 0-5 day	**Pollutant:** PM_{10} **Averaging Time:** 24 h **5 day Mean (SD):** 43 (10) **Monitoring Stations:** NR **Co-pollutant:** $PM_{2.5}$, SO_2, NO, NO_2, CO **Co-pollutant Correlation:** N/A	**PM Increment:** 1 SD **Beta (Lower CI, Upper CI), P, R2:** Flow-mediated brachial artery dilation: 0.07 (-0.62, 0.76), NS, 0.03 Reactive hyperemia: 15.91 (7.74, 24.0), <0.001, 0.16

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Choi et al. (2007, 093196) **Period of Study:** 2001-2003 **Location:** Incheon, South Korea	**Outcome:** Blood pressure **Study Design:** Cross-sectional **N:** 10459 subjects with a hospital health examination **Statistical Analyses:** Linear regression **Covariates: Season:** Effect modification by season	**Pollutant:** PM_{10} **Averaging Time:** Measured hourly and calculated 24-h means **Percentiles:** Warm season: Median: 36.7 Cold season: Median: 45.7 **Monitoring Stations:** 9 stations **Copollutant:** NO_2, SO_2	**PM Increment:** 10 $\mu g/m^3$ **Effect Estimate [Lower CI, Upper CI]:** Estimate (p-value) for the relationship between systolic blood pressure (SBP) and diastolic blood pressure (DBP) and an increase in PM_{10} on lag day 1 SBP: Warm season: 0.0798 ($p < 0.001$) DBP: Warm season: 0.0240 ($p < 0.001$) **Note:** No evidence of associations between PM_{10} and BP during the cold season
Reference: Chuang et al. (2007, 091063) **Period of Study:** Between Apr-Jun 2004 or 2005 **Location:** Taipei, Taiwan	**Outcome:** High-sensitivity C-reactive protein (hs-CRP) Fibrinogen, plasminogen activator fibrinogen inhibitor-1 (PAI-1), tissue-type plasminogen activator (tPA), 8-hydroxy-2'-deoxyguanosine (8-OHdG), and log-transformed HRV indices (SDNN = standard deviation of NN intervals, r-MSSD = square root of the mean of the sum of the squares of differences between adjacent NN intervals, LF = low frequency [0.04-0.15Hz], and HF = high frequency [0.15-0.40Hz]) **Age Groups:** 18-25 yr **Study Design:** Panel (cross-sectional) **N:** 76 students **Statistical Analyses:** Linear mixed-effects models **Covariates:** Age, sex, BMI, weekday, temperature of previous day, relative humidity **Season:** Only 1 season of data collection **Dose-response Investigated?** No **Statistical Package:** NR	**Pollutant:** PM_{10} **Averaging Time:** Hourly data used to calculate avg over 1- to 3-day periods **Mean (SD):** 1-day avg: 49.2 (18.0) 2-day avg: 55.3 (18.6) 3-day avg: 54.9 (18.2) **Range (Min, Max):** 1-day avg: 29.5, 83.4 2-day avg: 25.5, 85.1 3-day avg: 22.2, 87.2 **Monitoring Stations:** 2 sites (each pollutant measured at one site only) **Copollutant:** $PM_{2.5}$, Sulfate, Nitrate, OC, EC, NO_2, CO, SO_2, O_3	**PM Increment:** IQR (1-day avg: 32.7 2-day avg: 34.5 3-day avg: 26.0) **Effect Estimate [Lower CI, Upper CI]:** % change in health endpoint per increase in IQR of PM_{10} (1-3 day averaging period single pollutant models) **hs-CRP:** 1-day: 135.8 (1.8, 269.7) 2-day: 108.2 (-10.9, 227.3) 3-day: 109.6 (2.5, 216.7) **8-OHdG:** 1-day: -9.2 (-21.5, 3.2) 2-day: -6.1 (-17.0, 4.8) 3-day: -5.6 (-13.8, 2.6) **PAI-1:** 1-day: 30.0 (12.4, 47.7) 2-day: 19.1 (3.6, 34.7) 3-day: 21.2 (9.7, 32.8) **tPA:** 1-day: 16.0 (-4.1, 36.2) 2-day: 10.4 (-6.3, 27.2) 3-day: 8.8 (-2.8, 20.5) **Fibrinogen:** 1-day: 5.3 (1.5, 15.2) 2-day: 1.5 (-4.4, 7.5) 3-day: 3.3 (-1.1, 7.7) **Heart Rate Variability** **SDNN:** 1-day: -4.9 (-7.8, -2.1) 2-day: -4.0 (-6.6, -1.4) 3-day: -4.1 (-6.1, -2.2) **r-MSSD:** 1-day: -4.8 (-12.3, 2.7) 2-day: -2.2 (-9.0, 4.7) 3-day: -4.0 (-9.0, 0.9) **LF:** 1-day: -6.1 (-10.1, -2.1) 2-day: -3.0 (-7.2, 1.2) 3-day: -4.3 (-7.0, -1.6) **HF:** 1-day: -5.5 (-13.0, 2.1) 2-day: -2.7 (-9.5, 4.1) 3-day: -2.0 (-7.2, 3.2)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ebelt et al. (2005, 056907) **Period of Study:** Summer of 1998 **Location:** Vancouver, Canada	**Outcome:** CVD **Age Groups**: Range from 54-86 yr mean age= 74 yr **Study Design:** Extended analysis of a repeated-measures panel study **N:** 16 persons with COPD **Statistical Analyses:** Earlier analysis expanded by developing mixed-effect regression models and by evaluating additional exposure indicators **Dose-response Investigated?** No **Statistical Package**: SAS V8	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** Ambient PM_{10}: 17 ± 6 Exposure to ambient PM_{10}: 10.3 ± 4.6 **Range (Min, Max):** Ambient $PM_{10-2.5}$: 7−36 Exposure to ambient $PM_{10-2.5}$: 1.5−23.8 **Monitoring Stations**: 5 **Copollutant (correlation):** Ambient concentrations and exposure to ambient PM were highly correlated for each respective metric: r ≥ 0.71 $PM_{10-2.5}$: r ≥ 0.72 $PM_{2.5}$: r ≥ 0.92	**Note:** Total personal fine particle exposure (T) were dominated by exposures to non ambient particles which were not correlated with ambient fine particle exposure (A) or ambient concentrations (C). Results for each of these metrics are listed. **Effect estimates and 95% CI for IQR range increases in exposure** Increment: C10: IQR = 7 μg/m^3 SBP (mm Hg): -2.2 (-4.78-0.38) DBP (mm Hg): -0.78 (-2.65-1.09) Ln-SVE (bph): 0.16 (-0.07-0.40) HR (bpm): 1.02 (-0.79-2.82) SDNN (ms): -2.14 (-6.94-2.65) R-MSSD (ms): -2.24 (-4.27-0.21) Increment: A10: IQR = 6.5μg/m^3 SBP (mm Hg): -2.81 (-5.67-0.05) DBP (mm Hg): -0.59 (-2.79-1.62) Ln-SVE (bph): 0.27 (0.03-0.52) HR (bpm): 0.86 (-1.61-3.33) SDNN (ms): -3.91 (-9.73-1.91) R-MSSD (ms): -0.81 (-4.94-3.31)
Reference: Folino et al. (2009, 191902) **Period of Study:** Jun 2006-May 2007 **Location:** Padua, Italy	**Outcome:** HRV & Inflammatory Markers **Age Groups:** 45-65 yr **Study Design:** Panel **N:** 39 patients w/ myocardial infarction **Statistical Analyses:** Linear Regression Model, ANOVA **Covariates:** Temperature, relative humidity, atmospheric pressure, beta-blocker, aspirin, or nitrate consumption, smoking habit **Dose-response Investigated?** No **Statistical Package:** Stata **Lags Considered:** NR	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** Summer: 46.4 (16.1) Winter: 73.0 (30.9) Spring: 38.3 (15.4) **Monitoring Stations:** NR **Copollutant:** $PM_{2.5}$, $PM_{0.25}$ **Co-pollutant Correlation:** NR	**PM Increment:** 1 μg/m^3 **Beta (SE), p-value:** SDNN: 0.115 (0.093), 0.218 SDANN: 0.138 (0.103), 0.182 RMSSD: 0.049 (0.034), 0.146 pH: 0.002 (0.001), 0.033 LTB4: 0.427 (0.0279), 0.126 eNO: 0.000 (0.002), 0.851 PTX3: -0.003 (0.001), 0.033 C-reactive protein: -0.006 (0.004), 0.161 CC16: -0.002 (0.002), 0.280 IL-8: 0.000 (0.003), 0.895
Reference: Forbes et al. (2009, 190351) **Period of Study:** 1994, 1998, 2003 **Location:** England	**Outcome:** Inflammation markers **Age Groups:** 16+ yr **Study Design: C**ross-sectional **N:** 25,000 white adults w/ fibrinogen measurements & 17,000 white adults w/ C-reactive protein measurements **Statistical Analyses:** Multilevel Linear Regression Models **Covariates:** Age, sex, BMI, social class, region, cigarette smoking **Dose-response Investigated?** No **Statistical Package:** Stata **Lags Considered:** NR	**Pollutant:** PM_{10} **Averaging Time:** Yearly 1994 **Median:** 19.5 **Range:** 12.5-36.1 **IQR:** 3.7 1998 **Median:** 17.9 **Range:** 12.6-27.0 **IQR:** 2.7 2003 **Median:** 16.2 **Range:** 11.0-22.7 **IQR:** 2.6 **Monitoring Stations:** NR **Copollutant:** NO_2, SO_2, O_3 **Co-pollutant Correlation:** N/A	**PM Increment:** 1 μg/m^3 **Percent Change (Lower CI, Upper CI):** Fibrinogen 1994 Crude: -0.068 (-0.367, 0.231) 1994 Adjusted: 0.080 (-0.164, 0.326) 1998 Crude: -0.592 (-0.902, -0.280) 1998 Adjusted: -0.388 (-0.727, -0.047) 2003 Crude: -0.339 (-0.696, 0.019) 2003 Adjusted: -0.069 (-0.458, 0.322) Combined: -0.077 (-0.254, 0.100) C-reactive protein 1998 Crude: -0.914 (-2.206, 0.395) 1998 Adjusted: -0.266 (-1.782, 1.274) 2003 Crude: 0.286 (-1.327, 1.925) 2003 Adjusted: 0.661(-1.068, 2.421) Combined: 0.140 (-1.003, 1.296)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Kaufman (1987, 190960) **Period of Study:** Nov 2004-2005 **Location:** Isfahan, Iran	**Outcome:** Inflammation **Age Groups:** 10-18 yr **Study Design:** Panel **N:** 374 children **Statistical Analyses:** Linear Regression, Logistic Regression **Covariates:** Age, gender, BMI, waist circumference, healthy eating index, physical activity level **Dose-response Investigated?** No **Statistical Package:** SPSS **Lags Considered:** 0- to 7-day avg	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 122.08 (33.63) **0th:** 11.00 **25th:** 86.50 **50th:** 153.0 **75th:** 191.00 **Monitoring Stations:** 3 **Copollutant:** O_3, SO_2, NO_2, CO **Co-pollutant Correlation:** NR	**PM Increment:** NR **Beta (SE):** CRP: 1.5 (0.2) Ox-LDL: 1.4 (0.1) MDA: 1.3 (0.1) CDE: 1.1 (0.1) HOMA-IR: 1.1 (0.3)
Reference: Liao et al. (2004, 056590) **Period of Study:** 1996-1998 **Location:** ARIC study cohort (Washington County, MD Forsyth County, NC and selected suburbs of Minneapolis, MN). The 4th quarter of the ARIC cohort was sampled exclusively from black residents of Jackson, MS.	**Outcome:** 5-min HR, HRV indices (HF, LF, SDNN) **Study Design:** Cross-sectional **Statistical Analyses:** Linear regression	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 24.3 (11.5) **Copollutant:** O_3 CO SO_2 NO_2	**PM Increment:** SD **Effect Estimate [Lower CI, Upper CI]:** Estimate (SE) HF: -0.06 ms2 (0.018) SDNN: -1.03 ms (0.31) H: 0.32 beats/min (0.158)
Reference: Liao et al. (2005, 088677) **Period of Study:** 1987-1989 baseline health exam **Location:** 3 centers in the U.S. (Forsyth County, NC suburbs of Minneapolis, MN black residents of Jackson, MS)	**Outcome:** Fibrinogen, factor VIII co-agulant activity (VIII-C), von Willebrand factor (vWF), white blood cell count (WBC), and serum albumin **Age Groups:** 45-64 yr **Study Design:** Cross-sectional **N:** 10,208 participants (7705 for PM) **Statistical Analyses:** Multiple linear regression **Covariates:** Age, sex, ethnicity-center, education, smoking, drinking status, BMI, history of chronic respiratory disease, humidity, season, cloud cover, and temperature **Dose-response Investigated?** Yes, examined higher-ordered terms for each pollutant **Statistical Package:** SAS v8.2	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg (1, 2, and 3 days prior to the exam) **Mean (SD):** 29.9 (29.9) **Mean (SD) within Quartiles:** Q1-3: 24.0 (6.96) Q4: 47.3 (10.11) **Copollutant:** CO, SO_2, NO_2, O_3	**PM Increment:** 1 SD (12.8 µg/m^3) **Effect Estimate:** Adjusted regression coefficient (SE): Fibrinogen (mg/dl): 0.163 (0.755) Factor VIII-C (%): Non-linear association: β (PM_{10}) = -5.30, $p < 0.01$ β (PM_{10})2 = 0.80, $p < 0.05$ vWF (%): Diabetics: 3.93 (1.80) Nondiabetics: -0.54 (0.58) Albumin (g/dl): CVD: -0.006 (0.003) Non-CVD: 0.029 (0.017) $p < 0.05$

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Liao et al. (2007, 180272) **Period of Study:** 1999-2004 **Location:** 24 U.S. states	**Outcome:** Ectopy **Age Groups:** Women 50-79 yr **Study Design:** Panel **N:** 57,422 **Statistical Analyses:** Logistic regression & random effects modeling **Covariates:** Age, race, center, education, history of CVD/chronic lung disease, rel. humidity, temperature, smoking **Dose-response Investigated?** No **Statistical Package:** SAS, Stata **Lags Considered:** Lags 0-365 day ‡ Monitors used in model for spatial interpolation of daily PM values.	**Pollutant:** PM_{10} **Averaging Time:** Daily **Mean (SD)*:** All: 27.5 (12.1) No Ectopy: 27.5 (12.1) Any Ectopy: 27.5 (11.9) **5th, 95th percentile*:** All: 12.2, 48.9 No Ectopy: 12.3, 48.8 Any Ectopy: 11.8, 49.3 **Monitoring Stations:** NR‡ **Copollutant:** $PM_{2.5}$ **Co-pollutant Correlation:** NR *Lag 1	**PM Increment:** 10 µg/m^3 **Percent Change (Lower CI, Upper CI):** All Ventricular Ectopy Lag 0: 1.01 (0.95, 1.07) Lag 1: 1.02 (0.96, 1.09) Lag 2: 0.99 (0.93, 1.06) Current Smoker Ventricular Ectopy Lag 0: 1.21 (0.96, 1.53) Lag 1: 1.32 (1.07, 1.65) Lag 2: 1.22 (0.95, 1.56) Nonsmoker Ventricular Ectopy Lag 0: 1 (0.93, 1.06) Lag 1: 1.01 (0.94, 1.07) Lag 2: 0.98 (0.92, 1.05) All Supraventricular Ectopy Lag 0: 1 (0.95, 1.06) Lag 1: 1 (0.95, 1.05) Lag 2: 0.99 (0.94, 1.04) All Ventricular or Supraventricular Ectopy Lag 0: 1 (0.95, 1.04) Lag 1: 1 (0.96, 1.04) Lag 2: 0.98 (0.94, 1.02)
Reference: Liu et al. (2007, 156705) **Period of Study:** May 2005-Jul 2005 **Location:** Windsor, Ontario, Canada	**Outcome:** Heart rate, blood pressure, brachial arterial diameter, flow-mediated vasodilatation (FMD), plasma cytokines, and thiobarbituric acid reactive substances (TBARS) **Age Groups:** 18-65 yr **Study Design:** Panel **N:** 24 nonsmoking subjects with type I or II diabetes over a 7 week period (2-14 visits for subjects) 170 total vascular measurements and 134 total blood samples collected **Statistical Analyses:** Mixed effects regression models **Covariates:** (Time-dependent covariates) Daily temperature, relative humidity, blood glucose level, also checked for confounding by ambient air pollutant concentrations (controlled for ambient $PM_{2.5}$) **Season:** No adjustment since testing was completed within a 7-wk period during early summer **Dose-response Investigated?** No **Statistical Package:** S-Plus	**Pollutant:** PM_{10} (personal) **Averaging Time:** Real-time monitor measured exposure during 24-h period prior to clinic measures **Median (5th-95th percentile):** 0-24 h: 25.5 (9.8-133.0) 0-6 h: 15.3 (5.3-83.2) 7-12 h: 17.0 (7.1-186.3) 13-18 h: 28.5 (11.4-167.0) 19-24 h: 30.5 (10.1-148.2) **Monitoring Stations:** Personal monitoring **Copollutant (correlation):** Ambient $PM_{2.5}$ (r = 0.34)	**PM Increment:** 10 µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** **p < 0.05 *p < 0.10. Regression coefficients (SE) **End-diastolic basal diameter (µm):** All subjects (n=24): -2.52 (3.27) subjects not taking vasoactive meds (n=17): -3.93 (3.66) subjects w/BMI ≤ 29kg/m2 (n=14): 8.85 (5.85) **End-systolic basal diameter (µm):** All subjects (n=24): -9.02 (3.58)** subjects not taking vasoactive meds (n=17): -10.59 (4.36)** subjects w/BMI ≤29kg/m2 (n=14): 3.85 (5.49) **End-diastolic FMD (%):** All subjects (n=24): 0.20 (0.08)** subjects not taking vasoactive meds (n=17): 0.23 (0.09)** subjects w/BMI ≤29kg/m2 (n=14): 0.12 (0.05)** **End-systolic FMD (%):** All subjects (n=24): 0.38 (0.18)** subjects not taking vasoactive meds (n=17): 0.51 (0.22)** subjects w/BMI ≤ 29kg/m2 (n=14): 0.18 (0.10)* **Flow (cm/s):** All subjects (n=24): -0.16 (0.19) subjects not taking vasoactive meds (n=17): -0.48 (0.21)** subjects w/BMI ≤ 29kg/m2 (n=14): -0.39 (0.23)* **Heart rate (bpm):** All subjects (n=24): 0.01 (0.11) subjects not taking vasoactive meds (n=17): -0.06 (0.12) subjects w/BMI ≤ 29kg/m2 (n=14): 0.15 (0.12) **Diastolic blood pressure (mm Hg):** All subjects (n=24): 0.19 (0.16) subjects not taking vasoactive meds

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			(n=17): 0.40 (0.18)** subjects w/BMI ≤ 29kg/m2 (n=14): 0.27 (0.21) **Systolic blood pressure (mm Hg):** All subjects (n=24): 0.17 (0.19) subjects not taking vasoactive meds (n=17): 0.43 (0.24)* subjects w/ BMI ≤ 29kg/m2 (n=14): 0.38 (0.24) **CRP (µg/mL):** All subjects (n=24): 0.11 (0.07) subjects not taking vasoactive meds (n=17): 0.10 (0.09) subjects w/ BMI ≤ 29kg/m2 (n=14): 0.02 (0.03) **ET-1 (pg/mL):** All subjects (n=24): 0.00 (0.00) subjects not taking vasoactive meds (n=17): 0.00 (0.00) subjects w/BMI ≤ 29kg/m2 (n=14): 0.00 (0.01) **IL-6 (pg/mL):** All subjects (n=24): 0.00 (0.05) subjects not taking vasoactive meds (n=17): 0.01 (0.05) subjects w/BMI ≤ 29kg/m2 (n=14): -0.00 (0.03) **TNF-α (pg/mL):** All subjects (n=24): 0.03 (0.05) subjects not taking vasoactive meds (n=17): 0.02 (0.05) subjects w/ BMI ≤ 29kg/m2 (n=14): 0.03 (0.08) **TBARS (pmol/mL)** All subjects (n=24): 16.12 (4.00)** subjects not taking vasoactive meds (n=17): 8.10 (9.18) subjects w/ BMI ≤ 29kg/m2 (n=14): -0.28 (6.60) regression coefficients (SE) among subjects not taking vasoactive medications, with lag time **End-diastolic basal diameter (µm):** 0-6 h: 29.91 (10.64)** 7-12 h: 0.72 (3.95) 13-18 h: -3.62 (2.80) 19-24 h: -0.57 (1.7) **End-systolic basal diameter (µm):** 0-6 h: 28.88 (11.22)** 7-12 h: -0.78 (4.58) 13-18 h: -7.70 (3.30)** 19-24 h: -2.87 (2.05) **End-diastolic FMD (%):** 0-6 h: -0.12 (0.10) 7-12 h: 0.04 (0.05) 13-18 h: 0.11 (0.03)** 19-24 h: 0.12 (0.04)** **End-systolic FMD (%):** 0-6 h: 0.36 (0.08)** 7-12 h: 0.48 (0.32) 13-18 h: 0.19 (0.06)** 19-24 h: 0.34 (0.13)** **Flow (cm/s):** 0-6 h: -0.34 (0.22) 7-12 h: -0.26 (0.27 13-18 h: -0.27 (0.15)* 19-24 h: -0.30 (0.11)** **Heart rate (bpm):** 0-6 h: 0.31 (0.13)** 7-12 h: 0.26 (0.12)**

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			13-18 h: 0.01 (0.09) 19-24 h: -0.08 (0.05) **Diastolic blood pressure (mm Hg):** 0-6 h: -0.29 (0.12)** 7-12 h: 0.24 (0.12)** 13-18 h: 0.46 (0.17)** 19-24 h: 0.18 (0.14) **Systolic blood pressure (mm Hg):** 0-6 h: -0.65 (0.18)** 7-12 h: 0.17 (0.19) 13-18 h: 0.86 (0.24)** 19-24 h: 0.11 (0.10) **CRP (µg/mL):** 0-6 h: 0.15 (0.13) 7-12 h: 0.15 (0.13) 13-18 h: 0.03 (0.06) 19-24 h: 0.04 (0.03) **ET-1 (pg/mL):** 0-6 h: 0.02 (0.00)**: 7-12 h: -0.00 (0.00) 13-18 h: -0.00 (0.00) 19-24 h: 0.00 (0.00) **IL-6 (pg/mL):** 0-6 h: 0.03 (0.06) 7-12 h: 0.00 (0.06) 13-18 h: 0.02 (0.03) 19-24 h: 0.00 (0.02) **TNF-α (pg/mL):** 0-6 h: 0.01 (0.07) 7-12 h: 0.09 (0.04)** 13-18 h: 0.01 (0.04) 19-24 h: -0.00 (0.03) **TBARS (pmol/mL):** 0-6 h: -4.44 (6.72) 7-12 h: 11.94 (5.08)** 13-18 h: 5.06 (4.03) 19-24 h: 1.06 (4.64) **Note:** Adding ambient $PM_{2.5}$ data as a covariate in the model yielded similar regression coefficients for personal PM_{10}
Reference: Lipsett et al. (2006, 088753) **Period of Study:** Feb-May 2000 **Location:** Coachella Valley, CA	**Outcome:** HRV parameters: SDNN, SDANN, r-MSSD, LF, HF, total power, triangular index (TRII). **Study Design:** Panel study **N:** 19 non-smoking adults with coronary artery disease **Statistical Analysis:** Mixed linear regression models with random effects parameters	**Pollutant:** PM_{10} **Averaging Time:** 2 h **Mean (range):** Indio: 23.2 (6.3-90.4) Palm Springs: 14 (4.7-52) **Monitoring Stations:** 2 **Copollutant:** O_3	**PM Increment:** SE*1000 **Effect Estimate (change in HRV per unit increase in PM concentration):** SDNN: -0.71 msec (SE = 0.268) **Notes:** Weekly ambulatory 24 h ECG recordings (once per week for up to 12 wk), using Holter monitors, were made. Subjects' residences were within 5 miles of 1 of 2 PM monitoring sites. Regressed HRV parameters against 18:00-20:00 mean particulate pollution.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ljungman et al. (2008, 180266) **Period of Study:** Aug 2001-Dec 2006 **Location:** Gothenburg & Stockholm, Sweden	**Outcome:** Ventricular Arrhythmia **Age Groups:** 28-85 yr **Study Design:** Case-crossover **N:** 88 patients w/ implantable cardioverter defibrillators **Statistical Analyses:** Conditional logistic regression **Covariates:** Temperature, humidity, pressure, ischemic heart disease, ejection fraction, heart disease, diabetes, use of beta-blockers, age, BMI, location at time of arrhythmia, distance from air pollution monitor **Dose-response Investigated?** No **Statistical Package:** Stata, S-plus **Lags Considered:** Lags 2-24 h	**Pollutant:** PM_{10} **Averaging Time:** Hourly Gothenburg, Stockholm **Median:** 2h: 18.95, 14.62 24 h: 19.92, 15.23 **Min:** 2h: 0.00, 0.33 24 h: 2.13, 3.96 **Max:** 2h: 203.75, 159.79 24 h: 78.01, 90.50 **IQR:** 2h: 14.16, 11.59 24 h: 11.49, 9.59 **Monitoring Stations:** 2 **Copollutant:** $PM_{2.5}$, NO_2 **Co-pollutant Correlation** 2 h NO_2: 0.36 24 h NO_2: 0.29	**PM Increment:** Interquartile Range **Odds Ratio (Lower CI, Upper CI):** 2 h: 1.31 (1.00, 1.72) 24 h: 1.24 (0.87, 1.76) **Notes:** OR of ventricular arrhythmia for an IQR increase of air pollutants in different subgroups (Fig 2)
Reference: Ljungman et al. (2009, 191983) **Period of Study:** May 2003-Jul 2004 **Location:** Athens, Greece Helsinki, Finland Ausburg, Germany Barcelona, Spain Rome, Italy Stokholm, Sweeden	**Outcome:** Interleukin-6 Response **Age Groups:** 35-80 yr **Study Design:** Panel **N:** 955 male myocardial infarction survivors **Statistical Analyses:** Additive Mixed Models **Covariates:** Age, sex, BMI, city, HDL/total cholesterol, smoking, alcohol intake, HbA1c, NT-proBNP, history of MI, heart failure, or diabetes, phlegm **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 1 day	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean:** 31.6 **25th:** 21.1 **75th:** 38.4 **Monitoring Stations:** NR **Copollutant:** CO, NO_2, PNC, $PM_{2.5}$ **Co-pollutant Correlation** $PM_{2.5}$: 0.81	**PM Increment:** Interquartile Range (17.4 µg/m^3) **Change of IL-6 (Lower CI, Upper CI), p-value:** 0.0 (-1.3, 1.3), 1.0
Reference: Mar et al. (2005, 087566) **Period of Study:** 1999-2001 **Location:** Seattle, WA	**Outcome:** Change in arterial O_2 saturation, heart rate, and blood pressure (SBP and DBP) **Age Groups:** >75 yr **Study Design:** Panel study **N:** 88 elderly subjects **Statistical Analysis:** GEE	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** Indoor: 12.6 (7.8) Outdoor: 14.5 (7.0)	**PM Increment:** 10 µg/m^3 **Unit change in measure(95% CI): Among all subjects:** Each increase in outdoor same day PM_{10} was associated with: SBP: -0.10 mmHg (95% CI: -1.37, 1.18) DBP: -0.03 mmHg (95% CI: -0.79, 0.73) HR: -0.48 beats/min (95% CI: -1.03, 0.06) **Each increase in indoor same day $PM_{2.5}$ was associated with:** SBP: 0.92 mmHg (95% CI: -0.95, 2.78) DBP: 0.63 mmHg (95% CI: -0.29, 1.56) HR: 0.02 beats/min (95% CI: -0.54, 0.58) **Notes:** Results by health status presented in Fig 1. Used 2 sessions that each were 10 consecutive days of measurement. Used personal, indoor, and outdoor measures of $PM_{2.5}$

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Metzger et al. (2007, 092856) **Period of Study:** Jan 1993-Dec 2002 **Location:** Atlanta, GA	**Outcome:** Days with any event recorded by the ICD, days with ICD shocks/defibrillation and days with either cardiac pacing or defibrillation **Study Design:** Repeated measures **N:** 884 subjects **Statistical Analysis:** Logistic regression with GEE to account for residual autocorrelation within subjects	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 28.0 (12.2) **Median:** 26.4 **Copollutant:** O_3, NO_2, CO, SO_2. Aug1998-Dec2002: Oxygenated hydrocarbons	**PM Increment: OR (95% CI):** Outcome = Any event recorded by ICD OR = 1.00 (95% CI: 0.97, 1.03)
Reference: Min et al. (2008, 191901) **Period of Study:** Dec 2003-Jan 2004 **Location:** Taein Isalnd, South Korea	**Outcome:** Heart Rate Variability **Age Mean (SD):** 44.3 (21.9) **Study Design:** Panel **N:** 1.349 participants **Statistical Analyses:** Linear Regression **Covariates: A**ge, sex, BMI, smoking **Dose-response Investigated?** No **Statistical Package:** SAS, R **Lags Considered:** 0-72 h	**Pollutant:** PM_{10} **Averaging Time:** 1 h **Mean (SD):** 33.244 (19.017) **Percentiles:** 25th: 18.000 50th: 26.000 75th: 41.000 **Range:** 187.000. 16.000 **Monitoring Stations:** 1 **Copollutant:** NO_2, SO_2	**PM Increment:** 1 SD (19 µg/m^3) **Percent Change: [Lower CI, Upper CI]:** SDNN 6-h avg: -4.34 (-7.99, -0.55)** 9-h avg: -5.48 (-9.61, -1.17)**h^ 12-h avg: -6.23 (-10.47, -1.79)*** 24-h-avg: -4.73 (-9.73, 0.56)- 48-h avg: -1.25 (-5.59, 3.29) 72-h avg: -0.85 (-5.35, 3.86) LF 6-h avg: -10.32 (-18.05, -1.86)** 9-h avg: -13.79 (-22.26, -4.39)*** 12-h avg: -14.48 (-23.18, -4.80)*** 24-h-avg: -13.15 (-23.36, -1.57)** 48-h avg: -0.10 (-9.99, 10.87) 72-h avg: -7.61 (-17.04, 2.88) HF 6-h avg: -1.07 (-10.43, 9.28) 9-h avg: -3.28 (-13.72, 8.43) 12-h avg: -4.06 (-14.77, 8.00) 24-h-avg: -1.22 (-13.96, 13.41) 48-h avg: -3.55 (-14.01, 8.18) 72-h avg: -3.88 (-14.64, 8.23) **Notes:** Percent change in HRV for air pollution children, adults, and the elderly (Fig 2) Percent change in HRV for PM_{10} exposure in all ages (Fig 3)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Peters et al. (2009, 191992) **Period of Study:** May 2003-Jul 2004 **Location:** Helsinki, Finland Ausburg, Germany Barcelona, Spain Rome, Italy Stokholm, Sweeden	**Outcome:** Plasma Fibrinogen **Age Groups:** 37-81 **Study Design:** Panel **N:** 854 adults **Statistical Analyses:** Additive Mixed Models **Covariates:** Age, sex, BMI, city, HDL/total cholesterol, smoking, HbA1c, NT-proBNP, history of arrhythmia, asthma, arthrosis, stroke, bronchitis, season, apparent temperature, relative humidity, weekday, hour of visit **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 0- to 5-day avg	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 30.3 **Min:** 0 **Max:** 194 **Monitoring Stations:** NR **Copollutant:** $PM_{2.5}$, $PM_{10-2.5}$ **Co-pollutant Correlation:** NR	**PM Increment:** 13.5 µg/m^3 **Change (Lower CI, Upper CI):** Genotype 1 1 rs2070006: 1.22 (0.47, 1.96) rs2070011: 1.16 (0.41, 1.90) rs1800790: 0.27 (-0.36, 0.91) rs2227399: 0.27 (-0.36, 0.91) rs6056: 0.19 (-0.45, 0.83) rs4220: 0.19 (-0.45, 0.83) Haplotype in cluster 2: 0.09 (-0.53, 0.76) rs1800791: 0.18 (0.21, 1.40) Genotype 1 2 rs2070006: 0.5 (-0.19, 2.15) rs2070011: 0.42 (-0.28, 1.13) rs1800790: 1.28 (0.54, 2.01) rs2227399: 1.28 (0.55, 2.02) rs6056: 1.26 (0.49, 2.04) rs4220: 1.27 (0.49, 2.04) Haplotype in cluster 2: 1.17 (0.35, 1.99) rs1800791: 0.40 (-0.48, 1.28) Genotype 2 2 rs2070006: 0.11 (-1.94, 2.15) rs2070011: 0.08 (-2.08, 2.24) rs1800790: 2.15 (0.71, 3.60) s2227399: 2.18 (0.73, 3.63) s6056: 2.24 (0.72, 3.77) s4220: 2.25 (0.73, 3.78) Haplotype in cluster 2: 2.16 (0.61, 3.71) rs1800791: -0.13 (-1.84, 1.58)
Reference: Rosenlund et al. (2007, 114679) **Period of Study:** 1985-1996 **Location:** Stockholm County	**Outcome:** Myocardial Infarction **Age Groups:** 15-79 yr **Study Design:** Case-control **N:** 24,387 first event of myocardial infarction cases and 276,926 population based controls **Statistical Analyses:** Logistic Regression **Covariates:** Age, sex, calendar yr, SES **Dose-response Investigated?** No **Statistical Package:** Stata **Lags Considered:** 5 yr	**Pollutant:** PM_{10} **Averaging Time:** 5 yr **Median:** 2.4 **5th-95th:** 0.3-6.2 **Median:** 2.2 **5th-95th:** 0.3-6.0 **Monitoring Stations:** NR **Copollutant:** NO_2, CO **Co-pollutant Correlation:** HNR	**PM Increment:** 5th-95th percentile (5µg/m^3) **Odds Ratio (Lower CI, Upper CI):** All Subjects Controls: 1.0 All Cases: 1.04 (1.00, 1.09) Nonfatal Cases: 0.98 (0.963, 1.03) Fatal Cases: 1.16 (1.09, 1.24) In-hospital death: 1.05 (0.95, 1.17) Out-of-hospital death: 1.23 (1.14, 1.33) Subjects who did not move b/t population censuses Controls: 1.0 All Cases: 1.11 (1.02, 1.21) Nonfatal Cases: 1.05 (0.96, 1.15) Fatal Cases: 1.56 (1.28, 1.91) In-hospital death: 1.58 (1.13, 2.19) Out-of-hospital death: 1.56 (1.22, 1.98)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ruckerl et al. (2007, 156931) **Period of Study:** May 2003-Jul 2004 **Location:** Athens, Augsburg, Barcelona, Helsinki, Rome, and Stockholm	**Outcome:** Interleukin-6 (IL-6), fibrinogen, C-reactive protein (CRP) **Age Groups:** 35-80 yr **Study Design:** Repeated measures/ longitudinal **N:** 1003 MI survivors **Statistical Analyses:** Mixed-effect models **Covariates:** City-specific confounders (age, sex, BMI) long-term time trend and apparent temperature RH, time of day, day of week included if adjustment improved model fit **Season:** Long-term time trend **Dose-response Investigated?** Used p-splines to allow for nonparametric exposure-response functions **Statistical Package:** SAS v9.1	**Pollutant:** PM_{10} **Averaging Time:** Hourly and 24 h (lag 0-4, mean of lags 0-4, mean of lags 0-1, mean of lags 2-3, means of lags 0-3) **Mean (SD):** Presented by city only **Percentiles:** NR **Range (Min, Max):** NR **Monitoring Stations:** Central monitoring sites in each city **Copollutant:** SO_2 O_3 NO NO_2	**PM Increment:** IQR **Effect Estimate [Lower CI, Upper CI]:** % change in mean blood markers per increase in IQR increase of air pollutant. **IL-6:** Lag (IQR): % change in GM (95%CI) Lag 0 (17.4): -0.34 (-1.66, 0.99) Lag 1 (17.4): -0.69 (-1.95, 0.58) Lag 2 (17.4): -1.59 (-3.99, 0.88) 5-day avg (13.5): -0.87 (-2.28, 0.55) **Fibrinogen:** Lag (IQR): % change in AM (95%CI) Lag 0 (17.4): 0.06 (-0.43, 0.55) Lag 1 (17.4): 0.14 (-0.35, 0.63) Lag 2 (17.4): 0.24 (-0.24, 0.72) 5-day avg (13.5): 0.60 (0.10, 1.09) **CRP:** Lag (IQR): % change in GM (95%CI) Lag 0 (17.4): -0.71 (-2.75, 1.37) Lag 1 (17.4): -0.63 (-2.61, 1.39) Lag 2 (17.4): -1.42 (-4.23, 1.47) 5-day avg (13.5): -1.35 (-3.45, 0.79)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ruckerl et al. (2006, 088754) **Period of Study:** Oct 2000-Apr 2001 **Location:** Erfurt, Germany	**Outcome:** C-reactive protein (CRP) serum amyloid A (SAA) E-selectin vWF intercellular adhesion molecule-1 (ICAM-1) fibrinogen Factor VII prothrombin fragment 1+2 D-dimer **Age Groups:** 50+ yr **Study Design:** Panel (12 repeated measures at 2-wk intervals) **N:** 57 male subjects with coronary disease **Statistical Analyses:** Fixed effects linear and logistic regression models **Covariates:** Models adjusted for different factors based on health endpoint CRP: RH, temperature, trend, ID ICAM-1: temperature, trend, ID vWF: air pressure, RH, temperature, trend, ID FVII: air pressure, RH, temperature, trend, ID, weekday **Season:** Time trend as covariate **Dose-response Investigated?** Sensitivity analyses examined nonlinear exposure-response functions **Statistical Package:** SAS v8.2 and S-Plus v6.0	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 20.0 (13.0) **Percentiles:** 25th: 10.8 50th: 15.6 75th: 26.0 **Range (Min, Max):** 5.4, 74.5 **Monitoring Stations:** 1 site **Copollutant:** UFPs AP $PM_{2.5}$ PM_{10} OC EC NO_2 CO	**PM Increment:** IQR (15.2 5-day avg: 12.8) **Effect Estimate [Lower CI, Upper CI]:** Effects of air pollution on blood markers presented as OR (95%CI) for an increase in the blood marker above the 90th percentile per increase in IQR air pollutant. **CRP:** Time before draw: 0-23 h: 1.2 (0.8, 1.9) 24-47 h: 2.0 (1.1, 3.6) 48-71 h: 2.2 (1.2, 3.8) 5-day mean: 2.0 (1.2, 3.7) **ICAM-1:** Time before draw: 0-23 h: 1.3 (0.9, 1.8) 24-47 h: 3.1 (2.0, 4.8) 48-71 h: 3.4 (2.2, 5.2) 5-day mean: 3.4 (2.2, 5.3) Effects of air pollution on blood markers presented as % change from the mean/GM in the blood marker per increase in IQR air pollutant. **vWF:** Time before draw: 0-23 h: 4.0 (-0.6, 8.5) 24-47 h: 6.0 (0.6, 11.5) 48-71 h: 1.1 (-4.9, 7.0) 5-day mean: 6.1 (-0.6, 12.8) **FVII:** Time before draw: 0-23 h: -6.6 (-10.4--2.5) 24-47 h: -8.4 (-12.3--4.3) 48-71 h: -5.9 (-9.6, -2.0) 5-day mean: -8.0 (-12.4, -3.4) **Note:** Summary of results presented in figures. SAA results indicate increases in association with PM (not as strong and consistent as with CRP) No association observed between E-selectin and PM An increase in prothrombin fragment 1+2 was consistently observed, particularly with lag 4 Fibrinogen results revealed few significant associations, potentially due to chance D-dimer results revealed null associations in linear and logistic analyses

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ruckerl et al. (2007, 091379) **Period of Study:** Oct 2000-Apr 2001 **Location:** Erfurt, Germany	**Outcome:** Soluble CD40 ligand (sCD40L), platelets, leukocytes, erythrocytes, hemoglobin **Age Groups:** 50+ yr **Study Design:** Panel (12 repeated measures at 2-wk intervals) **N:** 57 male subjects with coronary disease **Statistical Analyses:** Fixed effects linear regression models **Covariates:** Long-term time trend, weekday of the visit, temperature, RH, barometric pressure **Season:** Time trend as covariate **Dose-response Investigated?** No **Statistical Package:** SAS v8.2 and S-Plus v6.0	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 20.0 (13.0) **Percentiles:** 25th: 10.8 50th: 15.6 75th: 26.0 **Range (Min, Max):** 5.4, 74.5 **Monitoring Stations:** 1 site **Copollutant:** UFPs AP $PM_{2.5}$ PM_{10} NO	**PM Increment:** IQR (15.2 5-day avg: 12.8) **Effect Estimate [Lower CI, Upper CI]:** Effects of air pollution on blood markers presented as % change from the mean/GM in the blood marker per increase in IQR air pollutant. **sCD40L, % change GM (pg/mL):** lag0: 1.6 (-3.5, 7.0) lag 1: 1.1 (-5.4, 7.9) lag 2: -3.5 (-8.9, 2.2) lag 3: -1.4 (-6.0, 3.4) 5-day mean: -1.2 (-7.8, 5.8) **Platelets, % change mean (103/µl):** lag 0: -0.4 (-1.9, 1.0) lag 1: 0.4 (-1.4, 2.3) lag 2: 0.5 (-1.4, 2.3) lag 3: -0.1 (-1.6, 1.4) 5-day mean: 0.0 (2.1, 0.0) **Leukocytes, % change in mean (103/µl):** lag0: -1.1 (-2.8, 0.7) lag 1: -0.5 (-2.6, 1.5) lag 2: 0.1 (-2.1, 2.4) lag 3: -0.7 (-2.6, 1.2) 5-day mean: -1.1 (-3.6, 1.4) **Erythrocytes, % change mean (106/µl):** lag0: 0.0 (-0.4, 0.5) lag 1: -0.4 (-1.0, 0.1) lag 2: -0.7 (-1.2, -0.2) lag 3: -0.4 (-0.8, 0.0) 5-day mean: -0.6 (-1.2, -0.1) **Hemoglobin, % change mean (g/dl):** lag 0: -0.1 (-0.7, 0.6) lag 1: -0.4 (-1.2, 0.3) lag 2: -0.7 (-1.3, 0.0) lag 3: -0.3 (-0.9, 0.2) 5-day mean: -0.7 (-1.5, 0.1)
Reference: Steinvil et al. (2008, 188893) **Period of Study:** 2003-2006 **Location:** Tel-Aviv, Israel	**Outcome:** Inflammation **Age Groups:** Mean (SD): 46 (12) yr **Study Design:** Panel **N:** 3659 **Statistical Analyses:** Linear Regression **Covariates:** Age, waist circumference, BMI, HDL, OLDL, triglycerides, diastolic & systolic BP, alcohol consumption, sports intensity, medications, smoking status, family history of CHD, temperature, humidity, precipitation, season, & yr **Dose-response Investigated?** No **Statistical Package:** SPSS **Lags Considered:** 0-7 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 64 (100.8) **25th:** 33.1 **50th:** 43.0 **75th:** 60.7 **Monitoring Stations:** NR **Copollutant:** SO_2, NO_2, O_3, CO **Co-pollutant Correlation:** SO_2: 0.043 NO_2: 0.082 O_3: -0.113 CO: 0.075	**PM Increment:** Interquartile Range (27.6 µg/m^3) **hs-CRP Relative % Change (Lower CI, Upper CI):** Men: Lag 0: -1 (-2, 1) Lag 1: 0 (-1, 1); Lag 2: -1 (-2, 1) Lag 3: -1 (-2, 0) Lag 4: 0 (-1, 1) Lag 5: 0 (-1, 2) Lag 6: 1 (0, 2) Lag 7: 1 (0, 1) 0-7 avg: -2 (-5, 1) Women: Lag 0: 0 (-2, 2) Lag 1: 0 (-1, 2) Lag 2: 1 (0, 2) Lag 3: 0 (-1, 1) Lag 4: 0 (-1, 2) Lag 5: 0 (-1, 2) Lag 6: -1 (-3, 1) Lag 7: 0 (-2, 1) 0-7 avg: 1 (-2, 4) **Fibrinogen Absolute % Change (Lower CI, Upper CI):** Men: Lag0: 0.7(0.0,1.5); Lag1: 0.4(-0.2, 0.9); Lag2: -0.1(-0.9, 0.6) Lag3: -0.1(-0.7, 0.6); Lag4: 0.0(-0.7, 0.7); Lag5: 0.1(-0.7, 1.0) Lag6: 0.6(-0.1, 1.3); Lag7: 0.4(0.0, 0.8);

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			0-7 avg: -0.4(-1.9, 1.0) Women: Lag0: 0.3(-0.6, 1.2); Lag1: -0.1(-0.8, 0.7); Lag2: -0.3(-0.9, 0.3) Lag3: -0.1(-0.7, 0.5); Lag4: 0.2(-0.4, 0.9); Lag5: 0.2(-0.7, 1.2) Lag6: -0.3(-1.4, 0.8); Lag7: 0.7(-0.1, 1.5); 0-7 avg: 0.0(-1.5, 1.5) **WBC Absolute Change (Lower CI, Upper CI):** Men: Lag0: 2 (-22, 27) Lag1: 3 (-14, 19) Lag2: 1 (-22, 24) Lag3: -7 (-28, 14) Lag4: -22 (-44, -1) Lag5: -20 (-46, 7) Lag6: -5 (-27, 16) Lag7: -4(-16, 9) 0-7avg: -11(-58, 36) Women: Lag 0: 20 (-6, 46)
Reference: Su et al. (2006, 157022) **Period of Study:** Feb-Apr 2002 **Location:** Taipei, Taiwan	**Outcome:** Total cholesterol, HDL, tryglycerides, LDL, hs-CRP, IL-6, TNF-α, tPA, PAI-1, and fibrinogen **Age Groups:** 40-75 yr **Study Design:** Panel study **N:** 49 subjects (31 males and 18 females) with coronary heart disease or multiple risk factors for CHD **Statistical Analysis:** Linear mixed effects regression	**Pollutant:** PM_{10} **Averaging Time:** 1 h (High pollution day = PM_{10} from 08: 00-18: 00 >100) **Copollutant:** O_3	**PM Increment:** High vs.. Low pollution days **Effect Estimate [Lower CI, Upper CI]: CHD patients (n = 23):** P-value for paired t-test comparing health endpoint means on high and low pollution days hs-CRP: p = 0.568 IL-6: p = 0.856 TNF-α: p = 0.246 PAI-1: p = 0.008 tPA: p = 0.322 Fibrinogen: p = 0.189 P-value for health endpoint in mixed-effects models PAI-1: p = 0.010 tPA: p = 0.329 Fibrinogen: p = 0.747 **Patients with multiple CHD risk factors (n = 26):** P-value for paired t-test comparing health endpoint means on high and low pollution days hs-CRP: p = 0.475 IL-6: p = 0.561 TNF-α: p = 0.572 PAI-1: p = 0.098 tPA: p = 0.260 Fibrinogen: p = 0.087 P-value for health endpoint in mixed-effects models PAI-1: p = 0.891 tPA: p = 0.789 Fibrinogen: p = 0.923 **Notes:** Subjects had paired fasting blood samples taken during high and low air pollution days.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Vedal et al., (2004, 055630) **Period of Study:** 1997-2000 **Location:** Vancouver, British Columbia	**Outcome:** Implantable cardioverter defibrillator (ICD) discharge **Age Groups:** All **Study Design:** Time series (Retrospective, longitudinal panel study) **N:** 50 ICD patients with 1+ discharges (40,328 person-days and 257 arrhythmia event days) **Statistical Analyses:** Multiple logistic regression with GEE **Covariates:** Temperature, relative humidity, barometric pressure, rainfall, wind direction and speed **Season:** Summer (May-Sep) and winter (Oct-Apr) **Dose-response Investigated:** No **Statistical Package:** NR **Lags Considered:** -3 day	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (min-max):** 12.9 (3.8-49.3) SD = 5.6 **Monitoring Stations:** 8 **Copollutant (correlation):** O_3: r = 0.11 SO_2: r = 0.70 NO_2: r = 0.49 CO: r = 0.43 **Other variables:** Temp: r = 0.43 Humidity: r = -0.35 Baro Pressure: r = 0.26 Rain: r = -0.63 Wind: r = -0.53	**PM Increment:** 5.6 µg/m^3 (SD) Percent Change [CI]: Values NR **Notes**: The author states that significant negative associations were found for ICD discharge with same-day lag, and also for 3-day lag with more arrhythmia-prone patients. All other non-significant percent change estimates are shown in Fig 3 and 4.
Reference: Vedal et al. (2004, 055630) **Period of Study:** 1997-2000 **Location:** Vancouver, British Columbia, Canada	**Outcome:** ICD discharges (arrhythmias) **N:** 150 patients w/ICD, 4 yr **Statistical Analysis:** Logistic regression, GEE **Covariates:** Temporal trends, temperature, relative humidity, wind speed, rain **Season:** Summer, winter **Dose-response Investigated?** No **Lags Considered:** 0, 1, 2, and 3 days	**Pollutant:** PM_{10} **Mean:** 12.9 (SD = 5.6) **Copollutant):** O_3, SO_2, NO_2, CO	**Increment:** 1 SD Effect Estimates, e.g., % change in the rate of arrhythmia, were presented in Fig 3. No association with PM_{10} was observed while SO_2 was associated with an increase in the rate of arrhythmia among 16 patients with at least 2 discharges per yr.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Whitsel et al. (2009, 191980) **Period of Study:** 1993-2004 **Location:** U.S.	**Outcome:** Heart Rate Variability **Age Groups:** 50-79 yr **Study Design:** Panel **N:** 4,295 women **Statistical Analyses:** Random Effects Model **Covariates:** Temperature, humidity **Dose-response Investigated?** No **Statistical Package:** SUDAAN **Lags Considered:** 0	**Pollutant:** PM_{10} **Averaging Time:** 24 h Amsterdam **Mean:** 20.0 **Min:** 3.8 **25th:** 10.4 **50th:** 16.9 **75th:** 23.9 **Max:** 82.2 Erfurt **Mean:** 23.1 **Min:** 4.5 **25th:** 10.5 **50th:** 16.3 **75th:** 27.4 **Max:** 118.1 Helsinki **Mean:** 12.7 **Min:** 3.1 **25th:** 8.1 **50th:** 10.6 **75th:** 16.0 **Max:** 39.8 **Monitoring Stations: 3** **Copollutant:** NR **Co-pollutant Correlation:** N/A	**PM Increment:** 10 µg/m^3 **Beta (Lower CI, Upper CI):** Supine Position, Amsterdam Lag 0: -0.06 (-0.95, 0.84) Lag 1: 0.18 (-0.74, 1.10) Lag 2: 0.93 (0.01, 1.85) 5-day avg: 0.49 (-0.74, 1.72) Supine Position, Erfurt Lag 0: -0.36 (-0.83, 0.11) Lag 1: -0.40 (-0.91, 0.11) Lag 2: -0.68 (-1.20, -0.17) 5-day avg: -0.68 (-1.44, 0.09) Supine Position, Helsinki Lag 0: -0.44 (-2.27, 1.40) Lag 1: -0.17 (-1.69, 1.3.5) Lag 2: -1.14 (-2.51, 0.23) 5-day avg: -0.59 (-3.08, 1.90) Supine Position, Pooled Lag 0: -0.30 (-0.71, 0.11) Lag 1: -0.25 (-0.68, 0.18) Lag 2: -0.26 (-1.22, 0.70)* 5-day avg: -0.36 (-0.99, 0.27) Standing Position, Amsterdam Lag 0: -0.44 (-1.6, 0.72) Lag 1: -0.61 (-1.8, 0.59) Lag 2: 0.32 (-0.88, 1.51) 5-day avg: -0.55 (-2.15, 1.04) Standing Position, Erfurt Lag 0: -0.59 (-1.24, 0.06) Lag 1: -0.70 (-1.42, 0.03) Lag 2: -0.65 (-1.37, 0.07) 5-day avg: -0.68 (-1.74, 0.39) Standing Position, Helsinki Lag 0: 1.17 (-1.46, 3.80) Lag 1: 0.01 (-2.17, 2.19) Lag 2: -0.63 (-2.60, 1.34) 5-day avg: -1.96 (-5.51, 1.60) Standing Position, Pooled Lag 0: -0.48 (-1.03, 0.07) Lag 1: -0.62 (-1.21, -0.03) Lag 2: -0.41 (-1.00, 0.17) 5-day avg: -0.72 (-1.57, 0.14) *p < 0.1
Reference: Yeatts et al. (2007, 091266) **Period of Study:** 12-wk period b/t Sep 2003-Jul 2004 **Location:** Chapel Hill, NC	**Outcome:** Heart Rate Variability **Age Groups:** 21-50 yr **Study Design:** Panel **N:** 12 asthmatics **Statistical Analyses:** Linear Mixed Model **Covariates:** Temperature, humidity, pressure **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 1 day	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 17.5 (7.8) **Min:** 1.4 **Max:** 45.6 **Monitoring Stations:** 1 **Copollutant:** $PM_{2.5}$, $PM_{10-2.5}$ **Co-pollutant Correlation** $PM_{2.5}$ = 0.90* $PM_{10-2.5}$ = 0.73* *p < 0.01	**PM Increment:** 1 µg/m^3 **Beta, SE, p-value (Lower CI, Upper CI):** NR

[1]All units expressed in µg/m^3 unless otherwise specified.

Table E-2. Short-term exposure - cardiovascular morbidity studies: $PM_{10-2.5}$.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Chuang et al. (2007, 091063) **Period of Study:** Nov 2002-Mar 2003 **Location:** Taipei, Taiwan	**Outcome:** Heart Rate Variability **Age Groups:** 52-76 yr **Study Design:** Panel **N:** 10 CHD & 16 Hypertensive Patients **Statistical Analyses:** Linear Mixed Effects Model **Covariates:** Age, sex, BMI, time of day, temperature, humidity, pressure, HRV **Dose-response Investigated?** No **Statistical Package:** S-PLUS **Lags Considered:** 1- to 4-h ma	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 1 h among CHD, among hypertensive **Mean (SD):** 16.4 (10.7), 14.0 (11.1) **IQR:** 14.8, 11.9 **Min:** 0.7, 0.3 **Max:** 59.6, 66.5 **Monitoring Stations:** 1 personal monitor each **Copollutant:** $PM_{1.0-2.5}$, $PM_{0.3-1.0}$ **Co-pollutant Correlation:** NR	**PM Increment:** Interquartile range **Percent Change (Lower CI, Upper CI):** Cardiac Patients- SDNN 1h moving: -1.73 (-3.53, 0.08) 2h moving: -1.97 (-4.43, 0.49) 3h moving: -1.70 (-4.39, 0.89) 4h moving: -1.75 (-5.42, 1.92) Cardiac Patients- r-MSSD 1h moving: -4.39 (-9.54, 0.03) 2h moving: -4.36 (-8.99, 0.27) 3h moving: -4.20 (-9.02, 0.61) 4h moving: -2.70 (-9.24, 3.84) Cardiac Patients- LF 1h moving: -1.85 (-4.33, 0.62) 2h moving: -3.87 (-8.22, 0.47 3h moving: -2.98 (-6.65, 0.69) 4h moving: -3.11 (-8.22, 1.99) Cardiac Patients- HF 1h moving: -4.46 (-9.23, 0.32) 2h moving: -4.41 (-9.55, 0.72) 3h moving: -3.80 (-9.12, 1.53) 4h moving: -3.39 (-10.62, 3.84) Cardiac Patients- LF: HF ratio 1h moving: 8.45 (-3.48, 20.38) 2h moving: 1.66 (-15.22, 18.55) 3h moving: 11.69 (-7.27, 30.64) 4h moving: 8.18 (-17.22, 33.57) Hypertensive Patients- SDNN 1h moving: -2.64 (-3.93, 0.55 2h moving: -3.51 (-7.87, 0.85) 3h moving: -2.74 (-6.22, 0.74) 4h moving: -2.49 (-6.13, 1.15) Hypertensive Patients- r-MSSD 1h moving: -2.53 (-5.10, 0.04) 2h moving: -5.42 (-10.92, 0.09) 3h moving: -3.15 (-6.32, 0.03) 4h moving: -4.23 (-8.88, 0.42) Hypertensive Patients- LF 1h moving: -4.38 (-8.78, 0.03) 2h moving: -5.23 (-10.95, 0.05) 3h moving: -3.34 (-1.72, 0.04) 4h moving: -2.96 (-6.63, 0.71) Hypertensive Patients- HF 1h moving: -4.92 (-9.94, 0.10) 2h moving: -6.07 (-12.28, 0.13) 3h moving: -1.94 (-5.44, 1.55) 4h moving: -2.78 (-6.78, 1.21) Hypertensive Patients- LF: HF ratio 1h moving: 5.94 (-3.27, 15.15) 2h moving: 10.70 (-2.19, 23.59) 3h moving: -1.51 (-17.02, 14.00) 4h moving: 3.41 (-16.91, 23.74) *p < 0.05

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ebelt et al. (2005, 056907) **Period of Study:** Summer of 1998 **Location:** Vancouver, Canada	**Outcome:** CVD **Age Groups**: range from 54-86 yr mean age= 74 yr **Study Design:** extended analysis of a repeated-measures panel study **N:** 16 persons with COPD **Statistical Analyses:** Earlier analysis expanded by developing mixed-effect regression models and by evaluating additional exposure indicators **Dose-response Investigated?** No **Statistical Package**: SAS V8	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 24 h **Mean (SD):** Ambient $PM_{10-2.5}$: 5.6 (3.0) Exposure to ambient $PM_{10-2.5}$: 2.4 (1.7) **Range (Min, Max):** Ambient $PM_{10-2.5}$: (-1.2-11.9) Exposure to ambient $PM_{10-2.5}$: (-0.4-7.2) **Monitoring Stations**: 5 **Copollutant (correlation):** Ambient concentrations and exposure to ambient PM were highly correlated for each respective metric: r ≥ 0.71	**Note:** Total personal fine particle exposure (T) were dominated by exposures to non ambient particles which were not correlated with ambient fine particle exposure (A) or ambient concentrations (C). Results for each of these metrics are listed. **PM Increment:** Increment: C10-2.5: IQR = 4.5 μg/m^3 SBP (mm Hg): -2.12 (-5.07-0.82) DBP (mm Hg): -0.92 (-3.37-0.36) Ln-SVE (bph): 0.06 (-0.24-0.36) HR (bpm): 1.09 (-0.69-2.86) SDNN (ms): 2.64 (-2.85-8.13) R-MSSD (ms): -0.33 (-4.49-3.82) Increment: A10-2.5: IQR = 2.4 μg/m^3 SBP (mm Hg): -2.55 (-6.15-1.05) DBP (mm Hg): -0.75 (-3.50-2.01) Ln-SVE (bph): 0.26 (-0.07-0.58) HR (bpm): 1.04 (-0.95-3.03) SDNN (ms): 0.68 (-3.07-4.42) R-MSSD (ms): 1.10 (-3.08-5.28)
Reference: Lipsett et al. (2006, 088753) **Period of Study:** Feb-May 2000 **Location:** Coachella Valley, CA	**Outcome:** HRV parameters, specifically SDNN, SDANN, r-MSSD, LF, HF, total power, triangular index (TRII). **Study Design:** Panel study **N:** 19 non-smoking adults with coronary artery disease **Statistical Analysis:** Mixed linear regression models with random effects parameters	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 2 h **Monitoring Stations:** 2 **Copollutant:** O_3	**PM Increment:** SE*1000 **Effect Estimate (change in HRV per unit increase in PM concentration):** SDNN: -0.72 msec (SE = 0.296) **Notes:** $PM_{10-2.5}$ calculated by subtracting $PM_{2.5}$ concentration from PM_{10} concentration. Weekly ambulatory 24-h ECG recordings (once per wk for up to 12 wk), using Holter monitors, were made. Subjects' residences were within 5 mi of 1 of 2 PM monitoring sites. Regressed HRV parameters against 18: 00-20: 00 mean particulate pollution
Reference: Metzger et al. (2007, 092856) **Period of Study:** Aug 1998-Dec 2002 **Location:** Atlanta, GA	**Outcome:** Days with any event recorded by the ICD, days with ICD shocks/defibrillation and days with either cardiac pacing or defibrillation **Study Design:** Repeated measures **N:** 884 subjects between 1993 and 2002 **Statistical Analysis:** Logistic regression with GEE to account for residual autocorrelation within subjects	**Pollutant:** $PM_{10-2.5}$ (n/cm^3) **Averaging Time:** 24 h **Mean (SD):** 9.6 (5.4) **Median:** 8.7 **Copollutant:** O_3, NO_2, CO, SO_2, oxygenated hydrocarbons	**PM Increment: OR (95% CI):** OR = 1.03 (95% CI: 1.00, 1.07)
Reference: Pekkanen et al. (2002, 035050) **Period of Study:** Winter 1998-1999 **Location:** Helsinki, Finland	**Outcome**: ST Segment Depression (>0.1mV) **Study Design**: Panel of ULTRA Study participants **N**: 45 subjects, 342 biweekly submaximal exercise tests, 72 exercise induced ST Segment Depressions **Statistical Analysis:** Logistic regression / GAM	**Pollutant:** $PM_{10-2.5}$ (n/cm^3) **Averaging Time:** 24 h **Median**: 4.8 **IQR**: 5.5 **Monitoring Stations**: 1 **Copollutant:** NO_2, CO, $PM_{2.5}$, PM_1, ACP, ultrafine	**PM Increment:** IQR **Effect Estimate(s):** $PM_{10-2.5}$: OR = 1.99 (0.70, 5.67), lag 2 **Notes**: The effect was strongest for ACP and $PM_{2.5}$, which in 2 pollutant models appeared independent. Increases in NO_2 and CO were also associated with increased risk of ST segment depression, but not with coarse particles.
Reference: Timonen et al. (2006, 088747) **Period of Study:** 1998-1999 **Location:** Amsterdam, Netherlands Erfurt, Germany Helsinki, Finland	**Outcome:** HRV measurements: [LF, HF, LFHFR, NN interval, SDNN, r-MSSD] **Study Design:** Panel study **N:** 131 elderly subjects with stable coronary heart disease **Statistical Analysis:** Linear mixed models	**Pollutant:** $PM_{10-2.5}$ **Means:** Amsterdam: 15.3 Erfurt: 3.7 Helsinki: 6.7 **Copollutant:** NO_2, CO	**PM Increment:** 10 μg/m^3 **Effect Estimate:** SDNN 0.69ms (95% CI: -1.24, 2.63) HF: 2.9% (95% CI: -7.3, 13.1) LFHFR: -3.3 (95% CI: -12.7, 6.1) **Notes:** Followed for 6 mo with biweekly clinic visits 2-day lag. ULTRA Study

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Yeatts et al. (2007, 091266) **Period of Study:** 12-wk period b/t Sep 2003-Jul 2004 **Location:** Chapel Hill, NC	**Outcome:** Heart Rate Variability **Age Groups:** 21-50 yr **Study Design:** Panel **N:** 12 asthmatics **Statistical Analyses:** Linear Mixed Model **Covariates:** Temperature, humidity, pressure **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 1 day	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 24 h **Mean (SD):** 5.3 (2.8) **Min:** 0 **Max:** 14.6 **Monitoring Stations:** 1 **Copollutant:** $PM_{2.5}$, PM_{10} **Co-pollutant Correlation:** $PM_{2.5}$ = 0.46* PM_{10} = NR *p < 0.01	**PM Increment:** 1 µg/m^3. **Beta, SE (Lower CI, Upper CI), p-value** HRV Max Heart Rate: -1.95, 0.88 (-3.67, -0.23), 0.03 ASDNN5: -0.77, 0.37 (-1.580, -0.04), 0.05 SDANN5: -3.76, 1.53 (-6.76, -0.76), 0.02 SDNN24HR(mesc): -3.36, 1.38 (-6.06, -0.65), 0.02 rMSSD: -0.75, 0.53 (-1.79, 0.28), 0.16 pNN50_24hr: -0.50, 0.27 (-1.03, 0.03), 0.07 pNN50_7min: -1.88, 0.55 (-2.95, -0.81), 0.07 Low-frequency power: -0.19, 0.42 (-1.01, 0.63), 0.65 Percent low frequency: 0.57, 1.08 (-1.55, 2.69), 0.60 High-frequency power: -0.46, 0.17 (-0.79, -0.14), 0.01 Percent high frequency: -2.14, 0.94 (-3.98, -0.30), 0.03 Blood Lipids Triglycerides: 4.78, 2.02 (0.81, 8.74), 0.02 VLDL: 1.15, 0.44 (0.29, 2.02), 0.01 Total cholesterol: 0.78, 0.54 (-0.28, 1.84), 0.15 Hematologic Factors Circulating eosinophils: 0.16, 0.06 (0.04, 0.28), 0.01 Platelets: -1.71, 1.11 (-3.89, 0.47), 0.13 Circulating Proteins Plasminogen: -0.01, 0.01 (-0.02, 0.00), 0.08 Fibrenogen: -0.04, 0.02 (-0.08, 0.00), 0.07 Von Willibrand factor: -1.23, 0.66 (-2.53, 0.06), 0.07 Factor VII: -0.90, 0.85 (-2.58, 0.77), 0.29

[1]All units expressed in µg/m^3 unless otherwise specified.

Table E-3. Short-term exposure - cardiovascular morbidity studies: $PM_{2.5}$ (including PM components/sources).

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Adar et al. (2007, 001458) **Period of Study:** Mar-Jun 2002 **Location:** St. Louis, Missouri	**Outcome:** Heart rate variability: heart rate, standard deviation of all normal-to-normal intervals (SDNN), square root of the mean squared difference between adjacent normal-to-normal intervals (rMSSD), percentage of adjacent normal-to-normal intervals that differed by more than 50 ms (pNN50), high frequency power (HF in the range of 0.15-0.4Hz), low frequency power (LF, in the range of 0.04-0.15Hz), and the ratio of LF/HF **Age Groups:** ≥ 60 yr **Study Design:** Panel (4 planned repeated measures surrounding bus	**Pollutant:** $PM_{2.5}$ (µg/m^3) **Averaging Time:** Measurements collected over 48 h period surrounding the bus trip (during which health endpoints were measured) used to calculate 5-, 30-, 60-min, 4-h, 24-h ma **Median (IQR):** All: 7.7 (6.8) Facility: 6.8 (5.1) Bus: 17.2 (10.3) Activity: 8.2 (16.1) Lunch: 11.2 (5.9) **Monitoring Stations:** 2 portable carts **Copollutant:**	**PM Increment:** IQR **Effect Estimate [Lower CI, Upper CI]:** % change (95%CI) in HRV per IQR in the 24-h ma of the microenvironmental pollutant (IQr = 4.5 µg/m^3) **Single-pollutant models:** SDNN: -5.5 (-6.3, -4.8) rMSSD: -9.1 (-9.8, -8.4) pNN50 + 1: -12.2 (-13.3, -11.1). LF: -10.8 (-12.3, -9.3) HF: -15.1 (-16.7, -13.7) LF/HF: 5.1 (3.9, 6.4) H: 1.0 (0.9, 1.2) **Two-pollutant models (with particle**

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
	trips with a total of 158 person-trips, 35 participating in all 4 trips) **N:** 44 participants **Statistical Analyses:** Generalized additive models **Covariates:** Subject, weekday, time, apparent temperature, trip type, activity, medications, and autoregressive terms **Season:** Limited data collection period **Dose-response Investigated?** No **Statistical Package:** SAS v8.02, R v2.0.1	$PM_{2.5}$ BC Fine particle counts coarse particle counts **Correlation notes:** 24-h mean $PM_{2.5}$, BC, and fine particle count concentrations ranged from 0.80-0.98 r = 0.76-0.97 when limited to time spent on the bus r = 0.55-0.86 when comparing bus concentrations to 24-h ma r = -0.003-0.51 when comparing 5-min avg and 24-h ma Poor correlations found between coarse particle count concentrations and all fine particulate measures during all times periods	**number count coarse):** SDNN: -5.7 (-6.5, -4.9) rMSSD: -9.4(-10.1, -8.6) pNN50+1: -13.1(-14.3, -11.9). LF: -10.7(-12.4, -9.1) HF: -14.9(-16.5, -13.3); LF/HF: 4.9 (3.6, 6.2)' H: 0.9 (0.7,1.1) Independent short- and medium-term associations with HRV across all time periods % change per IQR (95%CI) IQR 5-min means = 6.8 $\mu g/m^3$ and 23: 55-h means = 4.2 $\mu g/m^3$ SDNN: 5-min mean: -0.5 (-0.8, -0.1) 23: 55-h mean: -4.6 (-5.3, -4.0) rMSSD: 5-min mean: -0.9 (-1.3, -0.5) 23: 55-h mean: -7.5 (-8.1 to -6.8) pNN50 + 1 5-min mean: -1.1 (-1.7 to -0.5) 23: 55-h mean: -9.9 (-10.9 to -8.9). LF 5-min mean: 0.4 (-0.5, 1.2) 23: 55-h mean: -10.0 (-11.4 to -8.6) HF 5-min mean: -1.5 (-2.3 to -0.6) 23: 55-h mean: -12.9 (-14.2 to -11.5) LF/HF 5-min mean: 1.9 (1.3, 2.4) 23: 55-h mean: 3.2 (2.1, 4.3) H: 5-min mean: 0.1 (0.1, 0.2) 23: 55-h mean: 0.8 (0.7, 0.9) Independent associations of short-term avg (5-min means) of PM with HRV by bus and nonbus periods IQR for bus = 10 $\mu g/m^3$) and nonbus = 5.6 $\mu g/m^3$) % change (95%CI) p-value of interaction SDNN Bus: -5.0 (-6.3 to -3.7) Nonbus: -0.5 (-0.9 to -0.2) p-value for interaction: <0.0001. rMSSD Bus: -4.8 (-6.2 to -3.5) Nonbus: -0.7 (-1.1 to -0.4. p-value for interaction: <0.0001 pNN50 + 1 Bus: -6.3 (-8.4 to -4.2) Nonbus: -0.8 (-1.4 to -0.3) p-value for interaction: <0.0001 LF: Bus: -7.0 (-9.8 to -4.1) Nonbus: 0.6 (-0.1, 1.4) p-value for interaction: <0.0001. HF: Bus: -10.7 (-13.5 to -7.9)' Nonbus: -0.7 (-1.5, 0.04) p-value for interaction: <0.0001. LF/HF: Bus: 3.9 (1.7, 6.0) Nonbus: 1.4 (0.8, 1.9) p-value for interaction: 0.39. H: Bus: 0.7 (0.5, 1.0) Nonbus: -0.01 (-0.08, 0.1) p-value for interaction: <0.0001 **Note:** Exposure to health associations by all lag periods presented in Fig 2 (magnitude of associations increased with averaging period, with the largest associations consistently found for 24-h ma)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Adar et al. (2007, 001458) **Period of Study:** Mar-Jun 2002 **Location:** St. Louis, Missouri	**Outcome:** Heart rate variability: heart rate, standard deviation of all normal-to-normal intervals (SDNN), square root of the mean squared difference between adjacent normal-to-normal intervals (rMSSD), percentage of adjacent normal-to-normal intervals that differed by more than 50 ms (pNN50), high frequency power (HF in the range of 0.15-0.4Hz), low frequency power (LF, in the range of 0.04-0.15Hz), and the ratio of LF/HF **Age Groups:** ≥ 60 yr **Study Design:** Panel (4 planned repeated measures with a total of 158 person-trips 35 participating in all 4 trips) **N:** 44 participants **Statistical Analyses:** Generalized additive models **Covariates:** Subject, weekday, time, apparent temperature, trip type, activity, medications, and autoregressive terms **Season:** Limited data collection period **Dose-response Investigated?** No **Statistical Package:** SAS v8.02, R v2.0.1	**Pollutant:** BC (ng/m^3) **Averaging Time:** Measurements collected over 48 h period surrounding the bus trip (during which health endpoints were measured) used to calculate 5-, 30-, 60-min, 4-h, 24-h ma **Median (IQR):** All: 330 (337) Facility: 285 (270) Bus: 2911 (2464) Activity: 482 (1168) Lunch: 434 (276) **Monitoring Stations:** 2 portable carts **Copollutant:** $PM_{2.5}$ BC Fine particle counts Coarse particle counts **Correlation notes:** 24-h mean $PM_{2.5}$, BC, and fine particle count concentrations ranged from 0.80 to 0.98 r = 0.76 to 0.97 when limited to time spent on the bus r = 0.55 to 0.86 when comparing bus concentrations to 24-h ma r = -0.003 to 0.51 when comparing 5-min avg and 24-h ma Poor correlations found between coarse particle count concentrations and all fine particulate measures during all times periods	**PM Increment:** IQR **Effect Estimate [Lower CI, Upper CI]:** % change (95%CI) in HRV per IQR in the 24-h ma of the microenvironmental pollutant (IQr = 459 ng/m^3) Single-pollutant models SDNN: -5.3 (-6.5 to -4.1) rMSSD: -10.7 (-11.9 to -9.5) pNN50 + 1: -13.2 (-15.0 to -11.4) LF: -11.3 (-13.7 to -8.8) HF: -18.8 (-21.1 to -16.5) LF/HF: 9.3 (7.2, 11.4) H: 1.0 (0.8, 1.3) Independent short- and medium-term associations with HRV across all time periods % change per IQR (95%CI) IQR 5-min means = 337 ng/m^3 and 23: 55-h means = 490 ng/m^3) SDNN: 5-min mean: -0.3 (-0.5 to -0.1) 23: 55-h mean: -4.7 (-5.9 to -3.5) rMSSD: 5-min mean: -0.3 (-0.5 to -0.1) 23: 55-h mean: -9.3 (-10.5 to -8.1) pNN50 + 1: 5-min mean: -0.3 (-0.6 to -0.1) 23: 55-h mean: -10.5 (-12.3 to -8.7) LF: 5-min mean: -0.5 (-0.9 to -0.1) 23: 55-h mean: -9.8 (-12.4 to -7.2) HF: 5-min mean: -0.9 (-1.2 to -0.5) 23: 55-h mean: -15.4 (-17.8 to -12.9) LF/HF: 5-min mean: 0.3 (0.1, 0.6) 23: 55-h mean: 6.5 (4.5, 8.6) H: 5-min mean: 0.1 (0.1, 0.2) 23: 55-h mean: 0.4 (0.2, 0.7) Independent associations of short-term avg (5-min means) of PM with HRV by bus and nonbus periods IQR for bus = 2.6 $\mu g/m^3$) and nonbus = 0.27 $\mu g/m^3$) % change (95%CI) p-value of interaction SDNN: Bus: -4.6 (-6.1 to -3.0)' Nonbus: -0.1 (-0.3, 0.1) p-value for interaction: <0.0001 rMSSD: Bus: -2.6 (-4.2 to -0.9): Nonbus: -0.3 (-0.5 to -0.1) p-value for interaction: 0.64 pNN50 + 1: Bus: -2.0 (-4.5, 0.5): Nonbus: -0.5 (-0.8 to -0.1) p-value for interaction: 0.34 LF: Bus: -6.0 (-9.3 to -2.5): Nonbus: -0.2 (-0.7, 0.3) p-value for interaction: 0.028 HF: Bus: -5.8 (-9.1 to -2.3) Nonbus: -0.9 (-1.4 to -0.4) p-value for interaction: 0.50 LF/HF: Bus: -0.8 (-3.1, 1.7) Nonbus: 0.8 (0.5, 1.1) p-value for interaction: <0.0001 H: Bus: -0.5 (-0.8 to -0.2) Nonbus: 0.3 (0.26, 0.34) p-value for interaction: <0.0001 **Note:** Exposure to health associations by all lag periods presented in Fig 2 (magnitude of associations increased with averaging period, with the largest associations consistently found for 24-h ma)
Reference: Auchincloss et al. (2008, 156234)	**Outcome:** Blood pressure: Systolic (SBP), diastolic (DBP), mean arterial	**Pollutant:** $PM_{2.5}$	**PM Increment:** 10 $\mu g/m^3$ (approx. equivalent to difference between 90th

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Period of Study: Jul 2000-Aug 2002 **Location:** 6 U.S. communities (Baltimore City and Baltimore County, Maryland Chicago, Illinois Forsyth County, North Carolina Los Angeles, California Northern Manhattan and the Bronx, New York and St. Paul, Minnesota) Part of MESA (Multi-ethnic Study of Atherosclerosis)	(MAP), pulse pressure (PP) Avg of 2nd and 3rd BP measurement used for analyses **Age Groups:** 45-84 yr **Study Design:** Cross-sectional (Multi-Ethnic Study of Atherosclerosis baseline examination) **N:** 5,112 persons (free of clinically apparent cardiovascular disease) **Statistical Analyses:** Linear regression secondary analyses used log binomial models to fit a binary hypertension outcome **Covariates:** Age, sex, race/ ethnicity, per capita family income, education, BMI, diabetes status, cigarette smoking status, exposure to ETS, high alcohol use, physical activity, BP medication use, meteorology variables, and copollutants Examined site as a potential confounder and effect modifier Heterogeneity of effects also examined by traffic-related exposures, age, sex, type 2 diabetes, hypertensive status, cigarette use, by levels of SO_2 and CO, and for weather variables **Season:** Adjusted for temperature and barometric pressure to adjust for seasonality (because seasons vary by the study sites) Also performed sensitivity analyses adjusting for season to examine the potential for residual confounding not accounted for by weather variables **Dose-response Investigated?** Assessed nonlinear relationships-no evidence of strong threshold/nonlinear effects for $PM_{2.5}$ **Statistical Package:** NR	**Averaging Time:** 5 exposure metrics constructed: prior day, avg of prior 2 days, prior 7 days, prior 30 days, and prior 60 days **Mean (SD):** Prior day: 17.0 (10.5) Prior 2 days: 16.8 (9.3) Prior 7 days: 17.0 (6.9) Prior 30 days: 16.8 (5.0) Prior 60 days: 16.7 (4.4) **Percentiles:** NR **Range (Min, Max):** NR **Monitoring Stations:** Used monitor nearest the participant's residence to calculate exposure metrics **Copollutant:** SO_2 NO_2 CO Traffic-related exposures (straight-line distance to a highway total road length around a residence) **Correlations with PM2.5 averaged over prior 30 days:** O_3 Cool: r = -0.67 Moderate: r = -0.30 Warm: r = 0.23 CO Cool: r = 0.20 Moderate: r = 0.71 Warm: r = 0.23 SO_2 Cool: r = 0.36 Moderate: r = -0.17 Warm: r = -0.11 NO_2 Cool: r = 0.55 Moderate: r = 0.66 Warm: 0.32	and 10th percentile for prior 30 day mean) **Effect Estimate [Lower CI, Upper CI]:** Adjusted mean difference (95% CI) in PP and SBP (mmHg) per 10 $\mu g/m^3$ increase in $PM_{2.5}$ (avgd for the prior 30 days) **Pulse Pressure** ($PM_{2.5}$ avgd for prior 30 days) Adjustment variables: Person-level Covariates**:** 1.04 (0.25, 1.84), p = 0.010 Person-level cov., weather: 1.12 (0.28, 1.97), p = 0.009 Person-level cov., weather, gaseous copollutants: 2.66 (1.61, 3.71), p = 0.000 Person-level cov., study site: 0.93 (-0.04, 1.90), p = 0.060 Person-level cov., study site, weather: 1.11 (0.01, 2.22), p = 0.049 Person-level cov., study site, weather, gaseous copollutants: 1.34 (0.10, 2.59) , p = 0.035 **Systolic Blood Pressure** Adjustment variables: Person-level Covariates**:** 0.66 (-0.41, 1.74) , p = 0.226 Person-level cov., weather: 0.99 (-0.15, 2.13) , p = 0.089 Person-level cov., weather, gaseous copollutants: 2.8 (1.38, 4.22) , p = 0.000 Person-level cov., study site: 0.86 (-0.45, 2.17) , p = 0.200 Person-level cov., study site, weather: 1.32 (-0.18, 2.82) , p = 0.085 Person-level cov., study site, weather, gaseous copollutants: 1.52 (-0.16, 3.21) , p = 0.077 **Additional results:** Associations became stronger with longer averaging periods up to 30 days. For example: Adjusted (personal covariates and weather) mean differences in PP: Prior day: -0.38 (-0.76, 0.00) Prior 2 days: -0.22 (-0.65, 0.21) Prior 7 days: 0.52 (-0.08, 1.11) Prior 30 days: 1.12 (0.28, 1.97) Prior 60 days: 1.08 (0.11, 2.05) (Pattern held for additional adjustments and for SBP results therefore, only results for 30-day mean differences were presented) **Additional results (not presented):** None of DBP results were statistically significant Results for MAP were similar to SBP, though weaker and generally not significant **Effect modification:** Associations between $PM_{2.5}$ and BP were stronger for persons taking medications, with hypertension, during warmer weather, in the presence of high NO_2, residing ≤ 300m from a highway, and surrounded by a high density of roads (Fig 1) associations were not modified by age, sex, diabetes, cigarette smoking, study site, high levels of CO or SO_2, season , nor residence ≤ 400m fro a highway

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Note: Supplementary material available on-line shows results for DBP and MAP, among others
Reference: Baccarelli et al. (2009, 188183) **Period of Study:** Nov 2000-Jun 2005 **Location:** Boston, Mass	**Outcome:** Heart rate variability **Age Groups:** Elderly **Study Design:** Panel **N:** 549 men **Statistical Analyses:** Mixed-effects model **Covariates:** Age, past/current CHD, BMI, mean arterial pressure, fasting blood glucose, smoking, alcohol consumption, use of beta-blockers, CA channel blockers, angiotensin-converting enzyme inhibitors, room temperature, season, apparent temperature **Season:** No **Dose-response Investigated?** No **Statistical Package:** SAS	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 48-h ma **Geometric Mean (95%CI):** All Visits: 10.5 (10.0, 10.9) Visits w/ Genotype Data: 10.4 (9.9, 11.0) Visits w/o Genotype Data: 10.5 (9.8, 11.4) **Monitoring Stations:** 1 **Copollutant:** NR **Correlation:** N/A	**PM Increment:** 10 $\mu g/m^3$ **Percent Change [Lower CI, Upper CI], P:** All Subjects w/ Genotype Data SDNN: -6.0 (-13.5, 2.0), 0.14 HF: -17.1 (-32.3, 1.6), 0.07 LF: -8.2 (-22.1, 8.2), 0.31 All Subjects SDNN: -7.1 (-13.2, -0.6), 0.03 HF: -18.7 (-31.1, -4.0), 0.01 LF: -11.8 (-23.2, -1.3), 0.08

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Barclay et al. (2007, 192229) **Period of Study:** Jan 2003-May 2005 **Location:** Aberdeen, Scotland	**Outcome:** Haematological outcomes, Heart Rhythm outcomes, & Heart Rate Variability outcomes **Age Groups:** 70.4 (8.9) **Study Design:** Panel **N:** 132 patients w/ chronic heart failure **Statistical Analyses:** Linear & Mixed Effects Regression Model **Covariates:** Age, temperature, humidity, pressure **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** Lags 0-2 day	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily **Mean:** 7.454 **Min:** 1.092 **Max:** 21.97 **Monitoring Stations:** 0 **Copollutant:** PM_{10}, PNC, NO_2 **Co-pollutant Correlation** NO_2 city: 0.164 NO city: 0.048 PM_{10} city: 0.476* NO_2 personal: 0.169 PNC DEOM: 0.115 $PM_{2.5}$ traffic: 0.522* PNC total: 0.367* PNC traffic: 0.234 *correlations based on 3-day avg concentrations **Notes:** $PM_{2.5}$ values model predicted	**PM Increment:** NR **Beta (Lower CI, Upper CI):** Haemoglobin: -0.509 (-1.560, 0.542) Mean corpuscular haemoglobin: 0.188 (-0.481, 0.857) Platelets: 3.022 (0.403, 5.642) Haematocrit: -0.813 (-1.892, 0.267) White blood cells: -1.652 (-4.727, 1.424) C reactive protein: 4.924 (-13.022, 22.869) IL-6: -5.980 (-23.649, 11.690) von Willebrand factor: 1.363 (-6.561, 9.287) E-selectin: 2.136 (-2.946, 7.217) Fibrinogen: -5.579 (-10.403, -0.755)* Factor VII: 3.747 (-1.959, 9.452) day-dimer: 5.211 (-2.974, 13.397) All arrhythmias: -7.082 (-28.789, 14.626) Ventricular ectopic beats: -12.203 (-39.021, 14.615) Ventricular couplets: -1.255 (-25.678, 23.168) Ventricular runs: -2.548 (-17.448, 12.351) Supraventricular ectopic beats: 4.898 (-19.772, 29.568) Supraventricular couplets: 6.138 (-16.242, 28.518) Supraventricular runs: -0.545 (-17.577, 16.487) Avg HR: 0.617 (-0.782, 2.016) 24 h SDNN: 3.645 (-0.227, 7.517) 24 h SDANN: 4.437 (0.030, 8.844)* 24 h RMSSD: 0.617 (-0.782, 2.016) 24 h PNN 50%: 11.247 (-6.228, 28.722) 24 h LF power: 4.439 (-6.823, 15.701) 24 h LF normalized: -5.659 (-11.815, 0.497) 24 h HF power: 3.800 (-10.863, 18.464) 24 h HF normalized: -6.597 (-13.724, 0.531) 24 h LF/HF ratio: 1.033 (-8.355, 10.414) *p < 0.05 **Notes:** Estimates also available for $PM_{2.5}$ traffic LF= low frequency HF= high frequency
Reference: Briet et al. (2007, 093049) **Period of Study:** NR **Location:** Paris, France	**Outcome:** Endothelial Function **Age Groups:** 20-40 yr **Study Design:** Panel **N:** 40 white male nonsmokers **Statistical Analyses:** Multiple Robust Regrssion **Covariates:** R53R/R53H genotype, diet, subject factor, visit, temperature **Dose-response Investigated?** No **Statistical Package:** NCSS **Lags Considered:** 0-5 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **5 day Mean (SD):** 28 (6) **Monitoring Stations:** NR **Co-pollutant:** PM_{10}, SO_2, NO, NO_2, CO **Co-pollutant Correlation:** N/A	**PM Increment:** 1 SD **Beta (Lower CI, Upper CI), P, R2:** Flow-mediated brachial artery dilation: -0.32 (-1.10, 0.46), NS, 0.04 Reactive hyperemia: 15.68 (7.11, 23.30), <0.0001, 0.24 Changes in Endothelial function b/t visits: 1.98 (0.67, 3.259), 0.004, 0.44

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Cárdenas et al. (2008, 191900) **Period of Study:** NR **Location:** Mexico City, Mexico	**Outcome:** Heart Rate Variability **Age Groups:** 20-40 yr **Study Design:** Panel **N:** 54 subjects **Statistical Analyses:** Linear GEE models **Covariates:** Localization, supine position, gender, age, humidity, heart rate, orthostatic position, head-up tilt test result **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** NR	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **25th, 50th, 75th percentile:** Indoor: 14.8, 28.3, 47.9 Outdoor: 6.4, 10.8, 16.8 **Monitoring Stations:** NR **Co-pollutant:** NR **Co-pollutant Correlation:** N/A	**PM Increment:** NR **Mean Difference (Lower CI, Upper CI), lag:** Ln low frequency Indoors: -0.028 (-0.0423, -0.0138) Outdoors: -0.194 (-0.4509, 0.0627) Ln high frequency Indoors: -0.019 (-0.0338, -0.0044) Outdoors: -0.298 (-0.5553, -0.0401) Ln LF/HF ratio Indoors: -0.017 (-0.0330, -0.0007) Outdoors: -0.278 (-0.5540, 0.0030)
Reference: Cavallari et al. (2007, 157425) **Period of Study:** 1999-2006 **Location:** Massachusetts	**Outcome:** Heart Rate Variability **Age Groups:** 22-63 **Study Design:** Panel **N:** 36 males **Statistical Analyses:** Mixed Effects Regression Model **Covariates:** Age, smoking, heart rate at work **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** Lags 0-14 h	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Hourly **Mean (SD):** 1.12 (0.76) **Min:** 0.12 **Max:** 3.99 **Monitoring Stations:** NR **Copollutant:** NR **Co-pollutant Correlation:** N/A	**PM 1 mg Increment:** m^3 **Beta (Lower CI, Upper CI):** Model 1 Lag 1 h: -1.44 (-7.75, 4.87) Lag 2 h: -5.33 (-10.97, 0.31)* Lag 3 h: -6.86 (-11.91, -1.81)‡ Lag 4 h: -2.17 (-9.33, 4.99) Lag 5 h: -4.73 (-11.99, 2.53) Lag 6 h: -3.52 (-9.89, 2.84) Lag 7 h: -1.59 (-7.53, 4.35) Lag 8 h: -0.72 (-7.63, 6.20) Lag 9 h: -5.55 (-10.65, -0.45)‡ Lag 10 h: -3.66 (-8.85, 1.53) Lag 11 h: -8.60 (-17.45, 0.24)* Lag 12 h: -5.98 (-14.67, 2.70) Lag 13 h: -8.27 (-17.00, 0.46)* Lag 14 h: -4.19 (-12.71, 4.33) Model 2 Lag 1 h: 4.10 (-0.39, 8.60)* Lag 2 h: -3.21, (-8.78, 2.37) Lag 3 h: -6.45 (-11.59, -1.31)‡ Lag 4 h: -0.01 (-6.96, 6.94) Lag 5 h: -2.03 (-8.27, 4.22) Lag 6 h: -1.99 (-8.46, 4.48) Lag 7 h: -0.34 (-6.22, 5.54) Lag 8 h: 0.72 (-6.35, 7.78) Lag 9 h: -5.26 (-10.62, 0.11)* Lag 10 h: -3.68 (-9.17, 1.80) Lag 11 h: -9.41 (-18.60, -0.23)‡ Lag 12 h: -6.45 (-15.62, 2.72) Lag 13 h: -7.33 (-16.55, 1.89) Lag 14 h: -4.75 (-13.81, 4.32) *p < 0.05, ‡p < 0.10 **Notes:** Model 1 adjusted for smoking status and age only. Model 2 adjusted for smoking status, age, and heart rate during work.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Chahine et al. (2007, 156327) **Period of Study:** Jan 2000-Jun 2005 **Location:** Boston, MA	**Outcome:** Heart Rate Variability **Age Groups: M**ean 72.8(6.6) yr **Study Design:** Panel **N:** 539 white males **Statistical Analyses:** Mixed Effects Model **Covariates: A**ge, BMI, mean arterial pressure, fasting blood glucose, smoking, alcohol consumption, use of beta-blockers, calcium channel blockers, ACE inhibitors, room temperature, season, outdoor temperature **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 0- to 2-day ma	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 1 h **Mean (SD):** 11.7 (7.8) **Monitoring Stations:** 1 **Copollutant:** $PM_{1.0}$ **Co-pollutant Correlation:** N/A	**PM Increment:** 10 µg/m^3 **Percent Change (Lower CI, Upper CI), p-value:** log10 SDNN Total: -6.8 (-12.9, -0.2), 0.0436 GSTM1 wildtype: -2.0 (-11.3, 8.3), 0.6908 GSTM1 null: -10.5 (-18.2, -2.2), 0.0150 HMOX-1 <25 repeats: 7.4 (-8.7, 26.2), 0.3891 HMOX-1 ≥25 repeats: -8.5 (-14.8, -1.8), 0.0137 log10 HF Total: -17.3 (-30.0, -2.3), 0.0263 GSTM1 wildtype: -4.0 (-24.8, 22.6), 0.7442 GSTM1 null: -24.2 (-39.2, -5.5), 0.0139 HMOX-1 <25 repeats: 8.9 (-27.1, 62.8), 0.6759 HMOX-1 ≥25 repeats: -20.1 (-32.9, -5.0), 0.0115 log10 LF Total: -11.2 (-22.8, 2.2), 0.0986 GSTM1 wildtype: -0.6 (-19.0, 22.0), 0.9545 GSTM1 null: -17.0 (-31.0, -0.2), 0.0478 HMOX-1 <25 repeats: 14.0 (-18.6, 59.5), 0.4465 HMOX-1 ≥25 repeats: -14.0 (-25.7, -0.5), 0.0430
Reference: Chen and Schwartz (2008, 190106) **Period of Study:** 1989-1991 **Location:** U.S.	**Outcome:** White Blood Cell count **Age Groups:** 20-89 yr **Study Design:** Panel **N:** 2,978 participants **Statistical Analyses:** Mixed Effects Models **Covariates: A**ge, sex, race, SES, smoking, alcohol consumption, MS abnormalities, indoor air pollutants, exercise **Dose-response Investigated?** No **Statistical Package:** Stata **Lags Considered:** NR	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** 36.8 (13.0) **Median(range) for** **Q1:** 23.1(14.6-27.8) **Q2:** 31.2 (27.9-34.3) **Q3:** 38.8 (34.3-43.3) **Q4:** 53.7 (43.3-78.5) **Monitoring Stations:** NR **Copollutant:** NR **Co-pollutant Correlation:** N/A	**PM Increment:** Quartile, 1yr avg (36.8 µg/m^3) **Avg WBC count(SE) by PM quartile:** **Q1:** 6760 (79) **Q2:** 6942 (99) **Q3:** 6895 (84) **Q4:** 7109 (61) **Beta(Lower CI, Upper CI), p-value:** Crude: 239 (58, 420), 0.01 Model 1: 145 (10, 281), 0.035 Model 2: 141 (6, 277), 0.041 Model 3: 138 (2, 273), 0.046 Model 1: Age, sex, race, SES, smoking, alcohol consumption, MS abnormalities. Model 2: Model 1 plus indoor air pollutants, exercise. Model 3: Clean areas (Q1) vs.. other more polluted areas

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Chuang et al. (Chuang et al., 2007, 091063) **Period of Study:** Between Apr-Jun 2004 or 2005 **Location:** Taipei, Taiwan	**Outcome:** High-sensitivity C-reactive protein (hs-CRP) Fibrinogen, plasminogen activator fibrinogen inhibitor-1 (PAI-1), tissue-type plasminogen activator (tPA), 8-hydroxy-2'-deoxyguanosine (8-OHdG), and log-transformed HRV indices (SDNN = standard deviation of NN intervals, r-MSSD = square root of the mean of the sum of the squares of differences between adjacent NN intervals, LF = low frequency [0.04-0.15Hz], and HF = high frequency[0.15-0.40Hz]) **Age Groups:** 18-25 yr **Study Design:** Panel (cross-sectional) **N:** 76 students **Statistical Analyses: L**inear mixed-effects models **Covariates:** Age, sex, BMI, weekday, temperature of previous day, relative humidity **Season:** Only 1 season of data collection **Dose-response Investigated?** No **Statistical Package:** NR	**Pollutant:** PM_{10}, nitrate, sulfate **Averaging Time:** Hourly data used to calculate avg over 1- to 3-day periods **Mean (SD):** 1-day avg: 31.8 (10.6) 2-day avg: 36.4 (12.6) 3-day avg: 36.5 (12.6) **Range (Min, Max):** 1-day avg: 16.2, 50.1 2-day avg: 15.0, 53.4 3-day avg: 12.7, 59.5 **Monitoring Stations:** 2 sites (each pollutant measured at 1 site only) **Copollutant:** PM_{10} Sulfate Nitrate OC EC NO_2 CO SO_2 O_3	**$PM_{2.5}$ Increment:** IQR (1-day avg: 20.4 2-day avg: 25.2 3-day avg: 20.0) **Effect Estimate [Lower CI, Upper CI]:** % change in health endpoint per increase in IQR of $PM_{2.5}$ (1-3 day averaging period single pollutant models) hs-CRP: 1-day: 90.2 (-10.2, 190.1) 2-day: 99.1 (-26.1, 224.3) 3-day: 100.4 (-2.9, 203.7) 8-OHdG: 1-day: -5.0 (-14.3, 4.4) 2-day: -5.5 (-15.6, 4.6) 3-day: -5.6 (-13.8, 2.6) PAI-1: 1-day: 20.4 (17.3, 33.5) 2-day: 16.2 (1.9, 30.5) 3-day: 20.0 (18.5, 31.5) tPA: 1-day: 12.0 (-2.4, 26.3) 2-day: 12.0 (-2.9, 26.9); 3-day: 12.0 (-2.7, 26.6) Fibrinogen: 1-day: 2.6 (-2.7, 7.8) 2-day: 1.5 (-4.1, 7.1); 3-day: 3.6 (-0.8, 8.1) **Heart Rate Variability** SDNN: 1-day: -4.0 (-6.1 to -1.9) 2-day: -2.5 (-4.6 to -0.4) 3-day: -3.0 (-5.0 to -1.1) r-MSSD: 1-day: -3.0 (-8.7, 2.7) 2-day: -2.0 (-8.4, 4.4); 3-day: -3.6 (-8.8, 1.6) LF: 1-day: -3.1 (-6.1 to -0.1) 2-day: -3.2 (-4.6, 0.1); 3-day: -3.4 (-6.1 to -0.6) HF: 1-day: -3.7 (-9.4, 2.1) 2-day: -2.1 (-8.4, 4.3); 3-day: -4.0 (-9.3, 1.2)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Chuang et al. (2007, 091063) **Period of Study:** Between Apr-Jun 2004 or 2005 **Location:** Taipei, Taiwan	**Outcome:** High-sensitivity C-reactive protein (hs-CRP) Fibrinogen, plasminogen activator fibrinogen inhibitor-1 (PAI-1), tissue-type plasminogen activator (tPA), 8-hydroxy-2'-deoxyguanosine (8-OHdG), and log-transformed HRV indices (SDNN = standard deviation of NN intervals, r-MSSD = square root of the mean of the sum of the squares of differences between adjacent NN intervals, LF = low frequency [0.04-0.15Hz], and HF = high frequency[0.15-0.40Hz]) **Age Groups:** 18-25 yr **Study Design:** Panel (cross-sectional) **N:** 76 students **Statistical Analyses:** Linear mixed-effects models **Covariates:** Age, sex, BMI, weekday, temperature of previous day, relative humidity **Season:** Only 1 season of data collection **Dose-response Investigated?** No **Statistical Package:** NR	**Pollutant:** Nitrate **Averaging Time:** Hourly data used to calculate avg over 1-3 day periods **Mean (SD):** 1-day avg: 4.5 (2.7) 2-day avg: 4.7 (2.4) 3-day avg: 4.4 (2.2) **Range (Min, Max):** 1-day avg: 0.7, 10.6 2-day avg: 0.7, 8.9 3-day avg: 0.8, 7.5 **Monitoring Stations:** 2 sites (each pollutant measured at 1 site only) **Copollutant:** PM_{10} Sulfate $PM_{2.5}$ OC EC NO_2 CO SO_2 O_3	**Nitrate Increment:** IQR (1-day avg: 2.5 2-day avg: 4.0 3-day avg: 3.4) **Effect Estimate [Lower CI, Upper CI]:** % change in health endpoint per increase in IQR of nitrate (1-3 day averaging period single pollutant models) hs-CRP: 1-day: -2.1 (-21.9, 17.8) 2-day: -11.6 (-58.6, 35.5) 3-day: -18.7 (-69.9, 32.5) 8-OHdG: 1-day: 9.0 (4.0, 14.1) 2-day: 15.1 (5.9, 24.3) 3-day: 15.0 (4.9, 25.0) PAI-1: 1-day: 4.0 (-2.5, 10.4) 2-day: 11.6 (0.1, 23.1) 3-day: 16.9 (4.3, 29.4) tPA: 1-day: 2.0 (-6.2, 10.3) 2-day: 12.9 (-1.6, 27.5) 3-day: 10.0 (-5.8, 25.8) Fibrinogen: 1-day: 1.6 (-1.3, 4.5) 2-day: 1.3 (-3.9, 6.5) 3-day: 1.0 (-4.6, 6.6) **Heart Rate Variability** SDNN: 1-day: -1.5 (-2.6 to -0.3) 2-day: -2.6 (-4.7 to -0.5) 3-day: -3.0 (-5.3 to -0.7) r-MSSD: 1-day: -5.5 (-8.7 to -2.2) 2-day: -7.1 (-14.0 to -0.2) 3-day: -8.1 (-14.5 to -1.8) LF: 1-day: -1.0 (-1.6 to -0.5) 2-day: -2.0 (-5.6, 1.6) 3-day: -2.0 (-5.2, 1.2) HF: 1-day: -2.0 (-5.3, 14[potential typo, possibly 1.4]) 2-day: -4.9 (-10.9, 0.9) 3-day: -6.9 (-13.4 to -0.3)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Chuang et al. (2007, 091063) **Period of Study:** Between Apr-Jun 2004 or 2005 **Location:** Taipei, Taiwan	**Outcome:** High-sensitivity C-reactive protein (hs-CRP) Fibrinogen, plasminogen activator fibrinogen inhibitor-1 (PAI-1), tissue-type plasminogen activator (tPA), 8-hydroxy-2'-deoxyguanosine (8-OHdG), and log-transformed HRV indices (SDNN = standard deviation of NN intervals, r-MSSD = square root of the mean of the sum of the squares of differences between adjacent NN intervals, LF = low frequency [0.04-0.15Hz], and HF = high frequency[0.15-0.40Hz]) **Age Groups:** 18-25 yr **Study Design:** Panel (cross-sectional) **N:** 76 students **Statistical Analyses:** Linear mixed-effects models **Covariates:** Age, sex, BMI, weekday, temperature of previous day, relative humidity **Season:** Only 1 season of data collection **Dose-response Investigated?** No **Statistical Package:** NR	**Pollutant:** Sulfate **Averaging Time:** Hourly data used to calculate avg over 1- to 3-day periods **Mean (SD):** 1-day avg: 4.1 (3.6) 2-day avg: 4.1 (3.7) 3-day avg: 3.9 (3.5) **Range (Min, Max):** 1-day avg: 0.4, 10.9 2-day avg: 0.4, 11.9 3-day avg: 0.4, 11.5 **Monitoring Stations:** 2 sites (each pollutant measured at 1 site only) **Copollutant:** PM_{10} $PM_{2.5}$ Nitrate OC EC NO_2 CO SO_2 O_3	**Sulfate Increment:** IQR (1-day avg: 3.9 2-day avg: 4.3 3-day avg: 3.8) **Effect Estimate [Lower CI, Upper CI]:** % change in health endpoint per increase in IQR of sulfate (1-3 day averaging period single pollutant models) hs-CRP: 1-day: 80.0 (9.8, 150.2) 2-day: 87.1 (14.9, 159.4) 3-day: 71.1 (13.0, 129.2) 8-OHdG: 1-day: 1.0 (0.3, 1.3) 2-day: -0.4 (-5.4, 4.7) 3-day: -0.3 (-4.3, 3.7) PAI-1: 1-day: 12.0 (5.4, 18.7) 2-day: 13.3 (6.6, 19.9) 3-day: 11.2 (5.7, 16.6) tPA: 1-day: 2.0 (-4.6, 8.7) 2-day: 3.8 (-2.8, 10.3) 3-day: 3.0 (-2.3, 8.2) Fibrinogen: 1-day: 2.9 (0.2, 5.5) 2-day: 2.8 (0.1, 5.5) 3-day: 2.2 (0.4, 4.7) **Heart Rate Variability** SDNN: 1-day: -3.1 (-4.1 to -2.1) 2-day: -4.1 (-5.2 to -3.1) 3-day: -2.0 (-2.9 to -1.2) r-MSSD: 1-day: -5.0 (-8.0 to -2.0) 2-day: -6.0 (-8.9 to -2.9) 3-day: -5.7 (-8.2 to -3.2) LF: 1-day: -3.4 (-4.9 to -1.8) 2-day: -3.0 (-4.5 to -1.5) 3-day: -3.0 (-4.3 to -1.7) HF: 1-day: -3.5 (-6.5 to -0.4) 2-day: -3.9 (-7.0 to -0.8) 3-day: -3.0 (-5.5 to -0.5)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Chuang et al. (2007, 098629) **Period of Study:** NR **Location:** Boston, MA	**Outcome:** ST Segment Depression **Age Groups:** 43-75 yr **Study Design:** Panel **N:** 48 coronary artery disease patients **Statistical Analyses:** Linear & Mixed Logistic Regression models **Covariates:** Participant, day of week, order of visit, visit date, hour of day, hourly temperature **Dose-response Investigated?** No **Statistical Package:** R **Lags Considered:** Lags 1-72 h	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Hourly **25th, 50th, 75th percentile:** 12-h avg: 6.18, 8.91, 13.18 24-h avg: 6.38, 9.20, 13.31 **Max:** 12-h avg: 37.13 24-h avg: 40.38 **Monitoring Stations:** 1 **Co-pollutant:** BC, CO, O_3, NO_2, SO_2 **Co-pollutant Correlation** BC: 0.56 O_3: 0.20 NO_2: 0.38 SO_2: 0.25	**PM Increment:** Interquartile Increase **Change (Lower CI, Upper CI):** 12-h mean $PM_{2.5}$: -0.022 (-0.032, -0.012) $PM_{2.5}$+ NO_2: -0.023 (-0.034, -0.012) $PM_{2.5}$+ SO_2: -0.009 (-0.02, 0.001) $PM_{2.5}$+ BC: -0.011 (-0.023, 0.001) 24-h mean $PM_{2.5}$: -0.026 (-0.037, -0.015) $PM_{2.5}$+ NO_2: -0.017 (-0.029, 0.004) $PM_{2.5}$+ SO_2: -0.014 (-0.025, -0.002) $PM_{2.5}$+ BC: -0.012 (-0.026, 0.003) **Relative Risk (Lower CI, Upper CI):** 12-h mean $PM_{2.5}$: 1.02 (0.86, 1.21) $PM_{2.5}$+ NO_2: 0.99 (0.82, 1.21) $PM_{2.5}$+ SO_2: 0.87 (0.71, 1.05) $PM_{2.5}$+ BC: 0.92 (0.74, 1.14) 24-h mean $PM_{2.5}$: 1.22 (0.99, 1.50) $PM_{2.5}$+ NO_2: 1.00 (0.80, 1.25) $PM_{2.5}$+ SO_2: 1.04 (0.83, 1.30) $PM_{2.5}$+ BC: 0.87 (0.65, 1.17) **Mean (Lower CI, Upper CI):** 12-h mean Myocardial Infarction: -0.042 (-0.057, -0.026) No Myocardial Infarction: -0.012 (-0.023, 0.00) p- for interaction: 0.002 Visit 1: -0.102 (-0.12, -0.085) Visits 2-4: 0.006 (-0.005, 0.017) p- for interaction: <0.001 Diabetic: -0.097 (-0.119, -0.074) Non-diabetic: -0.009 (-0.019, 0.002) p- for interaction: <0.001 Diurnal daytime pattern: -0.032 (-0.043, -0.021) Diurnal nighttime pattern: -0.006 (-0.018, 0.006) p- for interaction: <0.001 24-h mean Myocardial Infarction: -0.027 (-0.043, -0.012) No Myocardial Infarction: -0.025 (-0.038, 0.011) p- for interaction: 0.787 Visit 1: -0.127 (-0.148, -0.105) Visits 2-4: 0.001 (-0.011, 0.013) p- for interaction: <0.001 Diabetic: -0.118 (-0.144, -0.091) Non-diabetic: -0.13 (-0.024, -0.002) p- for interaction: <0.001 Diurnal daytime pattern: -0.031 (-0.043, -0.020) Diurnal nighttime pattern: -0.018 (-0.030, -0.005) p- for interaction: 0.233 **Notes:** The effects of PM on half-h St segment levels (Fig 1)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Dales et al. (2007, 155743) **Period of Study:** NR **Location:** Ottawa, Canada	**Outcome:** Vascular Reactivity **Age Groups:** 18-50 yr **Study Design:** Panel **N:** 39 volunteers **Statistical Analyses:** Mixed Effects Model **Covariates:** Temperature, humidity, wind speed, time of day testing was done, site **Dose-response Investigated?** No **Statistical Package:** S-PLUS **Lags Considered:** NR	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 2 h **Mean (SD):** Downtown: 40 (20) Tunney's Pasture: 10 (10) p-value 0.000 **Monitoring Stations:** NR **Copollutant:** PM1.0 **Co-pollutant Correlation** N/A	**PM Increment:** Interquartile Range (27.02 µg/m^3) **Beta (SE), p-value:** Flow mediated vasodilation (%): -0.016 (0.0072) p=0.03 Heart Rate (beats/min): 0.081 (0.135) p=0.55 Diastolic blood pressure (mmHg): 0.088 (0.088) p=0.32 Systolic blood pressure (mmHg): -0.108 (0.006) p=0.48
Reference: de Hartog et al. (2009, 191904) **Period of Study:** 1998-1999 **Location:** Amsterdam, The Netherlands Erfurt, Germany and Helsinki, Finland	**Outcome:** Heart Rate Variability **Age Groups:** 50+ **Study Design:** Panel **N:** 122 coronary heart disease patients **Statistical Analyses:** Linear Regression **Covariates:** Time trend, temperature, humidity, pressure **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** Lags 0-3 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily **p25, p50, p75. p95:** Amsterdam: 10.4, 16.7, 23.9, 47.0 Erfurt: 10.8, 16.3, 26.7, 62.3 Helsinki: 8.3, 10.6, 15.9, 25.8 **Monitoring Stations:** NR **Copollutant:** PM <0.1, PM0.1-1.0, NO_2, SO_2 **Co-pollutant Correlation** NR **Note:** Correlations are provided for source-specific $PM_{2.5}$ & elements	**PM Increment:** 1 µg/m^3 **Beta (Lower CI, Upper CI):** SDNN Local traffic: -0.12 (-0.36, 0.12) Long-range transport: -0.04 (-0.14, 0.06) Oil combustion: -0.29 (-1.04, 0.45) Industry: 0.03 (-0.12, 0.19) Crustal: 0.11 (-0.35, 0.56) Salt: -0.19 (-1.92, 1.55) HF Local traffic: 0.43 (-0.91, 1.79) Long-range transport: 0.19 (-0.38, 0.77) Oil combustion: 1.05 (-2.70, 4.94) Industry: 0.62 (-0.34, 1.59) Crustal: 1.57 (-1.28, 4.50) Salt: -1.43 (-9.86, 7.78) SDNN ABS: -0.52 (-1.39, 0.31) S: -0.51 (-1.36, 0.33) V: -0.66 (-1.73, 0.41) Zn: 0.12 (-0.55, 0.79) Ca: 0.27 (-0.58, 1.11) Cl: 0.14 (-0.39, 0.67) Fe: 0.15 (-1.00, 1.30) Cu: -0.08 (-0.74, 0.57) SDNN ABS: 2.91 (-2.54, 8.67) S: 0.25 (-4.42, 5.14) V: 0.73 (-4.74, 6.53) Zn: 3.85 (-0.26, 8.13) Ca: 3.39 (-1.80, 8.86) Cl: 1.13 (-1.48, 3.81) Fe: 6.69 (0.11, 13.69) Cu: 3.00 (-0.85, 7.00) **Notes:** Estimates provided are for all subjects at lag 1, estimates are also available at lags 0, 2, and 3, as well as for subjects w/o beta-blockers at lags 0-3.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: DeMeo et al. (2004, 087346) **Period of Study:** Jul-Aug 1999 **Location:** Boston, MA	**Outcome:** Oxygen saturation **Age Groups**: 60.4-89.2 yr **Study Design:** Cross-sectional study **N:** 28 adult participants **Statistical Analyses:** GLM, Natural Spline Smoothing, Regression Analysis, Random-effects model **Covariates:** Mean temperature, Dew point temperature, Barometric pressure, Medication use **Season**: Summer **Dose-response Investigated?** No **Statistical Package**: S-PLUS, SAS **Lags Considered:** Hourly lags between 2 and 7 h	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 6 h, 12 h, 24 h, 48 h	**PM Increment:** IQR (13.42 µg/m^3) increase 6 h: 13.42 µg/m^3 12 h: 10.81 µg/m^3 24 h: 10.26µg/m^3 48: 10.57 µg/m^3 Overall: 0.172% (-0.313, 0.031) decrease 6 h: -0.769% (-1.21 to -0.327) decrease B-blocker users: -0.062% (-0.248, 0.123) Rest: 6 h: -0.173 (-0.345 to -0.001) 12 h: -0.160 (-0.308 to -0.012) 24 h: -0.169 (-0.316 to -0.022) 48 h: -0.153 (-0.304, 0.002) Exercise: 6 h: -0.005 (-0.215, 0.205) 12 h: -0.014 (-0.196, 0.168) 24 h: 0.001 (-0.180, 0.182) 48 h: -0.011 (-0.196, 0.174) Post exercise Rest: 6 h: -0.173 (-0.332 to -0.014) 12 h: -0.128 (-0.266, 0.010) 4 h: -0.113 (-0.250, 0.023) 48 h: -0.157 (-295 to -0.019) Paced breathing: 6 h: -0.142 (-0.292, 0.007) 12 h: -0.139 (-0.269 to -0.010) 24 h: -0.121 (-0.248, 0.007) 48 h: -0.082 (0.211, 0.047) Summary over protocol 6 h: -0.131 (-0.247 to -0.015) 12 h: -0.120 (-0.221, 0.020) 24 h: -0.112 (-0.212 to -0.013) **Notes:** Fig of the variation in oxygen saturation during the first rest period vs.. individual hourly lag measurements for $PM_{2.5}$
Reference: Diez-Roux et al. (2006, 156400) **Period of Study:** Baseline data collected Jun 2000-Aug 2002 **Location:** USA 6 field centers: Baltimore, MD Chicago, IL Forsyth Co, NC Los Angeles, CA New York, NY St. Paul, MN	**Outcome:** C-reactive protein (CRP) assessed continuously and as a dichotomous variable (cutpoint, 3 mg/L) interleukin-6 (IL-6) **Age Groups:** 45-84 yr **Study Design:** Cross-sectional **N:** 5634 persons **Statistical Analyses:** Linear regression & logistic regression **Covariates:** Age, sex, race/ethnicity, general health status, BMI, diabetes, cigarette status, secondhand smoke, physical activity, arthritis flare in last 2 wk, medications, infections in last 2 wk (also ran models including site, copollutants, and weather) **Season:** Examined seasonal patterns in the residuals of fully adjusted models stratified by season **Dose-response Investigated?** No **Statistical Package:** NR	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Prior day, prior 2 days, prior wk, prior 30 days, and prior 60 days **Mean (SD):** Presented in Fig 1 by site **Percentiles:** Presented in Fig 1 by site **Range:** NR **Monitoring Stations:** NR Long-term exposure to PM estimated based on residential history reported retrospectively All addresses geocoded Ambient AP obtained from U.S. EPA **Copollutant:** SO_2 NO_2 CO O_3	**PM Increment:** 10 µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** Adjusted (all personal-level covariates) relative difference in CRP (mg/L) per 10 µg/m^3 increase in $PM_{2.5}$ Prior day: 0.99 (0.96, 1.01) Prior 2 days: 0.99 (0.96, 1.01) Prior 7 days: 1.00 (0.96, 1.04) Prior 30 days: 1.03 (0.98, 1.10) Prior 60 days: 1.04 (0.97, 1.11) Odds Ratios of CRP of ≥ 3 mg/L per 10 µg/m^3 increase in $PM_{2.5}$ (adjusted for all personal-level covariates) Prior day: 0.98 (0.92, 1.04) Prior 2 days: 0.99 (0.93, 1.06) Prior 7 days: 1.05 (0.96, 1.15) Prior 30 days: 1.12 (0.98, 1.29) Prior 60 days: 1.12 (0.96, 1.32)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Dubowsky et al. (2006, 088750) **Period of Study:** Mar-Jun 2002 **Location:** St. Louis, Missouri	**Outcome:** White blood cells (WBC), C-reactive protein (CRP), interleukin-6 (IL-6) **Age Groups:** ≥ 60 yr **Study Design:** Panel (4 planned repeated measures n = 35 participated in 4 trips) **N:** 44 participants **Statistical Analyses:** Linear mixed models **Covariates:** Sex, obesity, diabetes, smoking history, time-varying parameters (apparent temperature, h, day, trip, residence, mold, pollen, illness, and juice intake), medication and vitamin consumption (day of blood draw) **Season:** Limited data collection period **Dose-response Investigated?** No **Statistical Package:** SAS v8.02	**Pollutant:** $PM_{2.5}$ (ambient) **Averaging Time:** Hourly data used to calculate avg concentrations over 1-7 days preceding the blood draw (ambient $PM_{2.5}$) Microenvironmental $PM_{2.5}$ measures were avgd over the 1-2 days preceding the blood draw **Mean (SD) (1-day):** 16 (6.0) **Percentiles (1-day):** 0: 6.5 25th: 12 75th: 22 100th: 28 **Monitoring Stations:** 1 ambient monitor **Copollutant:** $PM_{2.5}$ (ambient) BC (ambient) $PM_{2.5}$ (microenvironment) CO NO_2 SO_2 O_3	**PM Increment:** 6.1 µg/m^3 (5-day mean) **Effect Estimate [Lower CI, Upper CI]:** **Note:** Most results presented in figures. Selected result in abstract text: % change in WBC per increase in IQR (5.4 µg/m^3) of $PM_{2.5}$ avgd over the previous week: 5.5 (0.1, 11) Associations (% changes and 95%CI) between 5-day mean ambient concentrations and markers of inflammation per increase (IQR) in pollutant. CRP: All participants: 14 (-5.4, 37) Among those with all 3 conditions (diabetes, obesity, and hypertension): 81 (21, 172) Among those with at least 2 of the conditions: 11 (-7.3, 33) IL-6: All participants: -2.1 (-13, 11) Among those with all 3 conditions (diabetes, obesity, and hypertension): 23 (-5.3, 59) Among those with at least 2 of the conditions: -3.1 (-14, 9.7) WBC (x109/L): All participants: 3.4 (-1.8, 8.9) Among those with all 3 conditions (diabetes, obesity, and hypertension): 0.4 (-8.8, 11) Among those with at least 2 of the conditions: 3.6 (-1.7, 9.1)
Reference: Dubowsky et al. (2006, 088750) **Period of Study:** Mar-Jun 2002 **Location:** St. Louis, Missouri	**Outcome:** White blood cells (WBC), C-reactive protein (CRP), interleukin-6 (IL-6) **Age Groups:** ≥ 60 yr **Study Design:** Panel (4 planned repeated measures n = 35 participated in 4 trips) **N:** 44 participants **Statistical Analyses:** Linear mixed models **Covariates:** Sex, obesity, diabetes, smoking history, time-varying parameters (apparent temperature, h, day, trip, residence, mold, pollen, illness, and juice intake), medication and vitamin consumption (day of blood draw) **Season:** Limited data collection period **Dose-response Investigated?** No **Statistical Package:** SAS v8.02	**Pollutant:** BC (ng/m^3) (ambient) **Averaging Time:** Hourly data used to calculate avg concentrations over 1-7 days preceding the blood draw (ambient PM) microenvironmental $PM_{2.5}$ measures were avgd over the 1-2 days preceding the blood draw **Mean (SD) (1-day):** 900 (280) **Percentiles (1-day):** 0: 290 25th: 730 75th: 1,100 100th: 1,400 **Monitoring Stations:** 1 ambient monitor **Copollutant:** $PM_{2.5}$ (ambient) BC (ambient) $PM_{2.5}$ (microenvironment) CO NO_2 SO_2 O_3	**PM Increment:** 230 ng/m^3 (5-day mean) **Effect Estimate [Lower CI, Upper CI]:** **Note:** Most results presented in figures. **Associations (% changes and 95%CI) between 5-day mean ambient concentrations and markers of inflammation per increase (IQR) in pollutant.** CRP: All participants: 13 (-0.34, 28) Among those with all 3 conditions (diabetes, obesity, and hypertension): 49 (16, 90) Among those with at least 2 of the conditions: 9.0 (-3.8, 24) IL-6: All participants: -0.8 (-8.9, 8.0) Among those with all 3 conditions (diabetes, obesity, and hypertension): 15 (-2.2, 35) Among those with at least 2 of the conditions: -2.7 (-11, 6.2) WBC (x109/L): All participants: 1.3 (-2.1, 4.8) Among those with all 3 conditions (diabetes, obesity, and hypertension): 0.05 (-5.9, 6.3) Among those with at least 2 of the conditions: 1.5 (-2.0, 5.1)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ebelt et al. (2005, 056907) **Period of Study:** Summer of 1998 **Location:** Vancouver, Canada	**Outcome:** CVD **Age Groups**: Range from 54-86 yr mean age= 74 yr **Study Design: E**xtended analysis of a repeated-measures panel study **N:** 16 persons with COPD **Statistical Analyses:** Earlier analysis expanded by developing mixed-effect regression models and by evaluating additional exposure indicators **Dose-response Investigated?** No **Statistical Package**: SAS V8	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** Ambient $PM_{2.5}$: 11.4 ± 4.6 Exposure to ambient $PM_{2.5}$: 7.9 ± 3.7 **Range (Min, Max):** Ambient $PM_{2.5}$: 4.2-28.7 Exposure to ambient $PM_{2.5}$: 0.9-21.3 **Monitoring Stations**: 5 **Copollutant (correlation):** Ambient concentrations and exposure to ambient PM were highly correlated for each respective metric: r ≥ 0.71	**PM Increment:** Increment: C2.5: IQR = 5.8 SBP (mm Hg): -1.70 (-3.48-0.08) DBP (mm Hg): -0.58 (-2.02-0.85) Ln-SVE (bph): 0.20 (0.00-0.40) HR (bpm): 0.93 (-0.90-2.75) SDNN (ms): -4.37 (-9.40-0.65) R-MSSD (ms): -2.79 (-6.16-0.57) Increment: NS_C2.5: IQR = 4.2 SBP (mm Hg): -1.52 (-2.94- -0.09) DBP (mm Hg): -0.77 (-1.87-0.32) Ln-SVE (bph): 0.19 (-0.01-0.38) HR (bpm): 1.03 (-0.43-2.48) SDNN (ms): -3.83 (-7.77-0.11) R-MSSD (ms): -2.90 (-5.55- -0.25) Increment: S_C2.5: IQR = 1.5 SBP (mm Hg): -1.10 (-3.48-1.28) DBP (mm Hg): 0.76 (-1.15-2.68) Ln-SVE (bph): 0.09 (-0.05-0.23) HR (bpm): -0.42 (-2.28-1.44) SDNN (ms): -3.14 (-9.73-3.45) R-MSSD (ms): 0.24 (-5.14-5.63) Increment: A2.5: IQR = 4.4 SBP (mm Hg): -1.90 (-3.66- -0.14) DBP (mm Hg): -0.33 (-1.72-1.06) Ln-SVE (bph): 0.20 (0.02-0.37) HR (bpm): 0.57 (-1.34-2.47) SDNN (ms): -3.91 (-8.79-0.97) R-MSSD (ms): -1.05 (-4.79-2.17) Increment: NS_A2.5: IQR = 3.4 SBP (mm Hg): -1.70 (-3.27- -0.14) DBP (mm Hg): -0.51 (-1.71-0.70) Ln-SVE (bph): 0.20 (0.02-0.37) HR (bpm): 0.69 (-0.96-2.35) SDNN (ms): -4.18 (-8.51-0.15) R-MSSD (ms): -1.40 (-4.40-1.60) Increment: S_T2.5: IQR = 0.9 SBP (mm Hg): -1.55 (-3.35-0.26) DBP (mm Hg): 0.49 (-0.91-1.90) Ln-SVE (bph): 0.08 (-0.14-0.19) HR (bpm): -0.24 (-1.75-1.26) SDNN (ms): -0.68 (-4.74-3.38) R-MSSD (ms): 0.91 (-3.51-5.33) Increment: T2.5: IQR = 10.1 SBP (mm Hg): -1.26 (-2.60-0.08) DBP (mm Hg): 0.34 (-1.26-1.94) Ln-SVE (bph): 0.01 (-0.10-0.11) HR (bpm): -0.23 (-1.09-0.63) SDNN (ms): -2.11 (-4.90-0.68) R-MSSD (ms): -0.83 (-3.60-1.94) Increment: N2.5: IQR = 8.9 SBP (mm Hg): -0.81 (-2.15-0.53) DBP (mm Hg): 0.40 (-1.19-1.98) Ln-SVE (bph): -0.04 (-0.18-0.10) HR (bpm): -0.35 (-0.85-0.14) SDNN (ms): -1.10 (-3.10-0.90) R-MSSD (ms): -0.54 (-2.54-1.46) **Note:** Total personal fine particle exposure (T) were dominated by exposures to non ambient particles which were not correlated with ambient fine particle exposure (A) or ambient concentrations (C). Results for each of these metrics are listed.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Fan et al. (2008, 191979) **Period of Study:** Feb-May 2005 **Location:** Paterson, New Jersey	**Outcome:** Cardiopulmonary Health (FEV, FVC, PEF, SDNN, HR) **Age Groups:** 61.2 (13.7) **Study Design:** Panel **N:** 11 **Statistical Analyses:** Mixed Effects models, Linear Regression models **Covariates:** Temperature, humidity **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 0	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily **Mean (SD): |** $\Delta PM_{2.5}$ avg Morning: 35.2 (25.9) Afternoon: 24.1 (22.1) $\Delta PM_{2.5}$ peak Morning: 71.3 (56.1) Afternoon: 64.3 (43.5) **Range:** $\Delta PM_{2.5}$ avg Morning: 1.1 - 87 Afternoon: 1.2 - 98 $\Delta PM_{2.5}$ peak Morning: 4.0 - 278 Afternoon: 3.0 - 150 **Monitoring Stations:** NR **Copollutant:** NR **Co-pollutant Correlation:** N/A	**PM Increment:** 10 µg/m^3 **Beta (SE), p-value:** **∆SDNN** Morning, $\Delta PM_{2.5}$ avg 15min: -14.5 (6.9), 0.06 2h: -18.9 (4.2), 0.0002 4h: -2.5 (8.6), 0.78 Morning, $\Delta PM_{2.5}$ peak 15min: -9.2 (11.2), 0.43 2h: -5.1 (13.8), 0.72 4h: -7.4 (12.0), 0.55 Afternoon, $\Delta PM_{2.5}$ avg 15min: -2.4 (7.6), 0.77 2h: -20.2 (10.8), 0.10 4h: -0.7 (11.2), 0.95 Afternoon, $\Delta PM_{2.5}$ peak 15min: 0.6 (8.9), 0.95 2h: 19.2 (14.6), 0.23 4h: -6.8 (14.1), 0.64 **∆ HR** Morning, $\Delta PM_{2.5}$ avg 15min: 1.2 (3.1), 0.71 2h: -5.5 (2.9), 0.08 4h: -3.1 (4.6), 0.51 Morning, $\Delta PM_{2.5}$ peak 15min: 0.8 (4.4), 0.86 2h: -7.2 (4.2), 0.11 4h: -7.1 (6.3), 0.28 Afternoon, $\Delta PM_{2.5}$ avg 15min: -2.0 (4.0), 0.62 2h: 0.9 (5.4), 0.87 4h: 8.2 (5.2), 0.14 Afternoon, $\Delta PM_{2.5}$ peak 15min: -5.6 (5.3), 0.31 2h: 3.1 (8.1), 0.71 4h: 11.1 (8.1), 0.20 ∆ FEV_1 Morning, $\Delta PM_{2.5}$ avg: 0.02 (0.04), 0.68 Morning, $\Delta PM_{2.5}$ peak: -0.13 (0.08), 0.16 **∆ FVC** Morning, $\Delta PM_{2.5}$ avg: -0.10 (0.09), 0.31 Morning, $\Delta PM_{2.5}$ peak: -0.12 (0.17), 0.51 **∆ PEF** Morning, $\Delta PM_{2.5}$ avg: -0.54 (0.62), 0.42 Morning, $\Delta PM_{2.5}$ peak: -1.46 (1.12), 0.24 **Notes:** Estimates relative to increases in the avg and peak $PM_{2.5}$ concentrations
Reference: Folino et al. (2009, 191902) **Period of Study:** Jun 2006-May 2007 **Location:** Padua, Italy	**Outcome:** HRV & Inflammatory Markers **Age Groups:** 45-65 yr **Study Design:** Panel **N:** 39 patients w/ myocardial infarction **Statistical Analyses:** Linear Regression Model, ANOVA **Covariates:** Temperature, relative humidity, atmospheric pressure, beta-blocker, aspirin, or nitrate consumption, smoking habit **Dose-response Investigated?** No **Statistical Package:** Stata **Lags Considered:** NR	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** Summer: 33.9 (12.7) Winter: 62.1 (27.9) Spring: 30.8 (14.0) **Monitoring Stations:** NR **Copollutant:** PM_{10}, $PM_{0.25}$ **Co-pollutant Correlation:** NR	**PM Increment:** 1 µg/m^3 **Beta (SE), p-value:** SDNN: 0.109 (0.115), 0.345 SDANN: 0.127 (0.126), 0.314 RMSSD: 0.045 (0.040), 0.256 pH: 0.002 (0.001), 0.041 LTB4: 0.590 (0.324), 0.069 eNO: -0.002 (0.003), 0.503 PTX3: -0.004 (0.002), 0.013 C-reactive protein: -0.008 (0.005), 0.115 CC16: -0.002 (0.002), 0.410 IL-8: 0.000 (0.003), 0.989

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Folino et al. (2009, 191902) **Period of Study:** Jun 2006-May 2007 **Location:** Padua, Italy	**Outcome:** HRV & Inflammatory Markers **Age Groups:** 45-65 yr **Study Design:** Panel **N:** 39 patients w/ myocardial infarction **Statistical Analyses:** Linear Regression Model, ANOVA **Covariates:** Temperature, relative humidity, atmospheric pressure, beta-blocker, aspirin, or nitrate consumption, smoking habit **Dose-response Investigated?** No **Statistical Package:** Stata **Lags Considered:** NR	**Pollutant:** $PM_{0.25}$ **Averaging Time:** 24 h **Mean (SD):** Summer: 17.6 (7.5) Winter: 30.5 (17.4) Spring: 18.8 (10.8) **Monitoring Stations:** NR **Copollutant:** PM_{10}, $PM_{2.5}$ **Co-pollutant Correlation:** NR	**PM Increment:** 1 µg/m^3 **Beta (SE), p-value:** SDNN: 0.214 (0.204), 0.295 SDANN: 0.214 (0.214), 0.316 RMSSD: 0.081 (0.077), 0.291 pH: 0.005 (0.002), 0.004 LTB4: 0.835 (0.533), 0.117 eNO: -0.006 (0.005), 0.182 PTX3: -0.006 (0.003), 0.071 C-reactive protein: -0.011 (0.007), 0.104 CC16: 0.001 (0.004), 0.890 IL-8: -0.004 (0.006), 0.527
Reference: Goldberg et al. (2008, 180380) **Period of Study:** Jul 2002-Oct 2003 **Location:** Montreal, Canada	**Outcome:** Oxygen saturation & pulse rate **Age Groups:** 50-85 yr **Study Design:** Panel **N:** 31 **Statistical Analyses:** Mixed Random Effects Model **Covariates:** Body temperature, consumption of salt, intake of fluids, being ill the day before, ambient temperature, relative humidity, barometric pressure **Dose-response Investigated?** No **Statistical Package:** Splus **Lags Considered:** lags 1 day; 0- to 2-day avg	**Pollutant:** $PM_{2.5}$ **Averaging Time: D**aily **IQR:** 7.3 **Monitoring Stations:** 8 **Co-pollutant:** CO, NO_2, SO_2, O_3 **Co-pollutant Correlation** CO: 0.72 NO_2: 0.62	**PM Increment:** Interquartile Range (7.3 µg/m^3) **Mean Difference (Lower CI, Upper CI), lag:** Oxygen Saturation Unadjusted: -0.087 (-0.143, -0.031), lag 0 Unadjusted: -0.058 (-0.114, -0.002), lag 1 Unadjusted: -0.083 (-0.155, -0.010), lag 0-2-day avg Adjusted: -0.056 (-0.117, 0.005), lag 0 Adjusted: -0.019 (-0.079, 0.041), lag 1 Adjusted: -0.039 (-0.118, 0.039), lag 0-2-day avg Pulse Rate Unadjusted: 0.226 (-0.037, 0.489), lag 0 Unadjusted: 0.288 (0.022, 0.554), lag 1 Unadjusted: 0.420 (0.067, 0.772), lag 0-2-day avg Adjusted: 0.158 (-0.136, 0.451), lag 0 Adjusted: 0.246 (-0.040, 0.531), lag 1 Adjusted: 0.353 (-0.034, 0.740), lag 0-2-day avg

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Goldberg et al. (2008, 180380) **Period of Study:** Jul 2002-Oct 2003 **Location:** Montreal, Canada	**Outcome:** Shortness of Breath & General health **Age Groups:** 50-85 yr **Study Design:** Panel **N:** 31 **Statistical Analyses:** Mixed Random Effects Model **Covariates:** Body temperature, consumption of salt, intake of fluids, being ill the day before, ambient temperature, relative humidity, barometric pressure **Dose-response Investigated?** No **Statistical Package:** Splus **Lags Considered:** lags 0-4 days; 0- to 2-day avg	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily **Mean:** 9.5 **Median:** 7.0 **Min:** 0.8 **Max:** 50.2 **IQR:** 7.3 **Monitoring Stations:** 8 **Co-pollutant:** CO, NO_2, SO_2, O_3 **Co-pollutant Correlation** CO: 0.66 NO_2: 0.54 O_3: 0.32 SO_2: 0.50	**PM Increment:** Interquartile Range (7.3 µg/m^3) **Mean Difference (Lower CI, Upper CI), lag:** General Health Unadjusted: -0.317 (-0.699, 0.064), lag 0 Unadjusted: -0.284 (-0.670, 0.103), lag 1 Unadjusted: -0.048 (-0.427, 0.332), lag 2 Unadjusted: -0.241 (-0.620, 0.139), lag 3 Unadjusted: -0.010 (-0.390, 0.370), lag 4 Unadjusted: -0.482 (-1.053, 0.090), lag 0-2-day avg Adjusted: -0.125 (-0.545, 0.295), lag 0 Adjusted: -0.167 (-0.568, 0.234), lag 1 Adjusted: -0.081 (-0.464, 0.302), lag 2 Adjusted: -0.222 (-0.602, 0.157), lag 3 Adjusted: 0.016 (-0.364, 0.396), lag 4 Adjusted: -0.281 (-0.886, 0.325), lag 0-2-day avg Shortness of breath at night Unadjusted: -0.421 (-0.847, 0.006), lag 0 Unadjusted: -0.278 (-0.711, 0.155), lag 1 Unadjusted: -0.100 (-0.526, 0.327), lag 2 Unadjusted: -0.220 (-0.645, 0.206), lag 3 Unadjusted: -0.206 (-0.632, 0.220), lag 4 Unadjusted: -0.555 (-1.172, 0.063), lag 0-2-day avg Adjusted: -0.171 (-0.639, 0.297), lag 0 Adjusted: -0.130 (-0.579, 0.319), lag 1 Adjusted: -0.127 (-0.553, 0.299), lag 2 Adjusted: -0.192 (-0.616, 0.231), lag 3 Adjusted: -0.171 (-0.594, 0.253), lag 4 Adjusted: -0.301 (-0.952, 0.350), lag 0-2-day avg
Reference: Ibald-Mulli et al. (2004, 087415) **Period of Study: W**inter 1998-1999 **Location:** Helsinki, Finland Erfurt, Germany Amsterdam, the Netherlands	**Outcome:** Blood Pressure & Heart Rate **Age Groups:** 40-84 **Study Design:** Panel **N:** 131 adults w/ CHD **Statistical Analyses:** Linear Regression **Covariates: T**rend, day of week, temperature, barometric pressure, relative humidity, medication use **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 0-2, 5-day avg	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** Downtown: 40 (20) Tunney's Pasture: 10 (10) p-value 0.000 **Monitoring Stations:** NR **Copollutant:** $PM_{1.0}$ **Co-pollutant Correlation:** N/A	**PM Increment:** Interquartile Range (27.02 µg/m^3) **Beta (SE), p-value:** Flow mediated vasodilation (%): -0.016 (0.0072) p=0.03 Heart Rate (beats/min): 0.081 (0.135) p=0.55 Diastolic blood pressure (mmHg): 0.088 (0.088) p=0.32 Systolic blood pressure (mmHg): -0.108 (0.006) p=0.48
Reference: Langrish et al. (2009, 191908) **Period of Study:** Aug 2008 **Location:** Beijing, China	**Outcome:** Cardiovascular Effects **Age Groups:** Median 28 yr **Study Design:** Panel **N:** 15 **Statistical Analyses:** NR **Covariates:** NR **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** NR	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **Mean:** W/o mask: 86 W/ mask: 140 **Monitoring Stations:** NR **Co-pollutant:** CO, SO_2, NO_2 **Co-pollutant Correlation:** N/A	**PM Increment:** NR **Mean (Lower CI, Upper CI):** W/o Mask (Day) SBP: 100 (104, 116) DBP: 73 (69, 76) MAP: 85 (81, 88) Heart Rate: 79 (74, 84) Avg NN interval: 829 (789, 869) pNN50: 15.9 (10.7, 21.0) RMSSD: 35.1 (29.2, 41.0) SDNN: 61.2 (54.9, 67.5) Triangular index: 12.9 (11.9, 13.9) LF power: 816 (628, 1004) HF power: 460 (325, 595) LFn: 62.8 (56.7, 68.9) HFn: 29.2 (25.5, 32.8) HF/LF ratio: 0.738 (0.507, 0.970) W/ Mask (Day) SBP: 109 (104, 114) DBP: 73 (70-76) MAP: 85 (81, 89)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Heart Rate: 78 (73, 82) Avg NN interval: 850 (805, 896) pNN50: 17.9 (14.2, 21.6) RMSSD: 37.1 (32.2, 42.0) SDNN: 65.5 (59.0, 72.2)* Triangular index: 13.8 (13.0, 14.5) LF power: 919 (717, 1122)* HF power: 485 (400, 569) LFn: 64.5 (60.6, 68.4) HFn: 30.0 (27.0, 33.1) HF/LF ratio: 0.680 (0.519, 0.842) W/o Mask (During Walk) SBP: 121 (115, 127) DBP: 81 (75-87) MAP: 94 (89, 99) Heart Rate: 88 (82, 94) Avg NN interval: 594 (562, 627) pNN50: 3.3 (0.8, 5.7) RMSSD: 17.2 (13.4, 21.0) SDNN: 45.8 (36.8, 54.8) Triangular index: 10.7 (9.1, 12.4) LF power: 313 (170, 455) HF power: 76.5 (33.6, 120.0) LFn: 68.2 (60.9, 75.5) HFn: 16.1 (11.9, 20.3) HF/LF ratio: 0.259 (0.173, 0.344) W/ Mask (During Walk) SBP: 114 (108, 120) DBP: 79 (74, 83) MAP: 90 (86, 94) Heart Rate: 91 (85, 97) Avg NN interval: 613 (571, 655) pNN50: 2.1 (-0.1, -4.4) RMSSD: 20.0 (15.5, 24.6) SDNN: 54.8 (42.5, 67.0) Triangular index: 11.4 (9.4, 13.3) W/ Mask (During Walk) LF power: 414 (233, 595) HF power: 116.8 (52.6, 181.0) LFn: 67.9 (61.9, 73.9) HFn: 16.0 (12.5, 19.4) HF/LF ratio: 0.247 (0.180, 0.314) **Mean (SD):** W/o Mask (After Walk) Headache: 2.53 (5.55) Dizziness: 1.07 (2.22) Tiredness: 8.47 (12.14) Sickness: 1.07 (2.22) Cough: 1.80 (4.80) Difficulty Breathing: 0.67 (0.90) Eye irritation: 1.40 (3.60) Throat irritation: 1.47 (4.07) Nose irritation: 1.53 (3.78) Unpleasant Smell: 0.93 (1.22) Bad taste: 0.73 (0.96) Difficulty walking: 12.53 (13.24) Perception of Pollution: 19.80 (18.37) W/ Mask (After Walk) Headache: 0.73 (1.03) Dizziness: 0.80 (1.57 Tiredness: 7.40 (9.37) Sickness: 0.87 (1.51) Cough: 1.00 (1.73) Difficulty Breathing: 3.80 (8.10) Eye irritation: 1.67 (3.27) Throat irritation: 1.07 (2.63) Nose irritation: 1.07 (1.91) Unpleasant Smell: 0.60 (0.91) Bad taste: 0.60 (1.18) Difficulty walking: 15.13 (11.51) Perception of Pollution: 11.60 (10.44) *p < 0.05 **Notes:** Estimates also available for 24 h, night, before walk, and 24 h after walk.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Lanki et al. (2006, 088412) **Period of Study:** Fall 1998-spring 1999 **Location:** Helsinki, Finland	**Outcome:** ST segment depressions (2 endpoints: >0.1mV regardless of the direction of the ST slope and >0.1mV with horizontal or downward slope [stricter criteria]) **Age Groups:** Mean = 68.2 (6.5) yr **Study Design:** Panel **N:** 45 elderly nonsmoking persons with stable coronary heart disease 342 total exercise tests for analyses **Statistical Analyses:** Generalized additive models with penalized splines (logistic regression) principal components analysis and linear regression of 13 measured elements used to apportion $PM_{2.5}$ mass between different sources **Covariates:** Subject, linear terms for time trend, temperature, relative humidity, penalized spline for change in heart rate during the exercise test **Season:** NR **Dose-response Investigated?** No **Statistical Package:** S-plus 2000 and R	**Pollutant:** $PM_{2.5}$ (Analyses conducted for source specific $PM_{2.5}$) **Averaging Time:** Daily filter samples **Mean:** Crustal: 0.6 Long-range transported: 6.4 Oil combustion: 1.6 Salt: 0.9 Local traffic: 2.9 Total: 12.8 **Percentiles:** Crustal 25: 0.0 50: 0.4 75: 1.1; Max: 5.3 Long-range transported 25: 2.2 50: 5.5 75: 9.8; Max: 26.5 Oil combustion 25: 0.6 50: 1.3 75: 2.3; Max: 12.2 Salt 25: 0.3 50: 0.8 75: 1.2; Max: 5.9 Local traffic 25: 1.7 50: 2.5 75: 3.4; Max: 12.0 Total 25: 8.3 50: 10.6 75: 15.9; Max: 39.8 **Monitoring Stations:** 1 monitor **Copollutant (correlation):** Correlations with $PM_{2.5}$: Crustal: r = -0.01 Long-range transported: r = 0.82 Oil combustion: r = 0.35 Salt: r = 0.19 Local traffic: r = 0.26	**PM Increment:** 1 $\mu g/m^3$ **Effect Estimate [Lower CI, Upper CI]:** Adjusted ORs between daily source-specific $PM_{2.5}$ concentrations and ST-segment depressions. ST-segment depression defined as >0.1 mV (n = 62) **Crustal** Lag 0: 0.80 (0.47, 1.36) Lag 1: 0.66 (0.40, 1.10) Lag 2: 1.18 (0.68, 2.06) Lag 3: 1.87 (0.85, 4.09) **Long-range transport** Lag 0: 0.94 (0.84, 1.05) Lag 1: 1.00 (0.92, 1.08) Lag 2: 1.11 (1.02, 1.20) Lag 3: 1.06 (0.95, 1.18) **Oil combustion** Lag 0: 0.87 (0.57, 1.32) Lag 1: 1.04 (0.75, 1.45) Lag 2: 1.10 (0.83, 1.46) Lag 3: 1.12 (0.79, 1.58) **Salt** Lag0: 1.03 (0.57, 1.85) Lag1: 0.72 (0.37, 1.40) Lag2: 0.66 (0.31, 1.40) Lag3: 1.55 (0.83, 2.89) **Local traffic** Lag 0: 0.91 (0.69, 1.21) Lag 1: 1.22 (0.88, 1.69) Lag 2: 1.53 (1.19, 1.97) Lag 3: 0.98 (0.78, 1.23) ST-segment depression defined as >0.1 mV with horizontal or downward slope (n = 46) **Crustal** Lag0: 0.76 (0.42, 1.35) Lag1: 0.41 (0.22, 0.79) Lag2: 1.17 (0.65, 2.09) Lag3: 1.60 (0.72, 3.59) **Long-range transport** Lag 0: 0.98 (0.86, 1.10) Lag 1: 1.03 (0.95, 1.12) Lag 2: 1.11 (1.02, 1.21) Lag 3: 1.02 (0.95, 1.10) **Oil combustion** Lag 0: 0.95 (0.61, 1.49) Lag 1: 1.13 (0.76, 1.68) Lag 2: 1.33 (0.98, 1.80) Lag 3: 1.29 (0.90, 1.86) **Salt** Lag 0: 1.15 (0.56, 2.38) Lag 1: 0.90 (0.44, 1.81) Lag 2: 1.39 (0.63, 3.08) Lag 3: 1.93 (1.00, 3.72) **Local traffic** Lag 0: 0.89 (0.64, 1.23) Lag 1: 1.21 (0.86, 1.71) Lag 2: 1.37 (1.03, 1.83) Lag 3: 1.03 (0.80, 1.32) Adjusted ORs for the association of indicator elements of $PM_{2.5}$ sources and ST-segment depressions in multipollutant models (models include all 5 indicator elements). ST-segment depression defined as >0.1 mV (n = 62) **Si (Crustal)** Lag0: 0.73 (0.39, 1.38)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Lag1: 0.48 (0.25, 0.93) Lag2: 0.78 (0.35, 1.71) Lag3: 1.95 (0.69, 5.48) **S (Long-range transport)** Lag0: 0.70 (0.25, 1.95) Lag1: 0.58 (0.23, 1.47) Lag2: 1.08 (0.44, 2.63) Lag3: 1.60 (0.73, 3.48) **Ni (Oil combustion)** Lag0: 0.78 (0.30, 2.04) Lag1: 1.20 (0.58, 2.46) Lag2: 1.15 (0.61, 2.18) Lag3: 1.02 (0.41, 2.54) **Cl (Salt)** Lag0: 1.03 (0.79, 1.34) Lag1: 0.88 (0.56, 1.38) Lag2: 1.02 (0.62, 1.69) Lag3: 1.27 (0.85, 1.91) **ABS (Local traffic)** Lag0: 0.92 (0.36, 2.37) Lag1: 1.83 (0.73, 4.59) Lag2: 4.46 (1.69, 11.79) Lag3: 0.92 (0.40, 2.12) ST-segment depression defined as >0.1 mV with horizontal or downward slope (n = 46) **Si (Crustal)** Lag0: 0.67 (0.33, 1.36) Lag1: 0.34 (0.15, 0.81) Lag2: 0.81 (0.33, 2.00) Lag3: 1.90 (0.64, 5.65) **S (Long-range transport)** Lag0: 0.84 (0.29, 2.47) Lag1: 0.89 (0.34, 2.32) Lag2: 1.36 (0.54, 3.45) Lag3: 1.12 (0.53, 2.40) **Ni (Oil combustion)** Lag0: 1.10 (0.36, 3.37) Lag1: 1.16 (0.45, 2.96) Lag2: 1.64 (0.84, 3.20) Lag3: 1.63 (0.64, 4.14) **Cl (Salt)** Lag0: 1.13 (0.80, 1.62) Lag1: 0.99 (0.58, 1.68) Lag2: 1.55 (0.87, 2.76) Lag3: 1.45 (0.94, 2.25) **ABS (Local traffic)** Lag0: 0.74 (0.25, 2.23) Lag1: 1.76 (0.62, 5.00) Lag2: 4.86 (1.55, 15.26) Lag3: 0.97 (0.39, 2.41)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Lanki et al. (2008, 191984) **Period of Study:** Jan 1999-Apr 1999 **Location:** Helsinki, Finland	**Outcome:** ST Segment Depressions >0.1 mV **Age Groups:** 50+ **Study Design:** Panel **N:** 41 elderly people w/ CHD **Statistical Analyses:** Logistic Regression Model **Covariates:** Long-term time trend, temperature, humidity, change in heart rate following exercise test **Dose-response Investigated?** No **Statistical Package:** R **Lags Considered:** lags 0-24 h	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Hourly **25th, 50th, 75th, Max:** Personal $PM_{2.5}$ 1h: 6.9, 11.2, 15.8, 41.5 4h: 5.9, 10.0, 14.6, 41.3 8h: 5.0, 7.9, 13.0, 34.9 12h: 5.2, 7.8, 12.1, 28.8 22h: 6.6, 9.3, 13.0, 30.2 Outdoor $PM_{2.5}$ 1h: 8.9, 12.9, 17.8, 42.9 4h: 8.8, 12.5, 17.6, 40.8 8h: 8.3, 12.1, 17.2, 39.2 12h: 8.3, 11.9, 17.0, 37.0 24 h: 9.0, 12.5, 17.7, 30.5 **Monitoring Stations:** 1 **Co-pollutant:** PM<0.1 **Co-pollutant Correlation** Personal & Outdoor $PM_{2.5}$ 1 h & 1 h: 0.70 4 h & 4 h: 0.54 8 h & 8 h: 0.60 12 h & 12 h: 0.50 22 h & 24 h: 0.80 **Notes:** 1-22 h pollutant averaging times. Correlations also available for personal-personal and outdoor-outdoor.	**PM Increment:** 10 µg/m^3 **Odds Ratio (Lower CI, Upper CI):** Personal $PM_{2.5}$ 1-h avg: 3.26 (1.07, 9.99)* 4-h avg: 2.42 (0.75, 7.83) 8-h avg: 1.57 (0.49, 5.09) 12-h avg: 1.96 (0.44, 8.64) 22-h avg: 2.06 (0.30, 14.10) Outdoor $PM_{2.5}$ 1-h avg: 1.77 (0.87, 3.58) 4-h avg: 2.47 (1.05, 5.85)* 8-h avg: 1.83 (0.80, 4.20) 12-h avg: 1.90 (0.77, 4.65) 24-h avg: 1.60 (0.59, 4.39) *p < 0.05
Reference: Liao et al. (2007, 180272) **Period of Study:** 1999-2004 **Location:** 24 U.S. States	**Outcome:** Ectopy **Age Groups:** women 50-79 yr **Study Design:** Panel **N:** 57,422 **Statistical Analyses:** logistic regression & random effects modeling **Covariates:** Age, race, center, education, history of CVD/chronic lung disease, rel. humidity, temperature, smoking **Dose-response Investigated?** No **Statistical Package:** SAS, Stata **Lags Considered:** lags 0-365 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily **Mean (SD)*:** All: 13.8 (79) No Ectopy: 13.8 (7.9) Any Ectopy: 13.8 (7.6) **5th, 95th percentile*:** All: 5, 29.1 No Ectopy: 5, 29.2 Any Ectopy: 5.06, 28.5 **Monitoring Stations:** NR‡ **Copollutant:** PM_{10} **Co-pollutant Correlation:** NR *Lag 1 ‡Monitors used in model for spatial interpolation of daily PM values.	**PM Increment:** 10 µg/m^3 **Percent Change (Lower CI, Upper CI):** All Ventricular Ectopy Lag 0: 1.01 (0.91, 1.13) Lag 1: 1.07 (0.96, 1.20) Lag 2: 1.09 (0.98, 1.21) Current Smoker Ventricular Ectopy Lag 0: 1.52 (1.04, 2.24) Lag 1: 2 (1.32, 3.03) Lag 2: 1.59 (0.99, 2.55) Nonsmoker Ventricular Ectopy Lag 0: 0.99 (0.89, 1.11) Lag 1: 1.05 (0.94, 1.17) Lag 2: 1.08 (0.97, 1.21) All Supraventricular Ectopy Lag 0: 1.04 (0.96, 1.13) Lag 1: 1.01 (0.93, 1.10) Lag 2: 0.96 (0.87, 1.05) All Ventricular or Supraventricular Ectopy Lag 0: 1.03 (0.96, 1.11) Lag 1: 1.04 (0.97, 1.11) Lag 2: 1 (0.94, 1.07)
Reference: Lipsett et al. (2006, 088753) **Period of Study:** Feb-May 2000 **Location:** Coachella Valley, CA	**Outcome:** HRV parameters, specifically SDNN, SDANN, r-MSSD, LF, HF, total power, triangular index (TRII). **Study Design:** Panel study **N:** 19 non-smoking adults with coronary artery disease **Statistical Analysis:** Mixed linear regression models with random effects parameters	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 2 h **Mean (range)** Indio: 23.2 (6.3-90.4) Palm Springs: 14 (4.7-52) **Monitoring Stations:** 2 **Copollutant:** O_3	**PM Increment:** SE*100 **Effect Estimate (change in HRV per unit increase in PM concentration):** SDNN: -0.37 msec (SE = 1.01) **Notes:** Weekly ambulatory 24 h ECG recordings (once per week for up to 12 wk), using Holter monitors, were made. Subjects' residences were within 5 mi of 1 of 2 PM monitoring sites. Decreased HRV was associated with $PM_{2.5}$, but these effects were not statistically significant. Regressed HRV parameters against 18: 00-20: 00 mean particulate pollution.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ljungman et al. (2008, 180266) **Period of Study:** Aug 2001-Dec 2006 **Location:** Stockholm, Sweden	**Outcome:** Ventricular Arrhythmia **Age Groups:** 28-85 yr **Study Design: C**ase-crossover **N:** 88 patients w/ implantable cardioverter defibrillators **Statistical Analyses:** Conditional logistic regression **Covariates:** Temperature, humidity, pressure, ischemic heart disease, ejection fraction, heart disease, diabetes, use of beta-blockers, age, BMI, location at time of arrhythmia, distance from air pollution monitor **Dose-response Investigated?** No **Statistical Package:** Stata, S-plus **Lags Considered:** lags 2-24 h	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Hourly **Median:** 2 h: 9.17 24 h: 9.49 **Min:** 2 h: 0.15 24 h: 2.97 **Max:** 2 h: 99.25 24 h: 47.07 **IQR:** 2 h: 6.69 24 h: 5.27 **Monitoring Stations:** 1 **Copollutant:** PM_{10}, NO_2 **Co-pollutant Correlation:** NR	**PM Increment:** Interquartile Range **Odds Ratio (Lower CI, Upper CI):** 2 h: 1.23 (0.84, 1.80) 24 h: 1.28 (0.90, 1.84) **Notes:** OR of ventricular arrhythmia for an IQR increase of air pollutants in different subgroups (Fig 2)
Reference: Ljungman et al. **(2009, 191983)** **Period of Study:** May 2003-Jul 2004 **Location:** Athens, Greece Helsinki, Finland Ausburg, Germany Barcelona, Spain Rome, Italy Stokholm, Sweeden	**Outcome:** Interleukin-6 Response **Age Groups:** 35-80 yr **Study Design:** Panel **N:** 955 male myocardial infarction survivors **Statistical Analyses:** Additive Mixed Models **Covariates:** Age, sex, BMI, city, HDL/total cholesterol, smoking, alcohol intake, HbA1c, NT-proBNP, history of MI, heart failure, or diabetes, phlegm **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 1 day	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean:** 17.7 **25th:** 10.9 **75th:** 21.9 **Monitoring Stations:** NR **Copollutant:** CO, NO_2, PNC, $PM_{2.5}$ **Co-pollutant Correlation:** PM_{10}: 0.81	**PM Increment:** Interquartile Range (11.0 µg/m^3) **Change of IL-6 (Lower CI, Upper CI), p-value:** 0.6 (-0.8, 2.0), 0.40
Reference: Luttman-Gibson et al. (2006, 089794) **Period of Study:** Jun-Dec 2000 **Location:** Steubenville, OH	**Outcome:** Heart rate variability **Age Groups:** **Study Design:** Panel study **N:** 32 participants **Statistical Analysis:** Linear mixed models	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 1 h 24 h **Mean (IQR)** $PM_{2.5}$: 20.0 (15.2) Sulfate: 6.9 (5.1) EC: 1.1 (0.6) **Copollutant:** NO_2, SO_2, O_3	**PM Increment:** IQR **Percent change (95% CI):** Each 13.4 µg/m^3 increase in 24 h mean $PM_{2.5}$ concentration was associated with: SDNN: -4.0% (95% CI: -7.0% to -0.9%) r-MSSD: -6.5% (95% CI: -12.1% to -0.6%) HF: -11.4% (95% CI: -21.5% to -0.1%) Each 5.1 µg/m^3 increase in sulfates on the previous day was associated with: SDNN: -3.3% (95% CI: -6.0% to -0.5%) r-MSSD: -5.6% (95% CI: -10.7%, 0.2%) HF: -10.3% (95% CI: -19.5% to -0.1%) **Notes:** The authors conclude that increases in both traffic related particles and sulfates may adversely effect autonomic function.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Mar et al. (2005, 087566) **Period of Study:** 1999-2001 **Location:** Seattle, WA	**Outcome:** Change in arterial O_2 saturation, heart rate, and blood pressure (SBP and DBP) **Age Groups:** >75 yr **Study Design:** Panel study **N:** 88 elderly subjects **Statistical Analysis:** GEE	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** Personal: 9.3(8.4) Indoor: 7.4 (4.8) Outdoor: 9.0 (4.6)	**PM Increment:** 10 µg/m^3 **Unit change in measure (95% CI):** Among all subjects: Each increase in outdoor same day $PM_{2.5}$ was associated with: SBP: -0.81 mmHg (95% CI: -2.34, 0.73) DBP: -0.46 mmHg (95% CI: -1.49 to 0.57) H: -0.75 beats/min (95% CI: -1.42 to -0.07) Each increase in indoor same day $PM_{2.5}$ was associated with: SBP: 0.92 mmHg (95% CI: -2.04 to 3.87) DBP: 0.38 mmHg (95% CI: -1.43 to 2.20) H: 0.22 beats/min (95% CI: -0.71 to 1.16) Each increase in personal same day $PM_{2.5}$ was associated with: SBP: 0.37 mmHg (95% CI: -0.93 to 1.67) DBP: -0.20 mmHg (95% CI: -0.85 to 0.46) H: 0.44 beats/min (95% CI: 0.04 to 0.84) **Notes:** Results by health status presented in Fig 1 Used 2 sessions that each were 10 consecutive days of measurements Used personal, indoor, and outdoor measures of $PM_{2.5}$
Reference: Metzger et al. (2007, 092856) **Period of Study:** Aug 1998-Dec 2002 **Location:** Atlanta, GA	**Outcome:** Days with any event recorded by the ICD, days with ICD shocks/defibrillation and days with either cardiac pacing or defibrillation **Study Design:** Repeated measures **N:** 884 subjects between 1993 and 2002 **Statistical Analysis:** Logistic regression with GEE to account for residual autocorrelation within subjects	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** $PM_{2.5}$: 17.8 (8.6) $PM_{2.5}$ sulfates: 5.0 (3.4) $PM_{2.5}$ EC: 1.7 (1.2) $PM_{2.5}$ OC: 4.4 (2.4) $PM_{2.5}$ water-soluble metals: 0.029 (0.024) **Percentiles:** $PM_{2.5}$: Median: 16.2 $PM_{2.5}$ sulfates: Median: 4.1 $PM_{2.5}$ EC: Median: 1.4 $PM_{2.5}$ OC: Median: 3.9 $PM_{2.5}$ water-soluble metals: Median: 0.022 **Copollutant:** O_3 NO_2 CO SO_2 Oxygenated hydrocarbons	**PM Increment: OR (95% CI):** Outcome = Any event recorded by ICD $PM_{2.5}$ OR = 1.00 (95% CI: 0.95, 1.04) $PM_{2.5}$ EC OR = 1.01 (95% CI: 0.98, 1.05) $PM_{2.5}$ OC OR = 1.01 (95% CI: 0.98, 1.03) $PM_{2.5}$ Sulfates OR = 0.99 (95% CI: 0.93, 1.06) $PM_{2.5}$ Water soluble metals OR = 0.95 (95% CI: 0.90, 1.00
Reference: O'Neill et al. (2007, 091362) **Period of Study:** May 1998-Dec 2002 **Location:** Boston, MA	**Outcome:** Soluble intercellular adhesion molecule 1 (ICAM-1) Vascular cell adhesion molecule 1 (VCAM-1) von Willebrand factor (vWF) **Age Groups:** Mean (SD): 56.6 (10.6) **Study Design:** Cross-sectional **N:** 92 participants (type 2 diabetic patients)	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h (lagged ma of days 0 to 1, 2, 3, 4, and 5) **Mean (SD):** 11.4 (5.9) Descriptive statistics represent entire study period **Percentiles:** IQR range: 7.6 **Range (Min, Max):** 0.07, 33.7)	**PM Increment:** IQR (specific to lag period) **Effect Estimate [Lower CI, Upper CI]:** % change per IQR of $PM_{2.5}$ **ICAM-1 -** All subjects Lag 0: 2.87 (-4.63, 10.95) 2 dma: 2.25 (-5.15, 10.22) 3 dma: 1.48 (-5.63, 9.11) 4 dma: 1.80 (-4.98, 9.07) 5 dma: 1.51 (-5.30, 8.80) 6 dma: 2.12 (-4.23, 8.89)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
	Statistical Analyses: linear regression **Covariates:** Apparent temperature, season, age, race, sex, glycosylated hemoglobin, cholesterol, smoking history, BMI **Dose-response Investigated?** No **Statistical Package:** NR	**Monitoring Stations:** 1 site **Copollutant:** $PM_{2.5}$ BC SO_4^{2-}	**Subjects not known to be taking statins** Lag 0: 5.47 (-3.74, 15.57) 2 dma: 5.70 (-3.70, 16.01) 3 dma: 4.57 (-4.31, 14.27) 4 dma: 4.57 (-4.27, 14.23) 5 dma: 3.80 (-4.84, 13.22) 6 dma: 3.79 (-4.49, 12.80) **Subjects who report smoking in the past (but not within 6 mo)** Lag 0: 0.9 (-9.56, 12.66) 2 dma: 0.40 (-12.08, 14.65) 3 dma: 1.34 (-9.23, 13.14) 4 dma: 2.29 (-6.84, 12.30) 5 dma: 1.09 (-8.30, 11.44) 6 dma: 3.08 (-6.30, 13.40); **Subjects who did not report smoking in the past** Lag 0: 0.46 (-8.23, 9.97) 2 dma: 1.37 (-7.96, 11.65) 3 dma: -0.96 (-10.01, 9.00) 4 dma: -1.34 (-10.35, 8.58) 5 dma: -0.87 (-10.17, 9.40) 6 dma: -1.78 (-10.64, 7.94) **VCAM-1 -** All subjects Lag 0: 6.88 (-2.88, 17.62) 2 dma: 8.18 (-1.43, 18.72) 3 dma: 6.92 (-1.66, 16.25) 4 dma: 6.46 (-1.16, 14.66) 5 dma: 8.57 (0.05, 17.80) 6 dma: 11.76 (3.48, 20.70) **Subjects not known to be taking statins** Lag 0: 10.26 (-0.64, 22.35) 2 dma: 15.02 (3.76, 27.49) 3 dma: 14.59 (3.94, 26.34) 4 dma: 15.15 (4.54, 26.84) 5 dma: 16.16 (5.77, 27.58) 6 dma: 17.66 (7.77, 28.45) **Subjects who report smoking in the past (but not within 6 mo)** Lag 0: 13.2 (-1.30, 29.72) 2 dma: 18.4 (0.69, 39.33) 3 dma: 15.7 (1.19, 32.30) 4 dma: 13.1 (0.88, 26.78) 5 dma: 13.2 (0.49, 27.58) 6 dma: 16.2 (3.76, 30.10) **Subjects who did not report smoking in the past** Lag 0: -3.12 (-12.41, 7.17) 2 dma: -0.34 (-10.57, 11.05) 3 dma: -1.09 (-11.15, 10.12) 4 dma: -0.81 (-10.91, 10.43) 5 dma: 2.07 (-8.59, 13.96) 6 dma: 4.89 (-5.56, 16.50) **vWF -** All subjects Lag 0: 15.16 (-9.79, 47.01) 2 dma: 12.57 (-9.19, 39.55) 3 dma: 25.14 (-9.87, 73.74) 4 dma: 23.42 (-9.47, 68.25) 5 dma: 17.92 (-10.22, 54.87) 6 dma: 20.48 (-8.82, 59.22) **Subjects not known to be taking statins** Lag 0: 7.40 (-19.82, 43.88) 2 dma: 7.10 (-19.09, 41.76) 3 dma: 10.78 (-17.92, 49.52) 4 dma: 11.61 (-16.64, 49.42) 5 dma: 9.15 (-20.32, 49.53) 6 dma: 7.91 (-20.70, 46.85) **Subjects who report smoking in the**

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			past (but not within 6 mo) Lag 0: 19.23 (-24.29, 87.77) 2 dma: 19.92 (-29.65,104.41) 3 dma: 29.54 (-17.24, 102.76) 4 dma: 41.98 (-6.95, 116.63) 5 dma: 44.05 (-1.23, 110.07) 6 dma: 50.39 (9.35, 106.82) **Subjects who did not report smoking in the past** Lag 0: -14.21 (-53.20, 57.24) 2 dma: -20.66 (-63.14, 70.77) 3 dma: -28.89 (-68.43, 60.19) 4 dma: -23.51 (-55.11, 30.34) 5 dma: -29.18 (-60.08, 25.66) 6 dma: -30.68 (-55.95, 9.08)
Reference: O'Neill et al. (2007, 091362) **Period of Study:** May 1998-Dec 2002 **Location:** Boston, MA	**Outcome:** Soluble intercellular adhesion molecule 1 (ICAM-1) Vascular cell adhesion molecule 1 (VCAM-1) von Willebrand factor (vWF) **Age Groups:** Mean (SD): 56.6 (10.6) **Study Design:** Cross-sectional **N:** 92 participants (type 2 diabetic patients) **Statistical Analyses:** Linear regression **Covariates:** Apparent temperature, season, age, race, sex, glycosylated hemoglobin, cholesterol, smoking history, BMI **Dose-response Investigated?** No **Statistical Package:** NR	**Pollutant:** BC **Averaging Time:** 24 h (lagged ma of days 0 to 1, 2, 3, 4, and 5) **Mean (SD):** 1.1 (0.8) descriptive statistics represent entire study period **Percentiles:** IQR range: 0.8 **Range (Min, Max):** 0.2, 5.8 **Monitoring Stations:** 1 site **Copollutant:** $PM_{2.5}$ BC SO_4^{2-}	**PM Increment:** IQR (specific to lag period) **Effect Estimate [Lower CI, Upper CI]:** % change per IQR of BC **ICAM-1- -**All subjects Lag 0: 5.09 (-2.37, 13.11) 2 dma: 3.97 (-10.24, 20.42) 3 dma: 5.10 (-10.17, 22.96) 4 dma: 8.38 (-6.46, 25.56) 5 dma: 10.09 (-7.36, 30.83) 6 dma: 10.58 (-5.34, 29.18) **Subjects not known to be taking statins** Lag 0: 5.77 (-3.92, 16.44) 2 dma: 2.39 (-7.65, 13.52) 3 dma: 0.84 (-8.16, 10.73) 4 dma: 1.67 (-6.71, 10.80) 5 dma: 1.55 (-6.46, 10.24) 6 dma: 2.20 (-6.47, 11.68) **Subjects who report smoking in the past (but not within 6 mo)** Lag 0: 5.84 (0.87, 11.05) 2 dma: 5.08 (-2.34, 13.07) 3 dma: 4.44 (-2.70, 12.11) 4 dma: 5.02 (-1.78, 12.29) 5 dma: 5.89 (-2.14, 14.58) 6 dma: 6.73 (-1.54, 15.70) **Subjects who did not report smoking in the past** Lag 0: 6.04 (0.87, 11.48) 2 dma: 6.54 (-1.64, 15.39) 3 dma: 5.86 (-1.90, 14.22) 4 dma: 6.11 (-1.18, 13.94) 5 dma: 6.89 (-1.42, 15.89) 6 dma: 7.86 (-1.35, 17.94) **VCAM-1 -** All subjects Lag 0: 9.26 (2.98, 15.91) 2 dma: 10.18 (1.93, 19.10) 3 dma: 15.45 (2.70, 29.78) 4 dma: 17.97 (3.63, 34.30) 5 dma: 23.83 (8.41, 41.44) 6 dma: 27.51 (11.96, 45.21) **Subjects not known to be taking statins** Lag 0: 9.19 (3.23, 15.49) 2 dma: 14.64 (5.02, 25.14) 3 dma: 14.39 (5.30, 24.28) 4 dma: 14.19 (5.71, 23.36) 5 dma: 19.11 (9.44, 29.65) 6 dma: 22.60 (11.79, 34.45) **Subjects who report smoking in the past (but not within 6 mo)** Lag 0: 12.4 (2.77, 22.92) 2 dma: 28.5 (8.38, 52.24) 3 dma: 25.14 (3.50, 51.30) 4 dma: 23.1 (2.70, 47.58)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			5 dma: 32.0 (7.29, 62.30) 6 dma: 31.8 (9.74, 58.26) **Subjects who did not report smoking in the past** Lag 0: 5.15 (-5.63, 17.17) 2 dma: 2.09 (-9.07 ,14.61) 3 dma: 3.90 (-6.38, 15.31) 4 dma: 4.92 (-4.63, 15.43) 5 dma: 7.89 (-1.31, 17.95) 6 dma: 10.97 (0.98, 21.96) **vWF-** All subjects Lag 0: 7.96 (-4.34, 21.84) 2 dma: 14.87 (-2.85, 35.82) 3 dma: 15.34 (-3.22, 37.45) 4 dma: 15.47 (-7.60, 44.31) 5 dma: 19.50 (-8.89, 56.74) 6 dma: 20.53 (-9.80, 61.05) **Subjects not known to be taking statins** Lag 0: 3.23 (-8.91, 17.00) 2 dma: 9.82 (-8.39, 31.66) 3 dma: 17.79 (-16.03, 65.21) 4 dma: 13.14 (-18.71, 57.47) 5 dma: 16.14 (-20.43, 69.52) 6 dma: 13.25 (-22.09, 64.62) **Subjects who report smoking in the past (but not within 6 mo)** Lag 0: 7.63 (-17.01, 39.58) 2 dma: 37.64 (-7.18, 104.10) 3 dma: 75.41 (6.16, 189.85) 4 dma: 72.05 (-3.34, 206.22) 5 dma: 73.14 (6.94, 180.32) 6 dma: 71.23 (14.00, 157.19) **Subjects who did not report smoking in the past** Lag 0: 10.22 (-23.14, 58.04) 2 dma: 17.07 (-18.86, 68.91) 3 dma: 6.56 (-42.75, 98.36) 4 dma: -9.20 (-65.79, 140.99) 5 dma: -23.86 (-71.05, 100.29) 6 dma: -48.69 (-77.75, 18.29)
Reference: O'Neill et al. (2005, 088423) **Period of Study:** Baseline period: May 1998-Jan 2000 Time trial: 2000-2002 **Location:** Boston, MA	**Outcome:** Changes in vascular reactivity, specifically percent change in brachial artery diameter (flow-mediated and nitroglycerin-mediated) **N:** 270 patients with diabetes or at risk of diabetes, who participated in non-air pollution related studies at the Joselyn Diabetes Center in Boston **Statistical Analysis:** Linear regression	**Pollutant:** $PM_{2.5}$ **Mean (SD):** 11.5 (6.4) **Range:** 1.1-40.0 **Monitoring Stations:** 1 **Copollutant:** Sulfates BC Ultrafine particle counts	**PM Increment:** IQR (value not given) **Percent change (95% CI):** $PM_{2.5}$ 6-day ma Nitroglycerin-mediated reactivity: -7.6% (95% CI: 12.8% to -2.1%) **Notes:** $PM_{2.5}$ was positively associated with nitroglycerin-mediated reactivity an association was also reported with ultrafine particles. Effect estimates were larger in type II than type I diabetes. BC and sulfate increases were associated with decreased flow-mediated reactivity among those with diabetes. Although the largest associations were with the 6-day ma, similar patterns and quantitatively similar results appear in the other lags.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: O'Neill et al. (2007, 091362) **Period of Study:** May 1998-Dec 2002 **Location:** Boston, MA	**Outcome:** soluble intercellular adhesion molecule 1 (ICAM-1) vascular cell adhesion molecule 1 (VCAM-1) von Willebrand factor (vWF) **Mean Age:** 56.6 (10.6) **Study Design:** Cross-sectional **N:** 92 participants (type 2 diabetic patients) **Statistical Analyses:** Linear regression **Covariates:** Apparent temperature, season, age, race, sex, glycosylated hemoglobin, cholesterol, smoking history, BMI **Dose-response Investigated?** No **Statistical Package:** NR	**Pollutant:** SO_4^{2-} **Averaging Time:** 24 h (lagged ma of days 0 to 1, 2, 3, 4, and 5) **Mean (SD):** 3.0 (2.0) descriptive statistics represent entire study period **Percentiles:** IQR range: 2.2 **Range (Min, Max):** 0.5, 9.6) **Monitoring Stations:** 1 site **Copollutant:** $PM_{2.5}$, BC, SO_4^{2-}	**PM Increment:** IQR (specific to lag period) **Effect Estimate [Lower CI, Upper CI]:** % change per IQR of $PM_{2.5}$ **ICAM-1** All subjects Lag 0: 5.30 (-2.60, 13.83) 2 dma: 4.02 (-3.26, 11.85) 3 dma: 4.03 (-5.34, 14.34) 4 dma: -0.79 (-7.30, 6.18) 5 dma: 1.06 (-7.10, 9.93) 6 dma: 3.15 (-5.66, 12.78) **Subjects not known to be taking statins** Lag 0: 10.14 (0.44, 20.77) 2 dma: 9.39 (-1.28, 21.20) 3 dma: 10.93 (-2.23, 25.85) 4 dma: -0.24 (-9.66, 10.16) 5 dma: 4.03 (-8.66, 18.47) 6 dma: 5.66 (-7.52, 20.72) **Subjects who report smoking in the past (but not within 6 mo)** Lag 0: -4.00 (-24.79, 22.52) 2 dma: -4.82 (-18.01, 10.48) 3 dma: -7.19 (-23.66, 12.83) 4 dma: -9.8 (-27.96, 12.97) 5 dma: -10.4 (-29.92, 14.44) 6 dma: -6.8 (-25.72, 17.03) **Subjects who did not report smoking in the past** Lag 0: 6.67 (-4.34, 18.94) 2 dma: 5.65 (-4.67, 17.10) 3 dma: 10.21 (-5.83, 28.99) 4 dma: 0.80 (-9.94, 12.83) 5 dma: 2.80 (-10.85, 18.54) 6 dma: 5.15 (-7.78, 19.89) **VCAM-1** All subjects Lag 0: -0.04 (-3.75, 3.80) 2 dma: 0.94 (-4.79, 7.01) 3 dma: -0.87 (-3.50, 1.82) 4 dma: 0.13 (-2.02, 2.34) 5 dma: -0.47 (-2.67, 1.78) 6 dma: -0.46 (-1.99, 1.09) **Subjects not known to be taking statins** Lag 0: -1.34 (-11.23, 9.66) 2 dma: -0.19 (-11.13, 12.09) 3 dma: -2.84 (-13.90, 9.64) 4 dma: 4.28 (-6.18, 15.90) 5 dma: -0.26 (-13.44, 14.93) 6 dma: -3.44 (-16.51, 11.67) **Subjects who report smoking in the past (but not within 6 mo)** Lag 0: 0.07 (-23.40, 30.73) 2 dma: -5.62 (-20.77, 12.43) 3 dma: -26.92 (-33.31 to -19.91) 4 dma: -3.06 (-28.01,30.56) 5 dma: -6.42 (-30.75, 26.47) 6 dma: -6.46 (-28.55, 22.47) **Subjects who did not report smoking in the past** Lag 0: -3.28 (-12.66, 7.12) 2 dma: -3.17 (-11.75, 6.23) 3 dma: -9.67 (-22.07, 4.70) 4 dma: -5.51 (-14.28, 4.15) 5 dma: -12.17 (-22.05 to -1.05) 6 dma: -11.77 (-20.95 to -1.52) **vWF** (sulfate measures not available)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Park et al. (2008, 156845) **Period of Study:** Jan 1995-Jun 2005 **Location:** Greater Boston area, MA	**Outcome:** Total homocysteine (tHcy) **Mean Age:** 73.6 ± 6.9 yr **Study Design:** Cross-sectional and longitudinal analyses performed **N:** 960 men **Statistical Analyses:** Generalized additive models (also hierarchical mixed-effects regression models to assess repeated measures of tHcy) **Covariates:** Model 1: season, age, long-term trend, apparent temperature Model 2: further adjustment for BMI, systolic blood pressure, smoking status, pack yr of cigarettes, alcohol consumption Model 3: further adjustment for serum creatinine, plasma folate, vitamin B6, and vitamin B12 **Dose-response Investigated?** Modeled continuous covariates as penalized splines to determine if association with tHcy was linear **Statistical Package:** R software	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h (ma up to 7 days prior to blood collection) **Mean (SD):** 12.0 (6.6) **Median:** 10.6 **Range (Min, Max):** 2.0, 62.0 **Monitoring Stations:** 1 site **Copollutant:** $PM_{2.5}$ BC (r = 0.51) OC (r = 0.51) SO_4^{2-} (r = 0.85)	**PM Increment:** IQR **Effect Estimate [Lower CI, Upper CI]:** Estimated % change in tHcy per IQR increase in pollutant. Lag model Concurrent day. IQR: 7.66 Model 1: 1.32 (-0.83, 3.52) Model 2: 1.55 (-0.77, 3.91) Model 3: 1.57 (-0.38, 3.56) 1-day previous. IQR: 6.91 Model 1: -1.43 (-3.51, 0.69) Model 2: -1.41 (-3.53, 0.76) Model 3: -1.28 (-3.12, 0.60) 2-day ma. IQR: 6.47 Model 1: 0.04 (-2.13, 2.26) Model 2: -0.07 (-2.26, 2.17) Model 3: 0.25 (-1.69, 2.22) 3-day ma. IQR: 5.83 Model 1: -0.64 (-2.92, 1.69) Model 2: -0.74 (-3.04, 1.61) Model 3: -0.59 (-2.63, 1.49) 4-day ma. IQR: 5.21 Model 1: -0.63 (-2.94, 1.72) Model 2: -0.86 (-3.19, 1.52) Model 3: -0.73 (-2.78, 1.37) 5-day ma. IQR: 4.68 Model 1: -0.51 (-2.79, 1.83) Model 2: -0.82 (-3.13, 1.54) Model 3: -0.84 (-2.85, 1.22) 6-day ma. IQR: 4.50 Model 1: -0.91 (-3.32, 1.56) Model 2: -1.32 (-3.76, 1.17) Model 3: -1.44 (-3.58, 0.74) 7-day ma. IQR: 4.20 Model 1: -0.84 (-3.27, 1.64) Model 2: -1.19 (-3.64, 1.33) Model 3: -1.69 (-3.84, 0.51) Stratified analyses: No significant difference in effect of $PM_{2.5}$ among those with high and low levels of vitamins

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Park et al. (2008, 156845) **Period of Study:** Jan 1995-Jun 2005 **Location:** Greater Boston area, MA	**Outcome:** Total homocysteine (tHcy) **Mean Age:** 73.6 ± 6.9 yr **Study Design:** cross-sectional and longitudinal analyses performed **N:** 960 men **Statistical Analyses:** Generalized additive models (also hierarchical mixed-effects regression models to assess repeated measures of tHcy) **Covariates:** Model 1: season, age, long-term trend, apparent temperature Model 2: further adjustment for BMI, systolic blood pressure, smoking status, pack yr of cigarettes, alcohol consumption Model 3: further adjustment for serum creatinine, plasma folate, vitamin B6, and vitamin B12 **Dose-response Investigated?** Modeled continuous covariates as penalized splines to determine if association with tHcy was linear **Statistical Package:** R software	**Pollutant:** BC **Averaging Time:** 24 h (ma up to 7 days prior to blood collection) **Mean (SD):** 0.99 (0.56) **Median:** 0.87 **Range (Min, Max):** 0.07, 3.7 **Monitoring Stations:** 1 site **Copollutant (correlation):** $PM_{2.5}$ (r = 0.51) BC OC (r = 0.0.51) SO_4^{2-} (r = 0.50)	**PM Increment:** IQR **Effect Estimate [Lower CI, Upper CI]:** Estimated % change in tHcy per IQR increase in pollutant. Lag model Concurrent day. IQR: 0.66 Model 1: 2.64 (-0.12, 5.48) Model 2: 2.62 (-0.17, 5.48) Model 3: 3.13 (0.76, 5.55) 1-day previous. IQR: 0.66 Model 1: 1.46 (-0.98, 3.96) Model 2: 1.32 (-1.14, 3.85) Model 3: 0.95 (-1.12, 3.05) 2-day ma. IQR: 0.60 Model 1: 2.75 (-0.18, 5.76) Model 2: 2.63 (-0.33, 5.67) Model 3: 2.59 (0.10, 5.14) 3-day ma. IQR: 0.57 Model 1: 2.95 (-0.44, 6.46) Model 2: 2.97 (-0.46, 6.51) Model 3: 3.12 (0.21, 6.11) 4-day ma. IQR: 0.52 Model 1: 3.94 (0.24, 7.78) Model 2: 3.76 (0.02, 7.64) Model 3: 3.00 (-0.13, 6.22) 5-day ma. IQR: 0.49 Model 1: 3.26 (-0.60, 7.27) Model 2: 2.64 (-1.23, 6.67) Model 3: 2.38 (-0.89, 5.77) 6-day ma IQR: 0.44 Model 1: 1.63 (-1.99, 5.38) Model 2: 1.03 (-2.62, 4.80) Model 3: 0.93 (-2.15, 4.11) 7-day ma. IQR: 0.44 Model 1: 1.38 (-2.45, 5.36) Model 2: 0.69 (-3.16, 4.70) Model 3: 0.45 (-2.81, 3.83) % change in tHcy per IQR increase in BC, 24-h avg Among those with low folate: 5.31 (2.26, 8.42) Among those with low B12: 5.06 (2.03, 8.17) nearly null associations among those with high levels

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Park et al. (2008, 156845) **Period of Study:** Jan 1995-Jun 2005 **Location:** Greater Boston area, MA	**Outcome:** Total homocysteine (tHcy) **Mean Age:** 73.6 ± 6.9 yr **Study Design:** Cross-sectional and longitudinal analyses performed **N:** 960 men **Statistical Analyses:** Generalized additive models (also hierarchical mixed-effects regression models to assess repeated measures of tHcy) **Covariates:** Model 1: season, age, long-term trend, apparent temperature Model 2: further adjustment for BMI, systolic blood pressure, smoking status, pack yr of cigarettes, alcohol consumption Model 3: further adjustment for serum creatinine, plasma folate, vitamin B6, and vitamin B12 **Dose-response Investigated?** Modeled continuous covariates as penalized splines to determine if association with tHcy was linear **Statistical Package:** R software	**Pollutant:** OC **Averaging Time:** 24 h (ma up to 7 days prior to blood collection) **Mean (SD):** 3.5 (1.8) **Median:** 3.1 **Range (Min, Max):** 0.29, 11.8 **Monitoring Stations:** 1 site **Copollutant (correlation):** $PM_{2.5}$ (r = 0.51) BC (r = 0.51) OC SO_4^{2-} (r = 0.41)	**PM Increment:** IQR **Effect Estimate [Lower CI, Upper CI]:** Estimated % change in tHcy per IQR increase in pollutant. Lag model Concurrent day. IQR: NA Model 1: NA Model 2: NA Model 3: NA 1-day previous. IQR: 2.00 Model 1: 2.12 (-0.98, 5.31) Model 2: 1.69 (-1.51, 5.00) Model 3: 1.87 (-0.81, 4.62) 2-day ma. IQR: 1.93 Model 1: -0.39 (-3.67, 3.01) Model 2: -0.88 (-4.26, 2.61) Model 3: 1.05 (-1.86, 4.06) 3-day ma. IQR: 1.68 Model 1: 0.53 (-2.66, 3.83) Model 2: 0.14 (-3.15, 3.54) Model 3: 1.32 (-1.44, 4.16) 4-day ma. IQR: 1.64 Model 1: 1.57 (-1.89, 5.15) Model 2: 1.42 (-2.14, 5.12) Model 3: 1.89 (-1.15, 5.03) 5-day ma, IQR: 1.60 Model 1: 2.27 (-1.49, 6.16) Model 2: 2.11 (-1.77, 6.15) Model 3: 2.12 (-1.29, 5.65) 6-day ma. IQR: 1.43 Model 1: 2.83 (-0.74, 6.52) Model 2: 2.78 (-0.90, 6.60) Model 3: 2.53 (-0.59, 5.74) 7-day ma. IQR: 1.23 Model 1: 2.75 (-0.41, 6.02) Model 2: 2.55 (-0.71, 5.92) Model 3: 2.55 (-0.21, 5.39) % change in tHcy per IQR increase in OC, 7-day avg. Among those with low B12: 5.23 (1.59, 9.01) Nearly null associations among those with high levels

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Park et al. (2005, 057331) **Period of Study:** Nov 2000-Oct 2003 **Location:** Greater Boston area, MA	**Outcome:** Change in HRV (SDNN, HF, LF, LFHFR) **Mean age:** 72.7 yr **Study Design:** Cross-sectional **N:** 497 adult males living in the Greater Boston, MA area	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 4 h 24 h 48 h **Mean (SD):** 11.4 (8.0) **Range:** 6.45-62.9 **Copollutant:** O_3, Particle number count, BC, NO_2, SO_2, CO	**PM Increment:** 8 µg/m^3 **Percent change (95% CI):** 48h mean $PM_{2.5}$: 20.8% decrease in HF (95% CI: 4.6%, 34.2%) 18.6% increase in LFHFR (4.1%, 35.2%). **Notes:** Subjects were monitored during a 4-min rest period between 8 a.m. and 1 p.m. Modifying effects of hypertension, IHD, diabetes, and use of cardiac/anti-hypertensive medications also examined. Linear regression analyses. This subject group is from the VA Normative Aging Study. The 4-h averaging period was most strongly associated with HRV indices. The PM effect was robust in models including O_3. The HRV change per IQR increase in $PM_{2.5}$ were larger in subjects with hypertension (n = 335) IHD (n = 142), and diabetes (n = 72). In addition, those who did not use calcium-channel blockers had a greater decline in LF associated with each IQR increase in $PM_{2.5}$ than did those who did use calcium channel blockers. IQR increases in 48h mean BC concentration were also associated with adverse changes in HRV, suggesting traffic pollution may be particularly toxic.
Reference: Park et al. (2006, 091245) **Period of Study:** Nov 2000-Dec 2004 **Location:** Greater Boston area, MA	**Outcome:** Change in HF **Study Design:** Cross-sectional **N: Statistical Analysis:** Linear regression models	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 48 h **Mean (SD):** $PM_{2.5}$: 11.7 (7.8) Sulfates: 3.3 (3.3) BC: 0.92 (0.46) **Copollutant:** O_3	**PM Increment:** 10 µg/m^3 **Percent change (95% CI):** Wild-type HFE genotype: 31.7% (95% CI: 10.3, 48.1) Among those with either of the 2 HFE variants, there was no association between 48h $PM_{2.5}$ and HF (shown in a graph, ~10% non-significant increase). **Notes:** Normative Aging Study. Examining association between PM and HF among those with and without the wild-type HFE genotype.
Reference: Pekkanen et al. (2002, 035050) **Period of Study:** Winter 1998-1999 **Location:** Helsinki, Finland	**Outcome**: ST-Segment Depression (>0.1mV) **Study Design**: Panel of ULTRA Study participants **N**: 45 Subjects, n = 342 biweekly submaximal exercise tests, 72 exercise induced ST Segment Depressions **Statistical Analysis:** Logistic regression / GAM	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h Median: 10.6 IQR: 7.9 **Pollutant:** PM1 **Median:** 7.0 IQR: 5.6 **Pollutant:** ACP (100 to 1000nm) (n/cm^3) **Median:** 1200 IQR: 760 **Copollutant:** NO_2, CO, $PM_{10-2.5}$, ultrafine	**PM Increment:** IQR **Effect Estimate(s):** ACP: OR = 3.29 (1.57, 6.92), lag 2 PM_1: OR = 4.56 (1.73, 12.03), lag 2 $PM_{2.5}$: OR = 2.84 (1.42, 5.66), lag 2 **Notes**: The effect was strongest for ACP and $PM_{2.5}$, which in 2 pollutant models appeared independent. Increases in NO_2 and CO were also associated with increased risk of ST-segment depression, but not with coarse particles.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Park et al. (2008, 156845) **Period of Study:** Jan 1995-Jun 2005 **Location:** Greater Boston area, MA	**Outcome:** Total homocysteine (tHcy) **Mean Age:** 73.6 ± 6.9 yr **Study Design:** Cross-sectional and longitudinal analyses performed N: 960 men **Statistical Analyses:** Generalized additive models (also hierarchical mixed-effects regression models to assess repeated measures of tHcy) **Covariates:** Model 1: season, age, long-term trend, apparent temperature Model 2: further adjustment for BMI, systolic blood pressure, smoking status, pack yr of cigarettes, alcohol consumption Model 3: further adjustment for serum creatinine, plasma folate, vitamin B6, and vitamin B12 **Dose-response Investigated?** Modeled continuous covariates as penalized splines to determine if association with tHcy was linear **Statistical Package:** R software	**Pollutant:** SO_4^{2-} **Averaging Time:** 24 h (ma up to 7 days prior to blood collection) **Mean (SD):** 3.2 (3.0) **Median:** 2.4 **Range (Min, Max):** 0.39, 29.0 **Monitoring Stations:** 1 site **Copollutant (correlation):** $PM_{2.5}$ (r = 0.85) BC (r = 0.50) OC (r = 0.41) SO_4^{2-}	**PM Increment:** IQR **Effect Estimate [Lower CI, Upper CI]:** Estimated % change in tHcy per IQR increase in pollutant. Lag model Concurrent day: IQR: NA Model 1: NA Model 2: NA Model 3: NA 1-day previous: IQR: 2.61 Model 1: 0.91 (-0.77, 2.62) Model 2: 0.99 (-0.94, 2.95) Model 3: 0.91 (-0.72, 2.57) 2-day ma: IQR: 2.10 Model 1: -0.25 (-2.07, 1.60) Model 2: -0.29 (-2.35, 1.82) Model 3: 0.05 (-1.74, 1.86) 3-day ma: IQR: 1.73 Model 1: -0.15 (-1.97, 1.69) Model 2: -0.17 (-2.23, 1.93) Model 3: -0.01 (-1.78, 1.80) 4-day ma: IQR: 1.64 Model 1: -0.69 (-2.74, 1.41) Model 2: -0.60 (-2.95, 1.81) Model 3: -0.58 (-2.63, 1.51) 5-day ma: IQR: 1.60 Model 1: -1.14 (-3.53, 1.30) Model 2: -0.90 (-3.64, 1.92) Model 3: -1.09 (-3.48, 1.36) 6-day ma; ' IQR: 1.40 Model 1: 0.00 (-2.39, 2.44) Model 2: 0.36 (-2.36, 3.16) Model 3: 0.41 (-2.01, 2.89) 7-day ma IQR: 1.30 Model 1: -0.16 (-2.51, 2.24) Model 2: 0.30 (-2.37, 3.04) Model 3: 0.07 (-2.25, 2.43) Stratified analyses: No significant difference in effect of SO_4^{2-} among those with high and low levels of vitamins
Reference: Peters et al. (2005, 095747) Also Peters et al. (2005, 156859) **Period of Study:** Feb 1999-Jul 2001 **Location:** Augsburg, Germany	**Outcome:** Myocardial infarction **Study Design:** Case-crossover **N:** 691 myocardial infarction patients **Statistical Analysis:** Conditional logistic regression **Dose-response Investigated?** No	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 1 h: Median = 14.5 IQR: 9.1 24-h: Median = 14.9 IQR: 7.7 **Copollutant:** NO_2, SO_2, CO	**Effect Estimate:** 2-h lag: OR = 0.93 95% CI: 0,83, 1.04 24-h mean, 2-day lag: OR = 1.18 95% CI: 1.03, 1.34 **Notes:** Examined triggering for MI at various lags before MI onset (up to 6 h before MI, up to 5 days before MI). $PM_{2.5}$ levels 2 days before MI onset were associated with increased risk of MI, but not on the concurrent day, or lags 1, 3, 4, or 5. These findings are consistent with the prior Boston MI study for a 1- to 2-day lagged effect of $PM_{2.5}$.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Pope et al. (2004, 055238) **Period of Study:** Winter 1999-2000 (in Wasatch Front, UT). Summer 2000 (in Hawthorne, UT). Winter 2000-2001 (in Bountiful, UT and Lindon, UT) **Location:** Utah: Wasatch Front, Hawthorne, Bountiful, and Lindon	**Outcome:** Change in autonomic function (measured by changes in HRV), C-reactive protein (CRP), blood cell counts, platelets, and blood viscosity associated with short-term changes in $PM_{2.5}$ **Age Groups:** Elderly (specific age range not given) **Study Design:** Panel study **N:** 88 elderly subjects **Statistical Analysis:** Linear regression **Season:** Winter, summer **Dose-response Investigated?** No	**Pollutant:** $PM_{2.5}$ (TEOM) **Averaging Time:** 24 h **Mean (SD):** 18.9 (13.4) **Copollutant:** None	**PM Increment:** 100 µg/m^3 **Effect Estimate:** Each 100 µg/m^3 increase associated with: -35 (SE = 8) msec decline in SDNN 0.81 (SE 0.17) mg/dL increase in CRP 0.31 (SE 9.34) k/µL increase in platelets 0.07 (SE 0.21) cP increase in blood viscosity **Notes:** The study observed small but statistically significant adverse associations between daily mean $PM_{2.5}$ and HRV and C-reactive protein (CRP). The authors point out, however, that most of the variability in the temporal deviation of these physiological endpoints was not explained by $PM_{2.5}$. These observations therefore suggest that $PM_{2.5}$ may be 1 of multiple factors that influence HRV and CRP.
Reference: Pope et al. (2006, 091246) **Period of Study:** 1994-2004 **Location:** Wasatch Front, Utah	**Outcome:** Acute ischemic heart disease **Study Design:** Case-crossover study (time-stratified control selection) **N: Statistical Analysis:** Conditional logistic regression	**Pollutant:** $PM_{2.5}$ (FRM) **Averaging Time:** 24 h **Mean (SD):** Site 1: 10.1 Site 2: 10.8 Site 3: 11.3 **Monitoring Stations:** 3 **Copollutant:** PM_{10} (FRM) measured at 4 monitoring sites	**PM Increment:** 10 µg/m^3 **Effect Estimate:** For same-day increase in $PM_{2.5}$: OR = 1.045 95% CI: 1.011, 1.080 **Notes:** Case-crossover study (time-stratified control selection) triggering of acute ischemic heart disease by ambient $PM_{2.5}$ concentrations on the same and previous 3 days. $PM_{2.5}$ measured at 3 sites and estimated for missing days. Effect estimates were larger for those with angiographically demonstrated coronary artery disease.
Reference: Pope et al. (2004, 055238) **Period of Study:** 1999-2001 **Location:** Wasatch Front, Utah	**Outcome:** Heart rate variability (HRV) C-reactive protein (CRP) Blood cell counts, whole blood viscosity **Age Groups:** 54-89 yr **Study Design:** Panel study **N:** 88 participants **Statistical Analyses:** Linear regression **Covariates:** Subject-specific fixed effects Interactive spline smooths for temp, RH (partial control for H) **Season:** Temperature as covariate **Dose-response Investigated?** Yes, also assessed PM by including cubic smoothing splines with 3 df **Statistical Package:** SAS	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** 23.7 (20.2) **Range (Min, Max):** 1.7, 74.0 **Monitoring Stations:** NR **Copollutant:** None	**PM Increment:** 100 µg/m^3 **Effect Estimate [Lower CI, Upper CI]: Regression coefficients (SE) for associations with concurrent day pollutant:** Mean H: -4.49 (1.73) SDNN: -34.94 (8.32) SDANN: -18.98 (8.67) r-MSSD: -42.25 (10.90) CRP: 0.81 (0.18) Whole blood viscosity: 0.07 (0.21) WBC: -0.07 (0.38) Granulocytes: 0.02 (0.37) Lymphocytes: -0.07 (0.14) Monocytes: 0.12 (0.04) Basophils: -0.01 (0.01) Eosinophils: -0.01 (0.02) RBC: 0.03 (0.06) Platelets: 0.31 (9.34)
Reference: Rich et al. (2005, 079620) **Period of Study:** Jul 1995-Jul 2002 **Location:** Eastern Massachusetts, USA	**Outcome:** Confirmed ventricular arrhythmias **Study Design:** Case-crossover (time-stratified control selection) **N:** 203 patients with implantable cardioverter defibrillators **Statistical Analysis:** Conditional logistic regression	**Pollutant:** $PM_{2.5}$ (TEOM) **Averaging Time:** 1-h avg 24-h avg **Median (IQR):** 1-h avg: Median = 9.2 µg/m^3 24-h avg: Median = 9.8 µg/m^3 IQr = 7.8 **Copollutant:** O_3, BC, CO, NO_2, SO_2	**PM Increment:** 7.8 µg/m^3 **Effect Estimate:** For mean $PM_{2.5}$ in the 24 h before ventricular arrhythmia: OR = 1.19 95% CI: 1.02, 1.38 **Notes:** 794 ventricular arrhythmias among 84 subjects. **Lag h:** 0-2, 0-6, 0-23, 0-47

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Rich et al. (2006, 088427) **Period of Study:** Jul 1995-Jul 2002 **Location:** Eastern Massachusetts, USA	**Outcome:** Confirmed episodes of paroxysmal atrial fibrillation **Study Design:** Case-crossover (time-stratified control selection) **N:** 203 patients with implantable cardioverter defibrillators **Statistical Analysis:** Conditional logistic regression	**Pollutant:** $PM_{2.5}$ (TEOM) **Averaging Time:** 1-h avg 24-h avg **Median (IQR):** 1-h avg: Median = 9.2 µg/m^3 24-h avg: Median = 9.8 µg/m^3 IQr = 7.8 **Copollutant:** O_3, BC, CO, NO_2, SO_2	**PM Increment:** 9.4 µg/m^3 **Effect Estimate:** 0-h lag: OR 1.41 (0.82, 2.42) **Notes:** 91 paroxysmal atrial fibrillation (PAF) episodes among 29 subjects. **Lag h:** 0, 0-23 Positive, but not significant increases in the relative odds of PAF associated with $PM_{2.5}$ concentrations in the same h and 24-h before PAF episode onset. Authors note reduced statistical power for $PM_{2.5}$ analyses due to missing data.
Reference: Rich et al. (2006, 088427) **Period of Study:** Jul 1995-Jul 2002 **Location:** Eastern Massachusetts, USA	**Outcome:** Confirmed episodes of paroxysmal atrial fibrillation **Study Design:** Case-crossover (time-stratified control selection) **N:** 203 patients with implantable cardioverter defibrillators **Statistical Analysis:** Conditional logistic regression	**Pollutant:** BC **Averaging Time:** 1-h avg, 24-h avg **Median (IQR):** IQR: 0.91µg/m^3 **Copollutant:** O_3, $PM_{2.5}$, CO, NO_2, SO_2	**PM Increment:** 0.91µg/m^3 (IQR) **Effect Estimate:** 0- to 23-h lag period: OR 1.46 (95% CI: 0.67, 3.17) **Notes:** 91 paroxysmal atrial fibrillation (PAF) episodes among 29 subjects. **Lag h:** 0, 0-23 Positive, but not significant increases in the relative odds of PAF associated with BC concentrations in the same h and 24 h before PAF episode onset. Authors note reduced statistical power for BC analyses due to missing data.
Reference: Rich et al. (2006, 089814) **Period of Study:** May 2001-Dec 2002 **Location:** St. Louis, MO metropolitan area	**Outcome:** Confirmed ventricular arrhythmia **Study Design:** Case-crossover design (time-stratified control selection) **Dose-response Investigated?** No	**Pollutant:** $PM_{2.5}$ (CAMM) **Averaging Time:** 24 h **Median (IQR):** 16.2 µg/m^3 (IQr = 9.7) **Copollutant:** NO_2, SO_2, CO, O_3, EC, OC	**PM Increment:** 9.7 µg/m^3 (IQR) **Effect Estimate:** OR ($PM_{2.5}$) = 0.95 (95% CI: 0.72, 1.27) OR (SO_2) = OR = 1.24 (95% CI: 1.07, 1.44) **Notes:** 139 confirmed ventricular arrhythmia episodes among 56 subjects. Lags: 0-2h, 0-6h, 0-11h, 0-23h, 0-47h Authors did not find increased relative odds of VA associated with each IQR increase in 24-h mean $PM_{2.5}$, but did find non-significantly increased relative odds of VA associated with 24-h EC. Shorter and longer lag times' relative odds estimates provided no evidence of immediate ventricular arrhythmic effects of air pollution.
Reference: Rich et al. (2004, 055631) **Period of Study:** Feb-Dec 2000 **Location:** Vancouver, British Columbia, Canada	**Outcome:** ICD discharges (as a proxy for VT/VF) **Age Groups:** 15-85 yr **Study Design:** Case-crossover design (ambidirectional control selection ± 7 days) **N:** 34 patients with implantable cardioverter defibrillators **Statistical Analysis:** Conditional logistic regression **Dose-response Investigated?** No	**Pollutant:** $PM_{2.5}$ (Partisol) **Averaging Time:** 1 h **Mean (SD), IQR:** Mean: : 8.2 µg/m^3 (SD = 10.7) IQr = 5.2 **Copollutant:** O_3, EC, OC, SO_4^{2-}, CO, NO_2, SO_2, PM_{10} PM_{10}: Mean: : 13.3 µg/m^3 (SD = 4.9) IQr = 7.4	**PM Increment: Effect Estimate:** Odds ratios were less than 1.0 at all lags (0, 1, 2, 3) for $PM_{2.5}$. No consistent association between any of the air pollutants and implantable cardioverter defibrillators discharges. **Notes:** Same study as Vedal et al. (2004, 055630), except Rich (2004) used data from a shorter time period so as to estimate relative odds of ICD discharge associated with acute increases in more pollutants than Vedal (2004, 055630).

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Rich et al. (2008, 156910) **Period of Study:** NR **Location:** New Jersey	**Outcome:** Pulmonary Artery and Right Ventricular Pressures **Age Groups:** 25-68 **Study Design:** Panel **N:** 11 subjects **Statistical Analyses:** Repeated Measures **Covariates:** Long-term trends, calendar month, weekday, apparent temperature **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 0-6d	**Pollutant:** $PM_{2.5}$ **Averaging Time**: 24 h **Mean (SD):** NR **Monitoring Stations:** NR **Copollutant:** NR **Co-pollutant Correlation:** N/A	**PM Increment:** 11.62µg/m^3 **Change (Lower CI, Upper CI), p-value:** ePAD: 0.19 (0.05, 0.33), 0.01 RV diastolic pressure: 0.23 (0.11, 0.34), <0.001 RV systolic pressure: 0.12 (-0.07, 0.31), 0.23 MPAP: 0.12 (-0.05, 0.28), 0.16/
Reference: Riediker et al. (2004, 091261) **Period of Study:** Fall 2001 **Location:** Wake County, North Carolina	**Outcome:** Heart rate variability (measured 10 h after shift): mean cycle length of normal R-R intervals (MCL), the standard deviation of normal R-R intervals (SDNN), and percentage of normal R-R interval differences greater than 50 msec (PNN50), low frequency (0.04-0.15Hz), high frequency (0.15-0.40Hz), the ratio of low to high frequency. **Blood analysis (measured 15 h after shift)**: Uric acid, blood urea nitrogen, gamma glutamyl transpeptidase, white blood cell count, red blood cell count, hematocrit, hemoglobin, mean red blood cell volume (MCV), neutronphils (count and %), lymphocytes (count and %), C-reactive protein, plasminogen, plasminogen activator inhibitor type 1, von Willebrand factor (vWF), endo-vthzelin-1, protein C, and interleukin-6 **Age Groups:** 23-30 yr **Study Design:** Panel **N:** 9 healthy male troopers, repeated measures (36 person-days) **Statistical Analyses:** Mixed effects regression models (principal factor analysis for classification of exposure) **Covariates:** Potential confounders: temperature, relative humidity, number of law-enforcement activities during the shift and the avg speed during the shift Controlling had no effect on effect estimates for "crustal" and "speed-change" factors However, confounder inclusion in the "speed change" and blood urea nitrogen and vWF reduced the effect estimate and the CI included zero **Season:** Only 1 season included **Dose-response Investigated?** No **Statistical Package:** S-Plus 6.1	**Pollutant:** In-vehicle $PM_{2.5}$ components identified with factor analysis (crustal material, wear of steel automotive components, gasoline combustion, speed-changing traffic with engine emissions and brake wear **Averaging Time:** Exposure assessed during 3 p.m. to 12 a.m. work shifts **Mean:** $PM_{2.5}$mass = 23.0 µg/m^3 **Monitoring Stations:** Per vehicle **Copollutant (correlation):** Correlation to $PM_{2.5}$Mass Benzene: r = 0.50 Aldehydes: r = 0.34 CO: r = 0.52 Aluminum: r = 0.58 Silicon: r = 0.66 Sulfur: r = 0.58 Calcium: r = 0.37 Titanium: r = 0.41 Chromium: r = 0.51 Iron: r = 0.71 Copper: r = 0.16 Selenium: r = 0.38 Tungsten: r = 0.37 PM2.Lightscatter: r = 0.71	**PM Increment:** 1 SD change in source factor **Effect Estimate:** % change in the health outcome per 1 SD change in the "speed change" factor MCL: 7% HRV: 16% supraventricular ectopic beats: 39% % Neutrophils: 7% % lymphocytes: -10% red blood cell volume MCV: 1% vWF: 9% blood urea nitrogen: 7% protein C: -11% % change in the health outcome per 1 SD change in the "crustal" factor MCL: 3% serum uric acid concentrations: 5% **Note:** Results (including CIs) are reported in figures 2 & 3.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Riojas-Rodriguez et al. (2006, 156913) **Period of Study:** Dec 2001-Apr 2002 **Location:** Mexico City metropolitan area	**Outcome:** Heart rate variability (5-minute periods) **Study Design:** Panel study **N:** 30 patients from the outpatient clinic of the National Institute of Cardiology of Mexico, where each subject had existing ischemic heart disease. **Statistical Analysis:** Mixed models	**Pollutant:** $PM_{2.5}$ (nephelometry) **Averaging Time:** 5 min **Mean (SD), Range:** 46.8 µg/m^3 (SD = 1.82) **Range:** 0-483 µg/m^3 **Copollutant:** CO	**PM Increment:** 10 µg/m^3 **Effect Estimate:** Each 20 µg/m^3 increase in 5 min $PM_{2.5}$ was associated with a: -0.008 decrease in the ln(HF)(95% CI: -0.015, 0.0004 **Notes:** Population of subjects with known ischemic heart disease (25 men and 5 women who had at least 1 prior MI [not in last 6 mo]) Each 10 µg/m^3 increase in 5-min mean $PM_{2.5}$ was associated with non-significantly decreased HF, and with similar, but smaller changes in LF and VLF.
Reference: Romieu et al. (2005, 086297) **Period of Study:** 2000-2001 **Location:** Mexico City, Mexico	**Outcome:** Heart rate variability (HF, LF, VLF, PNN50, SDNN, r-MSSD) **Age Groups:** >60 yr of age **Study Design:** Double blind randomized controlled trial **N:** 50 elderly residents of a Mexico City nursing home	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Copollutant:** O_3, NO_2, SO_2, PM_{10}	**PM Increment:** 8 µg/m^3 **Effect Estimate:** In the group receiving the fish oil supplement, each 8 µg/m^3 change in 24-h mean total exposure $PM_{2.5}$ was associated with a: a) 54% reduction (95% CI: -72% to -24%) in HF (log transformed) in the pre-supplementation phase b) 7% reduction (95% CI: -20%, 7%) in the supplementation phase. Changes in other HRV parameters were also smaller in the supplementation phase. In the group receiving soy oil supplementation, the % reduction in HF was also smaller in the supplementation phase, but the differences were smaller and not statistically significant. **Notes:** Study of the effect of omega-3-fatty acid supplementation (2 g/day of fish oil vs.. 2 g/day of soy oil) to mitigate the effect of ambient $PM_{2.5}$ on HRV. Subjects had no cardiac arrhythmias, cardiac pacemakers, allergies to omega-3 fatty acids or fish, treatment with oral anticoagulants, or history of bleeding diathesis. $PM_{2.5}$ was measured and estimated indoors, outdoors, and with regards to total exposure (the same as Holguin et al. (2003)).

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Romieu et al. (2008, 156922) **Period of Study:** Sep 2001-Apr 2002 **Location:** Mexico City, Mexico	**Outcome:** Copper/zinc superoxide dismutase activity (Cu/Zn SOD) Lipoperoxidation (LPO) Reduced glutathione (GSH) **Age Groups:** 60-96 yr **Study Design:** Intervention (randomly assigned fish oil or soy oil) **N:** 52 participants **Statistical Analyses:** Linear mixed models **Covariates:** Time **Dose-response Investigated?** Assessed possible nonlinearity using generalized additive mixed models with p-splines **Statistical Package:** STATA v8.2 and SAS v9.1	**Pollutant:** $PM_{2.5}$ (indoor) **Averaging Time:** 24 h (same day) **Mean (SD):** 38.7 (14.7) **Percentiles:** 25th: 30.62 50th: 35.11 75th: 41.10 **Range (Min, Max):** 14.8, 70.9 **Monitoring Stations:** Indoor measured inside nursing home **Copollutant:** O_3	**PM Increment:** 10 µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** **Regression coefficient (SE** **p-value):** Cu/Zn SOD: -0.05 (0.02 0.001) LPO (square root transformed): 0.08 (0.09 0.381) GSH (log-transformed quadratic term for PM): -0.05 (0.01 0.002) Regression coefficient (SE p-value) by supplementation groups (same transformations as above): Cu/Zn SOD Soy Oil: -0.06 (0.02, <0.001) Fish Oil: * 0.04 (0.02, 0.009) LPO Soy Oil: -0.02 (0.14, 0.904) Fish Oil: * 0.16 (0.07, 0.024) GSH Soy Oil: -0.03 (0.04, 0.406) Fish Oil: -0.09 (0.04, 0.017) *Quadratic term for PM
Reference: Ruckerl et al. (2007, 156931) **Period of Study:** May 2003-Jul 2004 **Location:** Athens, Augsburg, Barcelona, Helsinki, Rome, and Stockholm	**Outcome:** Interleukin-6 (IL-6), fibrinogen, C-reactive protein (CRP) **Age Groups:** 35-80 yr **Study Design:** Repeated measures / longitudinal **N:** 1003 MI survivors **Statistical Analyses:** Mixed-effect models **Covariates:** City-specific confounders (age, sex, BMI) Long-term time trend and apparent temperature RH, time of day, day of week included if adjustment improved model fit **Season:** Long-term time trend **Dose-response Investigated?** Used p-splines to allow for nonparametric exposure-response functions **Statistical Package:** SAS v9.1	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Hourly and 24-h (lag 0-4, mean of lags 0-4, mean of lags 0-1, mean of lags 2-3, means of lags 0-3) **Mean (SD):** Presented by city only **Monitoring Stations:** Central monitoring sites in each city **Copollutant:** SO_2 O_3 NO NO_2	**PM Increment:** IQR **Effect Estimate [Lower CI, Upper CI]:** % change in mean blood markers per increase in IQR of air pollutant. IL-6 Lag (IQR): % change in GM (95%CI) Lag 0 (11.0): 0.46 (-0.89, 1.83) Lag 1 (11.0): -0.39 (-1.69, 0.93) Lag 2 (11.0): -0.23 (-1.53, 1.07) 5-day avg (8.6): 0.05 (-1.37, 1.50) Fibrinogen Lag (IQR): % change in AM (95%CI) Lag 0 (11.0): 0.05 (-0.48, 0.58) Lag 1 (11.0): 0.17 (-0.35, 0.69) Lag 2 (11.0): 0.20 (-0.32, 0.71) 5-day avg (8.6): 0.38 (-0.21, 0.96) CRP Lag (IQR): % change in GM (95%CI) Lag 0 (11.0): 0.11 (-1.95, 2.21) Lag 1 (11.0): -0.06 (-1.98, 1.90) Lag 2 (11.0): 0.11 (-1.80, 2.06) 5-day avg (8.6): -0.13 (-2.15, 1.92)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ruckerl et al. (2006, 088754) **Period of Study:** Oct 2000-Apr 2001 **Location:** Erfurt, Germany	**Outcome:** C-reactive protein (CRP) serum amyloid A (SAA) E-selectin von Willebrand Factor (vWF) intercellular adhesion molecule-1 (ICAM-1) fibrinogen Factor VII prothrombin fragment 1+2 D-dimer **Age Groups:** 50+ **Study Design:** Panel (12 repeated measures at 2-wk intervals) **N:** 57 male subjects with coronary disease **Statistical Analyses:** Fixed effects linear and logistic regression models **Covariates:** Models adjusted for different factors based on health endpoint CRP: RH, temperature, trend, ID ICAM-1: temperature, trend, ID vWF: air pressure, RH, temperature, trend, ID FVII: air pressure, RH, temperature, trend, ID, weekday **Season:** Time trend as covariate **Dose-response Investigated?** Sensitivity analyses examined nonlinear exposure-response functions **Statistical Package:** SAS v8.2 and S-Plus v6.0	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** 20.0 (15.0) **Percentiles:** 25th: 9.7 50th: 14.9 75th: 26.1 **Range (Min, Max):** 2.6, 83.7 **Monitoring Stations:** 1 site **Copollutant:** UFPs AP $PM_{2.5}$ PM_{10} OC EC NO_2 CO	**PM Increment:** IQR (16.4 5-day avg: 12.2) **Effect Estimate [Lower CI, Upper CI]:** Effects of air pollution on blood markers presented as OR (95%CI) for an increase in the blood marker above the 90th percentile per increase in IQR air pollutant. **CRP** Time before draw: 0 to 23 h: 1.1 (0.7, 1.8) 24-47 h: 1.5 (0.9, 2.5) 48-71 h: 1.2 (0.8, 1.9) 5-day mean: 1.4 (0.9, 2.3) **ICAM-1** Time before draw: 0-23 h: 0.7 (0.4, 0.9) 24-47 h: 1.3 (0.8, 1.8) 48-71 h: 1.8 (1.2, 2.7) 5-day mean: 1.1 (0.8, 1.5) Effects of air pollution on blood markers presented as % change from the mean/GM in the blood marker per increase in IQR air pollutant. **vWF** Time before draw: 0-23 h: 3.9 (-0.3, 8.1) 24-47 h: 3.1 (-1.6, 7.8) 48-71 h: 3.6 (-1.1, 8.3) 5-day mean: 5.6 (0.5, 10.8) **FVII** Time before draw: 0-23 h: -2.5 (-6.2 to 1.4) 24-47 h: -2.8 (-6.1 to 0.6) 48-71 h: -2.3 (-5.0 to 0.6) 5-day mean: -3.5 (-6.4 to -0.4) **Note:** Summary of results presented in figures. SAA results indicate increase in association with PM (not as strong and consistent as with CRP) No association observed between E-selectin and PM An increase in prothrombin fragment 1+2 was consistently observed, particularly with lag 4 Fibrinogen results revealed few significant associations, potentially due to chance D-dimer results revealed null associations in linear and logistic analyses

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ruckerl et al. (2006, 088754) **Period of Study:** Oct 2000-Apr 2001 **Location:** Erfurt, Germany	**Outcome:** C-reactive protein (CRP) serum amyloid A (SAA) E-selectin von Willebrand Factor (vWF) intercellular adhesion molecule-1 (ICAM-1) fibrinogen Factor VII prothrombin fragment 1+2 D-dimer **Age Groups:** 50+ yr **Study Design:** Panel (12 repeated measures at 2-wk intervals) **N:** 57 male subjects with coronary disease **Statistical Analyses:** Fixed effects linear and logistic regression models **Covariates:** Models adjusted for different factors based on health endpoint CRP: RH, temperature, trend, ID ICAM-1: temperature, trend, ID vWF: air pressure, RH, temperature, trend, ID FVII: air pressure, RH, temperature, trend, ID, weekday **Season:** Time trend as covariate **Dose-response Investigated?** Sensitivity analyses examined nonlinear exposure-response functions **Statistical Package:** SAS v8.2 and S-Plus v6.0	**Pollutant:** EC **Averaging Time:** 24 h **Mean (SD):** 2.6 (2.4) **Percentiles:** 25th: 1.0 50th: 1.8 75th: 3.2 **Range (Min, Max):** 0.2, 12.4 **Monitoring Stations:** 1 site **Copollutant:** UFPs AP $PM_{2.5}$ PM_{10} OC EC NO_2 CO	**PM Increment:** IQR (2.3 5-day avg: 1.8) **Effect Estimate [Lower CI, Upper CI]:** Effects of air pollution on blood markers presented as OR (95%CI) for an increase in the blood marker above the 90th percentile per increase in IQR air pollutant. **CRP** Time before draw: 0-23 h: 1.2 (0.7, 2.0) 24-47 h: 1.3 (0.7, 2.4) 48-71 h: 1.6 (0.9, 2.7) 5-day mean: 1.2 (0.7, 2.1) **ICAM-1** Time before draw: 0-23 h: 1.0 (0.7, 1.6) 24-47 h: 2.6 (1.7, 3.8) 48-71 h: 4.0 (2.5, 6.1) 5-day mean: 2.2 (1.4, 3.3) Effects of air pollution on blood markers presented as % change from the mean/GM in the blood marker per increase in IQR air pollutant. **vWF** Time before draw: 0-23 h: 5.0 (0.0, 10.1) 24-47 h: 7.6 (1.4, 13.7) 48-71 h: 1.1 (-5.2, 7.4) 5-day mean: 5.7 (-0.5, 12.0) **FVII** Time before draw: 0-23 h: -5.7 (-10.5 to -0.7) 24-47 h: -6.9 (-11.2 to -2.3) 48-71 h: -4.2 (-8.4, 0.2) 5-day mean: -6.0 (-10.5 to -1.2) **Note:** Summary of results presented in figures. SAA results indicate increase in association with PM (not as strong and consistent as with CRP) No association observed between E-selectin and PM An increase in prothrombin fragment 1+2 was consistently observed, particularly with lag 4 Fibrinogen results revealed few significant associations, potentially due to chance D-dimer results revealed null associations in linear and logistic analyses

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ruckerl et al. (2006, 088754) **Period of Study:** Oct 2000-Apr 2001 **Location:** Erfurt, Germany	**Outcome (ICD9 and ICD10):** C-reactive protein (CRP) Serum amyloid A (SAA) E-selectin von Willebrand Factor (vWF) intercellular adhesion molecule-1 (ICAM-1) Fibrinogen Factor VII Prothrombin fragment 1+2 D-dimer **Age Groups:** 50+ yr **Study Design:** Panel (12 repeated measures at 2-wk intervals) **N:** 57 male subjects with coronary disease **Statistical Analyses:** Fixed effects linear and logistic regression models **Covariates:** Models adjusted for different factors based on health endpoint CRP: RH, temperature, trend, ID ICAM-1: temperature, trend, ID vWF: air pressure, RH, temperature, trend, ID FVII: air pressure, RH, temperature, trend, ID, weekday **Season:** Time trend as covariate **Dose-response Investigated?** Sensitivity analyses examined nonlinear exposure-response functions **Statistical Package:** SAS v8.2 and S-Plus v6.0	**Pollutant:** OC **Averaging Time:** 24 h **Mean (SD):** 1.5 (0.6) **Percentiles:** 25th: 1.1 50th: 1.4 75th: 1.8 **Range (Min, Max):** 0.3, 3.4 **Monitoring Stations:** 1 site **Copollutant:** UFPs AP $PM_{2.5}$ PM_{10} OC EC NO_2 CO	**PM Increment:** IQR (0.7 5-day avg: 0.5) **Effect Estimate [Lower CI, Upper CI]:** Effects of air pollution on blood markers presented as OR (95%CI) for an increase in the blood marker above the 90th percentile per increase in IQR air pollutant. **CRP** Time before draw: 0-23 h: 1.2 (0.7, 1.9) 24-47 h: 1.3 (0.8, 2.1) 48-71 h: 1.4 (0.8, 2.4) 5-day mean: 1.2 (0.7, 1.8) **ICAM-1** Time before draw: 0-23 h: 0.9 (0.6, 1.3) 24-47 h: 2.0 (1.3, 3.2) 48-71 h: 3.0 (1.8, 4.8) 5-day mean: 1.3 (0.8, 2.0) Effects of air pollution on blood markers presented as % change from the mean/GM in the blood marker per increase in IQR air pollutant. **vWF** Time before draw: 0-23 h: 5.5 (0.2, 10.8) 24-47 h: 8.0 (2.1, 13.9) 48-71 h: 3.5 (-2.6, 9.6) 5-day mean: 7.4 (2.0, 12.8) **FVII** Time before draw: 0-23 h: -6.1 (-10.6 to -1.4) 24-47 h: -7.2 (-11.4 to -2.8) 48-71 h: -3.8 (-8.2, 0.9) 5-day mean: -5.6 (-9.8 to -1.1) **Note:** Summary of results presented in figures. SAA results indicate increase in association with PM (not as strong and consistent as with CRP) No association observed between E-selectin and PM An increase in prothrombin fragment 1+2 was consistently observed, particularly with lag 4 Fibrinogen results revealed few significant associations, potentially due to chance D-dimer results revealed null associations in linear and logistic analyses

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ruckerl et al. (2007, 091379) **Period of Study:** Oct 2000-Apr 2001 **Location:** Erfurt, Germany	**Outcome:** Soluble CD40 ligand (sCD40L), platelets, leukocytes, erythrocytes, hemoglobin **Age Groups:** 50+ yr **Study Design:** Panel (12 repeated measures at 2-wk intervals) **N:** 57 male subjects with coronary disease **Statistical Analyses:** Fixed effects linear regression models **Covariates:** Long-term time trend, weekday of the visit, temperature, RH, barometric pressure **Season:** Time trend as covariate **Dose-response Investigated?** No **Statistical Package:** SAS v8.2 and S-Plus v6.0	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** 20.0 (15.0) **Percentiles:** 25th: 9.7 50th: 14.9 75th: 26.1 **Range (Min, Max):** 2.6, 83.7 **Monitoring Stations:** 1 site **Copollutants:** UFPs AP $PM_{2.5}$ PM_{10} NO	**PM Increment:** IQR (16.4 5-day avg: 12.2) **Effect Estimate [Lower CI, Upper CI]:** Effects of air pollution on blood markers presented as % change from the mean/GM in the blood marker per increase in IQR air pollutant. **sCD40L, % change GM (pg/mL)** lag0: 1.5 (-4.0, 7.3) Lag1: 0.2 (-5.4, 6.2) Lag2: -2.6 (-8.0, 3.1) Lag3: 0.5 (-3.9, 5.0) 5-day mean: 0.2 (-5.4, 6.2) **Platelets, % change mean (103/µl)** Lag0: -0.6 (-1.9, 0.7) Lag1: 0.1 (-1.3, 1.5) Lag2: 0.5 (-0.9, 1.9) Lag3: 0.2 (-1.1, 1.5) 5-day mean: -0.4 (-1.9, 1.2) **Leukocytes, % change in mean (103/µl)** Lag0: -1.6 (-3.2, 0.0) Lag1: -0.4 (-2.2, 1.4) Lag2: -0.2 (-2.1, 1.7) Lag3: -0.8 (-2.4, 0.7) 5-day mean: -1.6 (-3.5, 0.3) **Erythrocytes, % change mean (106/µl)** Lag0: -0.1 (-0.5, 0.3) Lag1: -0.3 (-0.7, 0.2) Lag2: -0.4 (-0.8, 0.0) Lag3: -0.2 (-0.5, 0.1) 5-day mean: -0.4 (-0.8, 0.0) **Hemoglobin, % change mean (g/dl)** Lag0: 0.0 (-0.6, 0.5) Lag1: -0.2 (-0.8, 0.3) Lag2: -0.5 (-1.1, 0.0) Lag3: -0.2 (-0.7, 0.2) 5-day mean: -0.5 (-1.0, 0.1)
Reference: Sarnat et al. (2006, 090489) **Period of Study:** Summer and fall 2000 **Location:** Steubenville, OH	**Outcome:** Supraventricular ectopy (SVE) or ventricular ectopy (VE) **N:** 32 nonsmoking older adults **Statistical Analysis:** Logistic mixed effects regression **Season:** Summer and fall **Dose-response Investigated?** No	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 5 days **Median (IQR):** $PM_{2.5}$: Median: 19.0 µg/m^3 IQr = 10.0 Sulfate: Median: 6.1. IQR: 4.2 EC: Median: 0.9. IQR: 0.5 **Copollutants:** O_3, NO_2, SO_2	**PM Increment:** IQR **Effect Estimate:** $PM_{2.5}$: SVE: OR = 1.42 (95% CI: 0.99, 2.04) VE: OR = 1.02 (95% CI: 0.63-1.65) Sulfate: SVE: OR = 1.70 (95% CI: 1.12, 2.57) VE: OR = 1.08 (95% CI: 0.65, 1.80) EC: SVE: OR = 1.15 (95% CI: 0.73, 1.81) VE: OR = 1.00 (95% CI: 0.57, 1.75) **Notes:** Longitudinal study of 32 nonsmoking older adults who had ECG measurements made every week for 24 wk. PM measured within 1 mile of subjects' residences, and central site pollutant measurements were also made.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Schneider et al. (2008, 191985) **Period of Study:** Nov 2004-Dec 2005 **Location:** Chapel Hill, NC	**Outcome:** Endothelial Function Parameters **Age Groups:** 48-80 yr **Study Design:** Panel **N:** 22 diabetics **Statistical Analyses:** Mixed Models **Covariates:** Season, day of the week, temperature, relative humidity, barometric pressure **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 0-4 days; 5-day ma	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily **Mean (SD):** 13.6 (7.0) **Min:** 2.0 **Max:** 38.9 **Monitoring Stations:** 2 **Copollutant:** NR	**PM Increment:** 10 µg/m^3 **Percent Change: (Lower CI, Upper CI), lag:** FMD: ^I -17.3 (-34.6, 0.0), lag 0 -4.4 (-24.6, 15.8), lag 1 -18.6 (-44.8, 7.6), lag 2 1.6 (-23.6, 26.9), lag 3 18.4 (-3.5, 40.3), lag 4 -19.4 (-62.6, 23.8), 5-day ma NTGMD: 2.5 (-9.0, 13.9), lag 0 -13.6 (-24.5, -2.6), lag 1* -10.2 (-23.5, 3.0), lag 2 -8.0 (-22.4, 6.4), lag 3 3.6 (-7.9, 15.0), lag 4 -19.4 (-44.3, 5.5), 5-day ma LAEI: 0.4 (-4.2, 5.0), lag 0 -0.3 (-6.0, 5.4), lag 1 2.5 (-4.3, 9.4), lag 2 -7.3 (-13.5, -1.1), lag 3* -2.3 (-8.0, 3.3), lag 4 -4.6 (-15.3, 6.1), 5-day ma SAEI: -3.0 (-13.0, 7.0), lag 0 -17.0 (-27.5, -6.4), lag 1** -9.7 (-23.5, 4.2), lag 2 -15.1 (-29.3, -0.9)*, lag 3 -2.1 (-14.0, 9.7), lag 4 -25.4 (-45.4, -5.3), 5-day ma* SVR: -1.6 (-3.7, 0.4), lag 0 1.6 (-0.9, 4.1), lag 1 3.5 (0.5, 6.5), lag 2 2.4 (-0.5, 5.3), lag 3 3.2 (0.7, 5.6), lag 4* 4.5 (-0.3, 9.2), 5-day ma *p < 0.05, ** p < 0.01 **Notes:** Percent change (95% CI) per 10 µg/m^3 $PM_{2.5}$ by GSTM1 genotype (Fig 3)
Reference: Schwartz et al. (2005, 074317) **Period of Study:** 12 wk during the summer of 1999 **Location:** Boston, MA	**Outcome:** Heart rate variability (HRV), (SDNN, r-MSSD, PNN50, LFHFR) **Age Groups:** 61-89 yr **Study Design:** Panel study **N:** 28 elderly subjects **Statistical Analysis:** Mixed models. To examine heterogeneity of effects, hierarchical modeling was used. **Season:** Summer **Dose-response Investigated?** No	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 1 h, 24 h **Median:** 24-h: 10 µg/m^3 **Monitoring Stations:** 1 **Copollutant:** BC, O_3, CO, SO_2, NO_2	**PM Increment:** IQR (not given) **Effect Estimate:** 24 h: 2.6 ms decrease in SDNN (95% CI: 0.8 to -6.0) 10.1 ms decrease in r-MSSD (95% CI: -2.8 to -16.9). 1 h: 3.4 ms decrease in SDNN (95% CI: 0.6 to -7.3) 7.4 ms decrease in r-MSSD (95% CI: 1.6 to -15.5). **Notes:** Various log-transformed HRV parameters were measured for 30 minutes once a week. The random effects model indicated that the negative effect of BC on HRV was not restricted to a few subjects. Same study population as Gold et al. (2005). Boston Elders Study For each pollutant/averaging time, similarly sized changes were observed for PNN50 (%) and LFHFR.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Schwartz et al. (2005, 074317) **Period of Study:** 12 wk during the summer of 1999 **Location:** Boston, MA	**Outcome:** Heart rate variability (HRV), (SDNN, r-MSSD, PNN50, LFHFR) **Age Groups:** 61-89 yr **Study Design:** Panel study **N:** 28 elderly subjects **Statistical Analysis:** Mixed models. To examine heterogeneity of effects, hierarchical modeling was used. **Season:** Summer **Dose-response Investigated?** No	**Pollutant:** BC **Averaging Time:** 24 h **Median:** 1.0 µg/m^3 **Monitoring Stations:** 1 **Copollutant:** $PM_{2.5}$, O_3, CO, SO_2, NO_2	**PM Increment:** IQR **Effect Estimate:** 5.1 ms decrease in SDNN (-1.5 to -8.6) 10.1 ms decrease in r-MSSD (-2.4 to -17.2). **Notes:** Various log-transformed HRV parameters were measured for 30 minutes once a week. The random effects model indicated that the negative effect of BC on HRV was not restricted to a few subjects. Same study population as Gold et al. (2005). Boston Elders Study. Subjects with a prior MI experienced greater declines in BC associated HRV. For each pollutant/averaging time, similarly sized changes were observed for PNN50 (%) and LFHFR.
Reference: Schwartz et al. (2005, 074317) **Period of Study:** 2000 **Location:** Boston, Massachusetts	**Outcome:** HF (high frequency component of heart rate variability) **Study Design:** Cross-sectional **N:** 497 subjects **Statistical Analysis:** Linear regression, controlling for covariates	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 48 h **Mean (SD):** 11.4 µg/m^3 (8.0) **Copollutant:** None	**PM Increment:** 10 µg/m^3 **Effect Estimate:** 34% decrease in HF (95% CI: -9% to -52%) in subjects without the GSTM1 allele. In subjects with the allele, no effect was noted. Similar findings for obese subjects and those with high neutrophil counts. **Notes:** Study population: Normative Aging Study. Effects of $PM_{2.5}$ appear to be mediated by ROS.
Reference: Sorensen et al. (2005, 089428) **Period of Study:** Nov 1999-Aug 2000 **Location:** Copenhagen, Denmark	**Outcome:** 7-Hydro-8-Oxo-2'-Deoxyguanosine (8-oxodG) (measured in lymphocytes and urine) **Age Groups:** 20-33 yr **Study Design:** Panel (repeated measures) **N:** 49 students living and studying in central Copenhagen 50 students examined each season (66 subjects total 32 participated in each season total of 98 measurements) **Statistical Analyses:** Mixed models repeated measures **Covariates:** $PM_{2.5}$, season, subject (random factor) **Dose-response Investigated?** No **Statistical Package:** SAS v8e	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 48 h **Mean (SD):** Fall: 20.7 Summer: 12.6 **Percentiles:** IQR Fall: 13.1-27.7 IQR summer: 9.4-24.3 **Range (Min, Max):** NR **Monitoring Stations:** NA (personal assessment) **Copollutant (correlation):** Spearman correlations with $PM_{2.5}$ mass: chromium (r = 0.22) copper (r = 0.33) iron (r = 0.29) vanadium (p>0.5) nickel (p>0.5) platinum (p>0.5)	**PM Increment:** see below **Effect Estimate [Lower CI, Upper CI]:** Association between 8-oxodG in lymphocytes and personal exposure to transition metals in $PM_{2.5}$. % increase in 8-oxodG per increase in metal concentration indicated Vanadium: 1.9% per 1 µg/L (0.6, 3.3) Chromium: 2.2% per 1 µg/L (0.8, 3.5) Platinum: 6.1% per 1 ng/L (-0.6, 13.2) Nickel: 0.8% per 10 µg/L (-2.1, 3.7) Copper: -0.8% per 10 µg/L (-2.7, 1.0) Iron: 0.6% per 10 µg/L (-1.4, 2.6) **Note:** $PM_{2.5}$ mass was independently associated with 8-oxodG in 5 of 6 transition metal models (p < 0.02 in models with vanadium, chromium, nickel, copper, and iron p = 0.07 in platinum model). No transition metals were associated with 8-oxodG measured in urine

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Sorensen et al. (2003, 042700) **Period of Study:** Nov 1999-Aug 2000 **Location:** Copenhagen, Denmark	**Outcome:** RBC count, hemoglobin, platelet count, fibrinogen, PLAAS (2-aminoadipic semialdehyde in plasma proteins), HBGGS (γ-glutamyl semialdehyde in hemoglobin), HBAAS (2-aminoadipic semialdehyde in hemoglobin), MDA (malondialdehyde) **Age Groups:** 20-33 yr **Study Design:** Panel (repeated measures) **N:** 50 students living and studying in central Copenhagen 50 students examined each season (68 subjects total 31 participated in each season total of 195 measurements) **Statistical Analyses:** Mixed model repeated-measures analysis **Covariates:** Season, avg outdoor temperature, and sex **Season:** Repeated measures 4 times (once per season) **Dose-response Investigated?** No **Statistical Package:** SAS v8e	**Pollutant:** $PM_{2.5}$ (personal) **Averaging Time:** 48 h **Median:** 16.1 μg/m^3 **Percentiles:** Q25-Q75: 10.0-24.5 **Copollutant:** Urban background $PM_{2.5}$ Personal $PM_{2.5}$	**PM Increment:** 1 μg/m^3 **Effect Estimate [Lower CI, Upper CI]:** **Relationship between exposure and biomarkers** Estimate (p-value): Platelet count (x 106/g protein): 0.0008 (0.37) Fibrinogen (nmol/g protein): 0.0006 (0.69) PLAAS (pmol/mg protein): 0.0016 (0.061) HBGGS (pmol/mg protein): 0.0001 (0.94) HBAAS (pmol/mg protein): 0.0006 (0.64) **Increase (95%CI) in biomarkers per 10 μg/m^3 increase in** $PM_{2.5}$ RBC Men: 0% (-1.6, 1.6) Women: 2.3% (0.5, 4.1) Hemoglobin Men: 0.0% (-1.7, 1.5) Women: 2.6% (0.8, 4.5)
Reference: Sorensen et al. (2003, 042700) **Period of Study:** Nov 1999-Aug 2000 **Location:** Copenhagen, Denmark	**Outcome:** RBC count, hemoglobin, platelet count, fibrinogen, PLAAS (2-aminoadipic semialdehyde in plasma proteins), HBGGS (γ-glutamyl semi-aldehyde in hemoglobin), HBAAS (2-aminoadipic semialdehyde in hemoglobin), MDA (malondialdehyde) **Age Groups:** 20-33 yr **Study Design:** Panel (repeated measures) **N:** 50 students living and studying in central Copenhagen 50 students examined each season (68 subjects total 31 participated in each season total of 195 measurements) **Statistical Analyses:** Mixed model repeated-measures analysis **Covariates: S**eason, avg outdoor temperature, and sex **Season:** Repeated measures 4 times (once per season) **Dose-response Investigated?** No **Statistical Package:** SAS v8e	**Pollutant:** Personal exposure to black carbon (10-6/m) **Averaging Time:** 48 h **Median:** 8.1 **Percentiles:** Q25-Q75: 5.0-13.2 **Copollutant:** Urban background $PM_{2.5}$ Personal $PM_{2.5}$	**PM Increment:** 10-6/m **Effect Estimate [Lower CI, Upper CI]:** **Relationship between exposure and biomarkers** Estimate (p-value): RBC count (x 109/g protein): 0.0003 (0.75) Hemoglobin (μmol/g protein): 0.0004 (0.65) Platelet count (x 106/g protein): 0.0009 (0.51) Fibrinogen (nmol/g protein): -0.0027 (0.29) PLAAS (pmol/mg protein): 0.0041 (0.0009) HBGGS (pmol/mg protein): 0.0024 (0.25) HBAAS (pmol/mg protein): 0.0022 (0.20) MDA (pmol/mg protein): 0.0018 (0.30)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Sorensen et al. (2003, 042700) **Period of Study:** Nov 1999-Aug 2000 **Location:** Copenhagen, Denmark	**Outcome:** RBC count, hemoglobin, platelet count, fibrinogen, PLAAS (2-aminoadipic semialdehyde in plasma proteins), HBGGS (γ-glutamyl semialdehyde in hemoglobin), HBAAS (2-aminoadipic semialdehyde in hemoglobin), MDA (malondialdehyde) **Age Groups:** 20-33 yr **Study Design:** Panel (repeated measures) **N:** 50 students living and studying in central Copenhagen 50 students examined each season (68 subjects total 31 participated in each season total of 195 measurements) **Statistical Analyses:** Mixed model repeated-measures analysis **Covariates: S**eason, avg outdoor temperature, and sex **Season:** Repeated measures 4 times (once per season) **Dose-response Investigated?** No **Statistical Package:** SAS v8e	**Pollutant:** $PM_{2.5}$ (urban background concentration) **Averaging Time:** 48 h **Median:** 9.2 μg/m^3 **Percentiles:** Q25-Q75: 5.3-14.8 **Copollutant:** Urban background $PM_{2.5}$ Personal carbon black	**PM Increment:** 1 μg/m^3 **Effect Estimate [Lower CI, Upper CI]:** **Relationship between exposure and biomarkers** Estimate (p-value): RBC count (x 109/g protein): 0.0008 (0.36) Hemoglobin (μmol/g protein): 0.0005 (0.53) Platelet count (x 106/g protein): -0.0008 (0.49) Fibrinogen (nmol/g protein): 0.0004 (0.84) PLAAS (pmol/mg protein): 0.0004 (0.76) HBGGS (pmol/mg protein): -0.0020 (0.39) HBAAS (pmol/mg protein): -0.0021 (0.29) MDA (pmol/mg protein): 0.0012 (0.52)
Reference: Sullivan et al. (2007, 100083) **Period of Study:** Feb 2000-Mar 2002 **Location:** Seattle, Washington, USA	**Outcome:** Blood CRP, fibrinogen, D-dimer **Age Groups:** >55 yr of age **Study Design:** Panel study **N:** 47 elderly subjects	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Median (IQR):** 7.7 μg/m^3 (6.4) **Monitoring Stations:** 1 **Copollutant:** Indoor $PM_{2.5}$	**PM Increment:** 10 μg/m^3 **Effect Estimate:** Among those with CVD, $PM_{2.5}$ 1 day earlier: CRP: 1.25 (95% CI: 0.97, 1.58) Fibrinogen: 1.01 (95% CI: 0.97, 1.05) D-dimer: 1.04 (95% CI: 0.93, 1.15) With COPD: CRP: 0.69 (95% CI: 0.34, 1.42) Fibrinogen: 1.05 (95% CI: 0.97, 1.13) D-dimer: 1.10 (95% CI: 0.95, 1.28) Healthy: CRP: 1.01 (95% CI: 0.85, 1.19) Fibrinogen: 0.88 (95% CI: 0.81, 0.95) D-dimer: 1.10 (95% CI: 0.75, 1.58) **Notes:** Out of 47 subjects, n = 23 with CVD and n = 24 (n = 16 COPD and 8 healthy) without CVD. Blood markers were measured on 2-3 morning over a 5-10 day period, and outdoor $PM_{2.5}$ was measured at a central monitoring site. These findings are not consistent with and effect of fine PM on markers of inflammation and thrombosis in the elderly.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Sullivan et al. (2005, 109418) **Period of Study:** Feb 2000-Mar 2002 **Location:** Seattle, Washington, USA	**Outcome:** Heart rate variability (H, LF, HF, r-MSSD, SDNN) **Study Design:** Panel study **N:** 34 elderly subjects with (n = 21) and without (n = 13) CVD. **Statistical Analysis:** Linear mixed effects regression	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 1 h **Median (IQR):** 10.7 (7.6) **Copollutant:** CO, NO_2	**PM Increment:** 10 µg/m^3 **Effect Estimate:** 1 h: With CVD: HF: (3% increase, 95% CI: -19, 32) Without CVD: HF(5% decrease, 95% CI: -34, 36) Similarly, no association was found for 4-h or 24-h mean $PM_{2.5}$ concentrations. **Notes:** 285 daily 20 min HRV measures were made in the homes of study subjects over a 10-day period.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Sullivan et al. (2005, 109418) **Period of Study:** Feb 2000-Mar 2002 **Location:** Seattle area, WA	**Outcome (ICD9 and ICD10):** High-sensitivity C-reactive protein (hs-CRP) fibrinogen D-dimer Endothelin-1 (ET-1) Interleukin-6 (IL-6 Interleukin-6 receptor (IL-6r) Tumor necrosis factor-α (TNF-8- α) Tumor necrosis factor-receptors (p55, p75) Monocyte chemoattractant protein-1 (MCP-1) **Age Groups:** ≥ 55 yr **Study Design:** Panel (repeated measures) **N:** 47 participants with (23) and without (10 COPD and 8 healthy) CVD **Statistical Analyses:** Mixed models **Covariates:** Age, gender, medication use, meteorological variables (temperature and RH) **Dose-response Investigated?** No **Statistical Package:** SAS v8.02	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h (0-day and 1-day lags) **Mean (SD):** NR **Percentiles:** For all subject-days: 25th: 5.2 50th: 7.7 75th: 11.5 90th: 19.9 **Range (Min, Max):** 1.3, 33.9 **Monitoring Stations:** NA, measured at participant's residence **Copollutant:** None	**PM Increment:** 10 μg/m^3 **Effect Estimate [Lower CI, Upper CI]:** Multiplicative change in mean outcome associated with 10 μg/m^3 increase in PM **Among those with different disease status.** **CRP Fold-rise (95%CI)** CV 0-day lag: 1.21 (0.86, 1.70) CV 1-day lag: 1.25 (0.97, 1.58); COPD 0-day lag: 0.93 (0.48, 1.80) COPD 1-day lag: 0.69 (0.33, 1.46) Healthy 0-day lag: 0.98 (0.88, 1.08) Healthy 1-day lag: 1.01 (0.84 1.21) **Fibrinogen Fold-rise (95%CI)** CV 0-day lag: 1.02 (0.98, 1.06) CV 1-day lag: 1.0 (0.97, 1.03); COPD 0-day lag: 1.0 (0.91, 1.09) COPD 1-day lag: 1.08 (0.99, 1.17) Healthy 0-day lag: 0.94 (0.87, 1.01) Healthy 1-day lag: 0.99 (0.88, 1.17) **D-dimer Fold-rise (95%CI)** CV 0-day lag: 1.02 (0.88, 1.17) CV 1-day lag: 1.03 (0.93, 1.15); COPD 0-day lag: 1.04 (0.93, 1.16) COPD 1-day lag: 1.09 (0.94, 1.27) Healthy 0-day lag: 0.95 (0.79, 1.14) Healthy 1-day lag: 0.97 (0.71, 1.31) **Among those with cardiovascular disease** **MCP-1 Fold-rise (95%CI)** 0-day lag: 1.3 (1.1, 1.7) 1-day lag: 1.0 (0.9, 1.3) **ET-1 Fold-rise (95%CI)** 0-day lag: 1.1 (0.8, 1.2) 1-day lag: 1.1 (0.9, 1.2) **Note:** TNF-α and IL-6 measures were below the limit of detection of assays
Reference: Timonen et al. (2006, 088747) **Period of Study:** 1998-1999 **Location:** Amsterdam, Netherlands Erfurt, Germany Helsinki, Finland	**Outcome:** Heart variability (HRV) measurements: [LF, HF, LFHFR, NN interval, SDNN, r-MSSD] **Study Design:** Panel study **N:** 131 elderly subjects with stable coronary heart disease **Statistical Analysis:** Linear mixed models	**Pollutant:** $PM_{2.5}$ **Means:** Amsterdam: 20.0 Erfurt: 23.3 Helsinki: 12.7 **Copollutant:** NO_2, CO	**PM Increment:** 10 μg/m^3 **Effect Estimate:** SDNN -0.33ms (95% CI: -1.05, 0.38) HF: -0.3% (95% CI: -10.6, 5.4) LFHFR: -1.4 (95% CI: -5.9, 8.7) **Notes:** Followed for 6 mo with biweekly clinic visits 2-day lag. ULTRA Study

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Vallejo et al. (2006, 157081) **Period of Study:** Apr-Aug 2002 **Location:** Mexico City metropolitan area	**Outcome:** Heart rate variability measures (SDNN, pNN50) **Age Groups:** Mean age 27 yr **Study Design:** Panel study **N:** 40 young healthy participants (non-smokers, no meds or history of CVD, respiratory, neurological, or endocrine disease) **Statistical Analysis:** Linear mixed effects models	**Pollutant:** $PM_{2.5}$ (pDR nephelometric method-DataRAM) **Copollutant:** None	**PM Increment:** 30 µg/m^3 **Effect Estimate: pNN50:** 0 h lag: -0.01% (95% CI: -0.03, 0.01) 1 h: -0.01% (95% CI: -0.04, 0.02) 2 h: -0.05% (95% CI: -0.09, 0.00) 3 h: -0.07% (95% CI: -0.13 to -0.02) 4 h: -0.08% (95% CI: -0.14 to -0.01) 5 h: -0.06% (95% CI: -0.13, 0.02) 6 h: -0.05% (95% CI: -0.13, 0.04) **SDNN:** 0 h: 0.00% (95% CI: 0.00, 0.01) 1 h: 0.00% (95% CI: -0.01, 0.01) 2 h: 0.00% (95% CI: -0.02, 0.01) 3 h: -0.01% (95% CI: -0.02, 0.00) 4 h: -0.01% (95% CI: -0.02, 0.01) 5 h: -0.01% (95% CI: -0.02, 0.01) 6 h: 0.00% (95% CI: -0.02, 0.02) **Notes:** Subjects underwent 13 h of ECG monitoring and personal $PM_{2.5}$ measurement. HRV measures were regressed against different lags of $PM_{2.5}$ concentration.
Reference: Van Hee et al. (2009, 192110) **Period of Study:** Jul 2000-Aug 2002 **Location:** Baltimore, Maryland Chicago, Illinois Winston-Salem, North Carolina St. Paul Minnesota New York, New York Los Angeles, California	**Outcome:** Left Ventricular Mass Index and Ejection Fraction **Age Groups:** 45-84 yr **Study Design: C**ross-sectional **N:** 3,827 participants **Statistical Analyses:** Linear Regression Models **Covariates: A**ge, race, income, sex, education, medication use, LDL, HDL, physical activity, alcohol consumption, smoking, diabetes, systolic BP, diastolic BP **Dose-response Investigated?** No **Statistical Package:** Stata **Lags Considered:** NR	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **Mean (SD):** Fig only **Monitoring Stations:** N/A Interpolation used **Copollutant:** NR **Co-pollutant Correlation:** N/A	**PM Increment:** 10 µg/m^3 **Difference (Lower CI, Upper CI), p-value:** Left Ventricular Mass Index Unadjusted: -6.0 (-7.8, -4.2), <0.0001 All covariates except center, BP: -6.1 (-7.8, -4.4), <0.0001 All covariates except BP: 3.7 (-6.0, 13.4), 0.46 Full model: 4.6 (-4.7, 13.9), 0.33 Full model plus center/race interaction: 3.8 (-6.1, 13.7), 0.45 Left Ventricular Ejection Fraction Unadjusted: 3.0 (2.2, 3.8), <0.0001 All covariates except center, BP: 1.4 (0.5, 2.2), 0.001 All covariates except BP: -1.1(-5.8, 3.7), 0.66 Full model: -1.3 (-6.0, 3.5), 0.60 Full model plus center/race interaction: -3.0 (-8.0, 2.0), 0.24
Reference: Wellenius et al. (2007, 092830) **Period of Study:** Feb 2002-Mar 2003 **Location:** Boston, Massachusetts, USA	**Outcome:** Circulating levels of B-type natriuretic peptide (BNP Measured in whole blood at 0, 6, 12 wk) **Study Design:** Panel study **N:** 28 subjects (each with chronic stable HF and impaired systolic function) **Statistical Analysis:** Linear mixed effects models	**Pollutant:** $PM_{2.5}$ **Copollutant:** NO_2, SO_2, O_3, CO, BC	**PM Increment:** 10 µg/m^3 **Effect Estimate:** Same day $PM_{2.5}$: 0.8% increase in BNP (95% CI: -16.4, 21.5) **Notes:** The study found no association between any pollutant and measures of BNP at any lag. Further, the within subject coefficient of variation was large suggesting the magnitude of effected air pollutant health effects are small in relation to within subject variability in BNP.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Wellenius et al. (2007, 092830) **Period of Study:** Feb 2002-Mar 2003 **Location:** Boston, Massachusetts	**Outcome (ICD9 and ICD10):** B-type natriuretic peptide (BNP) (natural-log transformed) **Age Groups:** 33-88 yr **Study Design:** Panel (blood collected at 0, 6, and 12 wk) **N:** 28 patients with chronic stable heart failure and impaired systolic function **Statistical Analyses:** Linear mixed-effects models **Covariates:** Temperature, dew point, mean dew point over the past 3 days, calendar month of blood draw, measurement occasion, treatment assignment, measurement occasion by treatment assignment interaction **Season:** Adjusted for calendar month **Dose-response Investigated?** No **Statistical Package:** SAS v9.1	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily (assessed lags of 0-3 days) **Mean (SD):** 10.9 (8.4) **Percentiles:** 50th: 8.0 µg/m^3 **Range (Min, Max):** 0.7-50.9 µg/m^3 **Monitoring Stations:** 1 monitor **Copollutant (correlation):** CO (r = 0.35) NO_2 (r = 0.31) SO_2 (r = 0.18) O_3 (r = 0.35) BC(r = 0.68)	**PM Increment:** IQr = 8.1 µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** % change in BNP per IQR increase in $PM_{2.5}$ Lag0: 1.5 (-18.7, 19.2) Lag1: 2.1 (-20.0, 30.3) Lag2: 1.3 (12.3, 17.1) Lag3: 5.6 (-16.8, 34.0) **Note:** No significant associations observed between any pollutant and BNP levels at any lags (presented in Fig 2)
Reference: Wheeler et al. (2006, 088453) **Period of Study:** Fall 1999 and spring 2000 **Location:** Atlanta, GA	**Outcome:** Heart rate variability **Age Groups:** 49-76 yr **N:** 18 subjects with COPD and 12 subjects with a recent MI **Statistical Analysis:** Linear-mixed effect model **Season:** Fall and spring	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 1 h 4 h 24 h **Mean:** 24-h: 17.8 µg/m^3 **Copollutant:** O_3, CO, SO_2, NO_2	**PM Increment:** 11.65 µg/m^3 (IQR) in 4 h $PM_{2.5}$ **Effect Estimate:** Among COPD patients: 8.3% increase in SDNN (95% CI: 1.7, 15.3) Among MI patients: 2.9% decrease in SDNN (95% CI: -7.8, 2.3) Results for 1-h and 24-h averaging times were similar. **Notes:** Data was collected on 7 days in the fall of 1999 or spring of 2000. Effects were modified by medication use, baseline pulmonary function, and health status.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Yeatts et al. (2007, 091266) **Period of Study:** 12-wk period b/t Sep 2003-Jul 2004 **Location:** Chapel Hill, NC	**Outcome:** Heart Rate Variability **Age Groups:** 21-50 yr **Study Design:** Panel **N:** 12 asthmatics **Statistical Analyses:** Linear Mixed Model **Covariates:** Temperature, humidity, pressure **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 1 day	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** 12.5 (6.0) **Min:** 0.6 **Max:** 37.1 **Monitoring Stations:** 1 **Copollutant:** $PM_{10-2.5}$, PM_{10} **Co-pollutant Correlation:** $PM_{10-2.5}$ = 0.46* PM_{10} = NR *p < 0.01	**PM Increment:** 1 µg/m^3 **Beta, SE (Lower CI, Upper CI), p-value:** HRV Max Heart Rate: 0.40, 0.43 (-0.45, 1.24), 0.36 ASDNN5: -0.07, 0.15 (-0.37, 0.22), 0.63 SDANN5: 1.66, 0.65 (0.39, 2.93), 0.02 SDNN24HR(mesc): 1.16, 0.58 (0.02, 2.29), 0.06 rMSSD: 0.53, 0.20 (0.14, 0.91), 0.01 pNN50_24hr: -0.06, 0.11 (-0.27, 0.15), 0.58 pNN50_7min: 0.47, 0.42 (-0.35, 1.29), 0.27 Low-frequency power: -0.23, 0.14 (-0.51, 0.05), 0.11 Percent low frequency: -0.78, 0.41 (-1.59, 0.03), 0.07 High-frequency power: 0.14, 0.07 (-0.01, 0.28), 0.07 Percent high frequency: 0.64, 0.36 (-0.07, 1.34), 0.09 Blood Lipids Triglycerides: -0.63, 0.84 (-2.29, 1.02), 0.46 VLDL: -0.17, 0.22 (-0.61, 0.26), 0.44 Total cholesterol: -0.06, 0.22 (-0.49, 0.36), 0.77 Hematologic Factor Circulating eosinophils: -0.02, 0.00 (-0.02, -0.02), 0.27 Platelets: -0.01, 0.45 (-0.88, 0.86), 0.98 Circulating Proteins Plasminogen: 0.00, 0.00 (-0.01, 0.00), 0.82 Fibrenogen: 0.00, 0.01 (-0.01, 0.02), 0.59 Von Willibrand factor: -0.31, 0.29 (-0.87, 0.25), 0.28 Factor VII: -0.65, 0.33 (-1.29, -0.01), 0.05

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Yue et al. (2007, 097968) **Period of Study:** Oct 2000-Apr 2001 **Location:** Erfurt, Germany	**Outcome:** QT interval and T-wave amplitude for ECG recordings, and vWF, CRP from blood samples **Study Design:** Panel study **N:** 56 patients (male CAD patients with 12 clinical visits) **Statistical Analysis:** Linear and logistic regression models **Dose-response Investigated?** No	**Pollutant:** $PM_{2.5}$, PNC (n/cm^3) **Averaging Time: Mean:** Mass concentrations of PNC (0.1-2.84 n/cm^3) **Monitoring Stations:** 1 **Copollutant:** None	**PM Increment: .** IQR **Effect Estimate:** Each IQR increase in 0-23 h mean traffic particle concentration was associated with: QT interval: 0.6% (95% CI: -0.3, 1.4) T wave amplitude: -1.6% (95% CI: -3.3, 0.1) vWF: 3.2% (95% CI: -0.5, 7.0) CRP: (OR = 1.5 95% CI 1.0-2.3) Each IQR increase in 0-23 h mean combustion-generated particle concentration was associated with: QT interval: 0.1%(-0.3, 0.6) T wave amplitude: -0.2% (-1.2, 0.7) vWF: 2.8% (0.8, 4.8) CRP (OR = 1.0 0.8, 1.2) **Notes:** Five sources of particles were identified (airborne soil, local traffic-related ultrafine particles, combustion-generated aerosols, diesel traffic-related particles, and secondary aerosols).
Reference: Yue et al. (2007, 097968) **Period of Study:** Oct 12, 2000-Apr 27, 2001 **Location:** Erfurt, Germany	**Outcome:** QT interval, T wave amplitude, von Willebrand factor (vWF), C-reactive protein (CRP above 90th percentile compared to below) **Age Groups:** >50 yr **Study Design:** Panel (12 visits 625 observations for repolarization parameters and 578 observations for inflammatory markers) **N:** 57 male coronary artery disease patients **Statistical Analyses:** Linear and logistic fixed-effects regression models (generalized additive models) **Covariates:** Trend, weekday, and meteorological variables (temperature, relative humidity, barometric pressure) **Dose-response Investigated?** No **Statistical Package:** SAS v9.1 and S-Plus v6.0	**Pollutant:** Five particle source factors (airborne soil, local traffic-related ultrafine particles, combustion-generated aerosols, diesel traffic-related particles, and secondary aerosols); see below for size fractions (factor scores) **Averaging Time:** Used daily factor scores in analyses **Mean (SD):** Factor 1: particles from airborne soil (1.0-2.8 µm): 2390 (1696) Factor 2: ultrafine particles from local traffic (0.01-0.1 µm): 9931 (5858) Factor 3: secondary aerosols from local fuel combustion (0.1-0.5 µm): 3770 (6129) Factor 4: particles from traffic (0.01-0.5 µm): 6865 (5689) Factor 5: secondary aerosols from multiple sources (0.2-1.0 µm): 4732 (3890) **Median:** Factor 1: 2053 Factor 2: 8531 Factor 3: 1348 Factor 4: 5045 Factor 5: 3752 **IQR (5-day avg):** Factor 1: 1110 Factor 2: 5749 Factor 3: 4124 Factor 4: 5000 Factor 5: 3393 **Range (Min, Max):** Factor 1: 284, 12960 Factor 2: 866, 26632 Factor 3: 139, 39097 Factor 4: 283, 27605 Factor 5: 67, 20129 **Monitoring Stations:** 1 monitor	**PM Increment:** IQR **Effect Estimate [Lower CI, Upper CI]: QT interval, % change (95%CI)** **Factor 1:** 0-5 h: -0.1 (-0.6, 0.6) 6-11 h: -0.5 (-1.1, 0.2) 12-17 h: 0.1 (-0.4, 0.4) 18-23 h: -0.2 (-0.7, 0.2) 0-23 h: -0.2 (-0.9, 0.4) 1 day: -0.1 (-0.7, 0.6) 2 day: -0.3 (-0.9, 0.4) 3 day: -0.7 (-1.4, 0.1) 4 day: -0.2 (-0.9, 0.5) 0-4 day avg: -0.7 (-1.8, 0.3) **Factor 2:** 0-5 h: 0.2 (-0.4, 0.8) 6-11h: 0.8 (-0.0, 1.7) 12-17 h: 0.6 (-0.2, 1.4) 18-23 h: 0.5 (-0.4, 1.4) 0-23 h: 0.9 (-0.1, 2.0) 1 day: 1.5 (0.3, 2.7) 2 day: -0.4 (-1.7, 1.0) 3 day: 0.5 (-0.9, 1.9) 4 day: 0.1 (-1.2, 1.4) 0-4 day avg: 1.6 (-0.1, 3.3) **Factor 3:** 0-5 h: 0.1 (-0.3, 0.5) 6-11 h: 0.2 (-0.3, 0.6) 12-17 h: 0.2 (-0.3, 0.6) 18-23 h: 0.1 (-0.3, 0.4) 0-23 h: 0.1 (-0.3, 0.6) 1 day: 0.1 (-0.3, 0.4) 2 day: -0.1 (-0.4, 0.3) 3 day: -0.2 (-0.5, 0.2) 4 day: -0.1 (-0.5, 0.2) 0-4 day avg: -0.1 (-0.7, 0.6) **Factor 4:** 0-5 h: 0.2 (-0.4, 0.8) 6-11 h: 0.8 (0.0, 1.6) 12-17 h: 0.5 (-0.2, 1.3) 18-23 h: 0.5 (-0.2, 1.2) 0-23 h: 0.6 (-0.3, 1.4) 1 day: -0.4 (-1.5, 0.7) 2 day: -0.9 (-2.0, 0.1) 3 day: -0.5 (-1.4, 0.5)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
		Copollutant: NA	4 day: -0.5 (-1.3, 0.2) 0-4 day avg: -0.3 (-1.7, 1.1) **Factor 5**: n0-5 h: 1.0 (-0.1, 2.1) 6-11 h: 0.9 (-0.2, 2.0) 12-17 h: 0.3 (-0.7, 1.4) 18-23 h: -0.1 (-1.2, 1.0) 0-23h: 0.7 (-0.6, 1.9) 1 day: 0.1 (-1.1, 1.3) 2 day: -0.2 (-1.5, 1.1) 3 day: -0.6 (-1.9, 0.8) 4 day: -0.9 (-2.0, 0.2) 0-4 day avg: -0.4 (-1.9, 1.2) **T wave amplitude, % change (95%CI)** **Factor 1**: 0-5 h: -0.3 (-1.5, 0.9) 6-11 h: -0.6 (-1.9, 0.7) 12-17 h: 0.1 (-0.8, 0.9) 18-23 h: -0.6 (-1.5, 0.4) 0-23 h: -0.5 (-1.8, 0.9) 1 day: 0.4 (-0.9, 1.7) 2 day: 1.2 (-0.3, 2.7) 3 day: 0.2 (-1.2, 1.7) 4 day: -0.2 (-1.3, 1.0) 0-4 day avg: 0.8 (-1.1, 2.6) **Factor 2**: 0-5 h: -1.7 (-3.0 to -0.4) 6-11 h: -2.6 (-4.5 to -0.6) 12-17 h: -1.0 (-2.6, 0.7) 18-23 h: -1.1 (-2.8, 0.7) 0-23 h: -3.1 (-5.3 to -0.9) 1 day: -0.3 (-2.9, 2.2) 2 day: -1.2 (-4.1, 1.7) 3 day: -0.5 (-3.2, 2.1) 4 day: -3.4 (-9.9, 3.1) 0-4 day avg: -1.5 (-4.4, 1.5) **Factor 3**: 0-5 h: -0.3 (-1.1, 0.6) 6-11 h: -0.1 (-0.9, 0.9) 12-17 h: 0.1 (-0.9, 1.0) 18-23 h: -0.4 (-1.2, 0.4) 0-23 h: -0.2 (-1.2, 0.7) 1 day: 0.1 (-0.7, 0.8) 2 day: -0.1 (-0.7, 0.7) 3 day: 0.4 (-0.3, 1.1) 4 day: 0.1 (-0.7, 0.7) 0-4 day avg: 0.3 (-0.9, 1.5) **Factor 4**: 0-5 h: -1.5 (-2.8 to -0.2) 6-11 h: -1.3 (-3.0, 0.3) 12-17 h: -1.1 (-2.7, 0.4) 18-23 h: -0.9 (-2.4, 0.6) 0-23 h: -1.6 (-3.3, 0.1) 1 day: -1.2 (-3.3, 0.9) 2 day: -1.0 (-3.2, 1.2) 3 day: 0.2 (-1.5, 1.9) 4 day: 0.5 (-1.0, 2.0) 0-4 day avg: -1.7 (-4.1, 0.7) **Factor 5**: 0-5 h: -1.6 (-3.6, 0.4) 6-11 h: -0.1 (-2.1, 2.0) 12-17 h: -0.2 (-2.2, 1.8) 18-23 h: -1.8 (-3.8, 0.2) 0-23 h: -1.2 (-3.4, 1.0) 1 day: -1.8 (-4.2, 0.6) 2 day: -0.7 (-3.5, 2.1) 3 day: 0.8 (-1.5, 3.2) 4 day: 0.5 (-1.5, 2.5) 0-4 day avg: -1.4 (-4.0, 1.2) **vWF, % change (95%CI)Factor 1:** 0-5 h: 1.1 (-1.5, 3.6) 6-11 h: 1.6 (-1.2, 4.5) 12-17 h: 0.4 (-1.4, 2.1) 18-23 h: 1.4 (-0.6, 3.5) 0-23 h: 1.6 (-1.3, 4.4) 1 day: -1.0 (-3.9, 1.9) 2 day: -1.8 (-4.8, 1.2)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			3 day: -2.5 (-5.8, 0.9) 4 day: 0.5 (-2.9, 3.9) 0-4 day avg: -2.5 (-7.1, 2.2) **Factor 2**: 0-5 h: 0.4 (-2.4, 3.2) 6-11 h: -0.4 (-4.3, 3.4) 12-17 h: 2.1 (-1.4, 5.7) 18-23 h: 2.3 (-1.4, 5.9) 0-23 h: 1.9 (-2.8, 6.6) 1 day: 2.8 (-2.8, 8.3) 2 day: 5.1 (-0.8, 11.1) 3 day: 11.4 (5.3, 17.6) 4 day: 6.6 (0.0, 13.1) 0-4 day avg: 11.4 (3.7, 19.1) **Factor 3**: 0-5 h: 1.8 (0.1, 3.6) 6-11 h: 1.7 (-0.3, 3.7) 12-17 h: 2.2 (0.3, 4.2) 18-23 h: 2.8 (1.1, 4.5) 0-23 h: 2.8 (0.8, 4.8) 1 day: 2.7 (1.0, 4.4) 2 day: 3.4 (1.8, 5.0) 3 day: 2.3 (0.8, 3.8) 4 day: 1.4 (-0.2, 2.9) 0-4 day avg: 4.8 (2.0, 7.6) **Factor 4**: 0-5h: 1.5 (-1.4, 4.3) 6-11h: 2.0 (-1.7, 5.6) 12-17h: 2.6 (-0.8, 5.9) 18-23h: 3.5 (0.4, 6.6) 0-23h: 3.2 (-0.5, 7.0) 1 day: 5.4 (0.6, 10.2) 2 day: 4.5 (-0.6, 9.5) 3 day: 3.8 (-0.6, 8.1) 4 day: 3.0 (-0.6, 6.6) 0-4d avg: 11.3 (5.0, 17.6) **Factor 5**: 0-5 h: 1.9 (-2.8, 6.6) 6-11 h: 3.2 (-1.6, 8.0) 12-17 h: 2.4 (-2.3, 7.1) 18-23 h: 1.6 (-3.1, 6.2) 0-23 h: 2.9 (-2.5, 8.2) 1 day: -2.2 (-7.6, 3.2) 2 day: -1.3 (-7.4, 4.9) 3 day: 1.1 (-4.8, 7.1) 4 day: 1.3 (-4.2, 6.7) 0-4 day avg: 3.3 (-4.1, 10.6) **CRP, Odds Ratio (95%CI)** **Factor 1** 0-5 h: 0.9 (0.7, 1.1) 6-11 h: 1.4 (1.1, 1.8) 12-17 h: 1.2 (1.0, 1.4) 18-23 h: 1.0 (0.8, 1.3) 0-23 h: 1.1 (0.9, 1.5) 1 day: 1.4 (1.1, 1.8) 2 day: 1.3 (1.0, 1.7) 3 day: 1.0 (0.7, 1.4) 4 day: 1.1 (0.9, 1.5) 0-4 day avg: 1.6 (1.1, 2.2) **Factor 2** 0-5h: 0.8 (0.6, 1.0) 6-11h: 1.0 (0.7, 1.4) 12-17h: 1.1 (0.8, 1.5) 18-23h: 1.0 (0.8, 1.4) 0-23h: 0.9 (0.6, 1.4) 1 day: 0.9 (0.6, 1.5) 2 day: 2.1 (1.3, 3.3) 3 day: 1.9 (1.0, 3.6) 4 day: 1.4 (0.8, 2.3) 0-4d avg: 1.4 (0.8, 2.6) **Factor 3** 0-5 h: 1.0 (0.8, 1.1) 6-11 h: 0.9 (0.8, 1.1) 12-17 h: 1.0 (0.9, 1.2) 18-23 h: 1.0 (0.8, 1.2) 0-23 h: 1.0 (0.8, 1.2) 1 day: 1.1 (1.0, 1.3)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			2 day: 1.0 (0.9, 1.2) 3 day: 1.2 (1.1, 1.4) 4 day: 1.1 (1.0, 1.3) 0-4 dY avg: 1.2 (1.0, 1.5) **Factor 4** 0-5 h: 0.8 (0.6, 1.1) 6-11 h: 0.8 (0.6, 1.1) 12-17 h: 1.3 (1.0, 1.8) 18-23 h: 1.1 (0.8, 1.5) 0-23 h: 1.0 (0.7, 1.4) 1 day: 1.5 (1.0, 2.3) 2 day: 2.0 (1.3, 3.2) 3 day: 1.5 (0.9, 2.3) 4 day: 1.3 (0.9, 1.8) 0-4 day avg: 1.7 (1.0, 2.9) **Factor 5** 0-5 h: 0.7 (0.5, 1.1) 6-11 h: 1.4 (0.9, 2.1) 12-17 h: 1.9 (1.3, 2.8) 18-23 h: 1.4 (1.0, 2.0) 0-23 h: 1.4 (0.9, 2.2) 1 day: 1.6 (1.0, 2.6) 2 day: 1.6 (0.9, 2.6) 3 day: 2.3 (1.3, 4.1) 4 day: 1.6 (0.9, 2.8) 0-4 day avg: 2.1 (1.2, 3.8)
Reference: Zanobetti et al. (2004, 087489) **Period of Study:** 1999-2001 **Location:** Boston, Massachusetts, USA	**Outcome:** Blood pressure (systolic blood pressure, diastolic blood pressure, mean arterial blood pressure) **Age Groups:** Elderly **Study Design:** Panel study **N:** 62 elderly subjects with n = 631 repeated visits for cardiac rehabilitation **Statistical Analysis:** Linear mixed effects models	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Median (10th-90th percentile)** Median: 8.8 µg/m^3 10th-90th: 13.4 **Monitoring Stations:** 1 **Copollutant:** SO_2, O_3, CO, NO_2, BC 120-h avg Median: 0.651 10th-90th: 0.376	**PM Increment:** .10.4 µg/m^3 for 5-day mean, 13.9 µg/m^3 for 2-day mean **Effect Estimate:** Each 10.4 µg/m^3 increase in 5-day mean $PM_{2.5}$ concentration was associated with: Systolic BP: 2.8mmHg (95% CI: 0.1, 5.5) Diastolic BP: 2.7mmHg (95% CI: 1.2, 4.3) Mean arterial BP: 2.7mmHg (95% CI: 1.0, 4.5) Each 13.9 µg/m^3 increase in 2-day mean $PM_{2.5}$, during exercise in person with H.70bpm Diastolic: 7.0mmHg (95% CI: 2.3, 12.1) Mean arterial BP: 4.7mmHg (95% CI: 0.5, 9.1)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Zeka et al. (2006, 157177) **Period of Study:** Nov 2000-Dec 2004 **Location:** Greater Boston area (Massachusetts)	**Outcome:** White blood cells (WBC), C-reactive protein (CRP), sediment rate, fibrinogen **Age Groups:** Mean age (SD) = 73.0 (6.7) **Study Design:** Cross-sectional **N:** 710 subjects **Statistical Analyses:** Linear regression **Covariates:** Age, BMI, season (also assessed potential for confounding by temperature, RH, barometric pressure, hypertensive or cardiac medications, hypertension, smoking, alcohol, and fasting glucose levels) **Dose-response Investigated?** No	**Pollutant:** BC **Averaging Time:** Hourly (PN, BC, $PM_{2.5}$) and 24-h (SO_4^{2-}) measurements used to create 48-h, 1-wk, and 4-wk ma **Mean (SD):** 0.77 (0.63) **Percentiles:** 50th: 0.61 75th: 1.00 90th: 1.51 **Monitoring Stations:** 2 sites **Units:** ng/m^3 **Copollutant (correlation):** $PM_{2.5}$ (r = 0.52) BC PN (r = 0.30) SO_4^{2-} (r = 0.30)	**PM Increment:** 1 SD increase **Effect Estimate [Lower CI, Upper CI]:** % increase (95%CI) in biomarker per 1 SD increase in pollutant. **Fibrinogen** 48 h: 0.84 (-0.63, 2.31) 1 wk: 0.60 (-0.95, 2.15) 4 wk: 1.78 (0.19, 3.36) **CRP** 48 h: 4.51 (-2.03, 11.06) 1 wk: 1.07 (-5.55, 7.68) 4 wk: 5.41 (-1.00, 11.81) **Sediment rate** 48 h: -4.56 (-25.55, 16.43) 1 wk: 1.98 (-18.15, 22.11) 4 wk: 21.65 (1.48, 41.82) **WBC count** 48 h: -0.63 (-2.45, 1.19) 1 wk: -0.13 (-1.87, 1.60) 4 wk: -0.55 (-2.36, 1.26) **Note:** No statistically significant difference was reported for any category of effect modifiers (age, obesity, medications, homozygous for the deletion of GSTM1-null, hypertension) However, results suggested almost all the effect of BC on sediment rate was among the younger group (<78 yr) There was a 4-fold difference for the association between BC and CRP in the presence of obesity Also evidence for effect modification by obesity of the association between BC and sediment rate There was a suggestive greater effect of BC on CRP among GSTM1-null subjects (9.73% [1.48, 17.98]) vs.. GSTM1-present subjects (-2.97% [-14.05, 8.10] for concentrations 4-wk prior) A stronger effect of BC on sediment rate was seen among non-users of statins (36.01% [13.88, 58.13]) vs.. users (-12.29% [39.13, 14.55])
Reference: Zeka et al. (2006, 157177) **Period of Study:** Nov 2000-Dec 2004 **Location:** Greater Boston area (Massachusetts)	**Outcome:** White blood cells (WBC), C-reactive protein (CRP), sediment rate, fibrinogen **Age Groups:** Mean age (SD) = 73.0 (6.7) **Study Design:** Cross-sectional **N:** 710 subjects **Statistical Analyses:** Linear regression **Covariates:** Age, BMI, season (also assessed potential for confounding by temperature, RH, barometric pressure, hypertensive or cardiac medications, hypertension, smoking, alcohol, and fasting glucose levels) **Dose-response Investigated?** No	**Pollutant:** SO_4^{2-} **Averaging Time:** Hourly (PN, BC, $PM_{2.5}$) and 24-h (SO_4^{2-}) measurements used to create 48-h, 1-wk, and 4-wk ma **Mean (SD):** 2.29 (1.62) **Percentiles:** 50th: 1.84 75th: 2.81 90th: 4.10 **Monitoring Stations:** 2 sites **Copollutant (correlation):** $PM_{2.5}$ (r = 0.50) BC (r = 0.30) PN (r = -0.15) SO_4^{2-}	**PM Increment:** 1 SD increase **Effect Estimate [Lower CI, Upper CI]:** % increase (95%CI) in biomarker per 1 SD increase in pollutant. **Fibrinogen:** 48 h: 0.60 (-1.23, 2.42) 1 wk: 0.03 (-1.93, 1.99) 4 wk: 1.12 (-0.52, 2.77) **CRP:** 48 h: 1.57 (-7.13, 10.27) 1 wk: 0.21 (-8.27, 8.69) 4 wk: 5.29 (-1.91, 12.49) **Sediment rate:** 48 h: 4.05 (-23.26, 31.36) 1 wk: -5.87 (-32.39, 20.64) 4 wk: -1.60 (-25.24, 22.04) **WBC count:** 48 h: -0.12 (-2.35, 2.11) 1 wk: -0.48 (-2.87, 1.90) 4 wk: 0.75 (-1.30, 2.80) **Note:** No statistically significant difference was reported for any category of effect modifiers (age, obesity, medications, homozygous for the deletion of GSTM1-null, hypertension)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Zeka et al. (2006, 157177) **Period of Study:** Nov 2000-Dec 2004 **Location:** Greater Boston area (Massachusetts)	**Outcome (ICD9 and ICD10):** White blood cells (WBC), C-reactive protein (CRP), sediment rate, fibrinogen **Age Groups:** Mean age (SD) = 73.0 (6.7) **Study Design:** Cross-sectional **N:** 710 subjects **Statistical Analyses:** Linear regression **Covariates:** Age, BMI, season (also assessed potential for confounding by temperature, RH, barometric pressure, hypertensive or cardiac medications, hypertension, smoking, alcohol, and fasting glucose levels) **Dose-response Investigated?** No **Statistical Package:** NR	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Hourly (PN, BC, $PM_{2.5}$) and 24-h (SO_4^{2-}) measurements used to create 48-h, 1-wk, and 4-wk ma **Mean (SD):** 11.16 (7.95) **Percentiles:** 50th: 9.39 75th: 14.57 90th: 21.48 **Monitoring Stations:** 2 sites **Copollutant (correlation):** $PM_{2.5}$ BC (r = 0.52) PN (r = -0.02) SO_4^{2-} (r = 0.50)	**PM Increment:** 1 SD increase **Effect Estimate [Lower CI, Upper CI]:** % increase (95%CI) in biomarker per 1 SD increase in pollutant. **Fibrinogen:** 48 h: -0.18 (-1.93, 1.57) 1 wk: -1.39 (-3.46, 0.67) 4 wk: 1.14 (-0.60, 2.88) **CRP:** 48 h: -4.88 (-13.29, 3.53) 1 wk: -1.37 (-10.44, 7.71) 4 wk: 4.36 (-3.25, 11.96) **Sediment rate:** 48 h: -16.91 (-43.66, 9.84) 1 wk: -18.89 (-47.48, 9.70) 4 wk: 24.93 (0.68, 49.18) **WBC count:** 48 h: -3.18 (-5.39 to -0.97) 1 wk: -0.51 (-3.02, 2.00) 4 wk: -0.03 (-2.17, 2.10) **Note:** No statistically significant difference was reported for any category of effect modifiers (age, obesity, medications, homozygous for the deletion of GSTM1-null, hypertension)
Reference: Zhang et al. (2009, 191970) **Period of Study:** 1999-2003 **Location:** U.S.	**Outcome:** Myocardial Ischemia **Age Groups:** 52-90 **Study Design:** Panel **N:** 55,529 **Statistical Analyses:** Logistic & Linear Regression **Covariates: A**ge, race/ethnicity, education, exam site, BMI, current smoking status, history of CHD, diabetes, hypertension, SBP, chronic lung disease, or hypercholesterolemia, day of week, time of day, temperature, dew point, pressure, season **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 0-5-day	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **Mean (SD):** Lag 0: 14.1 (8) Lag 1: 13.8 (8) Lag 2: 13.8 (8) Lag 3: 13.8 (8) Lag 4: 13.9 (8) Lag 5: 14.1 (8) Lag 0-2: 13.9 (7) **Monitoring Stations:** NR‡ **Co-pollutant:** NR ‡ Monitors used in model for spatial interpolation of daily PM values.	**PM Increment:** 10 µg/m^3 **Odds Ratio (Lower CI, Upper CI), lag:** Minnesota Codes* MC4: 1.04 (0.97, 1.10), lag 0-2 MC4: 1.04 (0.98, 1.11), lag 3-5 MC5: 1.05 (1.00, 1.09), lag 0-2 MC5: 1.04 (1.00, 1.08), lag 3-5 MC 4 or 5: 1.04 (1.00, 1.09), lag 0-2 MC 4 or 5: 1.03 (0.99, 1.07), lag 3-5 **Change (Lower CI, Upper CI), lag:** ST-segment amplitude Lead I: -0.07 (-0.36, 0.21), lag 0-2 Lead I: 0.18 (-0.10, 0.46), lag 3-5 Lead II: -0.12 (-0.47, 0.23), lag 0-2 Lead II: 0.16 (-0.18, 0.50), lag 3-5 Lead aVL: -0.01 (-0.25, 0.23), lag 0-2 Lead aVL: 0.11 (-0.12, 0.34), lag 3-5 Lead V1: -0.02 (-0.39, 0.35), lag 0-2 Lead V1: -0.22 (-0.58, 0.14), lag 3-5 Lead V2: 0.07 (-0.57, 0.70), lag 0-2 Lead V2: -0.01 (-0.61, 0.62), lag 3-5 Lead V3: -0.11 (-0.68, 0.47), lag 0-2 Lead V3: -0.02 (-0.58, 0.54), lag 3-5 Lead V4: -0.0.3 (-0.51, 0.45), lag 0-2 Lead V4: 0.24 (-0.23, 0.71), lag 3-5 Lead V5: -0.01 (-0.41, 0.39), lag 0-2 Lead V5: 0.35 (-0.04, 0.74), lag 3-5 Lead V6: 0.02 (-0.30, 0.33), lag 0-2 Lead V6: 0.35 (0.04, 0.65), lag 3-5 T-wave amplitude Lead I: -1.60 (-3.07, -0.13), lag 0-2 Lead I: -0.31 (-1.73, 1.11), lag 3-5 Lead II: -0.54 (-1.99, 0.92), lag 0-2 Lead II: 0.71 (-0.70, 2.13), lag 3-5 Lead aVL: -1.21 (-2.50, 0.10), lag 0-2 Lead aVL: -0.55 (-1.18, 0.71), lag 3-5 Lead V1: 1.45 (-0.16, 3.06), lag 0-2 Lead V1: 0.03 (-1.53, 1.59), lag 3-5 Lead V2: -0.18 (-2.96, 2.60), lag 0-2 Lead V2: 0.57 (-2.12, 3.27), lag 3-5 Lead V3: -2.33 (-5.15, 0.49), lag 0-2 Lead V3: -0.13 (-2.87, 2.60), lag 3-5 Lead V4: -2.03 (-4.69, 0.63), lag 0-2 Lead V4: 0.64 (-1.94, 3.22), lag 3-5 Lead V5: -1.92 (-4.22, 0.38), lag 0-2 Lead V5: 0.55 (-1.69, 2.78), lag 3-5 Lead V6: -0.63 (-2.36, 1.10), lag 0-2 Lead V6: 0.82 (-0.86, 2.49), lag 3-5 QRS/T angles and heart rate (change)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			QRS/T angle-spatial (°): 0.19 (-0.21, 0.59), lag 0-2 QRS/T angle-spatial (°): -0.20 (-0.59, 0.19), lag 3-5 QRS/T angle-frontal (°): 0.13 (-0.24, 0.50), lag 0-2 QRS/T angle-frontal (°): 0.35 (-0.01, 0.71), lag 3-5 Heart Rate (beats/min): 0.16 (0.02, 0.30), lag 0-2 Heart Rate (beats/min): 0.04 (-0.10, 0.18), lag 3-5 *Any ST abnormality (MC 4.1-4.4) Any T abnormality (MC 5.1-5.4)

[1]All units expressed in μg/m^3 unless otherwise specified.

Table E-4. Short-term exposure-cardiovascular morbidity studies: Other size fractions.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Adar et al. (2007, 001458) **Period of Study:** Mar-Jun 2002 **Location:** St. Louis, Missouri	**Outcome:** Heart rate variability: heart rate, standard deviation of all normal-to-normal intervals (SDNN), square root of the mean squared difference between adjacent normal-to-normal intervals (rMSSD), percentage of adjacent normal-to-normal intervals that differed by more than 50 ms (pNN50), high frequency power (HF in the range of 0.15-0.4Hz), low frequency power (LF, in the range of 0.04-0.15Hz), and the ratio of LF/HF **Age Groups:** ≥ 60 yr **Study Design:** Panel (4 planned repeated measures with a total of 158 person-trips 35 participating in all 4 trips) **N:** 44 participants **Statistical Analyses:** Generalized additive models **Covariates:** Subject, weekday, time, apparent temperature, trip type, activity, medications, and autoregressive terms **Season:** Limited data collection period **Dose-response Investigated?** No **Statistical Package:** SAS v8.02, R v2.0.1	**Pollutant:** Particle count fine (PC fine) (particles/cm^3) **Averaging Time:** Measurements collected over 48-h period surrounding the bus trip (during which health endpoints were measured) used to calculate 5-, 30-, 60-min, 4-h, 24-h ma **Median (IQR):** All: 42 (57) Facility: 36 (45) Bus: 105 (96) Activity: 50 (133) Lunch: 69 (48) **Monitoring Stations:** 2 portable carts **Copollutant:** $PM_{2.5}$ BC Fine particle counts Coarse particle counts **Correlation notes:** 24-h mean $PM_{2.5}$, BC, and fine particle count concentrations ranged from 0.80 to 0.98 r = 0.76 to 0.97 when limited to time spent on the bus r = 0.55 to 0.86 when comparing bus concentrations to 24-h ma r = -0.003 to 0.51 when comparing 5-min avg and 24-h ma. Poor correlations found between coarse particle count concentrations and all fine particulate measures during all times periods	**PM Increment:** IQR **Effect Estimate [Lower CI, Upper CI]:** % change (95%CI) in HRV per IQR in the 24-h ma of the microenvironmental pollutant (IQr = 39 pt/cm^3) **Single-pollutant models** SDNN: -5.1 (-5.8 to -4.4) rMSSD: -8.0 (-8.7 to -7.2) pNN50 + 1: -10.2 (-11.3 to -9.0) LF: -9.9 (-11.4 to -8.4) HF: -13.7 (-15.1 to -12.2) LF/HF: 4.3 (3.1, 5.5) H: 0.9 (0.8, 1.1) **Note:** Exposure to health associations by all lag periods presented in Fig 2 (magnitude of associations increased with averaging period, with the largest associations consistently found for 24-h ma)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Adar et al. (Adar et al., 2007, 001458) **Period of Study:** Mar-Jun 2002 **Location:** St. Louis, Missouri	**Outcome:** Heart rate variability: heart rate, standard deviation of all normal-to-normal intervals (SDNN), square root of the mean squared difference between adjacent normal-to-normal intervals (rMSSD), percentage of adjacent normal-to-normal intervals that differed by more than 50 ms (pNN50), high frequency power (HF in the range of 0.15-0.4Hz), low frequency power (LF, in the range of 0.04-0.15Hz), and the ratio of LF/HF **Age Groups:** ≥ 60 yr **Study Design:** Panel (4 planned repeated measures with a total of 158 person-trips 35 participating in all 4 trips) **N:** 44 participants **Statistical Analyses:** Generalized additive models **Covariates:** Subject, weekday, time, apparent temperature, trip type, activity, medications, and autoregressive terms **Season:** Limited data collection period **Dose-response Investigated?** No **Statistical Package:** SAS v8.02, R v2.0.1	**Pollutant:** Particle count coarse (PT coarse) (pt/cm^3) **Averaging Time:** Measurements collected over 48-h period surrounding the bus trip (during which health endpoints were measured) used to calculate 5-, 30-, 60-min, 4-h, and 24-h ma **Median (IQR):** All: 0.02 (0.11) Facility: 0.01 (0.04) Bus: 0.16 (0.13) Activity: 0.29 (0.26) Lunch: 0.16 (0.36) **Monitoring Stations:** 2 portable carts **Copollutant:** $PM_{2.5}$ BC Fine particle counts Coarse particle counts **Correlation notes:** 24-h mean $PM_{2.5}$, BC, and fine particle count concentrations ranged from 0.80 to 0.98 r = 0.76 to 0.97 when limited to time spent on the bus r = 0.55 to 0.86 when comparing bus concentrations to 24-h ma r = -0.003 to 0.51 when comparing 5-min avg and 24-h ma. Poor correlations found between coarse particle count concentrations and all fine particulate measures during all times periods	**PM Increment:** IQR **Effect Estimate [Lower CI, Upper CI]:** % change (95%CI) in HRV per IQR in the 24-h ma of the microenvironmental pollutant (IQr = 0.066 pt/cm^3) **Single-pollutant models** SDNN: 2.4 (1.3, 3.6) rMSSD: 3.9 (2.6, 5.1) pNN50 + 1: 2.9 (1.0, 4.9) LF: 6.4 (3.7, 9.1) HF: 10.2 (7.4, 13.1) LF/HF: -3.3 (-5.0 to -1.6) H: -1.1 (-1.3 to -0.8) **Two-pollutant models (with $PM_{2.5}$):** SDNN: -0.7 (-1.9, 0.6) rMSSD: -1.3 (-2.6 to -0.05) pNN50 + 1: -4.3 (-6.3 to -2.4) LF: 0.2 (-2.5, 3.0) HF: 1.3 (-1.5, 4.1) LF/HF: -0.9 (-2.7, 1.0) H: -0.6 (-0.9 to -0.4) **Note:** Exposure to health associations by all lag periods presented in Fig 2 (magnitude of associations increased with averaging period, with the largest associations consistently found for 24-h ma)
Reference: Delfino et al. (2008, 156390) **Period of Study:** 2005-2006 **Location:** Los Angeles, California, air basin	**Outcome:** C-reactive protein (CRP) Fibrinogen, tumor necrosis factor-α (TNF-α) and its soluble receptor-II (TNF-RII) Interleukin-6 (IL-6) and its soluble receptor (IL-6sR) Fibrin D-dimer Soluble platelet selectin (sP-selectin) Soluble vascular cell adhesion molecule-1 (sVCAM-1) Intracellular adhesion molecule-1 (sICAM-1) and myeloperoxidase (MPO) Erythrocyte lysates for glutathione peroxidase-1 (GPx-1) Copper-zinc superoxide dismutase (cu, Zn-SOD) **Age Groups:** ≥ 65 yr **Study Design:** Panel (biomarkers measured weekly 12 times) **N:** 29 participants (nonsmoking with history of coronary artery disease) **Statistical Analyses:** Mixed models **Covariates:** temperature (infectious illnesses were excluded by excluding weeks with such observations) **Season:** Collected 6 wk of data during warm period and 6 wk of data during	**Pollutant:** PM (multiple size fractions and components) **Averaging Time:** 24-h avg preceding the blood draw (lag 0) and cumulative avg up to 5 days preceding the draw **Outdoor hourly PM:** EC: Mean (SD): 1.61 (0.62) Median: 1.56 IQR: 0.92 Min, Max: 0.24, 3.94 OC: Mean (SD): 5.94 (2.11) Median: 5.58 IQR: 2.79 Min-Max: 2.51, 13.60 BC: Mean (SD): 2.00 (0.77) Median: 1.89 IQR: 0.96 Min-Max: 0.58, 5.11 OCpri: Mean (SD): 3.37 (1.21) Median: 3.21 IQR: 1.63 Min-Max: 0.99, 7.11 Secondary OC: Mean (SD): 2.49 (1.50) Median: 2.10 IQR: 1.86 Min-Max: 0, 8.10 PN (p/cm^3): Mean (SD): 16,043 (5886) Median: 13,968 IQR: 7,386 Min-Max: 6837, 31263 **Indoor hourly PM** EC: Mean (SD): 1.31 (0.52) Median: 1.30 IQR: 0.70 Min-Max: 0.19, 2.89	**PM Increment:** IQR **Effect Estimate [Lower CI, Upper CI]:** **Note:** Nearly all results presented in figures **Results:** The authors found significant positive associations for CRP, IL-6, sTNF-RII, and sP-selectin with outdoor and/or indoor concentrations of quasi-ultrafine PM ≤ 0.25 µm in diameter, EC, OCpri, BC, PN, CO, and nitrogen dioxide from the current-day and multiday avg. There were consistent positive but largely nonsignificant coefficients for TNF-α, sVCAM-1, and sICAM-1, but not fibrinogen, IL-6sR, or D-dimer. The authors found inverse associations for erythrocyte Cu, Zn-SOD with these pollutants and other PM size fractions (0.25-2.5 and 2.5-10 µm). Inverse associations of GPx-1 and MPO with pollutants were largely nonsignificant. Indoor associations were often stronger for estimated indoor EC, OCpri, and PN of outdoor origin than for uncharacterized indoor measurements. There was no evidence for positive associations with SOA.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
	cool period **Dose-response Investigated?** No **Statistical Package:** NR	EC of outdoor origin: Mean (SD): 1.11 (0.39) Median: 1.06 IQR: 0.51 Min-Max: 0.41, 2.97 OC: Mean (SD): 5.69 (1.51) Median: 5.60 IQR: 1.96 Min-Max: 2.34, 10.79 OCpri of outdoor origin: Mean (SD): 2.18 (0.82) Median: 2.15 IQR: 1.07 Min-Max: 0.32, 5.21 Secondary OC of outdoor origin: Mean (SD): 2.08 (1.26) Median: 1.75 IQR: 1.45 Min-Max: 0, 6.87 PN (particles/cm^3): Mean (SD): 14,494 (6770) Median: 12,341 IQR: 7,337 Min-Max: 1016, 43027 PN of outdoor origin (p/cm^3): Mean (SD): 10,108 (3108) Median: 9,580 IQR: 3,684 Min-Max: 1016, 17700 **Outdoor PM mass** PM0.25: Mean (SD): 9.47 (2.97) Median: 9.4 IQR: 4.2 Min-Max: 3.31, 18.75 PM0.25-2.5: Mean (SD): 13.53 (10.67) Median: 11.7 IQR: 11.5 Min-Max: 1.29, 66.77 $PM_{10-2.5}$: Mean (SD): 10.04 (4.07) Median: 9.9 IQR: 5.9 Min-Max: 1.76, 22.38 **Indoor PM mass** PM0.25: Mean (SD): 10.45 (6.77) Median: 9.5 IQR: 4.5 Min-Max: 1.42, 69.86 PM0.25-2.5 (µg/m^3): Mean (SD): 7.36 (4.57) Median: 6.5 IQR: 5.7 Min-Max: 0.77, 30.86 $PM_{10-2.5}$: Mean (SD): 4.12 (4.76) Median: 2.8 IQR: 3.5 Min-Max: 0.12, 37.63 **Copollutant:** Outdoor hourly gases (NO_2, CO, O_3) and indoor hourly gases (NO_2, CO)	
Reference: Pekkanen et al. (2002, 035050) **Period of Study:** Winter 1998-1999 **Location:** Helsinki, Finland	**Outcome**: ST Segment Depression (>0.1mV) **Study Design**: Panel of ULTRA Study participants **N**: 45 Subjects, n = 342 biweekly submaximal exercise tests, 72 exercise induced ST Segment Depressions **Statistical Analysis:** Logistic regression / GAM	**Pollutant:** Ultrafine NC0.01-0.1 µm (n/cm^3) **Averaging Time:** 24 h **Median**: 14,890 **IQR**: 9830 **Monitoring Stations**: 1 **Copollutant:** NO_2, CO, $PM_{2.5}$, $PM_{10-2.5}$, PM_1, ACP	**PM Increment:** IQR **Effect Estimate(s):** NC0.01-0.1: OR = 3.14 (1.56, 6.32), lag 2 **Notes**: The effect was strongest for ACP and $PM_{2.5}$, which in 2 pollutant models appeared independent. Increases in NO_2 and CO were also associated with increased risk of ST segment depression, but not with coarse particles.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Peters et al. (2005, 095747) Also Peters et al, 2005 (2005, 156859) **Period of Study:** Feb 1999-Jul 2001 **Location:** Augsburg, Germany	**Outcome:** Myocardial infarction **Study Design:** Case-crossover **N:** 691 myocardial infarction patients **Statistical Analysis:** Conditional logistic regression **Dose-response investigated (yes/no)?** No	**Pollutant:** Ultrafine (TNC) (n/cm^3) **Averaging Time:** 1 h: Median = 10,001 IQR: 7919 24 h: Median = 10,934 IQR: 6276 **Copollutant:** NO_2, SO_2, CO	**PM Increment: Effect Estimate:** 2-h lag: OR = 0.95 95% CI: 0.84, 1.06 24-h mean, 2-day lag: OR = 1.04 95% CI: 0.90, 1.20 **Notes:** Examined triggering for MI at various lags before MI onset (up to 6 h before MI, up to 5 days before MI). No statistically significant increases in lagged ultrafine particle concentration were found.
Reference: Ruckerl et al. (2006, 088754) **Period of Study:** Oct 2000-Apr 2001 **Location:** Erfurt, Germany	**Outcome (ICD9 and ICD10):** C-reactive protein (CRP) Serum amyloid A (SAA) E-selectin von Willebrand Factor (vWF) Intercellular adhesion molecule-1 (ICAM-1) Fibrinogen Factor VII Prothrombin fragment 1+2 D-dimer **Age Groups:** 50+ yr **Study Design:** Panel (12 repeated measures at 2-wk intervals) **N:** 57 male subjects with coronary disease **Statistical Analyses:** Fixed effects linear and logistic regression models **Covariates:** Models adjusted for different factors based on health endpoint CRP: RH, temperature, trend, ID ICAM-1: temperature, trend, ID vWF: air pressure, RH, temperature, trend, ID FVII: air pressure, RH, temperature, trend, ID, weekday **Season:** Time trend as covariate **Dose-response Investigated?** Sensitivity analyses examined nonlinear exposure-response functions **Statistical Package:** SAS v8.2 and S-Plus v6.0	**Pollutant:** AP (n/cm^3) **Averaging Time:** 24 h **Mean (SD):** 1593 (1034) **Percentiles:** 25: 821 50: 1238 75: 2120 **Range (Min, Max):** 328, 4908 **Unit (i.e. µg/m^3):** n/cm^3 **Monitoring Stations:** 1 site **Copollutant:** UFPs AP $PM_{2.5}$ PM_{10} OC EC NO_2 CO	**PM Increment:** IQR (1299 5-day avg: 1127) **Effect Estimate [Lower CI, Upper CI]:** Effects of air pollution on blood markers presented as OR (95%CI) for an increase in the blood marker above the 90th percentile per increase in IQR air pollutant. **CRP** Time before draw: 0 to 23 h: 0.7 (0.5, 1.2) 24 to 47 h: 1.5 (0.9, 2.6) 48 to 71 h: 3.2 (1.7, 6.0) 5-day mean: 1.5 (0.8, 3.0) **ICAM-1** Time before draw: 0 to 23 h: 0.6 (0.4, 0.9) 24 to 47 h: 1.8 (1.2, 2.8) 48 to 71 h: 1.6 (1.0, 2.5) 5-day mean: 0.9 (0.6, 1.5) Effects of air pollution on blood markers presented as % change from the mean/GM in the blood marker per increase in IQR air pollutant. **vWF** Time before draw: 0 to 23 h: 4.8 (0.2, 9.3) 24 to 47 h: 5.9 (0.4, 11.5) 48 to 71 h: 7.0 (0.7, 13.4) 5-day mean: 13.5 (6.3, 20.6) **FVII** Time before draw: 0 to 23 h: 0.0 (-2.9, 3.0) 24 to 47 h: -2.9 (-6.1, 0.4) 48 to 71 h: -3.6 (-6.8 to -0.3) 5-day mean: -4.1 (-7.9 to -0.3) **Note:** Summary of results presented in figures. SAA results indicate increase in association with PM (not as strong and consistent as with CRP) No association observed between E-selectin and PM An increase in prothrombin fragment 1+2 was consistently observed, particularly with lag 4 Fibrinogen results revealed few significant associations, potentially due to chance D-dimer results revealed null associations in linear and logistic analyses

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ruckerl et al. (2006, 088754) **Period of Study:** Oct 2000-Apr 2001 **Location:** Erfurt, Germany	**Outcome:** Soluble CD40 ligand (sCD40L), platelets, leukocytes, erythrocytes, hemoglobin **Age Groups:** 50+ yr **Study Design**: Panel (12 repeated measures at 2-wk intervals) **N:** 57 male subjects with coronary disease **Statistical Analyses:** Fixed effects linear regression models **Covariates:** Long-term time trend, weekday of the visit, temperature, RH, barometric pressure **Season:** Time trend as covariate **Dose-response Investigated?** No **Statistical Package:** SAS v8.2 and S-Plus v6.0	**Pollutant:** AP (n/cm^3) **Averaging Time:** 24 h **Mean (SD):** 1593 (1034) **Percentiles:** 25th: 821 50th: 1238 75th: 2120 **Range (Min, Max):** 328, 4908 **Monitoring Stations:** 1 site **Copollutant:** UFPs AP $PM_{2.5}$ PM_{10} NO	**PM Increment:** IQR (1299 5-day avg: 1127) **Effect Estimate [Lower CI, Upper CI]:** Effects of air pollution on blood markers presented as % change from the mean/GM in the blood marker per increase in IQR air pollutant. **sCD40L, % change GM (pg/mL)** lag0: 6.9 (0.5, 13.8) lag1: -1.1 (-8.0, 6.4) lag2: -4.9 (-11.9, 2.7) lag3: -3.8 (-10.3, 3.2) 5-day mean: -1.3 (-9.9, 8.1) **Platelets, % change mean (103/µl)** lag0: -1.0 (-2.5, 0.5) lag1: -0.4 (-2.1, 1.6) lag2: 0.8 (-1.0, 2.4) lag3: 0.0 (-1.8, 1.7) 5-day mean: -0.9 (-3.0, 1.3) **Leukocytes, % change in mean (103/µl)** lag0: -1.9 (-3.8 to -0.1) lag1: -0.6 (-2.9, 1.6) lag2: -0.6 (-3.2, 2.0) lag3: -2.3 (-4.6, 0.1) 5-day mean: -2.7 (-5.5, 0.1) **Erythrocytes, % change mean (106/µl)** lag0: -0.1 (-0.5, 0.3) lag1: -0.4 (-0.9, 0.2) lag2: -0.4 (-0.9, 0.2) lag3: -0.4 (-0.6, 0.3) 5-day mean: -0.4 (-1.0, 0.2) **Hemoglobin, % change mean (g/dl)** lag0: -0.2 (-0.7, 0.4) lag1: -0.3 (-1.0, 0.4) lag2: -0.1 (-0.9, 0.7) lag3: -0.1 (-0.8, 0.6) 5-day mean: -0.2 (-1.1, 0.6)
Reference: Ruckerl et al. (2007, 156931) **Period of Study:** May 2003-Jul 2004 **Location:** Athens, Augsburg, Barcelona, Helsinki, Rome, and Stockholm	**Outcome:** Interleukin-6 (IL-6), fibrinogen, C-reactive protein (CRP) **Age Groups:** 35-80 yr **Study Design:** Repeated measures / longitudinal **N:** 1003 MI survivors **Statistical Analyses:** Mixed-effect models **Covariates:** City-specific confounders (age, sex, BMI) Long-term time trend and apparent temperature RH, time of day, day of week included if adjustment improved model fit **Season:** Long-term time trend **Dose-response Investigated?** Used p-splines to allow for nonparametric exposure-response functions **Statistical Package:** SAS v9.1	**Pollutant:** UFP (n/cm^3) **Averaging Time:** Hourly and 24 h (lag 0-4, mean of lags 0-4, mean of lags 0-1, mean of lags2-3, means of lags 0-3) **Mean (SD):** Presented by city only **Percentiles:** NR **Range (Min, Max):** NR **Monitoring Stations:** Central monitoring sites in each city **Copollutant:** SO_2 O_3 NO NO_2	**PM Increment:** IQR **Effect Estimate [Lower CI, Upper CI]:** % change in mean blood markers per increase in IQR of air pollutant. IL-6 Lag (IQR): % change in GM (95%CI) Lag 0 (11852): 1.88 (-0.16, 3.97) Lag 1 (11852): -0.67 (-2.56, 1.25) Lag 2 (11852): -2.12 (-4.03 to -0.17) 5-day avg (11003): -0.93 (-3.37, 1.56) Fibrinogen Lag (IQR): % change in AM (95%CI) Lag 0 (11852): 0.40 (-0.40, 1.19) Lag 1 (11852): 0.11 (-0.69, 0.91) Lag 2 (11852): 0.09 (-0.71, 0.90) 5-day avg (11003): 0.50 (-2.20, 3.20) CRP Lag (IQR): % change in GM (95%CI) Lag 0 (11852): 1.33 (-3.05, 5.90) Lag 1 (11852): -1.52 (-4.39, 1.45) Lag 2 (11852): -1.63 (-6.70, 3.71) 5-day avg (11003): -0.08 (-3.78, 3.75)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Pekkanen et al. (2002, 035050) **Period of Study:** Winter 1998-1999 **Location:** Helsinki, Finland	**Outcome**: ST Segment Depression (>0.1mV) **Age Groups: Study Design**: Panel of ULTRA Study participants **N**: 45 Subjects, n = 342 biweekly submaximal exercise tests, 72 exercise induced ST Segment Depressions **Statistical Analysis:** Logistic regression / GAM	**Pollutant:** Ultrafine NC0.01-0.1 µm (n/cm^3) **Averaging Time:** 24 h **Median**: 14,890 **IQR**: 9830 **Monitoring Stations**: 1 **Copollutant:** NO_2, CO, $PM_{2.5}$, $PM_{10-2.5}$, PM_1, ACP	**PM Increment:** IQR **Effect Estimate(s):** NC0.01-0.1: OR = 3.14 (1.56, 6.32), lag 2 **Notes**: The effect was strongest for ACP and $PM_{2.5}$, which in 2 pollutant models appeared independent. Increases in NO_2 and CO were also associated with increased risk of ST segment depression, but not with coarse particles.
Reference: Peters et al. (2005, 095747) Also Peters et al, 2005 (2005, 156859) **Period of Study:** Feb 1999-Jul 2001 **Location:** Augsburg, Germany	**Outcome:** Myocardial infarction **Study Design:** Case-crossover **N:** 691 myocardial infarction patients **Statistical Analysis:** Conditional logistic regression **Dose-response Investigated?** No	**Pollutant:** Ultrafine (TNC) (n/cm^3) **Averaging Time:** 1 h: Median = 10,001 IQR: 7919 24-h: Median = 10,934 IQR: 6276 **Copollutant:** NO_2, SO_2, CO	**PM Increment: Effect Estimate:** 2-h lag: OR = 0.95 95% CI: 0.84, 1.06 24-h mean, 2-day lag: OR = 1.04 95% CI: 0.90, 1.20 **Notes:** Examined triggering for MI at various lags before MI onset (up to 6 h before MI, up to 5 days before MI). No statistically significant increases in lagged ultrafine particle concentration were found.
Reference: Ruckerl et al. (2007, 091379) **Period of Study:** Oct 2000-Apr 2001 **Location:** Erfurt, Germany	**Outcome (ICD9 and ICD10):** Soluble CD40 ligand (sCD40L), platelets, leukocytes, erythrocytes, hemoglobin **Age Groups:** 50+ yr **Study Design**: Panel (12 repeated measures at 2-wk intervals) **N:** 57 male subjects with coronary disease **Statistical Analyses:** Fixed effects linear regression models **Covariates:** Long-term time trend, weekday of the visit, temperature, RH, barometric pressure **Season:** Time trend as covariate **Dose-response Investigated?** No **Statistical Package:** SAS v8.2 and S-Plus v6.0	**Pollutant:** UFP **Averaging Time:** 24 h **Mean (SD):** 12,602 (6455) **Percentiles:** 25th: 7326 50th: 11,444 75th: 17,332 **Range (Min, Max):** 328, 4908 **Monitoring Stations:** 1 site **Copollutant:** AP $PM_{2.5}$ PM_{10} NO	**PM Increment:** IQR (10,005 5-day avg: 6,821) **Effect Estimate [Lower CI, Upper CI]:** **sCD40L, % change GM (pg/mL)** lag 0: 7.1 (0.1, 14.5) lag 1: 0.3 (-6.6, 8.6) lag 2: 0.6 (-5.9, 8.6) lag 3: -8.5 (-15.8, -0.5) 5-day mean: -0.7 (-7.6, 6.8) **Platelets, % change mean (103/µl)** lag 0: -1.8 (-3.4, -0.2) lag 1: -1.1 (-2.9, 0.6) lag 2: 1.0 (-2.9, 0.8) lag 3: -2.4(4.5, -0.3) 5-day mean: -2.2 (-4.0, -0.3) **Leukocytes, [103/µl]** lag 0: -2.4 (-4.5, -0.2) lag 1: -2.1 (-4.4, 0.2) lag 2: -0.2 (-2.4, 2.8) lag 3: -1.5 (-4.4, 1.4) 5-day mean: -1.6 (-4.1, 0.8)

[1]All units expressed in µg/m^3 unless otherwise specified.

E.1.2. Cardiovascular Emergency Department Visits and Hospital Admissions

Table E-5. Short-term exposure-cardiovascular: ED/HA PM_{10}

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Anderson et al. (2003, 054820) **Period of Study:** 1992-1994 **Location:** London, U.K.	**Outcome:** Ischemic Heart Disease **Age Groups:** 0-15, 15-64, 65-74, 75+ **Study Design:** Time series **N:** NR **Statistical Analyses:** NR **Covariates:** NR **Dose-response Investigated?** No **Statistical Package:** NR	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (min-max):** NR **Monitoring Stations:** NR **Copollutant:** NR	**PM Increment:** 10th-90th percentile **% Change in Daily IHD Admissions by Age [CI]:** 0-15 yr: NR 15-64 yr: 2.6 [0.3,5] 65-74 yr: 2.5 [0.1,4.9] 75+ yr: 2.2 [0.2,4.6] **Notes:** RRs are presented in graph form showing little change with increasing age (PM increment of 10 $\mu g/m^3$). This article is primarily a systematic literature review of other studies.
Reference: Andersen et al. (2008, 189651) **Period of Study:** May 2001-Dec 2004 **Location:** Copenhagen, Denmark	**Outcome (ICD-10):** CVD, including angina pectoris (I20), myocardial infarction (I21-22), other acute ischemic heart diseases (I24), chronic ischemic heart disease (I25), pulmonary embolism (I26), cardiac arrest (I46), cardiac arrhythmias (I48-48), and heart failure (I50). **Age Groups:** >65 yr (CVD and RD), 5-18 yr (asthma) **Study Design:** Time series **N:** NR **Statistical Analyses:** Poisson GAM **Covariates:** Temperature, dew-point temperature, long-term trend, seasonality, influenza, day of the week, public holidays. **Season:** NR **Dose-response Investigated:** No **Statistical Package:** R (gam procedure, mgcv package) **Lags Considered:** Lag 0 -5 days, 4-day pollutant avg (lag 0 -3) for CVD.	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 24(14) **Median:** 21 **IQR:** 16-28 **99th percentile):** 72 **Monitoring Stations:** 1 **Copollutant (correlation):** NCtot: r = 0.39 NC100: r = 0.28 NCa12: r = 0.02 NCa23: r = -0.12 NCa57: r = 0.45 NCa212: r = 0.63 $PM_{2.5}$: r = 0.80 CO: r = 0.37 NO_2: r = 0.35 NO_X: r = 0.32 NO_X curbside: r = 0.18 O_3: r = -0.21 **Other variables:** Temperature: r = 0.12 Relative humidity: r = 0.05	**PM Increment:** 13 $\mu g/m^3$ (IQR) **Relative risk (RR) Estimate [CI]:** CVD hospital admissions (4-day avg, lag 0 -3), age 65+: One-pollutant model: 1.03 [1.01-1.05] Adj for NCtot: 1.04 [1.02-1.06] Adj for NCa212: 1.05 [1.01-1.09] RD hospital admissions (5-day avg, lag 0 -4), age 65+: One-pollutant model: 1.06 [1.02-1.09] Adj for NCtot: 1.05 [1.01-1.10] Adj for NCa212: 1.04 [0.98-1.11] Asthma hospital admissions (6-day avg lag 0-5), age 5 - 18: One-pollutant model: 1.02 [0.93-1.12] Adj for NCtot: 1.01 [0.91-1.12] Adj for NCa212: 0.94 [0.81-1.09] Estimates for individual day lags reported only in Fig form (see notes): **Notes:** Fig 2: Relative risks and 95% confidence intervals per IQR in single day concentration (0- to 5-day lag). Summary of Fig 2: CVD: Positive, marginally or statistically significant associations at Lag 0-Lag 2.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Anderson et al. (2007, 156214) **Period of Study:** January 1999−December 2004 **Location:** Copenhagen, Denmark	**Outcome (ICD10):** Hospital Admission, CVD, including angina pectoris (I20), myocardial infarction (I21-22), other acute ischemic heart diseases (I24), chronic ischaemic heart disease (I25), pulmonary embolism (I26), cardiac arrest (I46), cardiac arrhythmias (I48-48), and heart failure (I50). **Age Groups Analyzed:** Age >65 **Study Design:** Time series N: 2192 days, 9 Hospitals **Statistical Analyses:** Principal Component Analysis and Constrained Physical Receptor Model (COPREM), Poisson regression, GAM, **Covariates:** Season, day of the wk, public holidays, influenza epidemics and meteorology **Season:** All yr **Dose-response Investigated?** No **Statistical package:** R, gam/mgcv package **Lags Considered:** 0-6 days	**Pollutant:** Source specific PM_{10} components **Averaging Time:** 24 h **Mean (SD): Percentiles:** 25th: 16 50th (Median): NR 75th: 30 **Monitoring Stations:** 1 **Copollutant (correlation):** PM_{10}: Biomass: r = 0.53 Secondary: r = 0.73 Oil: r = 0.57 Crustal: r = 0.37 Sea salt: r = 0.04 Vehicle: r = 0.02 **Notes:** Correlations between source specific PM_{10} components presented in paper	**PM Increment:** IQR **RR Estimate** **Respiratory disease (age >65)** Single pollutant model: PM_{10}: 1.027 (1.013, 1.042), IQR=14 PM_{10} (other 5 sources): 1.045 (1.016, 1.074), IQR=13 Biomass: 1.040 (0.009, 1.072), IQR=5.4 Secondary: 1.050 (1.021, 1.081), IQR=6.1 Oil: 1.035 (1.006, 1.065), IQR=2.8 Crustal: 1.054 (1.028, 1.081), IQR=1.8 Sea salt: 0.98 (0.947, 1.017), IQR=2.2 Vehicle: 0.989 (0.949, 1.032), IQR=0.6 **Notes:** 2 pollutant model results for PM_{10} with source specific components and gases also presented in manuscript.
Reference: Baccarelli et al. (2007, 091310) **Period of Study:** Jan 1995-Aug 2005 **Location:** Lombardia region, Italy	**Outcome (ICD9 and ICD10):** Fasting and postmethionine-load total homocysteine (tHcy) **Age Groups:** 11-84 yr **Study Design:** Cross-sectional/Panel **N:** 1,213 participants **Statistical Analyses:** Generalized additive models **Covariates:** age, sex, BMI, smoking, alcohol, hormone use, temperature, day of the yr, and long-term trends **Season:** Adjusted for long-term trends to account for season **Dose-response Investigated?** No **Statistical Package:** R software v2.2.1	**Pollutant:** PM_{10} (some TSP measures used to predict PM_{10}) **Averaging Time:** Hourly concentrations used to calculate 24-h ma and 7-day ma **Mean (SD):** NR **Percentiles:** 25th: 20.1 50th: 34.1 75th: 52.6 **Range (Min, Max):** Max: 390.0 **Monitoring Stations:** 53 sites **Copollutant:** CO NO_2 SO_2 O_3	**PM Increment:** IQR **Effect Estimate [Lower CI, Upper CI]:** Estimates (%) per 32.5 µg/m^3 increase in 24-h ma of PM_{10} Homocysteine, fasting: 0.4 (-2.4, 3.3) Homocysteine, postmethionine-load: (-1.5, 3.7) Estimates (%) per 25.7m^3 increase in 7-day ma of PM_{10} Homocysteine, fasting: 1.0 (-1.9, 3.9) Homocysteine, postmethionine-load: 2.0 (-0.6, 4.7) Estimates of effect (%) on fasting homocysteine per IQR increase in 24-h PM_{10} levels Among smokers: 6.2 (0.0, 12.7) Among non-smokers: -1.6 (-5.5, 2.5) Estimates of effect (%) on postmethionine-load homocysteine per IQR increase in 24-h PM_{10} levels Among smokers: 6.0 (0.5, 11.8) Among non-smokers: -0.1 (-3.6, 3.5)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ballester et al. (2006, 088746) **Period of Study:** 1995-1999 **Location:** 5 Spanish cities: Granada, Huelva, Madrid, Seville, Zaragoza	**Outcome (ICD-9):** All cardiovascular disease (390-459), including all heart diseases (410-414, 427, 428) **Age Groups:** All ages **Study Design:** Time series **N:** NR **Statistical Analyses:** Poisson GAMs **Covariates:** Dily temp, barometric pressure relative humidity Daily influenza incidence, day of the week, holidays, unusual events (ex. medical strikes), seasonal variation, trend **Dose-response Investigated:** No **Statistical Package:** S-Plus GAM function **Lags Considered:** lag 0-3 days, lag 0-1 avg	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (10-90th percentile):** overall mean NR. City specific means Granada: 43.2 (24.8, 62.6) Huelva: 38.6 (23.1, 57.3) Madrid: 35.7 (21.4, 54.4) Seville: 41.9 (27.3, 57.6) Zaragoza: 32.8 (17.3, 50.3) **Monitoring Stations:** At least three stations/city (15+) **Copollutant (correlation):** Summary of the correlation coefficients between each pair of pollutants within cities: BS: r = 0.48 TSP: N/A NO_2: from r = 0.13 to r = 0.62 (median r = 0.40) SO_2: from r = 0.20 to r = 0.51 (median r = 0.46) CO: from r = 0.34 to r = 0.45 (median r = 0.37) O_3: from r = -0.07 to r = 0.16 (median r = 0.11)	**PM Increment:** 10 $\mu g/m^3$ **Relative risk [CI]:** Relative risks are expressed only in the form of figures (see notes). **Percentage change in risk [CI]:** All cardiovascular diseases (avg of lags 0 - 1): 0.91% [0.35, 1.47] Heart disease (avg of lags 0 -1) 1.56% [0.82, 2.31] **Notes: Relative risks for the single pollutant models are expressed in Fig 2.** Fig 2: Time sequence of the combined association between PM_{10} and hospital admissions for all CVD (A) and heart disease (B). Summary of results: Significant, positive association of PM_{10} with both overall CVD and heart disease hospitalizations at Lag 0 and Lag 1. **Relative risks for 2 pollutant models are expressed in Fig 3:** Fig 3: Combined estimates of the association between hospital admissions for heart diseases and air pollutants (avg of lags 0-1 Adjusted for CO, NO_2, O_3, or SO_2) Summary of results: Significant, positive association remains after adjusting for pollutants.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Bell et al. (2008, 091268) **Period of Study:** 1995-2002 **Location:** Taipei, Taiwan	**Outcome (ICD-9):** Hospital admissions for ischemic heart disease (410 , 411, 414), cerebrovascular disease (430-437). **Age Groups:** All **Study Design:** Time series **N:** 6,909 hospital admissions for ischaemic heart diseases, 11,466 for cerebrovascular disease. **Statistical Analyses:** Poisson regression **Covariates:** Day of the week, time, apparent temperature, long-term trends, seasonality **Season:** All **Dose-response Investigated:** No **Statistical Package:** NR **Lags Considered:** lags 0-3 days, avg of lags 0-3	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (range **IQR):** 49.1 (12.7-215.5 27.6) **Monitoring Stations:** Taipei area: 13 monitors Taipei City: 5 monitors Monitors with correlations of 0.75 + for PM_{10}: 12 monitors **Copollutant:** NR	**PM Increment:** 28 µg/m^3 (near IQR) **Percentage increase estimate [95% CI]: Ischemic heart disease:** Taipei area (13 monitors): L0: 1.91 (-1.25, 5.17) L1: 0.39 (-2.73, 3.61) L2: 1.80 (-1.33, 5.04) L3: 2.01 (-1.14, 5.26) L03: 2.91 (-1.52, 7.55) Taipei City (5 monitors): L0: 2.08 (-1.04, 5.30) L1: 0.43 (-2.64, 3.60) L2: 2.17 (-0.92, 5.36) L3: 2.16 (-0.94, 5.36) L03: 3.40 (-1.19, 8.20) Monitors with > = 0.75 between monitor correlations (12 monitors): L0: 1.82 (-1.29, 5.03) L1: 0.35 (-2.72, 3.52) L2: 1.93 (-1.15, 5.10) L3: 1.93 (-1.16, 5.12) L03: 2.86 (-1.63, 7.54) **Cerebrovascular disease:** Taipei area (13 monitors): L0: -1.41 (-3.80, 1.04) L1: -1.95 (4.31, 0.48) L2: 0.77 (-1.62, 3.23) L3: 2.64 (0.21, 5.12) L03: 0.01 (-3.33, 3.47) Taipei City (5 monitors): L0: -1.27 (-3.64, 1.16) L1: -2.13 (-4.47, 0.27) L2: 0.85 (-1.52, 3.28) L3: 2.52 (0.13, 4.97) L03: -0.07 (-3.53, 3.51) Monitors with > = 0.75 between monitor correlations (12 monitors): L0: -1.34 (-3.70, 1.07) L1: -1.98 (-4.31, 0.40) L2: 0.80 (-1.56, 3.22) L3: 2.61 (0.22, 5.05) L03: -0.02 (-3.40, 3.49)
Reference: Chan et al. (2007, 147787) **Period of Study:** Apr 1997-Dec 2002 **Location:** Boston, MA	**Outcome:** Cerebrovascular Emergency Admissions **Age Groups:** 50+ yr **Study Design:** Tme series **Statistical Analyses:** GAM Poisosn Regression **Covariates:** Yr, mo, day of wk, temperature, dew point **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 0-3 days	**Pollutant:** PM_{10} Averaging Time: 24 h **Mean (SD):** 50.2 (22.1) **Min:** 16.0 **Max:** 325.4 **IQR:** 25.4 **Monitoring Stations:** 16 **Copollutant:** O_3, CO, SO_2, NO_2, $PM_{2.5}$ **Co-pollutant Correlation:** O_3: 0.43 CO: 0.47 SO_2: 0.59 NO_2: 0.64 $PM_{2.5}$: 0.61	**PM Increment:** Interquartile Range (25.4 µg/m^3) **Percent Change (Lower CI, Upper CI), p-value:** Cerebrovascular Disease Lag 0: 1.001 (0.969, 1.033) Lag 1: 0.999 (0.9787, 1.020) Lag 2: 1.023 (0.989, 1.057) Lag 3: 1.030 (1.011, 1.049) Lag 3 + O_3: 1.018 (0.987, 1.049) Lag 3 + CO: 1.019 (0.988, 1.050) Lag 3 + O_3 + CO: 1.015 (0.985, 1.045) Stroke Lag 0: 0.969 (0.897, 1.041) Lag 1: 0.992 (0.918, 1.066) Lag 2: 1.004 (0.993, 1.015) Lag 3: 1.009 (0.988, 1.030) Ischaemic stroke Lag 0: 0.984 (0.932, 1.036) Lag 1: 0.993 (0.939, 1.047) Lag 2: 0.989 (0.927, 1.041) Lag 3: 1.042 (0.981, 1.103) Haemorrhagic stroke Lag 0: 0.966 (0.884, 1.048) Lag 1: 0.990 (0.908, 1.072) Lag 2: 1.002 (0.920, 1.084) Lag 3: 0.974 (0.902, 1.046)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Chan et al. (2008, 093297) **Period of Study:** 1995-2002 **Location:** Taipei Metropolitan area, Taiwan	**Outcome (ICD-9):** Emergency visits for ischaemic heart diseases (410-411, 414), cerebrovascular diseases (430-437), and COPD (493, 496) **Age Groups:** All **Study Design:** Time series **N:** NR **Statistical Analyses:** Poisson regression models **Covariates:** Yr, mo, day of wk, temperature, dew point temperature, $PM_{2.5}$, NO_2 **Season:** All **Dose-response Investigated:** No **Statistical Package:** SAS version 8.0 **Lags Considered:** 0- to 7-day lags	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** High dust events: Pre-dust periods: 45.5 (17.6) Asian dust events: 122.7 (24.4) Low dust events: Pre-dust periods: 59.4 (31.0) Asian dust events: 61.1 (17.8) **Monitoring Stations:** 1 **Copollutant:** NR	**PM Increment:** 25.4 µg/m^3 (IQR) **OR [95% CI]:** In environmental conditions without dust storms (results only shown for best-fitting model) Lag 3 days: 1.023 (1.003, 1.041)
Reference: Chang et al. (2007, 147621) **Period of Study:** 1997-2001 **Location:** Taipei, Taiwan	**Outcome:** CVD HA **Age Groups:** NR **Study Design:** Case-crossover **Statistical Analyses:** Conditional Logistic Regression **Covariates:** Temperature, humidity **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 0-2 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean:** 48.32 **Min:** 14.44 **25th:** 32.65 **50th:** 42.80 **75th:** 57.16 **Max:** 234.91 **Monitoring Stations:** 6 **Copollutant:** O_3, CO, SO_2, NO_2 **Co-pollutant Correlation:** NR	**PM Increment:** Interquartile Range (24.51 µg/m^3) **Odds Ratio (Lower CI, Upper CI):** ≥20°C PM_{10}: 1.085 (1.061, 1.110) PM_{10}+ SO_2: 1.131 (1.103, 1.161) PM_{10}+ NO_2: 10.977 (0.950, 1.006) PM_{10}+ CO: 1.025 (0.999, 1.052) PM_{10}+ O_3: 1.064 (1.039, 1.090) <20°C PM_{10}: 1.142 (1.105, 1.180) PM_{10}+ SO_2: 1.235 (1.184, 1.288) PM_{10}+ NO_2: 1.148 (1.103, 1.194) PM_{10}+ CO: 1.165 (1.121, 1.212) PM_{10}+ O_3: 1.142 (1.105, 1.180)
Reference: D'Ippoliti et al. (2003, 074311) **Period of Study:** Jan 1995-Jun 1997 **Location:** Rome, Italy	**Outcome:** Myocardial Infarction HA **Age Groups:** 18+ yr **Study Design:** Case-crossover **Statistical Analyses:** Conditional Logistic Regression **Covariates:** Temperature, humidity **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 0-4 days	**Pollutant:** TSP **Averaging Time:** 24 h **Mean (SD):** 66.9 (19.7) **25th:** 54.7 **50th:** 66.4 **75th:** 78.4 **IQR:** 23.7 **Monitoring Stations:** 3 **Copollutant:** CO, SO_2, NO_2 **Co-pollutant Correlation:** CO: 0.35 SO_2: 0.29 NO_2: 0.38	**PM Increment:** Quartiles **Odds Ratio (Lower CI, Upper CI):** Lag 0-2-day avg QI: 1.0 (ref) QII: 1.048 (0.957, 1.148) QIII: 1.105 (1.007, 1.214) QIV: 1.132 (1.023, 1.253) Various Lags Lag 0: 1.023 (1.004, 1.042) Lag 1: 1.015 (0.996, 1.034) Lag 2: 1.017 (0.999, 1.035) Lag 3: 0.989 (0.974, 1.003) Lag 4: 1.001 (0.987, 1.016)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Fung et al., (2005, 093262) **Period of Study:** Nov 1995-Dec 2000 **Location:** London, Ontario	**Outcome (ICD-9):** Cardiovascular diseases (410-414, 427-428) **Age Groups:** <65 yr, 65+ yr **Study Design:** Time series **N:** 12,947 CVD admissions **Statistical Analyses:** GAM with locally weighted regression smoothers (LOESS) **Covariates:** Maximum and minimum temp, humidity, day of the week, seasonal cycles, secular trends **Season:** NR **Dose-response Investigated?** No **Statistical Package:** S-Plus **Lags Considered:** Current to 3-day mean	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (min-max):** 38.0 (5-248) SD = 23.5 **Monitoring Stations:** 4 **Copollutant (correlation):** NO_2: r = 0.30 SO_2: r = 0.24 CO: r = 0.21 O_3: r = 0.53 COH: r = 0.29	**PM Increment:** 26 µg/m^3 **% Change in Daily Admission [CI]:** Age <65 Current day mean: 2.6 [-2.3,7.7] 2-day mean: -1.2 [-7.2,5.1] 3-day mean: -3 [-9.6,4] Age 65+ Current day mean: 0.9 [-2.3,4.2] 2-day mean: -0.9 [-4.8,3.2] 3-day mean: -0.1 [-4.4,4.5]
Reference: Hanigan et al. (2008, 156518) **Period of Study:** 1996-2005 (Apr-Nov of each yr) **Location:** Darwin, Australia	**Outcome:** Daily emergency hospital admissions for total cardiovascular (ICD-9: 390-459 ICD-10: I00-I99), ischemic heart disease (ICD-9: 410-414 ICD-10: I20-I25). **Age Groups:** All **Study Design:** Time series **N:** 8,279 hospital admissions **Statistical Analyses:** Poisson generalized linear models **Covariates:** Indigenous status, time in days, temperature, relative humidity, day of the week, influenza epidemics, change between ICD editions, holidays, yrly population **Season:** Apr-Nov (corresponding to the dry season) **Dose-response Investigated?** No **Statistical Package:** R version 2.3.1 **Lags Considered:** 0-3	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD** **range):** 21.2 (8.2 55.2) **Monitoring Stations:** N/A (see notes) **Copollutant:** NR	**PM Increment:** 10 µg/m^3 **Percent change [95% CI]:** Overall CVD: Lag 0 (indigenous): -3.78 [-13.4, 6.91] Lag 0 (non-indigenous): -3.43 [-9.00, 2.49] All unstratified associations either negative or zero and not statistically significant. All other results of stratified analysis (by indigenous status) reported in a Fig (see notes). **Notes:** Fig 3: Associations between hospitalizations for non-indigenous and indigenous people with estimated ambient PM_{10}. Summary: Confidence intervals were wide, but indigenous people generally had stronger associations with PM_{10} than non-indigenous people. Daily PM_{10} exposure levels were estimated for the population of the city from visibility data using a previously validated models.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Hanigan et al. (2008, 156518) **Period of Study:** 1996-2005 (Apr-Nov of each yr) **Location:** Darwin, Australia	**Outcome:** Cardiorespiratory Disease HA (ICD 9: 390-519 ICD 10: I00-99 & J00-99) **Age Groups:** NR **Study Design:** Time series **N:** 8279 events **Statistical Analyses:** poisson regression **Covariates:** Indigenous status, time in days, temperature, relative humidity, day of the week, influenza epidemics, change between ICD editions, holidays, yearly population **Dose-response Investigated?** No **Statistical Package:** R **Lags Considered:** lags 0-3	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 21.2 (8.2) **Range:** 55.2 **Monitoring Stations:** 2 (monitored & modeled) **Copollutant:** NR **Co-pollutant Correlation:** N/A	**PM Increment:** 10 µg/m^3 **Percent Change (Lower CI, Upper CI), lag:** Tot. Cardiovascular, Indigenous: -3.43 (-9.00, 2.49), lag 0 Tot Cardiovascular, Non-Indigenous: -3.78 (-13.4, 6.91), lag 0 *Fig 3. percent change in hospital admissions per 10 µg/m^3 increase in PM_{10}
Reference: Henrotin et al. (2007, 093270) **Period of Study:** Mar 1994-Dec 2004 **Location:** Dijon, France	**Outcome:** Ischemic and hemorrhagic strokes **Age Groups:** All **Study Design:** Bi-directional case-crossover **N:** 1487 (ischemic) and 220 (hemorrhagic) stroke patients **Statistical Analyses:** Conditional logistic regression **Covariates:** Temperature, relative humidity, influenza epidemics, holidays **Season:** NR **Dose-response Investigated?** Yes **Statistical Package:** STATA software v. 8.2 **Lags Considered:** 0-3 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (min-max):** 21.1 (2-103) SD = 11.3 **Monitoring Stations:** 1 **Copollutant:** NR	**PM Increment:** 10 µg/m^3 **OR Estimate [CI]:** Ischemic stroke Same-day lag: 1.009 [0.930,1.094] 1-day lag: 1.011 [0.998,1.094] 2-day lag: 0.960 [0.889,1.036] 3-day lag: 0.990 [0.919,1.066] Hemorrhagic stroke Same-day lag: 0.901 [0.730,1.111] 1-day lag: 1.014 [0.828,1.241] 2-day lag: 1.100 [0.903,1.339] 3-day lag: 0.991 [0.881,1.212] **Notes:** Ischemic stroke ORs were also categorized into male and female, yielding similar results (none were significant for any lag days).
Reference: Issever et al. (2005, 097736) **Period of Study:** Jan 1997-Dec 2001 **Location:** Istanbul, Turkey	**Outcome:** Acute coronary syndrome (ACS) **Age Groups:** All **Study Design:** Time series **N:** 2889 ACS admissions **Statistical Analyses:** Multiple stepwise regression, Pearson correlation **Covariates:** Humidity, temperature, pressure **Season:** NR **Dose-response Investigated?** No	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean:** NR **Monitoring Stations:** 1 **Copollutant (correlation):** ACS: r = 0.37 (p = 0.003) ACS controlled for temp: r = 0.29 (p = 0.02)	**PM Increment:** NR **RR Estimate [CI]:** NR **Notes:** This study focused more on the seasonal change in acute coronary syndrome admissions.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Jalaludin et al. (2006, 189416) **Period of Study:** Jan 1997-Dec 2001 **Location:** Sydney, Australia	**Outcome (ICD-9):** Cardiovascular disease (390-459), cardiac disease (390-429), ischemic heart disease (410-413) and cerebrovascular disease or stroke (430-438) **Age Groups:** 65+ yr **Study Design:** Time series **N:** NR **Statistical Analyses:** GAM, GLM **Covariates:** Temperature, humidity **Season:** Warm (Nov-Apr) and cool (May-Oct) **Dose-response Investigated?** No **Statistical Package:** S-Plus **Lags Considered:** 0-3	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (min-max):** 16.8 (3.8-103.9) SD = 7.2 **Monitoring Stations:** 14 **Copollutant (correlation):** Warm BSP: r = 0.82 $PM_{2.5}$: r = 0.89 O_3: r = 0.59 NO_2: r = 0.44; CO: r = 0.31 SO_2: r = 0.37 Cool BSP: r = 0.75 $PM_{2.5}$: r = 0.88 O_3: r = 0.22 NO_2: r = 0.67 CO: r = 0.48 SO_2: r = 0.46 **Other variables:** Warm Temp: r = 0.36 Rel humidity: r = -0.25 Cool Temp: r = 0.13 Rel humidity: r = 0.05	**PM Increment:** 7.8 µg/m^3 (IQR) **Percent Change Estimate [CI]:** All CVD Same-day lag: 0.72 [-0.14,1.60] Avg 0-1 day lag: 0.25 [-0.61,1.12] Cool (same-day lag): 1.34 [0.08,2.61] Warm (same-day lag): 0.33 [-0.83,1.50] Cardiac disease Same-day lag: 1.15 [0.14,2.18] Avg 0-1 day lag: 0.97 [-0.07,2.02] Cool (same-day lag): 1.35 [-0.16,2.89] Warm (same-day lag): 1.12 [-0.23,2.48] Ischemic heart disease Same-day lag: 0.59 [-0.95,2.17] Avg 0-1 day lag: 0.61 [-0.95,2.20] Cool (same-day lag): 0.33 [-2.00,2.72] Warm (same-day lag): 0.79 [-1.23,2.85] Stroke Same-day lag: -1.66 [-3.48,0.20] Avg 0-1 day lag: -2.05 [-3.88,-0.20] Cool (same-day lag): 0.46 [-2.17,3.17] Warm (same-day lag): -3.49 [-5.97,-0.95] **Notes:** All other lag-day ORs were provided, yet none were significant. Percent change in ED attendance was also reported graphically (Fig 1-5).
Reference: Johnston et al. (2007, 155882) **Period of Study:** 2000, 2004, 2005 (Apr-Nov of each yr) **Location:** Darwin, Australia	**Outcome (ICD-10):** All cardiovascular conditions (I00-I99), including ischemic heart disease (I20-I25). **Age Groups:** All **Study Design:** Case-crossover **N:** 2466 emergency admissions **Statistical Analyses:** Conditional logistic regression **Covariates:** Weekly influenza rates, temperature, humidity, days with rainfall >5mm, public holidays, school holiday periods (for respiratory conditions only) **Season:** Apr-Nov (dry season) **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 0-3	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Median:** 17.4 **IQR:** 13.6-22.3 **10-90th Percentile:** 10.3-27.7 **Range:** 1.1-70.0 **Monitoring Stations:** 1 **Copollutant:** NR	**PM Increment:** 10 µg/m^3 **OR Estimate [95% CI]: All respiratory conditions: Ischemic heart disease:** Lag 0: 0.82 [0.68-0.98] Lag 0 (non-indigenous): 0.75 [0.61-0.93] Lag 3 (indigenous): 1.71 [1.14-2.55] **Notes:** **Fig 5:** OR and 95% CI for hospital admissions for cardiovascular conditions. Summary: Negative associations in overall study population and in non-indigenous people. Positive associations in Indigenous people at Lag 1, Lag 2, and Lag 3. **Fig 6:** OR and 95% CI for hospital admissions for ischaemic heart disease. Summary: Negative associations in overall study population and non-indigenous people. Positive association in indigenous people.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Koken et al. (2003, 049466) **Period of Study:** Jul and Aug, 1993-1997 **Location:** Denver, Colorado	**Outcome (ICD-9):** Acute myocardial infarction (410.00-410.92), pulmonary heart disease (416.0-416.9), cardiac dysrhythmias (427.0-427.9), congestive heart failure (428.0) **Age Groups:** 65+ yr **Study Design:** Time series **N:** 298 days **Statistical Analyses:** GLM, GEE **Covariates:** Maximum temp and dew point temp **Season:** NR **Dose-response Investigated:** Yes **Statistical Package:** SAS (PROC GENMOD) **Lags Considered:** 0-4 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (min-max):** 24.2 (7.0-51.6) SD = 6.25 **Monitoring Stations:** 3 **Copollutant (correlation):** NO_2: r = 0.56 SO_2: r = 0.36 O_3: r = 0.03 CO: r = 0.25 **Other variables:** Max temp: r = 0.38 Dew point temp: r = -0.24	**PM Increment:** 8.0 µg/m^3 (IQR) **Percent Change Estimate [CI]:** No PM data reported
Reference: Lanki et al., (2006, 089788) **Period of Study:** 1992-2000 **Location:** Augsburg, Barcelona, Helsinki, Rome, and Stockholm	**Outcome (ICD-9):** Acute myocardial infarction (410 ICD-10: I21, I22) **Age Groups:** 35+ yr, <75 yr, 75+ yr **Study Design:** Time series **N:** 26,854 hospitalizations **Statistical Analyses:** GAM **Covariates:** Temperature, barometric pressure **Season:** Warm (Apr-Sep) and cold (Oct-Mar) **Dose-response Investigated:** No **Statistical Package:** R package mgcv 0.9-5 **Lags Considered:** 0-3 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Median:** Augsburg: 43.5 Barcelona: 57.4 Helsinki: 21.0 Rome: 48.5 Stockholm: 12.5 **Copollutant (correlation):** Augsburg PNC: r = 0.53 CO: r = 0.56 NO_2: r = 0.64 O_3: r = 0.43 Barcelona: PNC: r = 0.38 CO: r = 0.44 NO_2: r = 0.48 O_3: r = 0.01 Helsinki: PNC: r = 0.45 CO: r = 0.21 NO_2: r = 0.40 O_3: r = 0.40 Rome: PNC: r = 0.32 CO: r = 0.41 NO_2: r = 0.29 O_3: r = 0.59 Stockholm: PNC: r = 0.06 CO: r = 0.41 NO_2: r = 0.29 O_3: r = 0.59	**PM Increment:** 10 µg/m^3 **Pooled Rate Ratio [CI]:** All 5 cities (35+ yr) Same-day lag: 1.003 [0.995,1.011] 1-day lag: 1.001 [0.990,1.011] 2-day lag: 1.002 [0.994,1.010] 3-day lag: 1.002 [0.991,1.013] 3 cities with hospital discharge register (35+ yr) Same-day lag: 1.003 [0.994,1.012] 1-day lag: 0.997 [0.988,1.006] 2-day lag: 1.003 [0.995,1.012] 3-day lag: 1.003 [0.986,1.020] Warm season (35+ yr) Same-day lag: 1.006 [0.990,1.022] 1-day lag: 1.000 [0.985,1.016] 2-day lag: 1.005 [0.990,1.020] 3-day lag: 1.010 [0.995,1.025] Cold season (35+ yr) Same-day lag: 1.001 [0.991,1.012] 1-day lag: 0.998 [0.987,1.009] 2-day lag: 1.001 [0.991,1.012] 3-day lag: 0.991 [0.981,1.002] Age >75 Non-fatal Same-day lag: 1.012 [0.995,1.029] 1-day lag: 1.000 [0.983,1.017] 2-day lag: 0.999 [0.982,1.017] 3-day lag: 1.001 [0.984,1.018] Fatal Same-day lag: 1.009 [0.985,1.034] 1-day lag: 0.998 [0.974,1.023] 2-day lag: 1.003 [0.978,1.028] 3-day lag: 1.018 [0.975,1.063] **Notes:** Pooled rate ratios were also provided for groups <75 yielding similar results to the overall 3-city data.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Lee et al. (2003, 095552) **Period of Study:** Dec 1997-Dec 1999 **Location:** Seoul, Korea	**Outcome (ICD-10):** Angina pectoris (I20), acute/subsequent myocardial infarction (I21-I23), other acute ischemic heart diseases (I24) **Age Groups:** All ages, 64+ yr **Study Design:** Time series **N:** 822 days **Statistical Analyses:** GAM with LOESS, Pearson correlation **Covariates:** Temperature, relative humidity, day of the week **Season:** Summer (Jun-Aug) and winter **Dose-response Investigated:** Yes **Statistical Package:** NR **Lags Considered:** 0-6 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 64.0 (31.8) **Monitoring Stations:** 27 **Copollutant (correlation):** All yr SO_2: r = 0.59 NO_2: r = 0.74 O_3: r = 0.11 CO: r = 0.60 Temp: r = -0.07 Humidity: r = 0.02 Summer SO_2: r = 0.61 NO_2: r = 0.73 O_3: r = 0.64 CO: r = 0.55 Temp: r = -0.01 Humidity: r = -0.11	**PM Increment:** 40.4 µg/m^3 (IQR) **RR Estimate [CI]: All yr** All ages: 0.99 [0.96,1.01] 64+ yr: 1.05 [1.01,1.10] **Summer** All ages: 1.03 [0.97,1.09] 64+ yr: 1.09 [1.00,1.19] **Two-pollutant model** CO (1 ppm IQI): 1.04 [0.98,1.11] O_3 (21.7 ppb IQI): 1.07 [1.03,1.11] NO_2 (14.6 ppb IQI): 1.09 [1.02,1.16] SO_2 (4.4 ppb): 0.98 [0.94,1.03]
Reference: Lee et al. (2008, 192076) **Period of Study:** 1996-2005 **Location:** Taipei, Taiwan	**Outcome:** Congestive Heart Failure HA (ICD 9: 428) **Age Groups:** NR **Study Design:** Case-crossover **N:** 18593 events **Statistical Analyses:** conditional logistic regression **Covariates:** Temperature, humidity **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** Lags 0-2	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean:** 49.94 **Min:** 11.33 **25th:** 33.37 **50th:** 45.05 **75th:** 60.82 **Max:** 234.92 **Monitoring Stations:** 6 **Copollutant:** SO_2, CO, NO_2, O_3 **Co-pollutant Correlation** SO_2: 0.52 CO: 0.67 NO_2: 0.35 O_3: 0.39	**PM Increment:** Interquartile Range (27.45 µg/m^3) **Odds Ratio (Lower CI, Upper CI):** W/ Hypertension: 1.23 (1.15, 1.32) W/o Hypertension: 1.20 (1.15, 1.25) W/ Diabetes: 1.20 (1.12, 1.40) W/o Diabetes: 1.21 (1.15, 1.26) W/ Dysrhythmia: 1.17 (1.08, 1.27) W/o Dysrhythmia: 1.22 (1.17, 1.27) W/ COPD: 1.21 (1.07, 1.36) W/o COPD: 1.21 (1.16, 1.25)
Reference: Larrieu et al. (2007, 093031) **Period of Study:** 1998-2003 **Location:** 8 French urban area: Bordeaux, Le Havre, Lille, Lyon, Marseille, Paris, Rouen, and Toulouse	**Outcome (ICD-10):** Hospital admissions for cardiovascular disease (I00-I99), cardiac disease (I00-I52), ischemic heart disease (I20-I25), and stroke (cerebrovascular disease: I60-64 and transient ischemic attack: G45-G46). **Age Groups:** All, and 65 + **Study Design:** Time series **N: Statistical Analyses:** generalized additive Poisson regression **Covariates:** Temperature, holidays, influenza epidemic periods, long-term trend, season, day of the week, **Season:** NR **Dose-response Investigated:** No **Statistical Package:** R 2.2.1 **Lags Considered:** 0 –to 1-day lag (mean)	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean:** Bordeaux: 21.0 Le Havre: 21.7 Lille: 22.1 Lyon: 24.6 Marseille: 28.9 Paris: 23.1 Rouen: 21.2 Toulouse: 21.8 **Monitoring Stations:** 32 **Copollutant:** NR	**PM Increment:** 10 µg/m^3 **ERR [95% CI]:** CVD: All ages: 0.7 [0.1, 1.2] 65+ yr: 1.1 [0.5, 1.7] Cardiac diseases: All ages: 0.8 [0.2, 1.4] 65+ yr: 1.5 [0.7, 2.2] Ischemic heart diseases: All ages: 1.9 [0.8, 3.0] 65+ yr: 2.9 [1.5, 4.3] Strokes: All ages: 0.2 [-1.6, 1.9] 65+ yr: 0.8 [-0.9, 2.5]

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Le Tertre et al. (2002, 023746) **Period of Study:** 1990-1997 **Location:** Barcelona, Birmingham, London, Milan, the Netherlands, Paris, Rome, and Stockholm	**Outcome (ICD-9):** Cardiac diseases (390-429), ischemic heart disease (410-413), and stroke (430-438) **Age Groups:** <65 yr, 65+ yr **Study Design:** Time series **N:** NR **Statistical Analyses:** GAM **Covariates:** Long term trend, season, days of the week, holidays, influenza epidemics, temperature, and humidity **Season:** NR **Dose-response Investigated:** No **Statistical Package:** S-Plus **Lags Considered:** 0-3 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** Barcelona: 55.7 (18.4) Birmingham: 24.8 (13.1) London: 28.4 (12.3) Milan: 51.5 (22.7) Netherlands: 39.5 (19.9) Paris: 22.7 (10.8) Rome: 52.5 (12.9) Stockholm: 15.5 (7.2) **Monitoring Stations:** 1-12 **Copollutant:** NR	**PM Increment:** 10 µg/m^3 **Pooled Percent Increase [CI]:** Cardiac (all ages) Fixed: 0.5 [0.3,0.7] Random: 0.5 [0.2,0.8] Cardiac (over 65) Fixed: 0.7 [0.4,1.0] Random: 0.7 [0.4,1.0] IHD (<65) Fixed: 0.3 [-0.1,0.6] Random: 0.3 [-0.2,0.7] IHD (over 65) Fixed: 0.6 [0.3,0.8]; Random: 0.8 [0.3,1.2] Stroke (over 65) Fixed: 0.0 [-0.3,0.3]; Random: 0.0 [-0.3,0.3] Deaths: Cardiac: 0.5 [0.2,0.8]; Cardiac (65+): 0.7 [0.4,1.0] IHD (65+): 0.8 [0.3,1.2] **Notes:** Estimated percentage increases are also provided by city for cardiac admissions and ischemic heart disease in Fig 1-3.
Reference: Mann et al. (2002, 036723) **Period of Study:** 1988-1995 **Location:** South Coast Air Basin, California	**Outcome (ICD-9):** Ischemic heart disease (410-414), secondary congestive heart failure (sCHF) (428), and secondary arrhythmia (sARR) (426, 427) **Age Groups:** All, 40-59 yr, >60 yr **Study Design:** Time series **N:** 54,863 IHD admissions **Statistical Analyses:** GAM **Covariates:** Temperature, day of the week, relative humidity **Season:** NR **Dose-response Investigated:** No **Statistical Package:** S-Plus **Lags Considered:** 0-5 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (min-max):** 43.7 (0.22-251) SD = 27.7 **Monitoring Stations:** 20 **Copollutant (correlation):** Region 1: CO: r = 0.28 O_3: r = 0.20 NO_2: r = 0.36 Region 2: CO: r = 0.15 O_3: r = 0.57 NO_2: r = 0.53 Region 3: CO: r = 0.36 O_3: r = 0.30 NO_2: r = 0.46 Region 4: CO: r = 0.27 O_3: r = 0.33 NO_2: r = 0.50 Region 5: CO: r = 0.40 O_3: r = 0.43 NO_2: r = 0.53 Region 6: CO: r = 0.33 O_3: r = 0.20 NO_2: r = 0.42 Region 7: CO: r = 0.28 O_3: r = 0.48 NO_2: r = 0.60	**PM Increment:** 10 µg/m^3 **Percent Change in IHD Admissions [CI]:** Secondary ARR Same-day lag: 0.59 [-0.71,1.91] 1-day lag: 0.46 [-0.86,1.80] 2-day lag: -0.04 [-1.37,1.31] Secondary CHF Same-day lag: -0.62 [-1.77,0.55] 1-day lag: -0.45 [-1.60,0.71] 2-day lag: -0.36 [-1.52,0.82] No secondary diagnosis Same-day lag: -0.25 [-1.23,0.75] 1-day lag: 0.04 [-0.97,1.06] 2-day lag: 0.18 [-0.82,1.20] All IHD admissions: 0.19 [-0.576,0.955] MI admissions: -0.10 [-1.33,1.12] Other acute IHD admissions: 0.36 [-0.87,1.60]

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Metzger et al. (2004, 044222) **Period of Study:** Aug 1993-Aug 2000 **Location:** Atlanta Metropolitan area (Georgia)	**Outcome (ICD-9):** Emergency visits for ischemic heart disease (410-414), cardiac dysrhythmias (427), cardiac arrest (427.5), congestive heart failure (428), peripheral vascular and cerebrovascular disease (433-437, 440, 443-444, 451-453), atherosclerosis (440), and stroke (436). **Age Groups:** All **Study Design:** Time series **N:** 4,407,535 emergency department visits **Statistical Analyses:** Poisson generalized linear modeling **Covariates:** Day of the wk, hospital entry and exit indicator variables, federally observed holidays, temporal trends, temperature, dew point temperature **Season:** All **Dose-response Investigated:** No **Statistical Package:** SAS **Lags Considered:** 3-day ma, lags 0 -7	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Median (10% - 90% range):** 26.3 (13.2, 44.7) **Monitoring Stations:** NR **Copollutant (correlation):** O_3: r = 0.59 NO_2: r = 0.49 CO: r = 0.47 SO_2: r = 0.20 $PM_{2.5}$: r = 0.84 $PM_{10-2.5}$: r = 0.59 UFP: r = -0.13 $PM_{2.5}$ water-sol metals: r = 0.74 $PM_{2.5}$ sulfates: r = 0.74 $PM_{2.5}$ acidity: r = 0.68 $PM_{2.5}$ OC: r = 0.69 $PM_{2.5}$ EC: r = 0.56 oxygenated hydrocarbon: r = 0.58 **Other variables:** Temperature: r = 0.58 Dew point: r = 0.44	**PM Increment:** 10 µg/m^3 (approximately 1 SD) **RR [95% CI]:** For 3-day ma: All CVD: 1.009 [0.998, 1.019] Dysrhythmia: 1.008 [0.989, 1.029] Congestive heart failure: 0.992 [0.968-1.016] Ischemic heart disease: 1.011 [0.992-1.030] Peripheral vascular and cerebrovascular disease: 1.020 [0.999-1.043] **Notes:** Results for Lags 0-7 expressed in figures Fig 1: RR (95% CI) for single-day lag models for the association of ER visits for CVD with daily ambient PM_{10}. Summary: Statistically significant association at Lag 0. Positive but not statistically significant association at Lag 1. Negative, statistically significant association at Lag 7, and negative associations at Lag 2 through Lag 6.
Reference: Middleton et al. (2008, 156760) **Period of Study:** 1995-1998, 2000-2004 **Location:** Nicosia, Cyprus	**Outcome:** Hospital admissions for all cardiovascular disease (ICD-10: I00-I52). **Age Groups:** All, also stratified by age (<15 vs.. >15 yr) **Study Design:** Time series **Statistical Analyses:** Generalized additive Poisson models **Covariates:** Seasonality, day of the week, long- and short-term trend, temperature, relative humidity **Dose-response Investigated:** No **Statistical Package:** STATA SE 9.0, R 2.2.0 **Lags Considered:** Lag 0 -2 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD median 5% - 95% range):** Cold: 57.6 (52.5 50.8 20.0-103.0 5.0-1370.6) Warm: 53.4 (50.5 30.7 32.0-77.6 18.4-933.5) **Monitoring Stations:** 2 **Copollutant:** NR	**PM Increment:** 10 µg/m^3, and across quartiles of increasing levels of PM_{10} **Percentage increase estimate [CI]: All age/sex groups (Lag 0):** All admissions: 0.85 (0.55, 1.15) Cardiovascular: 1.18 (-0.01, 2.37) **Nicosia residents (Lag 0):** Cardiovascular: 0.73 (-0.62, 2.09) **Males (Lag 0):** All admissions: 0.96 (0.54, 1.39) Cardiovascular: 1.27 (-0.15, 2.72) **Females (Lag 0):** All admissions: 0.74 (0.31, 1.18) Cardiovascular: 0.99 (-1.11, 3.14) **Aged <15 yr (Lag 0):** All admissions: 0.47 (-0.13, 1.08) **Aged >15 yr (Lag 0):** All admissions: 0.98 (0.63, 1.33)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Peel et al. (2007, 090442) **Period of Study:** Jan 1993-Aug 2000 **Location:** Atlanta, GA	**Outcome (ICD-9):** Ischemic heart disease (410-414), dysrhythmia (427), congestive heart failure (428), peripheral vascular and cerebrovascular disease (433-437, 440, 443, 444, 451-453) **Age Groups:** All **Study Design:** Case-crossover **N:** 4,407,535 ED visits **Statistical Analyses:** Conditional logistic regression **Covariates:** Avg temp and dew point temp **Season:** NR **Dose-response Investigated:** No **Statistical Package:** SAS v. 9.1 **Lags Considered:** 0-2 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** Daily levels: 27.9 (12.3) Diff in case and control-day avg: 9.1 (7.5) **Monitoring Stations:** 1 **Copollutant:** NR	**PM Increment:** 10 µg/m^3 **OR Estimate [CI]:** All CVD: 1.010 [1.000,1.020] IHD: 1.009 [0.991,1.027] Dysrhythmia: 1.011 [0.991, 1.031] Peripheral/Cerebrovascular disease: 1.017 [0.996,1.039] CHF: 1.001 [0.978,1.024] With comorbid hypertension IHD: 1.003 [0.973,1.034] Dysrhythmia: 1.037 [0.988,1.089] Peripheral/Cerebrovascular disease: 1.024 [0.990,1.060] CHF: 1.041 [0.999,1.084] No comorbid hypertension IHD: 1.013 [0.991,1.036] Dysrhythmia: 1.006 [0.985,1.028] Peripheral/Cerebrovascular disease: 1.013 [0.987,1.040] CHF: 0.982 [0.955,1.010] With comorbid diabetes IHD: 1.022 [0.979,1.067] Dysrhythmia: 1.049 [0.968,1.137] Peripheral/Cerebrovascular disease: 1.016 [0.965,1.069] CHF: 1.029 [0.982,1.078] No comorbid diabetes IHD: 1.006 [0.987,1.026] Dysrhythmia: 1.009 [0.989,1.029] Peripheral/Cerebrovascular disease: 1.018 [0.995,1.042] CHF: 0.992 [0.966,1.019] With comorbid COPD IHD: 0.981 [0.921,1.044] Dysrhythmia: 0.984 [0.889,1.088] Peripheral/Cerebrovascular disease: 1.086 [0.998,1.181] CHF: 1.010 [0.954,1.069] No comorbid COPD IHD: 1.012 [0.993,1.031] Dysrhythmia: 1.012 [0.992,1.032] Peripheral/Cerebrovascular disease: 1.013 [0.991,1.035] CHF: 0.999 [0.974,1.025]
Reference: Pope et al., (2006, 091246) **Period of Study:** 1994-2004 **Location:** Wasatch Front area, Utah	**Outcome:** Myocardial infarction or unstable angina (ICD codes not reported) **Age Groups:** All **Study Design:** Case-crossover **N:** 12,865 patients who underwent coronary arteriography **Statistical Analyses:** Conditional logistic regression **Covariates:** Temperature and dew point temperature **Season:** NR **Dose-response Investigated:** No **Statistical Package:** NR **Lags Considered:** 0- to 3-day lag, 2- to 4-day lagged ma	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD maximum):** Ogden: 28.5 (16.5 163) SLC Hawthorne: 27.7 (17.4 162) Provo/Orem, Lindom: 32.7 (21.1 240) SLC AMC: 35.9 (20.4 161) SLC North: 45.1 (25.1 199) **Monitoring Stations:** 5 **Copollutant:** NR	**PM Increment:** 10 µg/m^3 **Percent increase in risk [95% CI]:** Results summarized in Fig (see notes). **Notes:** Fig 1: Percent increase in risk (and 95% CI) of acute coronary events associated with 10 µg/m^3 of PM_{10} for different lag structures. Summary of Fig 1: Positive, statistically significant or marginally significant associations between association seen for Lag 0, Lag 1 and 2-, 3-, and 4-day ma. Non-statistically significant associations

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Santos et al. (2008, 192004) **Period of Study:** Jan 1998-Aug 1999 **Location:** Sao Paulo, Bazil	**Outcome:** Cardiac Arrhythmia ER Visits (ICD 10: I45-I49) **Age Groups:** 17+ yr **Study Design:** Time series **N:** 3251 ER visits **Statistical Analyses:** Poisson **Covariates:** Temperature, humidity, seasonality **Dose-response Investigated?** Yes **Statistical Package:** S-Plus **Lags Considered:** Lags 0-13	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 48.64 (20.34) **Min:** 18.68 **Max:** 137.76 **Monitoring Stations:** 14 **Copollutant:** SO_2, CO, NO_2, O_3 **Co-pollutant Correlation:** SO_2: 0.675* CO: 0.580* NO_2: 0.781* O_3: 0.438* *p < 0.01	**PM Increment:** Interquartile Range (22.2 µg/m^3) **Percent Increase (Lower CI, Upper CI):** PM_{10}+ NO_2,CO: -5.6 (-12.7, 2.1) PM_{10}+ CO: -1.1 (-7.0, 5.1) PM_{10}+ NO_2: -2.4 (-9.4, 5.1) Fig 1. PM_{10} effects, reported as percent increase, on arrhythmia ER visits caused by interquartile range increases, lags 0-6. Fig 2. Relative risks and 95% CI for arrhythmia ER visits according to the division of air pollutant daily concentrations in quintiles.
Reference: Tolbert et al. (2007, 090316) **Period of Study:** 1993-2004 **Location:** Atlanta Metropolitan area, Georgia	**Outcome (ICD-9):** Combined CVD group, including: Ischemic heart disease (410-414), cardiac dysrhythmias (427), congestive heart failure (428), and peripheral vascular and cardiovascular disease (433-437, 440, 443-445, and 451-453). **Age Groups:** All **Study Design:** Time series **N:** 10,234,490 ER visits (283,360 and 1,072,429 visits included in the CVD and RD groups, respectively) **Statistical Analyses:** Poisson generalized linear models **Covariates:** Long-term temporal trends, season (for RD outcome), temperature, dew point, days of week, federal holidays, hospital entry and exit **Season:** All **Dose-response Investigated:** No **Statistical Package:** SAS version 9.1 **Lags Considered:** 3-day ma (lag 0-2)	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (median** **IQR, range, 10th-90th percentiles):** 26.6 (24.8 17.5-33.8 0.5-98.4 12.3-42.8) **Monitoring Stations:** NR **Copollutant (correlation):** O_3: r = 0.59 NO_2: r = 0.53 CO: r = 0.51 SO_2: r = 0.21 Coarse PM: r = 0.67 $PM_{2.5}$: r = 0.84 $PM_{2.5}$ SO_4: r = 0.69 $PM_{2.5}$ EC: r = 0.61 $PM_{2.5}$ OC: r = 0.65 $PM_{2.5}$ TC: r = 0.67 $PM_{2.5}$ water-sol metals: r = 0.73 OHC: r = 0.53	**PM Increment:** 16.30 µg/m^3 (IQR) **Risk ratio [95% CI]:** Single pollutant models: CVD: 1.008 (0.997-1.020)
Reference: Tsai et al. (2003, 080133) **Period of Study:** 1997-2000 **Location:** Kaohsiung, Taiwan	**Outcome (ICD-9):** Cerebrovascular diseases (430-438), subarachnoid hemorrhagic stroke (430), primary intracerebral hemorrhage (431-432), ischemic stroke (433-435), and others (436-438) **Age Groups:** All **Study Design:** Case-crossover **N:** 23,179 admissions **Statistical Analyses:** Conditional logistic regression **Covariates:** Temperature and humidity **Season:** NR **Dose-response Investigated:** No **Statistical Package:** SAS **Lags Considered:** Cumulative 0-2 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (min-max):** 78.82 (20.50-217.33) **Monitoring Stations:** 6 **Copollutant:** NR	**PM Increment:** 66.33 µg/m^3 (IQR) **OR Estimate [CI]: Two-pollutant model (all stroke admissions)** Primary intracerebral hemorrhage (PIH) Adj for SO_2: 1.55 [1.31,1.83] Adj for NO_2: 1.28 [1.01,1.61]; Adj for CO: 1.45 [1.20,1.74] Adj for O_3: 1.56 [1.27,1.91] Ischemic stroke (IS) Adj for SO_2: 1.46 [1.32,1.61] Adj for NO_2: 1.16 [1.01,1.34] Adj for CO: 1.35 [1.21,1.51] Adj for O_3: 1.51 [1.34,1.71] **Single-pollutant model** Temp >20ºC PIH: 1.54 [1.31,1.81] IS: 1.46 [1.32,1.61] Temp <20ºC PIH: 0.82 [0.48,1.40] IS: 0.97 [0.65,1.44]

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ulirsch et al. (2007, 091332) **Period of Study:** Nov 1994-Mar 2000 **Location:** Pocatello, Idaho and Chubbuck, Idaho	**Outcome (ICD-9):** CVD (390-429). **Age Groups:** 65 + **Study Design:** Time series **N:** 39,347 admissions/visits **Statistical Analyses:** Log-linear generalized linear models **Covariates:** Time, temperature, relative humidity, influenza, day of the week **Season:** All, and separate analyses were performed for the all-age group for cool months (Oct-Mar) vs.. warm months (Apr-Sep). **Dose-response Investigated:** No **Statistical Package:** S-plus version 6.1 **Lags Considered:** 0- to 4-day lags, and mean of days 0 -4	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (range 10th - 90th percentiles):** 24.2 (3.0-183.0 10.5-40.7) **Monitoring Stations:** 4 **Copollutant (correlation):** NO_2: r = 0.47 **Other variables:** Correlation for PM_{10} between monitors: r = 0.42-0.87	**PM Increment:** 50 µg/m^3 , and 24.3 µg/m^3 (mean increase in PM_{10}) **Mean percent of change (% change in the mean number of daily admissions and visits) [95% CI]:** **For 24.3 µg/m^3 increase in PM10:** All-age RD/CVD: 3.7 [1.3, 6.3] All-age CVD (Lag 0): -0.02 [-5.9, 6.3] All-age CVD (Lag 1): 1.9 [-4.1, 8.4] All-age CVD (Lag 2): -3.1 [-9.1, 3.4] All-age CVD (Lag 3): 0.5 [-5.6, 6.9] All-age CVD (Lag 4): -1.7 [-4.3, 0.9] Lag 0-4 days: -0.5 [-8.0, 7.6] **For 50 µg/m3 increase in PM10 (single pollutant models, CIs not given):** All-age respiratory disease: 8.4 All-age RD/CVD: 7.9 18-64 yr RD: 7.2 All-age CVD (Lag 3): 1.0 All-age CVD (Lag 4): -3.6 All-age CVD (Lag 0 -4): -1.1 **Notes:** Included urgent care visits as well as emergency department visits and hospital admissions.
Reference: Yang et al. (2007, 092847) **Period of Study:** 1996-2005 **Location:** Taipei, Taiwan	**Outcome:** Congestive Heart Failure HA (ICD 9: 428) **Age Groups:** NR **Study Design:** case-crossover **N:** 24,240 events **Statistical Analyses:** Poisson **Covariates:** Temperature, humidity **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** lags 0-3	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean:** 49.47 **Min:** 14.42 **25th:** 33.08 **50th:** 44.71 **75th:** 60.10 **Max:** 234.91 **Monitoring Stations:** 6 **Copollutant:** NR **Co-pollutant Correlation:** N/A	**PM Increment:** Interquartile Range (27.02 µg/m^3) **Odds Ratio (Lower CI, Upper CI):** Temp ≥20°C PM_{10}: 1.15 (1.10-1.21)* PM_{10}+ SO_2: 1.23 (1.17, 1.30)* PM_{10}+ NO_2: 1.03 (0.97, 1.10) PM_{10}+ CO_2: 1.09 (1.03, 1.15)* PM_{10}+ O_3: 1.10 (1.04, 1.15)* Temp <20°C PM_{10}: 0.99 (0.93, 1.05) PM_{10}+ SO_2: 0.96 (0.89, 1.03) PM_{10}+ NO_2: 0.97 (0.90, 1.04) PM_{10}+ CO_2: 0.96 (0.90, 1.03) PM_{10}+ O_3: 1.00 (0.94, 1.05) *p < 0.05
Reference: Yang et al. (2007, 092847) **Period of Study:** 1996-2001 **Location:** Taipei, Taiwan	**Outcome:** Congestive Heart Failure HA **Age Groups:** NR **Study Design:** case-crossover **N:** NR **Statistical Analyses:** Poisson **Covariates:** NR **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** Lags 0-3	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** Index days: 111.68 (38.32) Comparison days: 55.43 (24.66) **Monitoring Stations:** 7 **Copollutant:** NR **Co-pollutant Correlation:** N/A	**PM Increment:** Index (>125 µg/m^3) vs.. Comparison (≤125 µg/m^3) **Relative Risk (Lower CI, Upper CI), lag:** 0.915 (0.805, 1.041), lag 0 1.114 (0.993, 1.250), lag 1 0.983 (0.873, 1.106), lag 2 0.974 (0.870, 1.090), lag 3

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Villeneuve et al. (2006, 090191) **Period of Study:** Apr 1992-Mar 2002 **Location:** Edmonton, Canada	**Outcome (ICD-9):** Stroke (430-438), including ischemic stroke (434-436), hemorrhagic stroke (430,432), and transient ischemic attacks (TIA) (435). **Age Groups:** 65+ yr **Study Design:** Case-crossover N: 12,422 visits **Statistical Analyses:** Conditional logistic regression **Covariates:** Temperature and relative humidity **Season:** summer (Apr-Sep), winter (Oct-Mar) **Dose-response Investigated:** No **Statistical Package:** SAS (PHREG) **Lags Considered:** 0, 1, and 3 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** All yr: 24.2 (14.8) Summer: 25.9 (16.4) Winter: 22.6 (12.9) **Monitoring Stations:** 3 **Copollutant (correlation):** All yr SO_2: r = 0.19 NO_2: r = 0.34; CO: r = 0.30 O_3-mean: r = 0.07; O_3-max: r = 0.22 $PM_{2.5}$: r = 0.79 Summer SO_2: r = 0.18 NO_2: r = 0.57; CO: r = 0.38 O_3-mean: r = 0.20; O_3-max: r = 0.40 $PM_{2.5}$: r = 0.85 Winter SO_2: r = 0.27 NO_2: r = 0.48; CO: r = 0.53 O_3-mean: r = -0.26; O_3-max: r = -0.09 $PM_{2.5}$: r = 0.70	**PM Increment:** $\mu g/m^3$ (IQR) All yr: 16.0 Summer: 17.5 Winter: 16.0 Adjusted OR Estimate [CI]: Acute ischemic stroke All yr Same-day lag: 0.98 [0.94,1.03] 1-day lag: 1.00 [0.96,1.05] 3-day lag: 0.99 [.93,1.05] summer Same-day lag: 0.93 [0.87,1.00] 1-day lag: 1.01 [0.94,1.08] 3-day lag: 0.96 [0.88,1.04] Winter Same-day lag: 1.04 [0.97,1.11] 1-day lag: 1.00 [0.94,1.06]; 3-day lag: 1.05 [0.95,1.15] Hemorrhagic stroke All yr Same-day lag: 1.01 [0.90,1.12] 1-day lag: 1.03 [0.93,1.15] 3-day lag: 1.13 [0.98,1.30] summer Same-day lag: 1.02 [0.88,1.20] 1-day lag: 1.07 [0.91,1.26] 3-day lag: 1.20 [0.98,1.46] Winter Same-day lag: 1.05 [0.90,1.22] 1-day lag: 1.04 [0.91,1.19] 3-day lag: 1.11 [0.90,1.37] Transient cerebral ischemic attack All yr Same-day lag: 0.96 [0.90,1.02] 1-day lag: 0.99 [0.94,1.05] 3-day lag: 0.94 [0.87,1.01] summer Same-day lag: 0.97 [0.89,1.09] 1-day lag: 0.99 [0.91,1.08] 3-day lag: 0.94 [0.84,1.04] Winter Same-day lag: 0.95 [0.87,1.04] 1-day lag: 0.99 [0.92,1.07] 3-day lag: 0.93 [0.83,1.05] **Notes:** Adjusted ORs are provided for an IQR increase in the 3-day mean in Fig 1-4 for single and two-pollutant models.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: von Klot et al. (2005, 088070) **Period of Study:** 1992-2001 **Location:** Augsburg, Germany Barcelona, Spain Helsinki, Finland Rome, Italy Stockholm, Sweden	**Outcome (ICD-9):** Acute myocardial infarction (410 ICD-10: I21-I22), angina pectoris (411, 413 ICD-10: I20, I24), dysrhythmia (427 ICD-10: I46.0, 46.9, I47-I49, R00.1, R00.8), heart failure (428 ICD-10: 150) **Age Groups:** 35+ yr **Study Design:** Cohort N: 22,006 MI survivors **Statistical Analyses:** GAM, Spearman correlation **Covariates:** Temperature, dew point temp, avg barometric pressure, relative humidity **Season:** NR **Dose-response Investigated:** No **Statistical Package:** R **Lags Considered:** 0-3 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (5th-95th percentile):** Augsburg: 44.7 (16.8-81.4) Barcelona: 52.2 (25.3-89.2) Helsinki: 25.3 (9.5-57.6) Rome: 51.1 (23.3-89.4) Stockholm: 14.6 (6.4-30.0) **Monitoring Stations:** NR **Copollutant (correlation):** Augsburg PNC: r = 0.52 CO: r = 0.57; NO_2: r = 0.64 O_3: r = -0.32 Barcelona PNC: r = 0.29 CO: r = 0.39; NO_2: r = 0.36 O_3: r = -0.14 Helsinki PNC: r = 0.46 CO: r = 0.21; NO_2: r = 0.40 O_3: r = 0.02 Rome PNC: r = 0.33 CO: r = 0.31; NO_2: r = 0.48 O_3: r = -0.22 Stockholm PNC: r = 0.06 CO: r = 0.38; NO_2: r = 0.29 O_3: r = 0.15	**PM Increment:** 10 µg/m^3 Pooled RR Estimate [CI]: All cardiac admissions: 1.021 [1.005,1.048] Myocardial infarction: 1.026 [0.995,1.058] Angina pectoris: 1.008 [0.986,1.032] **Notes:** Rate ratios for 0-3 day lags are provided in graphical form (Fig 1). Same-day levels were significantly associated with cardiac readmissions.
Reference: Wellenius et al. (2005, 087483) **Period of Study:** Jan 1987-Nov 1999 **Location:** Pittsburgh, Pennsylvania	**Outcome (ICD-9):** Congestive heart failure (428.0-428.1) **Age Groups:** 65+ yr **Study Design:** Case-crossover N: 55,019 patients **Statistical Analyses:** Conditional logistic regression, Pearson's pairwise correlation **Covariates:** Temperature, barometric pressure, dew point **Season:** NR **Dose-response Investigated:** No **Statistical Package:** SAS **Lags Considered:** 0-3 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h Mean (5th-95th percentile): 31.06 (8.89-70.49) SD = 20.10 **Monitoring Stations:** 17 **Copollutant (correlation):** CO: r = 0.57 NO_2: r = 0.64 O_3: r = 0.29 SO_2: r = 0.51	**PM Increment:** 24 µg/m^3 (IQR) Percent Increase [CI]: Single-pollutant: 3.07 [1.59,4.57] Adj. for CO: -1.10 [-3.02,0.86] Adj. for NO_2: 0.52 [-1.46,2.53] Adj. for O_3: 2.80 [1.29,4.33] Adj. for SO_2: 2.18 [0.37,4.02] Percent Increase (with 10 µg/m^3 increment) 1.27 [0.66,1.88]

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Wellenius et al. (2005, 088685) **Period of Study:** Jan 1986-Nov 1999 **Location:** Birmingham, Chicago, Cleveland, Detroit, Minneapolis, New Haven, Pittsburgh, Salt Lake City, Seattle	Outcome (ICD-NR): Ischemic stroke and hemorrhagic stroke **Age Groups:** 65+ yr **Study Design:** Case-crossover (time-stratified) N: 115,503 hospital admissions **Statistical Analyses:** Conditional logistic regression **Covariates:** Temperature and humidity **Season:** NR **Dose-response Investigated:** No **Statistical Package:** SAS (v.9) and R-statistical package **Lags Considered:** 0-2 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h Mean (SD): 32.69 (19.75) **Monitoring Stations:** NR (data obtained from the U.S. EPA) **Copollutant (correlation):** CO: r = 0.43 NO_2: r = 0.53 SO_2: r = 0.39 Other variables: Temp: r = 0.22	**PM Increment:** 22.96 µg/m^3 (IQR) Percent Increase [CI]: Ischemic (same-day lag): 1.03 [0.04,2.04] Hemorrhagic: -0.58 [-5.48,4.58] **Notes:** Percent increase in rate for ischemic and hemorrhagic stroke are provided for each city in graphical form (Fig A and B).
Reference: Wellenius et al.,(2006, 088748) **Period of Study:** Jan 1986-Nov 1999 **Location:** Birmingham, Chicago, Cleveland, Detroit, Minneapolis, New Haven, Pittsburgh, Salt Lake City, Seattle	**Outcome (ICD-9):** Congestive heart failure (428) **Age Groups:** 65+ yr **Study Design:** Case-crossover (time-stratified) N: 292,918 admissions **Statistical Analyses:** Conditional logistic regression **Covariates:** Temperature and barometric pressure **Season:** NR **Dose-response Investigated:** No **Statistical Package:** SAS (v.9) and R-statistical package **Lags Considered:** 0-3 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h Median: Overall: 28.3 Birmingham: 33.0 Chicago: 31.5 Cleveland: 34.5 Detroit: 29.5 Minneapolis: 24.0 New Haven: 22. Seattle: 25.8 **Monitoring Stations:** NR (data obtained from the U.S. EPA) Copollutant: NR	**PM Increment:** 10 µg/m^3 Percent Increase [CI]: Same-day lag: 0.72 [0.35,1.10] p-value = 0.0002 **Notes:** City-specific percent increases are graphed in Fig 1 for same-day lag showing a significant association in Chicago, Detroit, Seattle, and the summary values. Percent increase in admission rate s are provided for lag 0-3 days in Fig 2 where same-day lag showed a significant association.
Reference: Yang et al. (2004, 094376) **Period of Study:** 1997-2000 **Location:** Kaohsiung, Taiwan	**Outcome (ICD-9):** Cardiovascular diseases (410-429) **Age Groups:** All **Study Design:** Case-crossover N: 29,661 admissions **Statistical Analyses:** Conditional logistic regression **Covariates:** Temperature and humidity **Season:** NR **Dose-response Investigated:** No **Statistical Package:** SAS **Lags Considered:** Cumulative 0-2 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Median (min-max):** 78.82 (20.50-217.33) **Monitoring Stations:** 6 **Copollutant:** NR	**PM Increment:** 66.33 µg/m^3 (IQR) OR Estimate [CI]: Temp >25ºC: 1.439 [1.316,1.573] Temp <25ºC: 1.568 [1.433,1.715] Adj for SO_2 Temp >25ºC: 1.460 [1.333,1.599] Temp <25ºC: 1.543 [1.404,1.696] Adj for NO_2 Temp >25ºC: 1.306 [1.154,1.478] Temp <25ºC: 0.912 [0.809,1.028] Adj for CO Temp >25ºC: 1.260 [1.144,1.388] Temp <25ºC: 1.259 [1.128,1.406] Adj for O_3 Temp >25ºC: 1.086 [0.967,1.220] Temp <25ºC: 1.703 [1.541,1.883]

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Yang et al. (2008, 157160) **Period of Study:** 1996-2004 **Location:** Taipei, Taiwan	**Outcome (ICD-9):** Congestive heart failure (428) **Age Groups:** All **Study Design:** Case-crossover N: 24,240 CHF hospital admissions **Statistical Analyses:** Conditional logistic regression **Covariates:** temperature, humidity **Season:** All **Dose-response Investigated:** No **Statistical Package:** SAS **Lags Considered:** Cumulative lag 0-2 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (median, range, IQR):** 49.47 (44.71, 14.42-234.91, 33.08-44.71) **Monitoring Stations:** 6 **Copollutant:** NR	**PM Increment:** 27.02 µg/m^3 (IQR) OR [95% CI]: Single pollutant models: >20 °C: 1.15 [1.10-1.21] <20 °C: 0.99 [0.93-1.05] Adjusted for SO_2: ≥ 20 °C: 1.23 [1.17-1.30] <20 °C: 0.96 [0.89-1.03] Adjusted for NO_2: ≥ 20 °C: 1.03 [0.97-1.10] <20 °C: 0.97 [0.90-1.04] Adjusted for CO: ≥ 20 °C: 1.09 [1.03-1.15] <20 °C: 0.96 [0.90-1.03] Adjusted for O_3: ≥ 20 °C: 1.10 [1.04-1.15] <20 °C: 1.00 [0.94-1.05]
Reference: Zanobetti and Schwartz (2002, 034821) **Period of Study:** 1988-1994 **Location:** Cook county (Chicago), Illinois Wayne county (Detroit), Michigan Allegheny county (Pittsburgh), Pennsylvania and King county (Seattle), Washington	**Outcome (ICD-9):** Cardiovascular disease (390-429) with/without diabetes (250) **Age Groups:** 65-74 and 75+ yr with diabetes, 65-74 and 75+ yr without diabetes **Study Design:** Time series N: NR **Statistical Analyses:** GAM, meta-regression **Covariates:** Temperature, prior day's temperature, relative humidity, barometric pressure, day of the week **Season:** NR **Dose-response Investigated:** No	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Median (25-75th percentile):** Chicago: 33 (23-46) Detroit: 32 (21-49) Pittsburgh: 30 (19-47) Seattle: 27 (18-39) **Monitoring Stations:** NR (obtained from USEPA Aerometric Information Retrieval System) **Copollutant:** NR	**PM Increment:** 10 µg/m^3 Percent Change [CI]: All 4 cities <75 (w/ diabetes): 1.6 [1.2,2.0] 75+ (w/ diabetes): 2.0 [1.6,2.4] <75 (w/o diabetes): 0.9 [0.6,1.1] 75+ (w/o diabetes): 1.3 [1.0,1.5] Chicago <75 (w/ diabetes): 1.9 [1.1,2.7] 75+ (w/ diabetes): 2.0 [1.1,3.0] <75 (w/o diabetes): 0.7 [0.2,1.2] 75+ (w/o diabetes): 1.2 [0.8,1.7] Detroit <75 (w/ diabetes): 1.3 [0.5,2.2] 75+ (w/ diabetes): 2.1 [1.0,3.1] <75 (w/o diabetes): 1.2 [0.7,1.7] 75+ (w/o diabetes): 1.2 [0.7,1.6] Pittsburgh <75 (w/ diabetes): 1.8 [0.9,2.7] 75+ (w/ diabetes): 0.9 [-0.2,2.0] <75 (w/o diabetes): 0.6 [0.1,1.2] 75+ (w/o diabetes): 1.6 [1.2,2.1] Seattle <75 (w/ diabetes): 1.9 [0.1,3.7] 75+ (w/ diabetes): 2.7 [0.7,4.8] <75 (w/o diabetes): 0.8 [0.0,1.6] 75+ (w/o diabetes): 0.9 [0.2,1.6] **Notes**: Overall percent increases were also provided for each city, yielding similar results.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Zanobetti and Schwartz (2005, 088069) **Period of Study:** 1985-1999 **Location:** 21 U.S. cities (Birmingham, Alabama Boulder, Colorado Canton, Ohio Chicago, Illinois Cincinnati, Ohio Cleveland, Ohio Colorado Springs, Colorado Detroit, Michigan Honolulu, Hawaii Houston, Texas Minneapolis-St. Paul, Minnesota Nashville, Tennessee New Haven, Connecticut Pittsburgh, Pennsylvania Provo-Orem, Utah Salt Lake City, Utah Seattle, Washington Steubenville, Ohio Youngstown, Ohio)	**Outcome (ICD-9):** Myocardial infarction (410) **Age Groups:** >65 yr **Study Design:** Case-crossover N: 302,453 admissions **Statistical Analyses:** Conditional logistic regression **Covariates:** Temperature **Season:** NR **Dose-response Investigated:** Yes **Statistical Package:** SAS (PROC PHREG) **Lags Considered:** 0-2 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Median:** Ranged from 15.5-34.1Avg across all cities = 27 **Monitoring Stations:** 1+ (data obtained from USEPA's Aerometric Information Retrieval System) Copollutant: NR	**PM Increment:** 10 $\mu g/m^3$ Percent Increase [CI]: MI only: 0.65 [0.3,1] Previous COPD admission: 1.3 [-0.1,2.8] Secondary pneumonia diagnosis: 1.4 [-0.8,3.6] **Notes**: Fig 1 presents percent change in MI per lag day, showing same-day lag to be significant. Fig 2 shows percent change with/without other co-morbidities.

[1]All units expressed in $\mu g/m^3$ unless otherwise specified.

Table E-6. Short-term exposure-cardiovascular-ED/HA - $PM_{10-2.5}$.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Halonen et al. (2009, 180379) **Period of Study:** 1998-2004 **Location:** Helsinki, Finland	**Outcome:** Cardiovascular Hospitalizations & Mortality (ICD 10: I00-99) **Age Groups:** 65+ yr **Study Design:** Time series **N:** NR **Statistical Analyses:** Poisson, GAM **Covariates:** Temperature, humidity, influenza epidemics, high pollen episodes, holidays **Dose-response Investigated?** No **Statistical Package:** R **Lags Considered:** lags 0-3 days; 5-day (0-4) mean	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** Daily **Mean (SD):** NR **Min:** 0.0 **25th percentile:** 4.9 **50th percentile:** 7.5 **75th percentile:** 12.1 **Max:** 101.4 **Monitoring Stations:** NR **Copollutant:** PM<0.03, PM0.03-0.1, PM<0.1, PM<0.10.29, $PM_{2.5}$, CO, NO_2 **Co-pollutant Correlation** PM<0.03: 0.14 PM0.03-0.1: 0.28 PM<0.1: 0.24 PM<0.10.29: 0.20 $PM_{2.5}$: 0.25	**PM Increment:** Interquartile Range **Percent Change (Lower CI, Upper CI):** All Cardiovascular Morality Lag 0: -0.01 (-1.52, 1.53) Lag 1: -0.26 (-1.69, 1.18) Lag 2: -0.61 (-2.03, 0.83) Lag 3: -0.57 (-1.98, 0.85) 5-day mean: -0.70 (-2.56, 1.20) Coronary Heart Disease HA Lag 0: 1.12 (-0.28, 2.55) Lag 1: -0.38 (-1.68, 0.94) Lag 2: 0.01 (-1.33, 1.37) Lag 3: -0.53 (-1.82, 0.78) 5-day mean: 0.23 (-0.29, 0.75) Stroke HA Lag 0: -1.33 (-3.26, 0.63) Lag 1: -1.90 (-3.82, 0.07) ‡ Lag 2: -1.09 (-3.04, 0.89) Lag 3: -0.51 (-2.40, 1.43) 5-day mean: -2.21 (-4.75, 0.39) Arrhythmia HA Lag 0: 0.57 (-1.33, 2.49) Lag 1: -0.65 (-2.55, 1.29) Lag 2: 0.02 (-1.93, 2.00) Lag 3: -1.34 (-3.26, 0.62) 5-day mean: -1.11 (-3.68, 1.53) *p < 0.05, ‡p < 0.10

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Host et al. (2008, 155852)(Host et al., 2008, 155852) **Period of Study:** 2000-2003 **Location:** Six French cities: Le Havre, Lille, Marseille, Paris, Rouen, and Toulouse	**Outcome (ICD-10):** Daily hospitalizations for all cardiovascular (I00-I99), cardiac (I00-I52), and ischemic heart diseases (I20-I25). **Age Groups:** For cardiovascular diseases: All ages, and restricted to ≥ 65 yr **Study Design:** Time series N: NR (Total population of cities: approximately 10 million) **Statistical Analyses:** Poisson regression **Covariates:** Seasons, days of the week, holidays, influenza epidemics, pollen counts, temperature, and temporal trends **Dose-response Investigated:** No **Statistical Package:** MGCV package in R software (R 2.1.1) **Lags Considered:** Avg of 0-1 days	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 24 h **Mean µg/m3 (5th -95th percentile):** Le Havre: 7.3 (2.5-14.0) Lille: 7.9 (2.2-13.7) Marseille: 11.0 (4.5-21.0) Paris: 8.3 (3.2-15.9) Rouen: 7.0 (3.0-12.5) Toulouse: 7.7 (3.0-15.0) **Monitoring Stations:** 13 total: 1 in Toulouse 4 in Paris 2 each in other cities **Copollutant (correlation):** $PM_{2.5}$: Overall: r>0.6 Ranged between r = 0.28 and r = 0.73 across the six cities.	**PM Increment:** 10 µg/m^3 , and an 18.8 µg/m^3 increase (corresponding to an increase in pollutant levels between the lowest of the 5th percentiles and the highest of the 95th percentiles of the cities' distributions) ERR (excess relative risk) Estimate [CI]: For all cardiovascular diseases (10 µg/m^3 increase): All ages: 0.5% [-1.2, 2.3] ≥ 65 yr: 1.0% [-1.0, 3.0] For all cardiovascular diseases (18 µg/m^3 increase): All ages: 1.0% [-2.3, 4.3] ≥ 65 yr: 1.9% [-2.0, 5.9] For cardiac diseases (10 µg/m^3 increase): All ages: 0.1% [-1.9, 2.1] ≥ 65 yr: 1.6% [-0.8, 4.1] For cardiac diseases (18.8 µg/m^3 increase): All ages: 0.1% [-3.6, 4.0] ≥ 65 yr: 3.1% [-1.5, 7.9] For ischemic heart diseases (10 µg/m^3 increase): All ages: 2.8% [-0.8, 6.6] ≥ 65 yr: 6.4% [1.6, 11.4] For ischemic heart diseases (18 µg/m^3 increase): All ages: 5.4% [-1.5, 12.8] ≥ 65 yr: 12.4 [3.1, 22.6]
Reference: Metzger et al. (2004, 044222) **Period of Study:** Aug 1998-Aug 2000 **Location:** Atlanta Metropolitan area (Georgia)	**Outcome (ICD-9):** Emergency visits for ischemic heart disease (410-414), cardiac dysrhythmias (427), cardiac arrest (427.5), congestive heart failure (428), peripheral vascular and cerebrovascular disease (433-437, 440, 443-444, 451-453), atherosclerosis (440), and stroke (436). **Age Groups:** All **Study Design:** Time series N: 4,407,535 emergency department visits between 1993-2000 (data not reported for 1998 - 2000) **Statistical Analyses:** Poisson generalized linear modeling **Covariates:** Day of the wk, hospital entry and exit indicator variables, federally observed holidays, temporal trends, temperature, dew point temperature **Season:** All **Dose-response Investigated:** No **Statistical Package:** SAS **Lags Considered:** 3-day ma; lags 0 -7	**Pollutant:** PM_{10} -2.5 **Averaging Time:** 24 h **Median µg/m3 (10% - 90% range):** 9.1 (4.4, 16.2) **Monitoring Stations:** 1 **Copollutant (correlation):** PM_{10}: r = 0.59 O_3: r = 0.35 NO_2: r = 0.46 CO: r = 0.32 SO_2: r = 0.21 $PM_{2.5}$: r = 0.43 UFP: r = 0.13 $PM_{2.5}$ water soluble metals: r = 0.47 $PM_{2.5}$ sulfates: r = 0.26 $PM_{2.5}$ acidity: r = 0.23 $PM_{2.5}$ OC: r = 0.51 $PM_{2.5}$ EC: r = 0.48 $PM_{2.5}$ oxygenated hydrocarbon: r = 0.31 Other variables: Temperature: r = 0.20 Dew point: r = 0.00	**PM Increment:** 5 µg/m^3 (approximately 1 SD) RR [95% CI]: For 3 day ma: All CVD: 1.012 [0.985, 1.040] Dysrhythmia: 1.021 [0.974, 1.070] Congestive heart failure: 1.020 [0.964-1.079] Ischemic heart disease: 0.994 [0.946-1.045] Peripheral vascular and cerebrovascular disease: 1.022 [0.972-1.074]] Results for Lags 0-7 expressed in figures (see notes). **Notes**: Fig 1: RR (95% CI) for single-day lag models for the association of ER visits for CVD with daily ambient $PM_{10-2.5}$. Summary of Fig 1 results: Positive association at Lag 0.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Peng et al. (2008, 156850) **Period of Study:** Jan 1999-Dec 2005 **Location:** 108 U.S. counties in the following states: Alabama, Arizona, California, Colorado, Connecticut, District of Columbia, Florida, Georgia, Idaho, Illinois, Indiana, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Missouri, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, Tennessee, Texas, Utah, Virginia, Washington, West Virginia, Wisconsin	**Outcome (ICD-9):** Emergency hospitalizations for: Cardiovascular disease, including heart failure (428), heart rhythm disturbances (426-427), cerebrovascular events (430-438), ischemic heart disease (410-414, 429), and peripheral vascular disease (440-448). **Age Groups:** 65 + yr, 65-74, 75+ **Study Design:** Time series N: approximately 12 million Medicare enrollees (3.7 million CVD and 1.4 million RD admissions) **Statistical Analyses:** Two-stage Bayesian hierarchical models: Overdispersed Poisson models for county-specific data. Bayesian hierarchical models to obtain national avg estimate **Covariates:** Day of the wk, age-specific intercept, temperature, dew point temperature, calendar time, indicator for age of 75 yr or older. Some models were adjusted for $PM_{2.5}$. **Dose-response Investigated:** No **Statistical Package:** R version 2.6.2 **Lags Considered:** 0-2 days	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 24 h **Mean µg/m3 (IQR)**: All counties assessed: 9.8 (6.9-15.0) Counties in Eastern U.S.: 9.1 (6.6-13.1) Counties in Western U.S.: 15.4 (10.3-21.8) **Monitoring Stations:** At least 1 pair of co-located monitors (physically located in the same place) for PM_{10} and $PM_{2.5}$ per county **Copollutant (correlation):** $PM_{2.5}$: r = 0.12 PM_{10}: r = 0.75 Other variables: Median within-county correlations between monitors: r = 0.60	**PM Increment:** 10 µg/m^3 Percentage change [95% CI]: CVD: Lag 0 (unadjusted for $PM_{2.5}$): 0.36 [0.05, 0.68] Lag 0 (adjusted for $PM_{2.5}$): 0.25 [-0.11, 0.60] **Notes**: Effect estimates for $PM_{10-2.5}$ (0-2 day lags) are showing in Fig 2-5. Fig 2: Percentage change in emergency hospital admissions for CVD per 10 µg/m^3 increase in PM (single pollutant model and model adjusted for $PM_{2.5}$ concentration) Fig 4: Percentage change in emergency hospital admissions rate for CVD and RD per a 10 µg/m^3 increase in $PM_{10-2.5}$ (0-2 day lags, Eastern vs.. Western USA) Fig 5: County-specific log relative risks of emergency hospital admissions for CVD per 10 µg/m^3 increase in $PM_{10-2.5}$ at Lag 0 (unadjusted for $PM_{2.5}$ and plotted vs.. percentage of urbanicity) No significant associations between $PM_{10-2.5}$ and cause-specific cardiovascular disease.
Reference: Tolbert et al. (2007, 090316) **Period of Study:** Aug 1998-Dec 2004 **Location:** Atlanta Metropolitan area, Georgia	**Outcome (ICD-9):** Combined CVD group, including: Ischemic heart disease (410-414), cardiac dysrhythmias (427), congestive heart failure (428), and peripheral vascular and cardiovascular disease (433-437, 440, 443-445, and 451-453) **Age Groups:** All **Study Design:** Time series N: NR for 1998-2004. For 1993-2004: 10,234,490 ER visits (283,360 visits). **Statistical Analyses:** Poisson generalized linear models **Covariates:** Long-term temporal trends, temperature, dew point, days of week, federal holidays, hospital entry and exit **Season:** All **Dose-response Investigated:** No **Statistical Package:** SAS version 9.1 **Lags Considered:** 3-day ma (lag 0-2)	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 24 h **Mean (µg/m3) (median IQR, range, 10th-90th percentiles):** 9.0 (8.2 5.6-11.5 0.5-50.3 3.6-15.1) **Monitoring Stations:** 1 **Copollutant (correlation):** PM_{10}: r = 0.67 O_3: r = 0.36 NO_2: r = 0.48 CO: r = 0.38SO_2: r = 0.16 $PM_{2.5}$: r = 0.47 $PM_{2.5}$ SO_4: r = 0.32 $PM_{2.5}$ EC: r = 0.49 $PM_{2.5}$ OC: r = 0.49 $PM_{2.5}$ TC: r = 0.51 $PM_{2.5}$ water-sol metals: r = 0.50 OHC: r = 0.41	**PM Increment:** 5.89 µg/m^3 (IQR) Risk ratio [95% CI]: CVD: 1.004 (0.990-1.019)

[1]All units expressed in µg/m^3 unless otherwise specified.

Table E-7. Short-term exposure – cardiovascular: ED/HA $PM_{2.5}$ (including PM components/sources)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Andersen et al. (2008, 189651) **Period of Study:** May 2001-Dec 2004 **Location:** Copenhagen, Denmark	**Outcome (ICD-10):** CVD, including angina pectoris (I20), myocardial infarction (I21-22), other acute ischemic heart diseases (I24), chronic ischaemic heart disease (I25), pulmonary embolism (I26), cardiac arrest (I46), cardiac arrhythmias (I48-48), and heart failure (I50). RD, including chronic bronchitis (J41-42), emphysema (J43), other chronic obstructive pulmonary disease (J44), asthma (J45), and status asthmaticus (J46). Pediatric hospital admissions for asthma (J45) and status asthmaticus (J46). **Age Groups:** > 65 yr (CVD and RD), 5-18 yr (asthma) **Study Design:** Time series **N:** NR **Statistical Analyses:** Poisson GAM **Covariates:** Temperature, dew-point temperature, long-term trend, seasonality, influenza, day of the week, public holidays, school holidays (only for 5-18 yr olds), pollen (only for pediatric asthma outcome) **Season:** NR **Dose-response Investigated:** No **Statistical Package:** R statistical software (gam procedure, mgcv package) **Lags Considered:** Lag 0-5 days, 4-day pollutant avg (lag 0-3) for CVD, 5-day avg (lag 0-4) for RD, and a 6-day avg (lag 0-5) for asthma.	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean µgm^3 (SD):** 10(5) **Median:** 9 **IQR:** 7-12 **99th percentile):** 28 **Monitoring Stations:** 1 **Copollutant (correlation):** NCtot: r = 0.40 NC100: r = 0.29 NCa12: r = 0.07 Nca23: r = -0.25 NCa57: r = 0.51 NCa212: r = 0.82 PM_{10}: r = 0.80 CO: r = 0.46 NO_2: r = 0.42 NO_X: r = 0.40 curbside: r = 0.28 O_3: r = -0.20 Other variables: Temperature: r = -0.01 Relative humidity: r = 0.21	**PM Increment:** 5 µg/m^3 (IQR) Relative risk (RR) Estimate [CI]: CVD hospital admissions (4-day avg, lag 0 - 3), age 65+: One-pollutant model: 1.03 [1.01-1.06] Adj for NCtot: 1.03 [1.01-1.06] RD hospital admissions (5-day avg, lag 0 -4), age 65+: One-pollutant model: 1.00 [0.95-1.00] Adj for NCtot: 1.00 [0.95-1.06] Asthma hospital admissions (6-day avg lag 0-5), age 5 - 18: One-pollutant model: 1.15 [1.00-1.32] Adj for NCtot: 1.13 [0.98-1.32] Estimates for individual day lags reported only in Fig form (see notes): **Notes**: Fig 2: Relative risks and 95% confidence intervals per IQR in single day concentration (0-5 day lag). Summary: CVD: Marginally significant association at Lag 0. RD: No statistically or marginally significant associations. Positive associations at Lag 4-5.Asthma: Wide confidence intervals make interpretation difficult. Positive associations at Lag 1, 2, 3.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ballester et al. (2006, 088746) **Period of Study:** 1995-1999 **Location:** 6 Spanish cities: Barcelona, Bilbao, Pamplona, Valencia, Vigo, Zaragoza	**Outcome (ICD-9):** The number of daily emergency admissions with primary diagnosis for all cardiovascular disease (390-459) and heart diseases (410-414, 427, 428) **Age Groups:** All ages **Study Design:** Time series **N:** NR **Statistical Analyses:** Poisson GAMs **Covariates: D**aily temperature, barometric pressure, and relative humidity Daily influenza incidence, day of the week, holidays, unusual events (ex. medical strikes), seasonal variation, trend of the series **Season:** NR **Dose-response Investigated:** No **Statistical Package:** S-Plus GAM function **Lags Considered:** 0-3 days, 0- to 1-day avg	**Pollutant:** Black smoke (BS) **Averaging Time:** 24 h **Mean µg/m3 (10-90th percentile):** Overall mean NR. City specific means Barcelona: 35.0 (19.4, 53.0) Bilbao: 18.5 (8.8, 31.0) Pamplona: 7.4 (2.3, 13.0) Valencia: 40.3 (20.3, 66.4) Vigo: 79.4 (43.9, 122.3) Zaragoza: 40.4 (23.8, 61.3) **Monitoring Stations:** NR (at least 3 stations per city) **Copollutant (correlation):** Summary of the correlation coefficients between each pair of pollutants within cities: PM_{10}: r = 0.48 TSP: from r = 0.16 to r = 0.69 (median r = 0.43) NO_2: from r = 0.23 to r = 0.69 (median r = 0.48) SO_2: from r = 0.09 to r = 0.59 (median r = 0.24) CO: from r = 0.62 to r = 0.69 (median r = 0.69) O_3: from r = -0.43 to r = -0.06 (median r = -0.16)	**PM Increment:** 10 µg/m^3 Relative risk [CI]: Relative risks are expressed only in the form of figures (see notes). Percentage change in risk [CI]: All cardiovascular diseases (avg of lags 0 - 1) 0.24% [-0.18, 0.67] Heart disease (avg of lags 0 -1) 0.71% [0.13, 1.29] **Notes**: Relative risks for the single pollutant models are expressed in Fig 2. Fig 2: Time sequence of the combined association between BS and hospital admissions for all CVD (A) and heart disease (B). Summary: Significant, positive association of TSP with both overall CVD and heart disease hospitalizations at Lag 0. Relative risks for 2 pollutant models are expressed in Fig 3: Combined estimates of the association between hospital admissions for heart diseases and air pollutants (avg of lags 0-1 Adjusted for CO, NO_2, O_3, or SO_2). Summary: Significant, positive association remains after adjusting for NO_2, O_3, and SO_2. Association remains positive but becomes marginally significant after adjusting for CO.
Reference: Ballester et al. (2006, 088746) **Period of Study:** 1993-1999 **Location:** 7 Spanish cities: Barcelona, Bilbao, Cartagena, Castellon, Gijon, Oviedo, Valencia	**Outcome (ICD-9):** The number of daily emergency admissions with primary diagnosis for all cardiovascular disease (390-459) and heart diseases (410-414, 427, 428) **Age Groups:** All ages **Study Design:** Time series **N:** NR **Statistical Analyses:** Poisson GAMs **Covariates:** Daily temperature, barometric pressure, and relative humidity Daily influenza incidence, day of the week, holidays, unusual events (ex. medical strikes), seasonal variation, trend of the series **Season:** NR **Dose-response Investigated:** No **Statistical Package:** S-Plus GAM function **Lags Considered:** 0-3 days, 0- to 1-day avg	**Pollutant:** TSP **Averaging Time:** 24 h **Mean µg/m3 (10-90th percentile):** Overall mean NR. City specific means Barcelona: 51.8 (29.4, 78.8) Bilbao: 58.3 (30.3, 92.3) Cartagena: 54.9 (32.5, 79.9) Castellon: 60.4 (32.0, 92.1) Gijon: 77.4 (47.4, 118.3) Oviedo: 76.0 (48.3, 111.8) Valencia: 61.0 (44.1, 80.7) **Monitoring Stations:** NR (at least three stations per city) **Copollutant (correlation):** Summary of the correlation coefficients between each pair of pollutants within cities: BS: from r = 0.16 to r = 0.69 (median r = 0.43) PM_{10}: NA NO_2: from r = -0.13 to r = 0.65 (median r = 0.48) SO_2: from r = 0.06 to r = 0.69 (median r = 0.31) CO: from r = 0.06 to r = 0.59 (median r = 0.47) O_3: from r = -0.27 to r = 0.07 (median r = -0.03)	**PM Increment:** 10 µg/m^3 Relative risk [CI]: Relative risks are expressed only in the form of figures (see notes). Percentage change in risk [CI]: All cardiovascular diseases: 0.07% [-0.23, 0.36] Heart disease 0.45% [0.04, 0.86] **Notes**: Relative risks for the single pollutant models are expressed in Fig 2. Fig 2: Time sequence of the combined association between TSP and hospital admissions for all CVD (A) and heart disease (B). Summary of results: Positive, marginally significant association of TSP with overall CVD at Lag 0. Positive, statistically significant relation between TSP and heart disease hospitalizations at Lag 0. Relative risks for 2 pollutant models are expressed in Fig 3: Fig 3: Combined estimates of the association between hospital admissions for heart diseases and air pollutants (avg of lags 0-1 adjusted for CO, NO_2, O_3, or SO_2). Summary of results: Small positive significant or marginally significant associations between TSP and general CVD and heart disease hospitalizations remain constant after adjustment for CO, NO_2, O_3, or SO_2.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Bell et al. (2008, 091268) **Period of Study:** 1995-2002 **Location:** Taipei, Taiwan	**Outcome (ICD-9):** Hospital admissions for ischemic heart disease (410, 411, 414), cerebrovascular disease (430-437), asthma (493), and pneumonia (486). **Age Groups:** All **Study Design:** Time series **N**: 6,909 hospital admissions for ischaemic heart diseases, 11,466 for cerebrovascular disease, 19,966 for pneumonia, and 10,231 for asthma **Statistical Analyses:** Poisson regression **Covariates:** Day of the week, time, apparent temperature, long-term trends, seasonality **Season:** All **Dose-response Investigated:** No **Statistical Package:** NR **Lags Considered:** lags 0-3 days, mean of lags 0-3	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean µg/m3 (range IQR)**: 31.6 (0.50-355.0 20.2) **Monitoring Stations:** 2 **Copollutant (correlation):** NR	**PM Increment:** 20 µg/m^3 (near IQR) Percentage increase estimate [95% CI]: Ischemic heart disease: L0: 3.48 (-0.39, 7.51) L1: 3.55 (-0.30, 7.56) L2: 3.32 (-0.50, 7.29) L3: 2.80 (-1.04, 6.79) L03: 8.38 (2.28, 14.84) Cerebrovascular disease: L0: -2.22 (-50.2, 0.67) L1: -1.30 (-4.08, 1.55) L2: 0.24 (-2.49, 3.040 L3: 1.21 (-1.41, 3.90) L03: -1.45 (-5.58, 2.87) Asthma: L0: 0.46 (-2.41, 3.42) L1: -1.36 (-4.33, 1.71) L2: -0.83 (-3.67, 2.10) L3: -0.78 (-3.63, 2.16) L03: -1.75 (-6.21, 2.92) Pneumonia: L0: 0.06 (-2.74, 2.94) L1: 0.34 (-2.446, 3.20) L2: -0.59 (-3.38, 2.29) L3: -0.44 (-3.22, 2.41) L03: -0.61 (-4.87, 3.85)
Reference: Bell et al. (2008, 091268) **Period of Study:** 1999-2005 **Location:** 202 U.S. counties	**Outcome (ICD-9):** Heart failure (428), heart rhythm disturbances (426-427), cerebrovascular events (430-438), ischemic heart disease (410-414, 429), peripheral vascular disease (440-449), COPD (490-492), respiratory tract infections (464 - 466, 480 - 487) **Age Groups:** 65+ **Study Design:** Time series **N:** NR **Statistical Analyses:** Two-stage Bayesian hierarchical model to find national avg First stage: Poisson regression (county-specific) **Covariates:** Day of the week, temperature, dew point temperature, temporal trends, indicator for persons 75+ yr, population size **Season:** All, Jun-Aug (Summer), Sep-Nov (Fall), Dec-Feb (Winter), Mar-May (Spring) **Dose-response Investigated:** No **Statistical Package:** NR **Lags Considered:** 0- to 2-day lags	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (µg/m3):** Descriptive information presented in Fig S2 (boxplots): **IQR:** 8.7 µg/m^3 **Monitoring Stations:** NR **Copollutant (correlation):** NR	**PM Increment:** 10 µg/m^3 **Percent increase [95% PI]:** **Cardiovascular admissions:** Lag 0 (all seasons): 0.80 [0.59-1.01] Lag 0 (winter, national): 1.49 [1.09-1.89] Lag 0 (winter, northeast): 2.01 [1.39-2.63] Lag 0 (winter, southeast): 1.06 [-0.07-2.21] Lag 0 (winter, northwest): 0.85 [-4.11-6.07] Lag 0 (winter, southwest): 0.76 [-0.25-1.79] Lag 0 (spring, national): 0.91 [0.47-1.35] Lag 0 (spring, northeast) 0.95 [0.32-1.58] Lag 0 (spring, southeast): 0.75 [-0.26-1.78] Lag 0 (spring, northwest): -0.07 [-12.40-13.98] Lag 0 (spring, southwest): 1.78 [-0.87-4.51] Lag 0 (summer, national): 0.18 [-0.23-0.58] Lag 0 (summer, northeast): 0.55 [0.08-1.02] Lag 0 (summer, southeast): -0.67 [-1.60-0.26] Lag 0 (summer, northwest): -1.55 [-15.22-14.31] Lag 0 (summer, southwest): -1.20 [-4.90-2.65] Lag 0 (fall, national): 0.68 [0.29-1.07] Lag 0 (fall, northeast): 1.03 [0.48-1.58] Lag 0 (fall, southeast): 0.17 [-0.72-1.07] Lag 0 (fall, northwest): -0.67 [-6.96-6.05] Lag 0 (fall, southwest): 0.30 [-0.98-1.59] Lag 1 (all seasons): 0.07 [-0.12-0.26] Lag 1 (winter): 0.56 [0.16-0.96] Lag 1 (spring): -0.10 [-0.58-0.39] Lag 1 (summer): -0.16 [-0.54-0.22] Lag 1 (fall): 0.04 [-0.28-0.35] Lag2 (all seasons): [0.06 [-0.12-0.23] Lag 2 (winter): 0.27 [-0.12-0.65] Lag 2 (spring): 0.19 [-0.23-0.60]

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Lag 2 (summer): -0.12 [-0.50-0.26] Lag 2 (fall): 0.02 [-0.30-0.34] **Respiratory admissions:** Lag 0 (all seasons): 0.22 [-0.12-0.56] Lag 0 (winter, national): 1.05 [0.29-1.82] Lag 0 (winter, northeast): 1.76 [0.60-2.93] Lag 0 (winter, southeast): 0.59 [-1.35-2.58] Lag 0 (winter, northwest): -0.07 [-6.74-7.08] Lag 0 (winter, southwest): 0.03 [-1.25-1.34] Lag 0 (spring, national): 0.31 [-0.47-1.11] Lag 0 (spring, northeast): 0.34 [-0.66-1.34] Lag 0 (spring, southeast): -0.06 [-1.77-1.68] Lag 0 (spring, northwest): -8.52 [-25.62-12.51] Lag 0 (spring, southwest): 1.87 [-2.00-5.90] Lag 0 (summer, national): -0.62 [-1.33-0.09] Lag 0 (summer, northeast): -0.8 [-1.65-0.07] Lag 0 (summer, southeast): -0.15 [-1.88-1.61] Lag 0 (summer, northwest): 0.25 [-21.46-27.96] Lag 0 (summer, southwest): 0.64 [-5.38-7.04] Lag 0 (fall, national): 0.02 [-0.63-0.67] Lag 0 (fall, northeast): -0.01 [-0.87-0.85] Lag 0 (fall, southeast): -0.58 [-2.06-0.91] Lag 0 (fall, northwest): -1.38 [-11.84-10.32] Lag 0 (fall, southwest): 1.77 [-0.73-4.33] Lag 1 (all seasons): 0.05 [-0.29-0.39] Lag 1 (winter): 0.50 [-0.27-1.27] Lag 1 (spring): -0.24 [-1.01-0.53] Lag 1 (summer): 0.28 [-0.39-0.95] Lag 1 (fall): 0.15 [-0.49-0.79 Lag 2 (all seasons): 0.41 [0.09-0.74] Lag 2 (winter, national): 0.72 [0.01-1.43] Lag 2 (winter, northeast): 0.79 [-0.21-1.80] Lag 2 (winter, southeast): 0.4 [-1.45, 2.27] Lag 2 (winter, northwest): -0.06 [-6.52-6.85] Lag 2 (winter, southwest): 1.2 [-0.10-2.52] Lag 2 (spring, national): 0.35 [-0.29-0.99] Lag 2 (spring, northeast): 0.04 [-0.88-0.97] Lag 2 (spring, southeast): 0.75 [-0.82-2.34] Lag 2 (spring, northwest): 2.29 [-14.26-22.03] Lag 2 (spring, southwest): 1.05 [-2.18-4.39] Lag 2 (summer, national): 0.57 [-0.07-1.23] Lag 2 (summer, northeast): 0.77 [-0.01-1.56] Lag 2 (summer, southeast): -0.52 [-2.07-1.06] Lag 2 (summer, northwest): 0.74 [-18.73-24.86] Lag 2 (summer, southwest): 2.41 [-2.61-7.69] Lag 2 (fall, national): 0.39 [-0.22-1.01] Lag 2 (fall, northeast): 0.12 [-0.82-1.07] Lag 2 (fall, southeast): 0.14 [-1.29-1.59]

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Lag 2 (fall, northwest): -0.74 [-10.08-9.58] Lag 2 (fall, southwest): 0.97[-1.36-3.36]
Reference: Bell et al. (2009, 191007) **Period of Study:** 1999-2005 **Location:** 168 U.S. Counties	**Outcome:** CVD hospital admissions **Study Design:** Retrospective Cohort **Covariates:** Socio-economic conditions, long term temperature **Statistical Analysis:** Bayesian hierarchical model **Age Groups:** ≥ 65 yr	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD) Unit:** NR **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** 20% of the population acquiring air conditioning **Percent Change (95% CI) in community-specific PM health effect estimates for CVD hospital admissions** Any AC, including window units Yearly health effect: -4.3 (-72.7 to 4.2) Summer health effect: -148 (-327 to 31.1) Winter health effect: -80.0 (-182 to 22.0) Central AC Yearly health effect: -42.5(-63.4-21.6) Summer health effect: -79.5 (-143 to 15.7) Winter health effect: -41.9 (-124 to 40.0)
Reference: Bell et al. (2009, 191997) **Period of Study:** 1999-2005 **Location:** U.S.	**Outcome:** Cardiovascular HA **Age Groups:** 65+ **Study Design:** time series **N:** NR **Statistical Analyses:** Bayesian Hierarchical Regression **Covariates:** time trend, day of week, seasonality, dew point, temperature **Statistical Package:** NR **Lags Considered:** 0-2	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily **Mean:** EC: 0.715 Ni: 0.002 V: 0.003 **Min:** EC: 0.309 Ni: 0.003 V: 0.001 **Max:** EC: 1.73 Ni: 0.021 V: 0.010 **Interquartile Range:** EC: 0.245 Ni: 0.001 V: 0.001 **Interquartile Range of Percents:** EC: 1.7 Ni: 0.01 V: 0.01 **Monitoring Stations:** NR **Copollutant:** Al, NH4+, As, Ca, Cl, Cu, EC, OMC, Fe, Pb, Mg. Ni, NO_3-, K, Si, Na+, SO_4=, Ti, V, Zn **Co-pollutant Correlation:** Ni, V: 0.48 V, EC: 0.33 Ni, EC: 0.30 **Note:** Pollutant concentrations available for all fractions of $PM_{2.5}$	**PM Increment:** Interquartile Range in the fraction of $PM_{2.5}$ **Percent Increase in PM Health Effect (Lower CI, Upper CI), lag** EC: 25.8 (4.4, 47.2), lag 0 EC + Ni: 14.0 (-7.6, 35.5), lag 0 EC + V: 14.9 (-7.8, 37.6), lag 0 EC+ V, HS education: 15.0 (3.3, 26.8), lag 0 EC+ V, median income: 15.8 (4.1, 27.5), lag 0 EC+ V, racial composition: 14.2 (2.8, 25.6), lag 0 EC+ V, percent living in urban area: 14.7 (3.1, 26.3), lag 0 EC+ V, population: 13.6 (2.2, 25.0), lag 0 EC + Ni, V: 11.9 (-10.4, 43.2), lag 0 Ni: 19.0 (9.9, 28.2), lag 0 Ni + EC: 17.3 (7.7, 26.9), lag 0 Ni + V: 15.5 (4.1, 26.9), lag 0 Ni + EC, V: 14.9 (3.4, 26.4), lag 0 V: 27.5 (10.6, 44.4), lag 0 V + EC: 23.1 (4.9, 41.4), lag 0 V+ Ni: 10.9 (-9.6, 31.5), lag 0 V + EC, Ni: 8.1 (-13.3, 29.5), lag 0 EC: 11.8 (-69.2, 92.8), lag 1 EC: 21.0 (-46.6, 88.6), lag 2 Ni: 20.6 (-15.5, 56.7), lag 1 Ni: -2.3 (-32.5, 27.9), lag 2 V: 34.0 (-31.2, 99.1), lag 1 V: 8.0 (-46.8, 62.7), lag 2 Percent HS education: -17.4 (-46.8, 11.9), lag 0 Median income: 21.3 (-20.0, 62.5), lag 0 Percent black: 26.9 (-15.8, 69.6), lag 0 Percent living in urban area: 34.4 (-29.0, 97.8), lag0 Population: -4.3 (-13.3, 4.8), lag 0 **Notes:** Interquartile ranges in percent HS education, median income, percent black, percent living in urban area, and population are 5.2 %, $9,223, 17.3%, 11.0%, and 549,283 respectively.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Chan et al. (2007, 147787) **Period of Study:** Apr 1997-Dec 2002 **Location:** Boston, MA	**Outcome:** Cerebrovascular Emergency Admissions **Age Groups:** 50+ yr **Study Design:** Time series **Statistical Analyses:** GAM Poisosn Regression **Covariates:** Yr, mo, day of wk, temperature, dew point **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 0-3 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** 31.5 (16.0) **Min:** 15.6 **Max:** 200.6 **IQR:** 19.7 **Monitoring Stations:** 16 **Copollutant:** O_3, CO, SO_2, NO_2, PM_{10} **Co-pollutant Correlation** O_3: 0.33 CO: 0.44 SO_2: 0.51 NO_2: 0.50 PM_{10}: 0.61	**PM Increment:** Interquartile Range (19.7 µg/m^3) **Percent Change (Lower CI, Upper CI), p-value:** Cerebrovascular Disease Lag 0: 1.006 (0.993, 1.019) Lag 1: 1.002 (0.990, 1.014) Lag 2: 1.015 (0.978, 1.052) Lag 3: 1.021 (1.005, 1.037) Lag 3 + O_3: 1.009 (0.987, 1.031) Lag 3 + CO: 1.014 (0.993, 1.035) Lag 3 + O_3 + CO: 1.009 (0.987, 1.031) Stroke Lag 0: 0.931 (0.831, 1.031) Lag 1: 0.936 (0.845, 1.027) Lag 2: 0.931 (0.820, 1.042) Lag 3: 0.991 (0.969, 1.013) Ischaemic stroke Lag 0: 0.981 (0.907, 1.055) Lag 1: 0.994 (0.920, 1.078) Lag 2: 0.960 (0.885, 1.035) Lag 3: 1.059 (0.984, 1.134) Haemorrhagic stroke Lag 0: 0.870 (0.740, 1.010) Lag 1: 0.882 (0.761, 1.003) Lag 2: 0.909 (0.810, 1.008) Lag 3: 0.921 (0.830, 1.012)
Reference: Chan et al. (2008, 093297) **Period of Study:** 1995-2002 **Location:** Taipei Metropolitan area, Taiwan	**Outcome (ICD-9):** Emergency visits for ischaemic heart diseases (410-411, 414), cerebrovascular diseases (430-437), and COPD (493, 496) **Age Groups:** All **Study Design:** Time series **N:** NR **Statistical Analyses:** Poisson regression **Covariates:** Yr, mo, day of wk, temperature, dewpoint temperature, PM_{10}, NO_2 **Season:** All **Dose-response Investigated:** No **Statistical Package:** SAS version 8.0 **Lags Considered:** 0- to 7-day lags	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean µg/m3 (SD):** NR **Monitoring Stations:** 1 **Copollutant (correlation):** NR	**PM Increment:** 19.7 µg/m^3 (IQR) OR [95% CI]: In environmental conditions without dust storms (results only given for best-fitting model) Lag 6 days: 1.024 (1.004, 1.044)
Reference: Delfino et al, (2008, 156390) **Period of Study:** October 2001−2003−November 2003 **Location:** Southern California	**Outcome:** Cardiovascular hospital admissions **Study Design:** Time series **Statistical Analysis:** Poisson regression with GEE **Age Groups:** All	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Hourly **Mean (SD) Unit by county:** Los Angeles Before Fires: 27.2 (12.4) µg/m^3 During Fires: 54.1 (21.0) µg/m^3 After Fires: 15.9 (5.5) µg/m^3 Orange Before Fires: 23.2 (9.6) µg/m^3 During Fires: 64.3 (26.5) µg/m^3 After Fires: 15.5 (10.2) µg/m^3 Riverside Before Fires: 32.7 (14.7) µg/m^3 During Fires: 42.1 (25.5) µg/m^3 After Fires: 16.9 (10.2) µg/m^3 San Bernadino Before Fires: 35.7 (16.6) µg/m^3 During Fires: 45.3 (28.7) µg/m^3 After Fires: 18.5 (8.3) µg/m^3 San Diego Before Fires: 18.5 (6.7) µg/m^3	**Increment:** 10 µg/m^3 **Relative Rate (Min CI, Max CI)** All Cardiovascular All Periods: 0.996 (0.989-1.003) Pre-Wildfire: 0.992 (0.976-1.009) Wildfire: 1.008 (0.999-1.018), p = 0.104 Post-Wildfire: 0.991 (0.964-1.019), p = 0.955 Ischaemic Heart Disease All Periods: 0.991 (0.980-1.003) Pre-Wildfire: 0.990 (0.963-1.017) Wildfire: 0.117 (0.990-1.024), p = 0.313 Post-Wildfire: 0.989 (0.950-1.030), p = 0.976 Congestive Heart Failure All Periods: 0.989 (0.974-1.004) Pre-Wildfire: 0.978 (0.942-1.015) Wildfire: 1.016 (0.933-1.039), p = 0.096 Post-Wildfire: 0.969 (0.914-1.027), p = 0.791

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
		During Fires: 76.1 (66.6) µg/m^3 After Fires: 14.2 (7.2) µg/m^3 Ventura Before Fires: 18.4 (8.3) µg/m^3 During Fires: 50.1 (50.5) µg/m^3 After Fires: 12.9 (4.3) µg/m^3 **Copollutant (correlation):** NR	Cardiac Dysrhythmia All Periods: 0.980 (0.962-0.998) Pre-Wildfire: 0.979 (0.935-1.025) Wildfire: 0.989 (0.961-1.017), p = 0.721 Post-Wildfire: 0.976 (0.912-1.044), p = 0.934 Cerebrovascular Disease and Stroke All Periods: 1.019 (1.004-1.035) Pre-Wildfire: 1.015 (0.980-1.052) Wildfire: 1.016 (0.997-1.036), p = 0.971 Post-Wildfire: 1.044 (0.987-1.104), p = 0.379 **Relative Rate (Min CI, Max CI) in relation to pre-wildfire period (1)** All Cardiovascular: Wildfire, unadjusted for $PM_{2.5}$: 0.958 (0.920-0.997) Wildfire, adjusted for $PM_{2.5}$: 0.947 (0.902-0.994) Post-wildfire, unadjusted for $PM_{2.5}$: 1.061 (1.006-1.119) Post-wildfire, adjusted for $PM_{2.5}$: 1.053 (0.994-1.114) Ischaemic Heart Disease: Wildfire, unadjusted for $PM_{2.5}$: 0.913 (0.852-0.978) Wildfire, adjusted for $PM_{2.5}$: 0.905 (0.832-0.985) Post-wildfire, unadjusted for $PM_{2.5}$: 1.029 (0.943-1.123) Post-wildfire, adjusted for $PM_{2.5}$: 1.029 (0.936-1.131) Congestive Heart Failure: Wildfire, unadjusted for $PM_{2.5}$: 0.981 (0.817-0.972) Wildfire, adjusted for $PM_{2.5}$: 0.911 (0.819-1.014) Post-wildfire, unadjusted for $PM_{2.5}$: 1.113 (0.997-1.242) Post-wildfire, adjusted for $PM_{2.5}$: 1.105 (0.982-1.244) Cardiac Dysrhythmia: Wildfire, unadjusted for $PM_{2.5}$: 0.968 (0.874-1.072) Wildfire, adjusted for $PM_{2.5}$: 0.964 (0.851-1.093) Post-wildfire, unadjusted for $PM_{2.5}$: 1.089 (0.949-1.251) Post-wildfire, adjusted for $PM_{2.5}$: 1.057 (0.914-1.223) Cerebrovascular Disease and Stroke: Wildfire, unadjusted for $PM_{2.5}$: 1.066 (0.981-1.159) Wildfire, adjusted for $PM_{2.5}$: 1.017 (0.922-1.123) Post-wildfire, unadjusted for $PM_{2.5}$: 1.013 (0.907-1.132) Post-wildfire, adjusted for $PM_{2.5}$: 1.013 (0.902-1.138)
Reference: Dominici et al. (2006, 088398) **Period of Study:** 1999-2002 **Location:** 204 U.S. counties, located in: Alabama, Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, District of Columbia, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, Tennessee, Texas,	**Outcome** (ICD-9): Daily counts of hospital admissions for primary diagnosis of heart failure (428), heart rhythm disturbances (426-427), cerebrovascular events (430-438), ischemic heart disease (410-414, 429), peripheral vascular disease (440-448), chronic obstructive pulmonary disease (490-492), and respiratory tract infections (464-466, 480-487). **Age Groups:** >65 yr **Study Design:** Time series N: 11.5 million Medicare enrollees **Statistical Analyses:** Bayesian 2-stage	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h Mean (µg/m^3) (IQR): 13.4 (11.3-15.2) **Monitoring Stations:** NR **Copollutant (correlation):** NR Other variables: Median of pairwise correlations among $PM_{2.5}$ monitors within the same county for 2000: r = 0.91 (IQR: 0.81-0.95)	**PM Increment:** 10 µg/m^3 (Results in figures; see notes) Percent increase in risk [95% PI]: Cerebrovascular disease (Lag 0): Age 65+: 0.81 [0.30, 1.32] Age 65-74: 0.91 [0.01, 1.82] Age 75+: 0.80 [0.21, 1.38] Peripheral vascular disease (Lag 0): Age 65+: 0.86 [-0.06, 1.79] Age 65-74: 1.21 [-0.26, 2.67] Age 75+: 0.86 [-0.39, 2.11] Ischemic heart disease (Lag 2): Age 65+: 0.44 [0.02, 0.86] Age 65-74: 0.37 [-0.22, 0.96] Age 75+: 0.52 [-0.01, 1.04]

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Utah, Virginia, Washington, West Virginia, Wisconsin	hierarchical models. First stage: Poisson regression (county-specific) Second stage: Bayesian hierarchical models, to produce a national avg estimate **Covariates:** Day of the week, seasonality, temperature, dew point temperature, long-term trends **Season:** NR **Dose-response Investigated**: No **Statistical Package:** R statistical software version 2.2.0 **Lags Considered:** 0-2 days, avg of days 0-2		Heart rhythm disturbances (Lag 0): Age 65+: 0.57 [-0.01, 1.15] Age 65-74: 0.46 [-0.63, 1.54] Age 75+: 0.72 [0.02, 1.42] Heart failure (Lag 0): Age 65+: 1.28 [0.78, 1.78] Age 65-74: 1.21 [0.35, 2.07] Age 75+: 1.36 [0.78, 1.94] COPD (Lag 0): Age 65 +: 0.91 [0.91, 1.64] Age 65-74: 0.42 [-0.64, 1.48] Age 75+: 1.47 [0.54, 2.40] Respiratory tract infection: Age 65+: 0.92 [0.41, 1.43] Age 65-74: 0.93 [0.04, 1.82] Age 75+: 0.92 [0.32, 1.53] Annual reduction in admissions attributable to a 10 μg/m^3 reduction in daily $PM_{2.5}$ level (95% PI): Cerebrovascular disease: Annual number of admissions: 226,641 Annual reduction in admissions: 1836 [680, 2992] Peripheral vascular disease: Annual number of admissions: 70,061 Annual reduction in admissions: 602 [-42, 1254] Ischemic heart disease: Annual number of admissions: 346,082 Annual reduction in admissions: 1523 [69, 2976] Heart rhythm disturbances: Annual number of admissions: 169,627 Annual reduction in admissions: 967 [-17, 1951] Heart failure: Annual number of admissions: 246,598 Annual reduction in admissions: 3156 [1923, 4389] COPD: Annual number of admissions: 108,812 Annual reduction in admissions: 990 [196, 1785] Respiratory tract infections: Annual number of admissions: 226,620 Annual reduction in admissions: 2085 [929, 3241] **Notes**: Fig 2: Point estimates and 95% posterior intervals of the % change in admissions rates per 10 μg/m^3 (national avg relative rates) for single lag (0, 1, and 2 days) and distributed lag models for 0 to 2 days (total) for all outcomes. Summary: Positive significant or marginally significant associations between $PM_{2.5}$ and cerebrovascular disease at Lag 0 Peripheral vascular disease at Lags 0 and 2 Ischemic heart disease at Lag 2 Heart rhythm disturbances at Lag 0

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Heart failure at Lag 0, Lag 2, and Lags 0 -2 COPD at Lag 0, Lag 1, and Lags 0-2 and respiratory tract infections at Lag 2 and Lags 0-2. Fig 3: Point estimates and 95% posterior intervals of the % change in admission rates per 10 μg/m^3 (regional relative rates). Summary: For cardiovascular diseases, all estimates in the Midwestern, Northeastern, and Southern regions were positive, while estimates in the other regions (South, West, Central, Northwest) were close to 0. For respiratory disease, there were larger effects in the Central, Southeastern, Southern, and Western regions than in the other regions. Fig 4: Point estimates and 95% posterior intervals of the % change in admission per 10 μg/m^3 (Eastern vs.. Western regions): Summary: All estimates for cardiovascular outcomes were positive in the U.S. Eastern region but not in the U.S. Western region. The estimates for respiratory tract infections were larger in the Western region than in the Eastern region. The estimates for CCPD were positive in the both regions.
Reference: Halonen et al. (2009, 180379) **Period of Study:** 1998-2004 **Location:** Helsinki, Finland	**Outcome:** Cardiovascular Hospitalizations & Mortality (ICD 10: I00-99) **Age Groups:** 65+ yr **Study Design:** Time series **N:** NR **Statistical Analyses:** Poisson, GAM **Covariates:** Temperature, humidity, influenza epidemics, high pollen episodes, holidays **Dose-response Investigated?** No **Statistical Package:** R **Lags Considered:** lags 0-3 days; 5-day (0-4) mean	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily **Mean (SD):** NR **Min:** 1.1 **25th percentile:** 5.5 **50th percentile:** 9.5 **75th percentile:** 11.7 **Max:** 69.5 **Monitoring Stations:** NR **Copollutant:** PM<0.03, PM0.03-0.1, PM<0.1, PM<0.10.29, $PM_{10-2.5}$, CO, NO_2 **Co-pollutant Correlation** PM<0.03: 0.14 PM0.03-0.1: 0.48 PM<0.1: 0.35 PM<0.10.29: 0.88 $PM_{10-2.5}$: 0.25	**PM Increment:** Interquartile Range **Percent Change (Lower CI, Upper CI):** All Cardiovascular Morality Lag 0: 0.73 (-0.66, 2.13) Lag 1: 0.74 (-0.63, 2.13) Lag 2: 0.74 (-0.62, 2.11) Lag 3: 0.06 (-1.29, 1.43) 5-day mean: 0.87 (-0.94, 2.70) Coronary Heart Disease HA Lag 0: -0.17 (-1.5.0, 1.18) Lag 1: -0.03 (-1.31, 1.26) Lag 2: -0.63 (-1.87, 0.62) Lag 3: 0.48 (-0.78, 1.76) 5-day mean: 0.80 (-0.94, 2.58) Stroke HA Lag 0: -0.99 (-2.78, 0.84) Lag 1: 0.02 (-1.74, 1.82) Lag 2: -1.38 (-3.13, 0.40) Lag 3: -0.17 (-1.92, 1.61) 5-day mean: -0.78 (-3.10, 1.60) Arrhythmia HA Lag 0: 0.82 (-1.03, 2.68) Lag 1: 0.18 (-1.58, 1.97) Lag 2: -0.09 (-1.82, 1.67) Lag 3: -0.48 (-2.22, 1.29) 5-day mean: 0.16 (-2.16, 2.54) *p < 0.05, ‡p < 0.10

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Host et al. (2008, 155852) **Period of Study:** 2000-2003 **Location:** Six French cities: Le Havre, Lille, Marseille, Paris, Rouen, and Toulouse	**Outcome (ICD-10):** Daily hospitalizations for all cardiovascular (I00-I99), cardiac (I00-I52), and ischemic heart diseases (I20-I25), all respiratory diseases (J00-J99), respiratory infections (J10-J22). **Age Groups:** For cardiovascular diseases: All ages, and restricted to ≥ 65 yr. For all respiratory diseases: 0-14 yr, 15-64 yr, and ≥ 65 yr. For respiratory infections: All ages **Study Design:** Time series **N:** NR (Total population of cities: approximately 10 million) **Statistical Analyses:** Poisson regression **Covariates:** Seasons, days of the wk, holidays, influenza epidemics, pollen counts, temperature, and temporal trends **Season:** NR **Dose-response Investigated:** No **Statistical Package:** MGCV package in R software (R 2.1.1) **Lags Considered:** Avg of 0-1 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (5th -95th percentile):** Le Havre: 13.8 (6.0-30.5) Lille: 15.9 (6.9-26.3) Marseille: 18.8 (8.0-33.0) Paris: 14.7 (6.5-28.8) Rouen: 14.4 (7.5-28.0) Toulouse: 13.8 (6.0-25.0) **Monitoring Stations:** 13 total: 1 in Toulouse 4 in Paris 2 each in other cities **Copollutant (correlation):** $PM_{10-2.5}$: Overall: r > 0.6 Ranged between r = 0.28 and r = 0.73 across the six cities.	**PM Increment:** 10 µg/m^3 increase, and a 27 µg/m^3 increase (corresponding to the difference between the lowest of the 5th percentiles and the highest of the 95th percentiles of the cities' distributions) ERR (excess relative risk) Estimate [CI]: For all cardiovascular diseases (10 µg/m^3 increase): All ages: 0.9% [0.1, 1.8] ≥ 65 yr: 1.9% [0.9, 3.0] For all cardiovascular diseases (27 µg/m^3 increase): All ages: 2.5% [0.2, 4.9] ≥ 65 yr: 5.3% [2.6, 8.2] For ischemic heart diseases (27 µg/m^3 increase): All ages: 5.2% [-0.6, 11.3] ≥ 65 yr: 12.7% [6.3, 19.5] For cardiac diseases (10 µg/m^3 increase): All ages: 0.9% [-0.1, 2.0] ≥ 65 yr: 2.4% [1.2, 3.7] For cardiac diseases (27 µg/m^3 increase): All ages: 2.5% [-0.3, 5.4] ≥ 65 yr: 6.8% [3.3, 10.3] For ischemic heart diseases (10 µg/m^3 increase): All ages: 1.9 % [-0.2, 4.0] ≥ 65 yr: 4.5% [2.3, 6.8] For all respiratory diseases (10 µg/m^3 increase): 0-14 yr: 0.4% [-1.2, 2.0] 15-64 yr: 0.8% [-0.7, 2.3]; ≥ 65 yr: 0.5% [-2.0, 3.0] For all respiratory diseases (27 µg/m^3 increase): 0-14 yr: 1.1% [-3.1, 5.5] 15-64 yr: 2.2% [-1.8, 6.4]; ≥ 65 yr: 1.3% [-5.3, 8.2] For respiratory infections (10 µg/m^3 increase): All ages: 2.5% [0.1, 4.8] For respiratory infections (27 µg/m^3 increase): All ages: 7.0% [0.7, 13.6]

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Jalaludin et al. (2006, 189416) **Period of Study:** Jan 1997-Dec 2001 **Location:** Sydney, Australia	**Outcome (ICD-9):** Cardiovascular disease (390-459), cardiac disease (390-429), ischemic heart disease (410-413) and cerebrovascular disease or stroke (430-438) **Age Groups:** 65+ yr **Study Design:** Time series **N:** NR **Statistical Analyses:** GAM, GLM **Covariates:** Temperature, humidity **Season:** Warm (Nov-Apr) and cool (May-Oct) **Dose-response Investigated:** No **Statistical Package:** S-Plus **Lags Considered:** 0-3 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (min-max):** 9.5 (2.4-82.1) SD = 5.1 **Monitoring Stations:** 14 **Copollutant (correlation):** Warm BSP: r = 0.93 PM_{10}: r = 0.89 O_3: r = 0.57 NO_2: r = 0.45 CO: r = 0.35 SO_2: r = 0.27 Cool BSP: r = 0.90 PM_{10}: r = 0.88 O_3: r = 0.05 NO_2: r = 0.68 CO: r = 0.60 SO_2: r = 0.46 **Other variables:** Warm Temp: r = 0.24 Rel humidity: r = -0.15 Cool Temp: r = -0.04 Rel humidity: r = 0.20	**PM Increment:** 4.8 µg/m^3 (IQR) Percent Change Estimate [CI]: All CVD Same-day lag: 1.26 [0.56,1.96] Avg 0-1 day lag: 0.85 [0.18,1.52] Cool (same-day lag): 2.23 [0.98,3.50] Warm (same-day lag): 0.73 [-0.05,1.52] Cardiac disease Same-day lag: 1.55 [0.74,2.38] Avg 0-1 day lag: 1.33 [0.54,2.13] Cool (same-day lag): 2.37 [0.87,3.89] Warm (same-day lag): 1.13 [0.22,2.04] Ischemic heart disease Same-day lag: 1.17 [-0.08,2.44] Avg 0-1 day lag: 1.24 [0.04,2.45] Cool (same-day lag): 0.57 [-1.74,2.94] Warm (same-day lag): 1.31 [-0.04,2.68] Stroke Same-day lag: -0.89 [-2.41,0.65] Avg 0-1 day lag: -1.08 [-2.54,0.41] Cool (same-day lag): 1.45 [-1.17,4.15] Warm (same-day lag): -2.19 [-4.00,-0.36] **Notes**: All other lag-day ORs were provided, yet none were significant. Percent change in ED attendance was also reported graphically (Fig 1-5).
Reference: Jalaludin et al. (2006, 189416) **Period of Study:** Jan 1997-Dec 2001 **Location:** Sydney, Australia	**Outcome (ICD-9):** Cardiovascular disease (390-459), cardiac disease (390-429), ischemic heart disease (410-413) and cerebrovascular disease or stroke (430-438) **Age Groups:** 65+ yr **Study Design:** Time series N: NR **Statistical Analyses:** GAM, GLM **Covariates:** Temperature, humidity **Season:** Warm (Nov-Apr) and cool (May-Oct) **Dose-response Investigated:** No **Statistical Package:** S-Plus **Lags Considered:** 0-3 days	**Pollutant:** BS,P **Averaging Time:** 24 h **Mean/104/m (min-max):** 0.26 (0.04-3.37) SD = 0.22 **Monitoring Stations:** 14 **Copollutant (correlation):** Warm $PM_{2.5}$: r = 0.93 PM_{10}: r = 0.82 O_3: r = 0.48 NO_2: r = 0.35 CO: r = 0.33 SO_2: r = 0.21 Cool $PM_{2.5}$: r = 0.90 PM_{10}: r = 0.75 O_3: r = -0.08 NO_2: r = 0.59 CO: r = 0.62 SO_2: r = 0.48 **Other variables:** Warm Temp: r = 0.23 Rel humidity: r = -0.04 Cool Temp: r = -0.09 Rel humidity: r = 0.36	**PM Increment:** 0.18/ 104/m (IQR) Percent Change Estimate [CI]: All CVD Same-day lag: 1.05 [0.44,1.66] Avg 0-1 day lag: 0.79 [0.20,1.38]; Cool (same-day lag): 2.38 [1.15,3.62] Warm (same-day lag): 0.45 [-0.18,1.09] Cardiac disease Same-day lag: 1.34 [0.63,2.05] Avg 0-1 day lag: 1.13 [0.44,1.82]; Cool (same-day lag): 2.50 [1.04,3.98] Warm (same-day lag): 0.80 [0.07,1.54] Ischemic heart disease Same-day lag: 0.91 [-0.17,2.02] Avg 0-1 day lag: 0.90 [-0.14,1.95]; Cool (same-day lag): 0.52 [-1.74,2.83] Warm (same-day lag): 0.93 [-0.15,2.03] Stroke Same-day lag: -0.93 [-2.27,0.42] Avg 0-1 day lag: -0.82 [-2.11,0.49]; Cool (same-day lag): 1.38 [-1.19,4.01]; Warm (same-day lag): -1.85 [-3.31,-0.36] **Notes**: All other lag-day ORs were provided, yet none were significant. Percent change in ED attendance was also reported graphically (Fig 1-5).

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Lisabeth et al. (2008, 155939) **Period of Study:** 2001-2005 **Location:** Nueces County, Texas	**Outcome:** Ischemic stroke and transient ischemic attacks (ICD codes not reported). **Age Groups:** 45+ yr **Study Design:** Time series **N:** 3,508 stroke/TIAs (2,350 strokes, and 1,158 TIAs) **Statistical Analyses:** Poisson regression **Covariates:** Temperature, day of week, temporal trends **Season:** All, but looked at potential effect modification by season (Summer: Jun-Sep; Non-summer: Oct-May) **Dose-response Investigated:** No **Statistical Package:** S-plus 7.0 **Lags Considered:** Lags 0-5 days, and avg lag effect (0-5 days)	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Median µg/m3 (IQR):** 7.0 (4.8-10.0) **Monitoring Stations:** 6 **Copollutant (correlation):** NR	**PM Increment:** 5.1 µg/m^3 (IQR) RR Estimate [CI]: Lag 0: 1.03 (0.99, 1.07) Lag 1: 1.03 (1.00-1.07) All other lags and avg (lag 0-5) were not statistically or marginally significant. Adjusted for O_3: Lag 0: 1.03 (0.99, 1.07) Lag 1: 1.03 (0.99-1.06) All other lags and avg (lag 0-5) were not statistically or marginally significant. **Notes**: Fig 3: % change in stroke/TIA risk associated with an IQR increase in $PM_{2.5}$
Reference: Metzger et al. (2004, 044222) **Period of Study:** Aug 1998-Aug 2000 **Location:** Atlanta Metropolitan area (Georgia)	**Outcome (ICD-9):** Emergency visits for ischemic heart disease (410-414), cardiac dysrhythmias (427), cardiac arrest (427.5), congestive heart failure (428), peripheral vascular and cerebrovascular disease (433-437, 440, 443-444, 451-453), atherosclerosis (440), and stroke (436). **Age Groups:** All **Study Design:** Time series **N:** 4,407,535 emergency department visits for 1993-2000 (data not reported for 1998-2000) **Statistical Analyses:** Poisson generalized linear modeling **Covariates:** Day of the wk, hospital entry and exit indicator variables, federally observed holidays, temporal trends, temperature, dew point temperature **Season:** All **Dose-response Investigated:** No **Statistical Package:** SAS **Lags Considered:** 3-day ma, lags 0 -7	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Median µg/m3 (10%-90% range):** $PM_{2.5}$: 17.8 (8.9, 32.3) $PM_{2.5}$ water soluble metals: 0.021 (0.006-0.061) $PM_{2.5}$ acidity: 4.5 (1.9-1.07) $PM_{2.5}$ OC: 0.010 (-0.001-0.045) $PM_{2.5}$ EC: 4.1 (2.2-7.1) **Monitoring Stations:** 1 **Copollutant (correlation):** PM_{10}: r = 0.84 O_3: r = 0.65 NO_2: r = 0.46 CO: r = 0.44 SO_2: r = 0.17 $PM_{10-2.5}$: r = .43 UFP: r = -0.16 $PM_{2.5}$ water-sol metals: r = 0.70 $PM_{2.5}$ sulfates: r = 0.77 $PM_{2.5}$ acidity: r = 0.58 $PM_{2.5}$ OC: r = 0.51 $PM_{2.5}$ EC: r = 0.48 oxygenated hydrocarbon: r = 31 **Other variables:** Temperature: r = 0.20 Dew point: r = 0.00	**PM Increment:** Approximately 1 SD increase: $PM_{2.5}$: 10 µg/m^3 $PM_{2.5}$ water-sol metals: 0.03 µg/m^3 $PM_{2.5}$ sulfates: 5 µg/m^3 $PM_{2.5}$ acidity: 0.02 µequ/m^3 $PM_{2.5}$ OC: 2 µg/m^3 $PM_{2.5}$ EC: 1 µg/m^3 RR [95% CI]: $PM_{2.5}$ (3-day ma): All CVD: 1.033 [1.010, 1.056] Dysrhythmia: 1.015 [0.976, 1.055] Congestive heart failure: 1.055 [1.006-1.105] Ischemic heart disease: 1.023 [0.983-1.064] Peripheral vascular and cerebrovascular disease: 1.050 [1.008-1.093] **$PM_{2.5}$ water soluble metals (3-day ma):** All CVD: 1.027[0.998, 1.056] Dysrhythmia: 1.031 [0.982, 1.082] Congestive heart failure: 1.040 [0.981-1.103] Ischemic heart disease: 1.000 [0.951-1.051] Peripheral vascular and cerebrovascular disease: 1.043 [0.991-1.098] **$PM_{2.5}$ sulfates (3-day ma):** All CVD: 1.003 [0.968, 1.039] Dysrhythmia: 0.986 [0.926, 1.048] Congestive heart failure: 1.009 [0.938-1.085] Ischemic heart disease: 0.997 [0.936-1.062] Peripheral vascular and cerebrovascular disease: 1.025 [0.964-1.090] **$PM_{2.5}$ acidity (3-day ma):**

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			All CVD: 0.994 [0.966, 1.022] Dysrhythmia: 0.991 [0.942, 1.043] Congestive heart failure: 0.989 [0.930-1.052] Ischemic heart disease: 0.992 [0.944-1.043] Peripheral vascular and cerebrovascular disease: 1.004 [0.955-1.056] **$PM_{2.5}$ OC (3-day ma)**: All CVD: 1.026 [1.006, 1.046] Dysrhythmia: 1.008 [0.975, 1.044] Congestive heart failure: 1.048 [1.007-1.091] Ischemic heart disease: 1.028 [0.994-1.064] Peripheral vascular and cerebrovascular disease: 1.026 [0.990-1.062] hydrocarbons simultaneously. **$PM_{2.5}$ OC (3-day ma):** All CVD: 1.020 [1.005, 1.036] Dysrhythmia: 1.011 [0.985, 1.037] Congestive heart failure: 1.035 [1.003-1.068] Ischemic heart disease: 1.019 [0.992-1.046] Peripheral vascular and cerebrovascular disease: 1.021 [0.994-1.049] Results for Lags 0-7 expressed in figures (see notes). **Notes**: Fig 1: RR (95% CI) for single-day lag models for the association of ER visits for CVD with daily ambient $PM_{2.5}$ and associated components. Summary of Fig 1 results: Statistically significant positive associations at Lag 0 and Lag 1 for $PM_{2.5}$, at Lag 0 for $PM_{2.5}$ water soluble metals (inverse association at Lag 7), at Lag 0, Lag 1, and Lag 3 for organic and EC (inverse association at Lag 7). Fig 2: RR (95%) of multipollutant models for the association of ER visits for CVD with daily ambient air quality measurements. Summary of Fig 2 results: Positive association after adjustment for NO_2, CO, and oxygenated hydrocarbons, but attenuated when adjusted for total carbon and null when adjusted for NO_2, CO, total carbon, and oxygenated

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Peng et al. (2008, 156850) **Period of Study:** Jan 1999-Dec 2005 **Location:** 108 U.S. counties in the following states: Alabama, Arizona, California, Colorado, Connecticut, District of Columbia, Florida, Georgia, Idaho, Illinois, Indiana, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Missouri, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, Tennessee, Texas, Utah, Virginia, Washington, West Virginia, Wisconsin	**Outcome (ICD-9):** Emergency hospitalizations for: Cardiovascular disease, including heart failure (428), heart rhythm disturbances (426-427), cerebrovascular events (430-438), ischemic heart disease (410-414, 429), and peripheral vascular disease (440-448). Respiratory disease, including COPD (490-492) and respiratory tract infections (464-466, 480-487) **Age Groups:** 65 + yr, 65-74, ,75 + **Study Design:** Time series **N:** ~12 million Medicare enrollees (3.7 million CVD and 1.4 million RD admissions) **Statistical Analyses:** Two-stage Bayesian hierarchical models: Overdispersed Poisson models for county-specific data Bayesian hierarchical models to obtain national avg estimate **Covariates:** Day of the week, age-specific intercept, temperature, dew point temperature, calendar time, indicator for age of 75 yr or older. Some models were adjusted for $PM_{10-2.5}$. **Season:** NR **Dose-response Investigated:** No **Statistical Package:** R version 2.6.2 **Lags Considered:** 0-2 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean µg/m3 (IQR):** All counties assessed: 13.5 (11.1-15.8) Counties in Eastern U.S.: 13.8 (12.3-15.8) Counties in Western U.S.: 11.1 (10.1-14.3) **Monitoring Stations:** At least 1 pair of co-located monitors (physically located in the same place) for PM_{10} and $PM_{2.5}$ per county Other variables: Median within-county correlations between monitors: r = 0.92	**PM Increment:** 10 µg/m^3 Percentage change [95% CI]: CVD and RD (unadjusted for PM_{10}-25): Lag 0: 0.71 [0.45, 0.96] Lag 2: 0.44 [0.06, 0.82] Most values NR (see note) **Notes**: Effect estimates for $PM_{10-2.5}$ (0-2 day lags) are showing in Fig 2-5. Fig 2: Percentage change in emergency hospital admissions for CVD per 10 µg/m^3 increase in $PM_{2.5}$ (single pollutant model and model adjusted for $PM_{10-2.5}$ concentration) Fig 3: Percentage change in emergency hospital admissions for RD per 10 µg/m^3 increase in $PM_{2.5}$ (single pollutant model and model adjusted for $PM_{10-2.5}$ concentration) No significant associations between $PM_{2.5}$ and cause-specific cardiovascular disease.
Reference: Peters et al. (2005, 156859) **Period of Study:** Feb 1999-Jul 31, 2001 **Location:** Germany: City of Augsburg, County Augsburg, and County Aichach-Friedlberg	**Outcome:** Transmural or nontransmural acute MI **Age Groups:** NR **Study Design:** Case-crossover and time series **N:** 851 MI survivors **Statistical Analyses:** Conditional logistic regression for case-crossover element. Poisson regression for time series element. **Covariates:** Case-crossover: Season, temperature, day of the week, time series: trend, season, influenza, weather, and day of the week **Season:** All **Dose-response Investigated:** No **Statistical Package:** SAS, version 8.2 Poisson: R, version 1.7.1 **Lags Considered:** Lags 0-6 h, 0-5 days Poisson: Single lagged days, 5-day, 15-day, 30-day, and 45-day ma	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 1 h and 24 h **Mean µg/m3 (range IQR/ median IQR):** 1-h avg: 16.3 (-6.9-355.2 10.7-19.8 14.5) 24-h avg: 16.3 (6.1-58.5 11.6-19.3 14.9) **Monitoring Stations:** 1 **Copollutant (correlation):** 24-h avg: TNC: r = 0.37 TSP: r = 0.89 PM_{10}: r= 0.92 CO: r = 0.57 NO_2: r = 0.67 NO: r = 0.59 SO_2: r = 0.58 O_3: r = -0.24 1hr avg: TNC: r = 0.42 CO: r = 0.52 NO_2: r = 0.58 NO: r = 0.50 SO_2: r = 0.48 O_3: r = -0.35 Other variables: 24-h avg: Temperature: r = 0.05 1-h avg: Temperature: r = -0.01	**PM Increment:** 1-h avg: 9.1 µg/m^3 (IQR) 24-h avg: 7.7 µg/m^3 (IQR) OR [95% CI]: Case-Crossover (control selection method (unidirectional with three control periods): **1-h avg:** Lag 0: 0.98 (0.88, 1.10) Lag 1: 0.97 (0.87, 1.09) Lag 2: 0.93 (0.83, 1.04) Lag 3: 0.98 (0.88, 1.09) Lag 4: 0.96 (0.86, 1.07) Lag 5: 0.94 (0.84, 1.05) Lag 6: 0.90 (0.80, 1.01). **24-h avg:** Lag 0: 0.95 (0.83, 1.080) Lag 1: 1.10 (0.96, 1.25) Lag 2: 1.18 (1.03, 1.34) Lag 3: 1.07 (0.94, 1.22) Lag 4: 0.94 (0.83, 1.07) Lag 5: 0.90 (0.79, 1.02) Case-Crossover (control selection method: bidirectional with 16 control periods): **24-h avg:** Lag 0: 1.03 (0.94, 1.12) Lag 1: 1.07 (0.98, 1.16) Lag 2: 1.08 (0.99, 1.17) Lag 3: 1.01 (0.92, 1.10) Lag 4: 0.96 (0.88, 1.04) Lag 5: 0.93 (0.85, 1.02) Lag 0 -4 (IQR = 5.8): 1.03 (0.94, 1.14) Unidirectional: Model 1 (unadjusted): 1.175 (1.033, 1.337) Model 2 (adjusted for day of week using indicator variables): 1.179 (1.035,

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			1.343) Model 3 (adjusted for temperature-quadratic, linear air pressure): 1.170 (1.028, 1.333) Model 4 (adjusted for temperature-quadratic, linear air pressure, day of week): 1.176 (1.031, 1.341) Model 5 (temperature-quadratic, air pressure-quadratic, relative humidity-quadratic, day of week using indicator variables): 1.170 (1.026, 1.336) Model 6 (temperature-penalized spline, 4.4 df, linear air pressure, day of week using indicator variables): 1.175 (1.030, 1.340 Model 7 (temperature-penalized spline, 4.4 df, linear air pressure, relative humidity-penalized spline, 7.8 df, day of week using indicator variables: 1.177 (1.030, 1.344) Bidirectional (16 control periods): Model 1 (unadjusted): 1.077 (0.988, 1.174) Model 2 (adjusted for day of the week using indicator variables): 1.078 (0.988, 1.175) Model 3 (adjusted for temperature-quadratic, linear air pressure): 1.060 (0.970, 1.160) Model 4 (adjusted for temperature-quadratic, linear air pressure, day of the week): 1.060 (0.969, 1.160) Model 5 (temperature-quadratic, air pressure-quadratic, relative humidity-quadratic, day of the week using indicator variables): 1.065 (0.973, 1.166) Model 6 (temperature-penalized spline, 4.4 df, linear air pressure, day of the week using indicator variables): 1.068 (0.976, 1.168) Model 7 (temperature-penalized spline, 4.4 df, linear air pressure, relative humidity-penalized spline, 7.8 df, day of the week using indicator variables: 1.077 (0.983, 1.179) Bidirectional (4 control periods): Model 1 (unadjusted): NR Model 2 (adjusted for day of the week by design): 1.049 (0.964, 1.141) Model 3 (adjusted for temperature-quadratic, linear air pressure): NR Model 4 (adjusted for temperature-quadratic, linear air pressure, day of the week): 1.032 (0.944, 1.128) Model 5 (temperature-quadratic, air pressure-quadratic, relative humidity-quadratic, day of the week by design): 1.033 (0.945, 1.130) Model 6 (temperature-penalized spline, 4.4 df, linear air pressure, day of the week by design): 1.036 (0.947, 1.132) Model 7 (temperature-penalized spline, 4.4 df, linear air pressure, relative

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			humidity-penalized spline, 7.8 df, day of the week by design): 1.039 (0.950, 1.136) Stratified: Model 1 (unadjusted): NR Model 2 (adjusted for day of week by design): 1.059 (0.972, 1.154) Model 3 (adjusted for temperature-quadratic, linear air pressure): NR Model 4 (adjusted for temperature-quadratic, linear air pressure, day of week): 1.047 (0.957, 1.145) Model 5 (temperature-quadratic, air pressure-quadratic, relative humidity-quadratic, day of week by design): 1.045 (0.954, 1.144) Model 6 (temperature-penalized spline, 4.4 df, linear air pressure, day of week by design): 1.054 (0.964, 1.153odel 7 (temperature-penalized spline, 4.4 df, linear air pressure, relative humidity-penalized spline, 7.8 df, day of week by design): 1.056 (0.965, 1.156) RR (95% CI): Time series (24 h avg): Lag 0: 0.97 (0.89, 1.07) Lag 1: 1.04 (0.96, 1.13) Lag 2: 1.07 (0.98, 1.15) Lag 3: 1.03 (0.95, 1.11) Lag 4: 0.98 (0.90, 1.07) Lag 5: 0.98 (0.90, 1.06) Lag 0-4: 1.03 (0.94, 1.12) Lag 0-14: 1.03 (0.95, 1.13) Lag 0-29: 1.09 (1.01, 1.18) Lag 0-44: 1.08 (1.00, 1.17) **Time series (OR [95% CI]):** Model 1 (unadjusted): 1.059 (0.981, 1.142) Model 2 (adjusted for day of week using indicator variables): 1.056 (0.979, 1.140) Model 3 (adjusted for temperature-quadratic, linear air pressure): 1.062 (0.982, 1.148) Model 4 (adjusted for temperature-quadratic, linear air pressure, day of week): 1.059 (0.979, 1.146) Model 5 (temperature-quadratic, air pressure-quadratic, relative humidity-quadratic, day of week using indicator variables): 1.063 (0.981, 1.151) Model 6 (temperature-penalized spline, 4.4 df, linear air pressure, day of week using indicator variables): 1.065 (0.985, 1.153) Model 7 (temperature-penalized spline, 4.4 df, linear air pressure, relative humidity-penalized spline, 7.8 df, day of week using indicator variables: 1.069 (0.988, 1.157)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Pope et al.(2006, 091246) **Period of Study:** 1994-2004 **Location:** Wasatch Front area, Utah	**Outcome:** Myocardial infarction or unstable angina (ICD codes not reported) **Age Groups:** All, <65, 65+ **Study Design:** Case-crossover **N:** 12,865 patients who underwent coronary arteriography **Statistical Analyses:** Conditional logistic regression **Covariates:** Temperature and dew point temperature **Season:** NR **Dose-response Investigated:** No **Statistical Package:** NR **Lags Considered:** 0- to 3-day lag, 2- to 4-day lagged ma	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (µg/m3) (SD maximum):** Ogden: 10.8 (10.6 108) SLC Hawthorne: 11.3 (11.9 94) Provo/Orem, Lindom: 10.1 (9.8 82) **Monitoring Stations:** 3 **Copollutant (correlation):** NR	**PM Increment:** 10 µg/m^3 Percent increase in risk [95% CI]: Same-day increase in $PM_{2.5}$ (Lag 0): Index MI and unstable angina: 4.81 [0.98-8.79] Subsequent MI: 3.23 [-3.87, 10.85] All acute coronary events: 4.46 [1.07-7.97] All acute coronary events excluding observations using imputed $PM_{2.5}$ data: 4.24 [0.33-8.31] Stable presentation: -2.57 [-5.39, 0.34] Remaining results summarized in figures (see notes). **Notes**: Fig 1: Percent increase in risk (and 95% CI) of acute coronary events associated with 10 µg/m^3 of $PM_{2.5}$ for different lag structures. Summary of Fig 1: Positive, statistically significant association seen for Lag 0, Lag 1 and 2, 3, and 4 day ma. Positive but non-statistically significant associations seen for Lags 2 and 3. Fig 2: Percent increase in risk (and 95% CI) of acute coronary events associated with 10 µg/m^3 of $PM_{2.5}$ stratified by various characteristics.
Reference: Pope et al. (2008, 191969) **Period of Study:** 1994-2006 **Location:** Ogden, Salt Lake City, & Provo/Orem, Utah	**Outcome:** Heart Failure Hospitalizations **Age Groups:** NR **Study Design:** Case-crossover **N:** 2,618 **Statistical Analyses:** Conditional Logistic Regression **Covariates:** Age, sex, length of stay, temperature, pressure, clearing index, day of the week, seasonality, and long-term trends **Season:** Adjusted for long-term trends to account for season **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 0- to 28-day ma.	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **Mean (SD):** Ogden: 10.6(9.9) SLC, Hawthorne: 11.1 (11.2) Provo/Orem, Lindon: 10.1 (9.3) **Max:** Ogden: 108 SLC, Hawthorne: 94 Provo/Orem, Lindon: 82 **Monitoring Stations:** NR **Copollutant:** PM_{10}	**PM Increment:** 10 µg/m^3 **Percent Increase: (Lower CI, Upper CI):** All HF Admissions All: 13.1 (1.3, 26.2)* Men: 13.4 (-1.7, 30.7)‡ Women: 12.7 (-5.1, 33.9) Age <65 yr: 3.5 (-13.5, 23.8) Age ≥65 yr: 19.6 (4.0, 37.5)* Length of stay 0-2 days: 24.4 (-0.8, 56.0) ‡ Length of stay 3-7 days: 10.8 (-4.6, 28.7) Length of stay 8+ days: 6.5 (-15.9, 34.8) First HF Admissions: 2.1 (-11.3, 17.5) Subsequent HF Admits: 32.4 (10.7, 58.4) † All HF Admissions All: 32.4 (10.7, 58.4) † Men: 29.2 (2.7, 62.6)* Women: 41.5 (5.4, 89.9)* Age <65 yr: -3.1 (-26.5, 27.8) Age ≥65 yr: 64.1 (28.6, 109) † Length of stay 0-2 days: 68.9 (12.5, 154)* Length of stay 3-7 days: 35.7 (5.9, 73.9)* Length of stay 8+ days: 2.6 (-28.5, 47.1) *p < 0.05, † p < 0.01, ‡p < 0.10

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Sarnat et al. (2008, 097972) **Period of Study:** Nov 1998-Dec 2002 **Location:** Atlanta (Georgia) metropolitan area	**Outcome (ICD-9):** Cardiovascular disease ED visits: Ischemic heart disease (410-414), cardiac dysrhythmias (427), congestive heart failure (428), and peripheral vascular and cerebrovascular disease (433-437, 440, 443-444, 451-453) **Age Groups:** All **Study Design:** Time series **N:** >4.5 million emergency department visits **Statistical Analyses:** Poisson generalized linear models **Covariates:** Day of the week, holidays, hospital, long-term trends, temperature, dew point temperature **Season:** All, warm season (Apr 15-Oct 14), and cool season (Oct 15-Apr 14). **Dose-response Investigated:** No **Statistical Package:** NR **Lags Considered:** 0-day lag	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (µg/m3) (median 10th-90th percentile):** Total $PM_{2.5}$: Cool season: 15.8 (14.3 7.5-25.5). Warm season: 18.2 (17.0 9.1-29.0) $PM_{2.5}$ EC: Cool: 1.7 (1.4 0.6-3.3). Warm: 1.4 (1.3 0.6-2.5) $PM_{2.5}$ Zn (ng/m^3): Cool: 15.7 (11.7 4.6-30.2) Warm: 10.9 (8.5 3.3-20.2) $PM_{2.5}$ K (ng/m^3): Cool: 63.0 (53.9 24.3-114.2) Warm: 52.7 (43.3 23.2-93.5) $PM_{2.5}$ Si (ng/m^3): Cool: 67.7 (54.1 24.3-123.5). Warm: 110.9 (89.0 32.9-186.3) $PM_{2.5}$ SO_4^{2-}: Cool: 3.4 (0.6 1.5-5.8). Warm: 6.0 (5.2 2.3-10.8) $PM_{2.5}$ NO_3-: Cool: 1.4 (1.2 0.5-2.6). Warm: 0.7 (2.9 0.3-1.2) $PM_{2.5}$ Se (ng/m^3): Cool: 1.4 (1.1 0.4-3.0). Warm: 1.2 (0.9 0.4-2.7) $PM_{2.5}$ OC: Cool: 4.6 (3.9 1.9-8.0) Warm: 4.0 (3.7 2.1-6.4) **Monitoring Stations:** 1 **Copollutants:** NR	**PM Increment:** IQR (specific values not given) Risk ratio [95% CI]: CVD (Lag 0): All seasons: Total $PM_{2.5}$: 1.022 [1.007, 1.038] $PM_{2.5}$ EC: 1.02 [1.013-1.037] $PM_{2.5}$ zinc: 1.013 [1.005-1.022] $PM_{2.5}$ potassium: 1.030 [1.018-1.042] $PM_{2.5}$ silicon: 1.008 [1.00-1.016] $PM_{2.5}$ sulfate: 1.007 [0.994-1.019] $PM_{2.5}$ nitrate: 1.002 [0.990-1.014] $PM_{2.5}$ selenium: 1.002 [0.991-1.012] $PM_{2.5}$ OC: 1.024 [1.013-1.035] Cool season: Total $PM_{2.5}$: 1.028 [1.012-1.044] $PM_{2.5}$ EC: 1.029 [1.015-1.044] $PM_{2.5}$ Zinc: 1.012 [1.002-1.022] $PM_{2.5}$ K: 1.037 [1.021-1.054] $PM_{2.5}$ Si: 1.022 [1.002-1.043] $PM_{2.5}$ sulfate: 1.014 [0.991-1.037] $PM_{2.5}$ nitrate: 1.006 [0.993-1.019] $PM_{2.5}$ Se: 1.012 [0.997-1.027] $PM_{2.5}$ OC: 1.027 [1.013-1.040] Warm season: Total $PM_{2.5}$: 1.006 [0.990-1.022] $PM_{2.5}$ EC: 1.021 [1.000-1.043] $PM_{2.5}$ Zinc: 1.017 [1.002-1.033] $PM_{2.5}$ K: 1.024 [1.007-1.041] $PM_{2.5}$ Si: 1.005 [0.996-1.014] $PM_{2.5}$ sulfate: 1.001 [0.988-1.015] $PM_{2.5}$ nitrate: 1.000 [0.969-1.033] $PM_{2.5}$ Se: 0.996 [0.981-1.011] $PM_{2.5}$ OC: 1.027 [1.004-1.051]

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Schreuder et al. (2006, 097959) **Period of Study:** Sep 1995-May 2002 **Location:** Spokane, WA	**Outcome:** Cardiac HA **Age Groups:** NR **Study Design:** Time series **Statistical Analyses:** GAM Poisosn Regression **Covariates:** Season, temperature, relative humidity, day of week **Dose-response Investigated?** No **Statistical Package:** S-Plus **Lags Considered:** 0-1 day	**Pollutant:** $PM_{2.5}$ (ng/m^3) **Averaging Time:** 24 h **Arithmetic Mean:** 10,580 **Geometric Mean:** 8,790 **Min:** 930 **Max:** 43,230 **IQR:** Entire period: 7.7 $\mu g/m^3$ Heating season: 10.1$\mu g/m^3$ Non-heating season: 5.5$\mu g/m^3$ **Monitoring Stations:** NR **Copollutant:** NR **Co-pollutant Correlation:** NR	**PM Increment:** Interquartile Range **Relative Risk (Lower CI, Upper CI):** Entire Period, Lag 0: 1.008 (0.985, 1.032) Entire Period, Lag 1: 1.000 (0.978, 1.023) Heating Season, Lag 1: 1.015 (0.968, 1.063) Non-Heating Season, Lag 1: 0.995 (0.969, 1.021)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Sullivan et al. (2005, 109418) **Period of Study:** 1988-1994 **Location:** King County, Washington	**Outcome:** Acute MI **Age Groups:** All, <50, 50-59, 70+ **Study Design:** Case-crossover **N:** 5793 cases of acute MI (5793 case days and 20,134 referent exposure days from these case individuals) **Statistical Analyses:** Conditional logistic regression **Covariates:** Relative humidity, temperature, season, day of week **Season:** All, and also conducted stratified analysis by season of event (heating season: Nov-Feb nonheating season: Mar-Oct) **Dose-response Investigated:** No **Statistical Package:** SAS version 8.0 and SPSS version 10 **Lags Considered:** Lag 1 and Lag 2 for 24-h avg	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 1 h, 2 h, 4 h, and 24 h Summary of $PM_{2.5}$ 1 h before MI onset: **Mean (µg/m3) (median IQR, 90th percentile range):** 12.8 (8.6 5.3-15.9 27.3 2.0-147) **Monitoring Stations:** 3 **Copollutant (correlation):** 1-h avg: PM_{10}: r = 0.78 CO: r = 0.47 SO_2: r = 0.16	**PM Increment:** 10 µg/m^3 **Odds ratio [95% CI]:** **1-h Averaging Time:** 1.01 [0.98, 1.05] **2-h Averaging Time:** 1.01 [0.97, 1.05] **4-h Averaging Time:** 1.02 [0.98, 1.04] **24-h Averaging Time:** 1.02 [0.98, 1.07] Association between $PM_{2.5}$ (24 h) lagged 1 or 2 days non-significant (data not shown) Season (1-h avg): Heating: 1.01 [0.98-1.05] Nonheating: 0.99 [0.91-1.09] Age (1-h avg): <50 yr: 1.04 [0.95, 1.14] 50-60 yr: 0.99 [0.94, 1.05] 70+ yr: 1.03 [0.98, 1.08] Age (24-h avg): <50 yr: 1.07 [0.98, 1.19] 50-69 yr: 0.99 [0.93, 1.06] 70+ yr: 1.04 [0.99, 1.11] Sex (1-h avg): Men: 1.02 [0.98, 1.06] Women: 1.00 [0.95, 1.06] Sex (24-h avg): Men: 1.03 [0.99, 1.08] Women: 1.00 [0.94, 1.07] Race (1-h avg): White: 1.01 [0.97, 1.04] Nonwhite: 1.06 [0.97, 1.17] Race (24-h avg): White: 1.01 [0.97, 1.06] Nonwhite: 1.10 [0.99, 1.23] Smoking status (1-h avg): Current: 0.99 [0.93, 1.06] Nonsmoker: 1.03 [0.97, 1.08] Smoking status (24-h avg): Current: 0.99 [0.95, 1.14] Nonsmoker: 1.03 [0.98, 1.09] Survivor of MI * (1-h avg): Yes: 1.02 [0.98, 1.06]; No: 0.96 [0.86, 1.08] Survivor of MI * (24-h avg): Yes: 1.03 [0.98, 1.07]; No: 0.97 [0.85, 1.10] Previous congestive heart failure (1 h avg): Yes: 1.06 [0.97, 1.16]; No: 1.00 [0.97, 1.04] Previous congestive heart failure (24-h avg): Yes: 1.08 [0.97, 1.2]; No: 1.00 [0.97, 1.04] Previous MI (1-h avg): Yes: 1.03 [0.97, 1.1]; No: 1.01 [0.96, 1.06] Previous MI (24-h avg): Yes: 1.04 [0.97, 1.17]; No: 1.02 [0.98, 1.08] Hypertension (1-h avg): Yes: 1.02 [0.97, 1.07]; No: 1.01 [0.96, 1.06] Hypertension (24-h avg): Yes: 1.02 [0.97, 1.07]; No: 1.02 [0.97, 1.08] Diabetes mellitus (1-h avg): Yes: 1.06 [0.98, 1.14]; No: 1.01 [0.97, 1.05] Diabetes mellitus (24-h avg): Yes: 1.04 [0.95, 1.14]; No: 1.01 [0.97, 1.06] *Compares those who survive hospitalization (yes) with those who died in hospital from complications of MI.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Symons et al. (2006, 091258) **Period of Study:** Apr-Dec 2002 **Location:** Baltimore, Maryland	**Outcome:** Congestive heart failure **Age Groups:** All **Study Design:** Case-crossover **N:** 125 patients **Statistical Analyses:** Conditional logistic regression **Covariates:** Temperature and humidity **Season:** NR **Dose-response Investigated:** Yes **Statistical Package:** SAS and S-Plus **Lags Considered:** 0-3 days (single and cumulative)	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 8 h & 24 h **Mean (min-max):** 8 h 17.0 (0.1-111.9) SD = 12.7 24 h 16.0 (3.5-69.2) SD = 10.0 **Monitoring Stations:** 8 **Copollutant (correlation):** NR	**PM Increment:** 9.2 µg/m^3 (IQR) RR Estimate [CI]: 8 h (participant's onset period) Same-day lag: 0.87 [0.69,1.09] 1-day lag: 0.96 [0.78,1.18] 2-day lag: 1.09 [0.91,1.30] 3-day lag: 0.99 [0.79,1.23] Cumulative 1-day lag: 0.89 [0.67,1.16] Cumulative 2-day lag: 0.99 [0.74,1.33] Cumulative 3-day lag: 0.98 [0.70,1.36] 24 h avg Same-day lag: 0.81 [0.65,1.01] 1-day lag: 0.90 [0.74,1.11] 2-day lag: 0.85 [0.68,1.07] 3-day lag: 0.86 [0.70,1.05] Cumulative 1-day lag: 0.82 [0.64,1.04] Cumulative 2-day lag: 0.76 [0.57,1.01] Cumulative 3-day lag: 0.70 [0.51,0.97] **Notes**: β coefficients presented in Fig 5
Reference: Tolbert et al. (2007, 090316) **Period of Study:** Aug 1998-Dec 2004 **Location:** Atlanta Metropolitan area, Georgia	**Outcome (ICD-9):** Combined CVD group, including: Ischemic heart disease (410-414), cardiac dysrhythmias (427), congestive heart failure (428), and peripheral vascular and cardiovascular disease (433-437, 440, 443-445, and 451-453) **Age Groups:** All **Study Design:** Time series **N:** NR for 1998-2004. For 1993-2004: 10,234,490 ER visits (283,360 and 1,072,429 visits included in the CVD and RD groups, respectively) **Statistical Analyses:** Poisson generalized linear models **Covariates:** Long-term temporal trends, season (for RD outcome), temperature, dew point, days of week, federal holidays, hospital entry and exit **Season:** All **Dose-response Investigated:** No **Statistical Package:** SAS version 9.1 **Lags Considered:** 3-day ma(lag 0 -2)	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (µg/m3) (median IQR, range, 10th -90th percentiles):** $PM_{2.5}$: 17.1 (15.6 11.0-21.9 0.8-65.8 7.9-28.8). $PM_{2.5}$ sulfate: 4.9 (3.9 2.4-6.2 0.5-21.9 1.7-9.5). $PM_{2.5}$ OC: 4.4 (3.8 2.7-5.3 0.4-25.9 2.1-7.2). $PM_{2.5}$ EC: 1.6 (1.3 0.9-2.0 0.1-11.9 0.6-3.0). $PM_{2.5}$ water-soluble metals: 0.030 (0.023 0.014-0.039 0.003-0.202 0.009-0.059) **Monitoring Stations:** 1 **Copollutant (correlation):** Between $PM_{2.5}$ and: PM_{10}: r = 0.84 O_3: r = 0.62 NO_2: r = 0.47 CO: r = 0.47 SO_2: r = 0.17 $PM_{10-2.5}$: r = 0.47 $PM_{2.5}$ SO_4: r = 0.76 $PM_{2.5}$ EC: r = 0.65 $PM_{2.5}$ OC: r = 0.70 $PM_{2.5}$ TC: r = 0.71 $PM_{2.5}$ water-sol metals: r = 0.69 OHC: r = 0.50 Between $PM_{2.5}$ SO_4 and: PM_{10}: r = 0.69 O_3: r = 0.56 NO_2: r = 0.14 CO: r = 0.14 SO_2: r = 0.09 $PM_{10-2.5}$: r = 0.32 $PM_{2.5}$: r = 0.76 $PM_{2.5}$ EC: r = 0.32 $PM_{2.5}$ OC: r = 0.33	**PM Increment:** $PM_{2.5}$: 10.96 µg/m^3 (IQR) $PM_{2.5}$ sulfate: 3.82 µg/m^3 (IQR) $PM_{2.5}$ total carbon: 3.63 µg/m^3 (IQR) $PM_{2.5}$ OC: 2.61 µg/m^3 (IQR) $PM_{2.5}$ EC: 1.15 µg/m^3 (IQR) $PM_{2.5}$ water-soluble metals: 0.03 µg/m^3 (IQR) Risk ratio [95% CI] (single pollutant models): $PM_{2.5}$: CVD: 1.005 [0.993-1.017] $PM_{2.5}$ sulfate: CVD: 0.999 [0.987-1.011] $PM_{2.5}$ total carbon: CVD: 1.016 [1.005-1.026] $PM_{2.5}$ OC: CVD: 1.015 [1.005-1.026] $PM_{2.5}$ EC: CVD: 1.015 [1.005-1.025] $PM_{2.5}$ water-soluble metals: CVD: 1.009 [0.997-1.021] **Notes**: Results of selected multi-pollutant models for cardiovascular disease are presented in Fig 1. Fig 1: $PM_{2.5}$ total carbon adjusted for CO, NO_2, or NO_2+CO **Summary of results:** $PM_{2.5}$ total carbon continued to have a positive, statistically significant association with CVD after adjustment for NO_2 but not after adjustment

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
		$PM_{2.5}$ TC: r = 0.34 $PM_{2.5}$ water-sol metals: r = 0.65 OHC: r = 0.47 Between $PM_{2.5}$ EC and: PM_{10}: r = 0.61 O_3: r = 0.40 NO_2: r = 0.64 CO: r = 0.66 SO_2: r = 0.22 $PM_{10-2.5}$: r = 0.49 $PM_{2.5}$: r = 0.65$PM_{2.5}$ SO_4: r = 0.32 $PM_{2.5}$ OC: r = 0.82 $PM_{2.5}$ TC: r = 0.91 $PM_{2.5}$ water-sol metals: r = 0.52 OHC: r = 0.35 Between $PM_{2.5}$ OC and: PM_{10}: r = 0.65 O_3: r = 0.54 NO_2: r = 0.62 CO: r = 0.59 SO_2: r = 0.17 $PM_{10-2.5}$: r = 0.49 $PM_{2.5}$: r = 0.70 $PM_{2.5}$ SO_4: r = 0.33 $PM_{2.5}$ EC: r = 0.82 $PM_{2.5}$ TC: r = 0.98 $PM_{2.5}$ water-sol metals: r = 0.49 OHC: r = 0.37 Between $PM_{2.5}$ total carbon and: PM_{10}: r = 0.67 O_3: r = 0.52 NO_2: r = 0.65 CO: r = 0.63 SO_2: r = 0.19 $PM_{10-2.5}$: r = 0.51 $PM_{2.5}$: r = 0.71 $PM_{2.5}$ SO_4: r = 0.34 $PM_{2.5}$ EC: r = 0.91 $PM_{2.5}$ OC: r = 0.98 $PM_{2.5}$ water-sol metals: r = 0.52 OHC: r = 0.38 Between $PM_{2.5}$ water-soluble metals and: PM_{10}: r = 0.73 O_3: r = 0.43 NO_2: r = 0.32 CO: r = 0.35 SO_2: r = 0.06 $PM_{10-2.5}$: r = 0.50 $PM_{2.5}$: r = 0.69 $PM_{2.5}$ SO_4: r = 0.65 $PM_{2.5}$ EC: r = 0.52 $PM_{2.5}$ OC: r = 0.49 $PM_{2.5}$ TC: r = 0.52	

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Villeneuve et al. (2006, 090191) **Period of Study:** Apr 1992-Mar 2002 **Location:** Edmonton, Canada	**Outcome (ICD-9):** Stroke (430-438), including ischemic stroke (434-436), hemorrhagic stroke (430,432), and transient ischemic attacks (TIA) (435). **Age Groups:** 65+ yr **Study Design:** Case-crossover **N:** 12,422 visits **Statistical Analyses:** Conditional logistic regression **Covariates:** Temperature and relative humidity **Season:** Summer (Apr-Sep), winter (Oct-Mar) **Dose-response Investigated:** No **Statistical Package:** SAS (PHREG) **Lags Considered:** 0, 1, and 3 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean µg/m3 (SD):** All yr: 8.5 (6.2) Summer: 8.7 (7.1) Winter: 8.3 (5.2) **Monitoring Stations:** 3 **Copollutant (correlation):** All yr SO_2: r = 0.22 NO_2: r = 0.41 CO: r = 0.43 O_3-mean: r = -0.07 O_3-max: r = 0.07 PM_{10}: r = 0.79 Summer SO_2: r = 0.20 NO_2: r = 0.52 CO: r = 0.42 O_3-mean: r = 0.11 O_3-max: r = 0.34 PM_{10}: r = 0.85 Winter SO_2: r = 0.28 NO_2: r = 0.57 CO: r = 0.71 O_3-mean: r = -0.45 O_3-max: r = -0.35 PM_{10}: r = 0.70	**PM Increment:** µg/m^3 (IQR) All yr: 6.3 Summer: 6.5 Winter: 6.0 Adjusted OR Estimate [CI]: Acute ischemic stroke All yr: Same-day lag: 1.00 [0.96,1.04] 1-day lag: 1.00 [0.96,1.05] 3-day lag: 1.01 [0.96,1.06] Summer: Same-day lag: 0.96 [0.90,1.03] 1-day lag: 1.01 [0.94,1.07] 3-day lag: 0.98 [0.89 [1.07] Winter: Same-day lag: 1.04 [0.99,1.10] 1-day lag: 1.01 [0.96,1.07] 3-day lag: 1.05 [0.98,1.13] Hemorrhagic stroke All yr: Same-day lag: 0.99 [0.90,1.08] 1-day lag: 1.07 [0.98,1.16] 3-day lag: 1.05 [0.93,1.19] Summer: Same-day lag: 0.99 [0.86,1.15] 1-day lag: 1.12 [0.97,1.30] 3-day lag: 1.08 [0.88,1.31] Winter: Same-day lag: 1.04 [0.92,1.18] 1-day lag: 1.08 [0.97,1.20] 3-day lag: 1.11 [0.94,1.31] Transient cerebral ischemic attack All yr: Same-day lag: 0.98 [0.93,1.03] 1-day lag: 0.99 [0.95,1.04] 3-day lag: 0.96 [0.90,1.03] Summer: Same-day lag: 1.00 [0.92,1.08] 1-day lag: 1.03 [0.95,1.12] 3-day lag: 0.98 [0.88,1.09] Winter: Same-day lag: 0.97 [0.90,1.05] 1-day lag: 0.97 [0.91,1.04] 3-day lag: 0.94 [0.86,1.03] **Notes**: Adjusted ORs are provided for an IQR increase in the 3-day mean in Fig 1-4 for single and two-pollutant models.
Reference: Zanobetti and Schwartz (2006, 090195) **Period of Study:** 1995-1999 **Location:** Boston Metropolitan area	**Outcome (ICD-9):** Myocardial infarction (410) or pneumonia (480-487) **Age Groups:** 65+ yr **Study Design:** Case-crossover **N:** 15,578 patients admitted for MI and 25,857 admitted for pneumonia **Statistical Analyses:** Conditional logistic regression **Covariates:** Temperature, day of the week. **Season:** All, and also tested for interaction by warm (Apr-Sep) vs.. cold season **Dose-response Investigated:** No **Statistical Package:** SAS version 8.2 (PROC PHREG) **Lags Considered:** Lag 0 , and mean of lags 0 -1	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Median (µg/m3) (IQR 5th-95th percentile):** 11.1 (7.23-16.14 3.87-26.31) **Monitoring Stations:** 1 **Copollutant (correlation):** BC: r = 0.66 NO_2: r = 0.55 CO: r = 0.52 O_3: r = 0.20 PM non-traffic: r = 0.74	**PM Increment:** Difference between the 90th and 10th percentile for $PM_{2.5}$ Myocardial infarction cohort (Lag 0): 17.17 µg/m^3 Myocardial infarction cohort (Lag 0-1): 16.32 µg/m^3 Pneumonia cohort (Lag 0): 17.14 µg/m^3 Pneumonia cohort (Lag 0): 16.32 µg/m^3 Percentage (%) increase in risk [95% CI]: Myocardial infarction cohort: Lag 0: 8.50 (1.89-14.43) Lag 0-1: 8.65 (1.22-15.38) Pneumonia cohort: Lag 0: 6.48 (1.13-11.43) Lag 0-1: 5.56 (-0.45, 11.27) **Notes**: Assessed for effect modification by season. Results are reported in Fig 2. Summary of results: $PM_{2.5}$ is associated with pneumonia hospitalization in the cold season but not the hot season. $PM_{2.5}$ is associated with MI hospitalization in the hot season but not the cold season.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Zanobetti and Schwartz (2006, 090195) **Period of Study:** 1995-1999 **Location:** Boston Metropolitan area	**Outcome (ICD-9):** Myocardial infarction (410) or pneumonia (480-487) **Age Groups:** 65 + yr **Study Design:** Case-crossover **N:** 15,578 patients admitted for MI and 25,857 admitted for pneumonia **Statistical Analyses:** Conditional logistic regression **Covariates: T**emperature, day of the week. **Season:** All, and also assessed for interaction by hot (Apr-Sep) vs.. cold season **Dose-response Investigated:** No **Statistical Package:** SAS Software Release 8.2 **Lags Considered:** Lag 0 , and mean of lags 0 -1	**Pollutant:** BC **Averaging Time:** 24 h **Median (µg/m3) (IQR 5th-95th percentiles):** 1.15 (0.74-1.72 0.42-2.83) **Monitoring Stations:** 1 **Copollutant (correlation):** $PM_{2.5}$: r = 0.66 NO_2: r = 0.70 CO: r = 0.82 O_3: r = -0.25 PM non-traffic: r = -0.01	**PM Increment:** Difference between the 90th and 10th percentile for BC Myocardial infarction cohort (Lag 0): 2.01 µg/m^3 Myocardial infarction cohort (Lag 0-1): 1.69 µg/m^3 Pneumonia cohort (Lag 0): 2.05 µg/m^3 Pneumonia cohort (Lag 0 -1): 1.69 µg/m^3 Percentage (%) increase in risk [95% CI]: Myocardial infarction cohort: Lag 0: 6.98 (-0.27-13.76) Lag 0-1: 8.34 (0.21-15.82) Pneumonia cohort: |Lag 0: 10.76 (4.54-15.89) Lag 0-1: 11.71 (4.79, 17.36) **Notes**: Assessed for effect modification by season. Results are reported in Fig 2. Summary of results: PM_2.BC is associated with pneumonia hospitalization in the cold season but not the hot season. BC had a stronger positive association with MI hospitalization in the cold season, but the confidence interval was wide.

[1]All units expressed in µg/m^3 unless otherwise specified.

Table E-8. Short-term exposure-cardiovascular-ED/HA-other size fractions.

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Andersen et al, (2008, 189651) **Period of Study:** May 2001-Dec 2004 **Location:** Copenhagen, Denmark	**Outcome (ICD-10):** CVD, including angina pectoris (I20), myocardial infarction (I21-22), other acute ischemic heart diseases (I24), chronic ischaemic heart disease (I25), pulmonary embolism (I26), cardiac arrest (I46), cardiac arrhythmias (I48-48), and heart failure (I50). RD, including chronic bronchitis (J41-42), emphysema (J43), other chronic obstructive pulmonary disease (J44), asthma (J45), and status asthmaticus (J46). Pediatric hospital admissions for asthma (J45) and status asthmaticus (J46). **Age Groups:** >65 yr (CVD and RD), 5-18 yr (asthma) **Study Design:** Time series **N:** NR **Statistical Analyses:** Poisson GAM **Covariates:** Temperature, dew-point temperature, long-term trend, seasonality, influenza, day of the week, public holidays, school holidays (only for 5-18 yr olds), pollen (only for pediatric asthma outcome) **Season:** NR	**Pollutant:** Total number concentration of ultrafine and accumulation mode particles (NCtot) (particles/cm^3) **Averaging Time:** 24 h **NCtotal** **Mean (SD):** 8,116 (3502) **Median:** 7,358 **IQR:** 5,738-9,645 **99th Percentile:** 19,895 **NCa12** **Mean (SD):** 493 (315) **Median:** 463 **IQR:** 308-650 **99th Percentile:** 1,263 **NCa23** **Mean (SD):** 2,253 (1,364) **Median:** 2,057 **IQR:** 1,280-3,066 **99th Percentile:** 6,096 **NCa57** **Mean (SD):** 5,104 (2,687) **Median:** 4,562 **IQR:** 3,248-6,274 **99th Percentile:** 14,410 **NCa100** **Mean (SD):** 6,847 (2,846) **Median:** 6,243 **IQR:** 4,959-8,218 **99th Percentile:** 16,189 **NCa212**	**PM Increment:** IQR increase in pollutant level: Nctot: 3907 particles/cm^3 (IQR) N_{ca12}: 342 particles/cm^3 (IQR) N_{ca23}: 1786 particles/cm^3 (IQR) N_{ca57}: 3026 particles/cm^3 (IQR) N_{C100}: 3259 particles/cm^3 (IQR) N_{ca212}: 495 particles/cm^3 (IQR) Relative risk (RR) Estimate [CI]: CVD hospital admissions (4-day avg, lag 0 - 3), age 65+ One-pollutant model (NCtot): 1.00 [0.99-1.02] Adj for PM_{10}: 0.98 [0.96-1.01] Adj for $PM_{2.5}$: 0.99 [0.95-1.03] Adj for CO: 0.99 [0.97-1.02] Adj for NO_2: 1.01 [0.98-1.03] Adj for O_3: 1.01 [0.96-1.06] One-pollutant model (NC100): 1.00 [0.98-1.02] One pollutant model (Nca12): 0.99 [.97-1.01] Adj for other size fractions: 0.99 [0.97-1.02] One pollutant model (Nca23): 0.99 [0.96-1.01] Adj for other size fractions: 0.99 [0.96-1.02] One pollutant model (NCa57): 1.01 [0.98-1.02] Adj for other size fractions: 0.99 [0.97-1.02] One pollutant model (Nca212): 1.02 [1.00-1.04]

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
	Dose-response Investigated: No **Statistical Package:** R statistical software (gam procedure, mgcv package) **Lags Considered:** Lag 0 -5 days, 4-day pollutant avg (lag 0 -3) for CVD, 5-day avg (lag 0-4) for RD, and a 6-day avg (lag 0-5) for asthma.	**Mean (SD):** 392 (441) **Median:** 246 **IQR:** 89-584 **99th Percentile:** 2,248 *NC, number concentration tot, total (all particles 6-700 in diameter) a12, size mode with mean diameter of 12 nm a23, size mode with median diameter of 23 nm a57, size mode with median diameter of 57 nm a212 size mode with median diameter of 212 nm NC100 = a12+a23+0.797*a57+0.084*a212. **Monitoring Stations:** 1 **Copollutant (correlation):** Correlation of NCtot with: PM_{10}: r = 0.39 $PM_{2.5}$: r = 0.40 NO_2: r = 0.68 : r = 0.66 NC_{100}: r = 0.98 NC_{a12}: r = 0.31 NC_{a23}: r = 0.57 NC_{a57}: r = 0.87 NC_{a212}: r = 0.29 CO: r = 0.54 NO_X curbside: r = 0.36 O_3: r = -0.12 **Other variables:** Temperature: r = -0.06 Relative humidity: r = -0.04	Adj for other size fractions: 1.02 [1.00-1.05] Adj for PM_{10}: 0.98 [0.95-1.01] RD hospital admissions (5-day avg, lag 0 -4), age 65+: One-pollutant model: 1.04 [1.00-1.07] Adj for PM_{10}: 1.00 [0.96-1.05] Adj for $PM_{2.5}$: 0.97 [0.89-1.05] Adj for CO: 1.03 [0.98-1.07] Adj for NO_2: 1.00 [0.95-1.05] Adj for O_3: 0.95 [0.87-1.04] One pollutant model (NC100): 1.03 [0.99-1.07] One pollutant model (Nca12): 1.01 [0.98-1.05] Adj for other size fractions: 1.01 [0.97-1.05] One pollutant model (Nca23): 0.99 [0.94-1.03] Adj for other size fractions: 0.98 [0.94-1.03] One pollutant model (Nca57): 1.04 [1.00-1.08] Adj for other size fractions: 1.02 [0.97-1.06] One pollutant model (Nca212): 1.04 [1.01-1.08] Adj for other size fractions: 1.03 [0.99-1.07] Adj for PM_{10}: 1.01 [0.96-1.07] Asthma hospital admissions (6-day avg lag 0-5), age 5-18: One-pollutant model: 1.07 [0.98-1.17] Adj for PM_{10}: 1.03 [0.92-1.15] Adj for $PM_{2.5}$: 1.04 [0.85-1.28] Adj for CO: 1.09 [0.99-1.21] Adj for NO_2: 1.07 [0.96-1.19] Adj for O_3: 1.08 [0.87-1.35] One pollutant model (NC100): 1.06 [0.97-1.16] One pollutant model (Nca212): 1.08 [0.99-1.18] Adj for other size fractions: 1.07 [0.97-1.19] One pollutant model (Nca23): 1.09 [0.98-1.21] Adj for other size fractions: 1.08 [0.97-1.21] One pollutant model (Nca57): 1.02 [0.94-1.12] Adj for other size fractions: 0.93 [0.83-1.04] One pollutant model (Nca212): 1.08 [1.00-1.17] Adj for other size fractions: 1.12 [1.02-1.23] Adj for PM_{10}: 1.10 [0.96-1.13] **Notes**: Fig 2: Relative risks and 95% confidence intervals per IQR in single day concentration (0-5 day lag). Summary of Fig 2: CVD: Positive, marginally or statistically significant associations at Lag 2 (Nctot, Nca57, Nca212), Lag 3 (Nca212), and Lag 1 (Nca212). RD: Positive, statistically or marginally significant associations at Lag 4 (Nctot, Nca57, NCa212) and Lag 5 (Nctot, Nca57, Nca212), and to a lesser extent Lag 2 (Nctot, Nca212) and Lag 3 (Nctot, Nca212). Asthma: Wide confidence intervals make interpretation difficult. Positive, significant association for Nca212 at Lag 1.

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Lanki et al. (2006, 089788) **Period of Study:** 1992-2000 **Location:** Augsburg, Barcelona, Helsinki, Rome, and Stockholm	**Outcome (ICD-9):** Acute myocardial infarction (410 ICD-10: I21, I22) **Age Groups:** 35+ yr, <75 yr, 75+ yr **Study Design:** Time series **N:** 26,854 hospitalizations **Statistical Analyses:** GAM **Covariates:** Temperature, barometric pressure **Season:** Warm (Apr-Sep) and cold (Oct-Mar) **Dose-response Investigated:** No **Statistical Package:** R package mgcv 0.9-5 **Lags Considered:** 0-3 days	**Pollutant: UFP (**PNC) **Averaging Time:** 24 h **Median particles/cm3:** Augsburg: 12,400 Barcelona: 76,300 Helsinki: 13,600 Rome: 46,000 Stockholm: 11,800 **Copollutant (correlation):** Augsburg PM_{10}: r = 0.53 CO: r = 0.63 NO_2: r = 0.65 O_3: r = 0.26 Barcelona: PM_{10}: r = 0.38 CO: r = 0.80 NO_2: r = 0.49 O_3: r = -0.35 Helsinki: PM_{10}: r = 0.45 CO: r = 0.48 NO_2: r = 0.82 O_3: r = 0.01 Rome: PM_{10}: r = 0.32 CO: r = 0.83 NO_2: r = 0.68 O_3: r = 0.03 Stockholm: PM_{10}: r = 0.06 CO: r = 0.56 NO_2: r = 0.83 O_3: r = -0.01	**PM Increment:** 10,000 particles/cm^3 Pooled Rate Ratio [CI]: All 5 cities (35+ yr) Same-day lag: 1.005 [0.996,1.015] 1-day lag: 0.997 [0.982,1.012] 2-day lag: 0.999 [0.990,1.008] 3-day lag: 0.998 [0.979,1.017] 3 cities with hospital discharge register (35+ yr) Same-day lag: 1.013 [1.000,1.026] 1-day lag: 0.995 [0.953,1.039] 2-day lag: 1.001 [0.989,1.014] 3-day lag: 1.009 [0.974,1.046] Warm season (35+ yr) Same-day lag: 1.009 [0.972,1.048] 1-day lag: 1.023 [0.988,1.060]; 2-day lag: 1.050 [1.016,1.085] 3-day lag: 1.022 [0.987,1.058] Cold season (35+ yr) Same-day lag: 1.014 [1.001,1.028] 1-day lag: 1.001 [0.956,1.048] 2-day lag: 1.001 [0.989,1.014] 3-day lag: 1.009 [0.971,1.049] Age >75Non-fatal Same-day lag: 1.032 [1.008,1.056] 1-day lag: 1.009 [0.985,1.032] 2-day lag: 0.989 [0.966,1.013] 3-day lag: 1.009 [0.969,1.051] Fatal Same-day lag: 1.016 [0.978,1.055] 1-day lag: 1.001 [0.966,1.038] 2-day lag: 1.005 [0.969,1.041] 3-day lag: 0.984 [0.948,1.021] **Notes**: Rate ratios for PNC are given for 0-5 lag days in graph form (Fig 1) for each city. Pooled rate ratios were also provided for groups <75 yielding similar results to the overall 3-city data.
Reference: Metzger et al. (2004, 044222) **Period of Study:** Aug 1998-Aug 2000 **Location:** Atlanta Metropolitan area (Georgia)	**Outcome (ICD-9):** Emergency visits for ischemic heart disease (410-414), cardiac dysrhythmias (427), cardiac arrest (427.5), congestive heart failure (428), peripheral vascular and cerebrovascular disease (433-437, 440, 443-444, 451-453), atherosclerosis (440), and stroke (436). **Age Groups:** All **Study Design:** Time series **N:** 4,407,535 emergency department visits between 1993-2000 (data not reported for 1998-2000) **Statistical Analyses:** Poisson generalized linear modeling **Covariates:** Day of the week, hospital entry and exit indicator variables, federally observed holidays, temporal trends, temperature, dew point temperature **Season:** All **Dose-response Investigated:** No **Statistical Package:** SAS **Lags Considered:** 3-day ma, lags 0-7	**Pollutant:** UFP (10-100 nm particle count) (no/cm^3) **Averaging Time:** 24 h **Median (10%-90% range):** 25,900 (11,500-74,600) **Monitoring Stations:** 1 **Copollutant (correlation):** PM_{10}: r = -0.13 O_3: r = -0.13 NO_2: r = 0.26 CO: r = 0.10 SO_2: r = 0.24 $PM_{2.5}$: r = -0.16 $PM_{2.5}$ water soluble metals: r = -0.27 $PM_{2.5}$ sulfates: r = -0.31; $PM_{2.5}$ acidity: r = -0.39; $PM_{2.5}$ OC: r = 0.08; $PM_{2.5}$ EC: r = 0.08; $PM_{2.5}$ oxygenated hydrocarbon: r = 0.05 **Other variables:** Temperature: r = -0.33 Dew point: r = -0.41	**PM Increment:** 30,000 no/cm^3 (approximately 1 SD)3 RR [95% CI]: For 3 day ma: All CVD: 0.985 [0.965, 1.005] Dysrhythmia: 0.972 [0.937, 1.008] Congestive heart failure: 0.983 [0.943-1.025] Ischemic heart disease: 0.989 [0.953-1.026] Peripheral vascular and cerebrovascular disease: 0.998 [0.960-1.039] Results for Lags 0-7 expressed in figures (see notes). **Notes**: Fig 1: RR (95% CI) for single-day lag models for the association of ER visits for CVD with daily ambient UFP. Summary of Fig 1 results: Null or negative associations.

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: von Klot et al. (2005, 088070) **Period of Study:** 1992-2001 **Location:** Augsburg, Germany Barcelona, Spain Helsinki, Finland Rome, Italy Stockholm, Sweden	**Outcome (ICD-9):** Acute myocardial infarction (410 ICD-10: I21-I22), angina pectoris (411, 413 ICD-10: I20, I24), dysrhythmia (427 ICD-10: I46.0, 46.9, I47-I49, R00.1, R00.8), heart failure (428 ICD-10: 150) **Age Groups:** 35+ yr **Study Design:** Cohort **N:** 22,006 MI survivors **Statistical Analyses:** GAM, Spearman correlation **Covariates:** Temperature, dew point temp, avg barometric pressure, relative humidity **Season:** NR **Dose-response Investigated:** No **Statistical Package:** R-software with "mgcv" package **Lags Considered:** 0-3 days	**Pollutant**: UFP (PNC) **Averaging Time:** 24 h **Mean particle/cm3 (5th-95th percentile):** Augsburg: Barcelona: Helsinki: Rome: Stockholm: **Monitoring Stations**: NR **Copollutant (correlation):** Augsburg PM_{10}: r = 0.52 CO: r = 0.63 NO_2: r = 0.64 O_3: r =-0.32 Barcelona PM_{10}: r = 0.29 CO: r = 0.71; NO_2: r = 0.44 O_3: r =-0.55 Helsinki PM_{10}: r = 0.46 CO: r = 0.47; NO_2: r = 0.83 O_3: r =-0.16 Rome PM_{10}: r = 0.33 CO: r = 0.80; NO_2: r = 0.71 O_3: r =-0.47 Stockholm PM_{10}: r = 0.06 CO: r = 0.54; NO_2: r = 0.80 O_3: r =-0.17	**PM Increment:** 10,000 particles/cm^3 Pooled RR Estimate [CI]: All cardiac admissions: 1.026 [1.005,1.048] Myocardial infarction: 1.039 [0.998.1.082] Angina pectoris: 1.020 [0.992,1.048]

[1]All units expressed in µg/m^3 unless otherwise specified.

E.2. Short-Term Exposure and Respiratory Outcomes

E.2.1. Respiratory Morbidity Studies

Table E-9. Short-term exposure-respiratory morbidity outcomes -PM_{10}.

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Aekplakorn, et al. (2003, 089908) **Period of Study**: 107 days, from Oct 1997-Jan 1998 **Location**: Mae Mo district, Lampang Province, North Thailand	**Outcome**: Upper respiratory symptoms, lower respiratory symptoms, cough **Age Groups**: 6-14 yr old **Study Design**: Logistic regression **N:** 98 asthmatic school children, 98 non-asthmatic school children **Statistical Analyses:** GEE, stratified analysis, PROC GENMOD **Covariates:** Temperature and relative humidity **Season**: Winter **Dose-response Investigated?** No **Statistical Package**: SAS v 8.1	**Pollutant**: PM_{10} **Averaging Time:** Daily **Mean (SD):** Sob Pad station: 31.92 Sob Mo station: 33.64 Hua Fai station: 37.45 **Range (Min, Max):** Sob Pad: 6.63, 153.25 Sob Mo: 4.23, 121.80 Hua Fai: 6.98, 113.30 **Monitoring Stations**: 3 **Copollutant:** $PM_{2.5}$, SO_2	**PM Increment:** 10 µg/m^3 Odds Ratios [Lower CI, Upper CI] lag: Asthmatics: URS: 1.03 (0.99, 1.07) lag 0 LRS: 1.04 (0.99, 1.09) lag 0 Cough: 1.04 (1.00, 1.07) lag 0 Non-Asthmatics: URS: 1.04 (0.99, 1.08) lag 0 LRS: 1.0 (0.93, 1.07) lag 0 Cough: 0.99 (0.94, 1.05) lag 0 PM_{10} + SO_2 Asthmatics: URS: 1.03 (0.99, 1.07) lag 0 LRS: 1.03 (0.98, 1.09) lag 0 Cough: 1.04 (1.00, 1.08) lag 0 Non-Asthmatics: URS: 1.04 (0.99, 1.08) lag 0 LRS: 1.0 (0.93, 1.07) lag 0 Cough: 0.99 (0.95, 1.05) lag 0

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Andersen et al. (2008, 189651) **Period of Study:** Dec 1998-Dec 2004 **Location:** Copenhagen, Denmark	**Outcome:** Daily symptoms (prospective daily recording of symptoms via diary) **Age Groups:** 0-3 yr **Study Design:** Panel study of children with genetic susceptibility to asthma (mothers had asthma) **N:** 205 children (living within a 15km radius of the central monitor during the first 3 yr of life) born between Aug 2, 1998 and Dec 12, 2001 **Statistical Analyses:** Logistic regression model (GEE) **Covariates: T**emperature, season, gender, age, exposure to smoking, and paternal history of asthma Effect modification: gender, medication use, and paternal history of asthma **Statistical Package:** SAS v9.1 **Lag:** 0,1,2,3,4,2-4	**Pollutant:** PM_{10} **Mean:** 25.1 **SD:** 16.7 **Percentiles:** 25th: 15.7 75th: 30.2 IQR: 14.5 **Copollutant (correlation):** $PM_{2.5}$ (r = 0.79) Number concentration of ultrafine particles, UFP (r = 0.37) NO_2 (r = 0.43) NO_X (r = 0.40) CO (r = 0.45) O_3 (r = -0.32) Temp (r = 0.25)	**PM Increment:** IQR (14.5 µg/m^3) increase Odds Ratios (95%CI) for incident wheezing symptoms Age 0-1 L0: 1.05 (0.88, 1.25) L1: 1.00 (0.82, 1.22) L2: 1.01 (0.83, 1.23) L3: 1.20 (0.98, 1.46) L4: 1.23 (1.02, 1.48) L2-4: 1.21 (0.99, 1.48) Age 1-2 L0: 1.00 (0.86, 1.15) L1: 1.02 (0.87, 1.19) L2: 1.05 (0.93, 1.19) L3: 0.96 (0.84, 1.09) L4: 1.04 (0.90, 1.21) L2-4: 1.03 (0.88, 1.22) Age 2-3 L0: 0.87 (0.72, 1.06) L1: 0.95 (0.78, 1.15) L2: 0.99 (0.82, 1.17) L3: 1.03 (0.84, 1.25) L4: 0.89 (0.74, 1.09) L2-4: 0.94 (0.74, 1.19) Age 0-3 L0: 0.97 (0.87, 1.08) L1: 0.99 (0.89, 1.10) L2: 1.01 (0.92, 1.12) L3: 1.03 (0.93, 1.14) L4: 1.04 (0.94, 1.15) L2-4: 1.04 (0.92, 1.17) Two pollutant models (lag 2-4) 1-pollutant model: 1.21 (0.99, 1.48) 2-pollutant (adj for NO_2): 1.13 (0.88, 1.45) 2-pollutant (adj for): 1.16 (0.90, 1.48) 2-pollutant (adj for CO): 1.23 (0.96, 1.57) 110 children living within 5km radius from monitor (sensitivity analysis): Age 0-1: 1.32 (0.95, 1.82) Age 1-2: 1.20 (0.87, 1.67) Age 2-3: 0.78 (0.52, 1.16) Age 0-3: 1.11 (0.88, 1.39)

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Boezen et al. (2005, 087396) **Period of Study:** Two consecutive winters (winter 1993-winter 1995) **Location: R**ural (Meppel, Nunspeet) and urban (Amsterdam) areas in the Netherlands	**Outcome:** FEV_1, airway hyperresponsiveness (AHR), serum total IgE and daily data on lower respiratory symptoms (LRS), upper respiratory symptoms (URS), cough and morning and evening peak expiratory flow **Age Groups:** 50-70 yr **Study Design:** Case-control study **N:** 327 patients **Statistical Analyses:** Logistic regression **Covariates:** daily minimum temperature, linear, quadratic and cubic time trend, weekend/holidays, and influenza incidence for the rural and urban areas and two winters separately **Season**: winter **Dose-response Investigated?** No **Lags Considered:** 0, 1, 2, and 5-day mean	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** Winter 93/94 Urban: 41.5 Winter 93/94 Rural: 44.1 Winter 94/95 Urban: 31.1 Winter 94/95 Rural: 26.6 **Percentiles:** 50th(Median): Winter 93/94 Urban: 34.6 Winter 93/94 Rural: 30.4 Winter 94/95 Urban: 28.9 Winter 94/95 Rural: 23.7 **Range (Min, Max):** 93/94 Urban: (12.1-112.7) 93/94 Rural: (7.9-242.2) 94/95 Urban: (8.8-89.9) 94/95 Rural: (7.1-96.9) **Copollutant:** SO_2 NO_2 BS	**PM Increment:** 10 µg/m^3 Effect Estimate [Lower CI, Upper CI]: AHR-/IgE- Upper Respiratory Symptoms Lag 0: OR = 0.99 (0.97-1.01) Lag 1: OR = 1.01 (0.99-1.03) Lag 2: OR = 1.00 (0.96-1.02) 5-day mean: OR = 1.00 (0.96-1.04) Cough Lag 0: OR = 1.00 (0.99-1.02) Lag 1: OR = 0.99 (0.98-1.01) Lag 2: OR = 1.00 (0.98-1.01) 5-day mean: OR = 0.98 (0.95-1.01) >10% fall in morning peak expiratory flow Lag 1: OR = 1.01 (0.98-1.04) Lag 2: OR = 0.97 (0.94-1.00) 5-day mean: OR = 0.97 (0.92-1.02) AHR-/IgE+ Upper Respiratory Symptoms Lag 0: OR = 1.01 (0.99-1.03) Lag 1: OR = 1.02 (1.00-1.04) Lag 2: OR = 1.01 (0.99-1.03) 5-day mean: OR = 1.08 (1.04-1.11) Cough Lag 0: OR = 1.01 (0.99-1.03) Lag 1: OR = 0.99 (0.98-1.01) Lag 2: OR = 1.00 (0.98-1.02) 5-day mean: OR = 1.01 (0.97-1.05) >10% fall in morning peak expiratory flow Lag 1: OR = 0.99 (0.97-1.02) Lag 2: OR = 0.99 (0.97-1.02) 5-day mean: OR = 0.97 (0.93-1.01) AHR+/IgE- Upper Respiratory Symptoms Lag 0: OR = 0.99 (0.95-1.03) Lag 1: OR = 1.01 (0.97-1.05) Lag 2: OR = 0.99 (0.96-1.03) 5-day mean: OR = 0.98 (0.91-1.06) Cough Lag 0: OR = 1.00 (0.97-1.02) Lag 1: OR = 1.01 (0.98-1.03) Lag 2: OR = 0.99 (0.96-1.02) 5-day mean: OR = 1.02 (0.96-1.08) >10% fall in morning peak expiratory flow Lag 1: OR = 0.99 (0.95-1.03) Lag 2: OR = 0.99 (0.95-1.03) 5-day mean: OR = 0.99 (0.93-1.06) AHR+/IgE+ Upper Respiratory Symptoms Lag 0: OR = 1.01 (0.98-1.04) Lag 1: OR = 1.03 (1.00-1.05) Lag 2: OR = 1.02 (0.99-1.05) 5-day mean: OR = 1.06 (1.00-1.11) Cough Lag 0: OR = 1.03 (1.01-1.06) Lag 1: OR = 1.00 (0.98-1.02) Lag 2: OR = 0.99 (0.97-1.01) 5-day mean: OR = 0.99 (0.95-1.04) Lag 2: OR = 0.99 (0.96-1.03) 5-day mean: OR = 0.99 (0.92-1.05) >10% fall in morning peak expiratory flow Lag 1: OR = 1.04 (1.00-1.07) Lag 2: OR = 1.03 (0.99-1.06) 5-day mean: OR = 1.05 (0.99-1.11)
Reference: Boezen et al. (1999, 040410) **Periods of Study:** 3 Winters (1992-1995) **Location:** Urban and rural areas of the Netherlands	**Outcome:** Respiratory symptoms Lower respiratory symptoms (wheeze, attacks of wheezing, shortness of breath) Upper respiratory symptoms (sore throat, runny or blocked nose)	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** Winter 1992-93 Urban: 54.8 Rural: 44.7 Winter 1993-94	**Increment:** 100 µg/m^3 **Odds Ratio (Lower CI, Upper CI) lag:** OR for respiratory symptoms and exposure to PM_{10} in children with BHR and high serum total IgE Lower Respiratory Symptoms 1.32 (1.07, 1.63) 0

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
	Bronchial hyperresponsiveness (BHR) **Study Design:** Time-series **Statistical Analyses:** Logistic regression (PROC model) **Age Groups:** 7-11	Urban: 41.5 3 Rural: 44.1 Winter 1994-95 Urban: 31.1 Rural: 26.6 **Range (Min, Max):** Winter 1992-93 Urban: (4.7, 145.6) Rural: (4.8, 103.8) Winter 1993-94 Urban: (12.1, 112.7) Rural: (7.9, 242.2) Winter 1994-95 Urban: (8.8, 89.9) Rural: (7.1, 96.9) **Copollutants:** BS SO_2 NO_2	1.36 (1.13, 1.64) 1 1.36 (1.13, 1.65) 2 2.39 (1.71, 3.35) 0-5 avg. Upper Respiratory Symptoms 1.13 (0.97, 1.32) 0 1.00 (0.87, 1.16) 1 0.96 (0.84, 1.11) 2 0.91 (0.70, 1.18) 0-5 avg >10% morning peak expiratory flow (PEF) decrease 1.10 (0.92, 1.33) 0 1.08 (0.90, 1.28) 1 1.03 (0.87, 1.23) 2 1.10 (0.83, 1.46) 0-5 avg >10% evening peak expiratory flow (PEF) increase 1.37 (1.16, 1.63) 0 1.09 (0.92, 1.29) 1 1.16 (0.98. 1.36) 2 1.35 (1.04, 1.77) 0-5 avg. OR for respiratory symptoms and exposure to PM_{10} in children without BHR and low serum total IgE Lower Respiratory Symptoms 1.08 (0.75, 1.57) 0 1.04 (0.70, 1.53) 1 0.98 (0.69, 1.39) 2 1.15 (0.61, 2.15) 0-5 avg. Upper Respiratory Symptoms 1.12 (0.99, 1.28) 0 1.01 (0.89, 1.15) 1 1.01 (0.89, 1.15) 2 0.93 (0.67, 1.28) 0-5 avg >10% morning PEF decrease 1.07 (0.93, 1.23) 0 0.86 (0.75, 0.99) 1 0.97 (0.85, 1.11) 2 0.99 (0.79, 1.23) 0-5 avg >10% evening PEF decrease 1.13 (0.98, 1.30) 0 1.05 (0.91, 1.21) 1 0.99 (0.87, 1.14) 2 0.94 (0.75, 1.17) 0-5 avg OR for respiratory symptoms and exposure to PM_{10} in children with BHR and low serum total IgE Lower Respiratory Symptoms 0.77 (0.48, 1.24) 0 1.34 (0.94, 1.93) 1 1.24 (0.86, 1.81) 2 1.92 (0.84, 4.41) 0-5 avg Upper Respiratory Symptoms 1.13 (0.92, 1.40) 0 0.98 (0.79, 1.22) 1 0.97 (0.79, 1.20) 2 0.83 (0.54, 1.25) 0-5 avg >10% morning PEF decrease 1.04 (0.78, 1.38) 0 0.86 (0.66, 1.12) 1 0.91 (0.71, 1.17) 2 0.78 (0.51, 1.20) 0-5 avg >10% evening PEF decrease 1.07 (0.82, 1.41) 0 0.98 (0.76, 1.26) 1 0.93 (0.73, 1.19) 2 0.83 (0.55, 1.26) 0-5 avg OR for respiratory symptoms and exposure to PM_{10} in children without BHR and high serum total IgE Lower Respiratory Symptoms 1.04 (0.80, 1.35) 0 1.21 (0.98, 1.51) 1 1.18 (0.96, 1.45) 2 1.35 (0.89, 2.04) 0-5 avg Upper Respiratory Symptoms 1.01 (0.85, 1.20) 0 0.95 (0.81, 1.12) 1 0.93 (0.80, 1.09) 2

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
			0.93 (0.69, 1.25) 0-5 avg >10% morning PEF decrease 0.97 (0.80, 1.17) 0 1.09 (0.91, 1.30) 1 1.02 (0.85, 1.21) 2 0.95 (0.71, 1.28) 0-5 avg >10% evening PEF decrease 1.02 (0.85, 1.22) 0 1.06 (0.90, 1.25) 1 1.08 (0.93, 1.27) 2 1.04 (0.80, 1.34) 0-5 avg.
Reference: Chattopadhyay et al. (2007, 147471) **Period of Study:** NR **Location:** Three different points in Kolkata, India: North, South, and Central	**Outcome:** pulmonary function tests (respiratory impairments) **Age Groups:** All ages **Study Design:** Cross-sectional **N:** 505 people studied for PFT total population of Kolkata not given **Statistical Analyses:** Frequencies **Covariates:** Meteorologic data (i.e. temperature, wind direction, wind speed, and humidity) **Dose-response Investigated?** No	**Pollutant:** PM_{10} **Averaging Time:** 8 h **Mean (SD):** North Kolkata: 535.9 Central Kolkata: 1114.5 South Kolkata: 909.2 **Monitoring Stations:** 1 **Copollutant:** PM<10-3.3 PM<3.3-0.4	**PM Increment:** NR Respiratory impairments (SD): North Kolkata Male (n = 137) Restrictive: 4 (2.92) Obstructive: 5 (3.64) Combined Res. And Obs.: 6 (4.37) Total: 15 (10.95) Female (n = 152) Restrictive: 3 (1.97) Obstructive: 5 (3.28) Combined Res. And Obs.: N/A Total: 8 (5.26) Total (n = 289) Restrictive: 7 (2.42) Obstructive: 10 (3.46) Combined Res. And Obs: 6 (2.07) Total: 23 (7.96) Central Kolkata Male (n = 44) Restrictive: 6 (13.63) Obstructive: 1 (2.27) Combined Res. And Obs.: 1 (2.27) Total: 8 (18.18) Female (n = 50) Restrictive: 3 (6.00) Obstructive: 2 (4.00) Combined Res. And Obs.: N/A Total: 5 (10.00) Total (n = 94) Restrictive: 9 (9.57) Obstructive: 3 (3.19) Combined Res. And Obs.: 1 (1.06) Total: 13 (13.82) South Kolkata Male (n = 52) Restrictive: 1 (1.92) Obstructive: 2 (3.84) Combined Res. And Obs.: 3 (5.76) Total: 6 (11.53) Female (n = 70) Restrictive: 2 (2.85) Obstructive: 1 (1.42) Combined Res. And Obs.: N/A Total: 3 (4.28) Total (n = 122) Restrictive: 3 (2.45) Obstructive: 3 (2.45) Combined Res. And Obs.: 3 (2.45) Total: 9 (7.37)

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Dales et al. (2006, 090744) **Period of Study:** Jan 1986-Dec 2000 **Location:** 11 Canadian Cities: Calgary, Edmonton, Halifax, London, Hamilton, Ottawa, St. John, Toronto, Vancouver, Windsor, Winnipeg	**Health Outcome:** Respiratory Illness: Asphyxia (799) Respiratory failure (799.1) Dyspnea and respiratory abnormalities (786) Respiratory distress syndrome (769) Unspecified birth asphyxia in live-born infant (768.9) Other respiratory problems after birth (770.8) Pneumonia (486) **Study Design:** Time-series **Statistical Analyses:** Poisson **Age Groups:** 0-27 days	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Copollutants (correlation):** O_3: r = -0.29 to 0.41 NO_2: r = -0.26 to 0.69 SO_2: r = -0.09 to 0.61 CO: r = -0.13 to 0.71	**Increment:** 10 µg/m^3 % Increase (Lower CI, Upper CI) Lag: In respiratory illness and exposure to PM_{10} in neonates PM_{10} alone: 2.13 (-0.50, 4.76) Multipollutant model PM_{10}: 1.45 (-1.90, 4.80) PM_{10}, O_3: 2.67 (0.98, 4.39) PM_{10}, NO_2: 2.48 (1.18, 3.80) PM_{10}, SO_2: 1.41 (0.35, 2.47) PM_{10}, CO: 1.30 (0.13, 2.49)
Reference: de Hartog et al. (2003, 001061) **Period of Study:** Winter of 1998-1999 Amsterdam, from Nov 1998 to Jun 1999 Erfurt, from Oct 1998 to Apr 1999 Helsinki, from Nov 1998 to Apr 1999 **Location:** Amsterdam, the Netherlands; Erfurt, Germany; Helsinki, Finland	**Outcome:** Respiratory symptoms **Age Groups:** ≥ 50 yr **Study Design:** Panel **N:** 131 subjects with history of coronary heart disease **Statistical Analyses:** Logistic regression **Covariates:** Ambient temperature, relative humidity, atmospheric pressure, incidence of influenza-like illness **Season:** Winter **Dose-response Investigated?** No **Statistical Package:** S-PLUS 2000 **Lags Considered:** 0-, 1-, 2-, 3-, and 5-day avg	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** Amsterdam: 36.5 Erfurt: 27.1 Helsinki: 19.6 **Range (Min, Max):** Amsterdam: (13.6-112.0) Erfurt: (5.2-104.2) Helsinki: (6.4-67.4) **Monitoring Stations:** 1 **Copollutant:** $PM_{2.5}$ $N_{C0.01-0.1}$ CO NO_2 SO_2	'There was a tendency toward positive associations between avoidance of activities and both particulate air pollution (PM_{10}) and gases, but none of the associations were statistically significant….In both incidence analyses and prevalence analyses, odds ratios for PM_{10} were generally similar to the corresponding odds ratios for $PM_{2.5}$, but were somewhat less significant.'
Reference: Delfino et al. (1998, 051406) **Period of Study:** Aug-Oct 1995 **Location:** Alpine, CA	**Outcome:** asthma symptom severity **Age Groups:** 9-17 **Study Design:** Panel Study **N:** 24 non-smoking pediatric asthmatics **Statistical Analyses:** GEE **Covariates:** Day of week, temperature, humidity, wind speed **Statistical Package:** SAS **Lags Considered:** 0-5, 0, 0-4	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 31 (8) 90th: 42 **Range (Min, Max):** 16, 54 **Copollutant (correlation):** O_3 (r = 0.32)	**PM Increment:** 42 µg/m^3 (90th percentile increase) Asthma symptoms: Everyone: 1.47 (0.90, 2.39) lag 0 Everyone: 1.73 (1.03, 2.89) lag 0-4 Less symptomatic: 2.47 (1.23-4.95) lag 0 Less symptomatic: 4.03 (1.22, 13.33) lag 0-4 More symptomatic: 1.50 (0.80, 2.80) lag 0 More symptomatic: 1.95 (1.12, 3.43) lag 0-4 PM_{10} + O_3 Asthma symptoms: 1.31 (0.84, 2.06) lag 0 1.65 (1.03, 2.66) lag 0-4 Less symptomatic: 2.08 (1.12-3.83) lag 0 Less symptomatic: 3.35 (1.06, 10.51) lag 0-4 More symptomatic: 1.40 (0.77, 2.53) lag 0 More symptomatic: 1.87 (1.11, 3.13) lag 0-4

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Delfino et al. (2002, 093740) **Period of Study:** Mar-Apr 1996 **Location:** Alpine, California (a semi-rural area)	**Outcome:** Asthma symptoms that interfere with daily activities **Age Groups:** 9-19 yr **Study Design:** Daily panel study **N:** 22 asthmatic children **Statistical Analyses:** GEE **Covariates:** Temperature, relative humidity, day-of-week trends, linear time trend across the 61 days, and upper or lower respiratory infection **Season:** "Early spring season" of Mar-Apr **Dose-response Investigated?** Yes **Statistical Package:** SAS, version 8 **Lags Considered:** 0-, 1-, 2-, 3-, 4-, 5-, and 3-day ma	**Pollutant:** PM_{10} **Averaging Time:** 1 h max **Mean (SD)**: 38(15) **Percentiles:** 90th: 63 **Range (Min, Max):** (12-69) **Averaging Time:** 8 h max **Mean (SD):** 28(12) **Percentiles:** 90th: 46 **Range (Min, Max):** (8-57) **Averaging Time:** 24 h **Mean (SD):** 20(9) **Percentiles:** 90th: 32 **Range (Min, Max):** (7-42) **Copollutant (correlation):** 1 h max PM_{10} 8 h max PM_{10}: r = 0.93 24 h PM_{10}: r = 0.84 1 h max O_3: r = 0.68 8 h max O_3: r = 0.95 1 h max NO_2: r = 0.49 8 h max NO_2: r = 0.55 8 h max PM_{10}: 1 h max PM_{10}: r = 0.93 24 h PM_{10}: r = 0.95 1 h max O_3: r = 0.72 8 h max O_3: r = 0.65 1 h max NO_2: r = 0.48 8 h max NO_2: r = 0.55 24 h PM_{10}: 1 h max PM_{10}: r = 0.84 8 h max PM_{10}: r = 0.95 1 h max O_3: r = 0.74 8 h max O_3: r = 0.71 1 h max NO_2: r = 0.37 8 h max NO_2: r = 0.44	**PM Increment:** 90th percentile increase Effect Estimate [Lower CI, Upper CI]: ORs for risk of asthma symptoms in those who report a respiratory infection compared to those who do not have a respiratory infection 1 h max PM_{10} lag 0: 4.88 (1.31-18.2) 8 h max PM_{10} lag 0: 6.78 (1.38-33.3) 24 h mean PM_{10} lag 0: 4.68 (0.71-30.7) 3-day ma 1 h max PM_{10}: 11.1 (1.10-112) 3-day ma 8 h max PM_{10}: 10.1 (1.42-72.0) 3-day ma 24 h PM_{10}: 2.67 (0.60-11.8) Effect modification by anti-inflammatory medication use on the relationship of asthma symptoms in children 1 h max PM_{10} lag 0: 1.41 (0.87-2.30) On medication: 0.96 (0.25-3.69) Not on medication: 1.92 (1.22-3.02) 8 h max PM_{10} lag 0: 1.19 (0.74-1.94) On medication: 0.75 (0.18-3.04) Not on medication: 1.68 (0.91-3.09) 24 h mean PM_{10} lag 0: 1.08 (0.73-1.61) On medication: 0.80 (0.24-2.69) Not on medication: 1.35 (0.82-2.22) 3-day ma 1 h max PM_{10}: 1.45 (0.76-2.76) On medication: 1.01 (0.14-7.02) Not on medication: 1.92 (0.99-3.71) 3-day ma 8 h max PM_{10}: 1.32 (0.76-2.29) On medication: 0.82 (0.17-3.94) Not on medication: 1.89 (1.10-3.24) 3-day ma 24 h PM_{10}: 1.22 (0.84-1.77) On medication: 0.75 (0.26-2.14) Not on medication: 1.75 (1.15-2.68) Dose-response results are found in Fig 2 and not quantitatively reported elsewhere.
Reference: Delfino et al. (2003, 090941) **Period of Study:** Nov 1999-Jan 2000 **Location:** Huntington Park, Los Angeles	**Outcome:** Asthma severity scale Peak Expiratory Flow Rate (PEF) **Age Groups:** Ages 10 to 16 **Study Design:** Longitudinal study panel **N:** 22 children **Statistical Analyses:** Regression analysis (GEE, GLM) multivariate regression models **Covariates:** Day of the week, Maximum Temperature, Respiratory Infections **Season:** Winter **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 0, 1	**Pollutant:** PM_{10} **Mean (SD):** 59.9 (24.7) **Range (Min, Max):** 20-126 IQR: 37 90th: 86.0 **Monitoring Stations:** 1 **Copollutant (correlation):** 8-h max NO_2 = 0.38 8-h max O_3 = -0.16 8-h max CO = 0.50 8-h max SO_2 = 0.73	**PM Increment:** IQR 37.0 $\mu g/m^3$ OR Estimate [Lower CI, Upper CI] lag: Lag 0 Symptom Scores >1: 1.45 (1.11, 1.90) Symptom Scores >2: NR Lag 1 Symptom Scores >1: 1.07 (0.64, 1.77) Symptom Scores >2: NR

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Delfino et al. (2004, 056897) **Period of Study:** Sep-Oct 1999 Apr-Jun 2000 **Location:** Alpine, California	**Outcome:** FEV_1 **Age Groups:** 9-19 yr old **Study Design:** Panel study **N:** 24 children **Statistical Analyses:** GLM Akaike's information criterion and Bayesian information criterion **Covariates:** Day of week, Personal temperature and relative humidity, time of FEV_1 maneuver (morning, afternoon, or evening), Season (fall 1999 or spring 2000) As-needed medication use Presence or absence of upper or lower respiratory infections **Season:** Spring, Fall **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** Lag 0-4	**Pollutant:** PM_{10} **Averaging Time:** 4 h, 8 h, 12 h, 24 h Personal Monitor 1-h max personal PM last 24-h **Mean (SD):** 151.0 (12.03) 90th: 292.4 **Range (Min, Max):** (9.1, 996.8) Mean personal PM last 24-h **Mean (SD):** 37.9 (19.9) 90th: 65.1 **Range (Min, Max):** (3.9, 113.8) Central outdoor stationary-site PM 1-h Maximum TEOM PM_{10} last 24-h Mean (SD): 54.4 (13.8) 90th: 71.0 **Range (Min, Max):** (24.4, 95.4) Mean TEOM PM_{10} last 24-h Mean (SD): 29.7 (8.6) 90th: 40.9 **Range (Min, Max):** (12.9, 50.7) 24-h mean PM_{10} Mean (SD): 23.6 (9.1) 90th: 34.6 **Range (Min, Max):** (3.2, 48.0) **Copollutant (correlation):** 8-h max personal PM 8-h max O_3 = 0.03 8-h Max NO_2 = 0.26 24-h Mean Personal PM = 0.94 8-h Max TEOM PM_{10} = 0.38 24-h Mean TEOM PM_{10} = 0.40 24-h Central HI PM_{10} = 0.37 24-h Central HI $PM_{2.5}$ = 0.38 24-h Outdoor HI PM_{10} = 0.32 24-h Outdoor HI $PM_{2.5}$ = 0.39 24-h Indoor HI PM_{10} = 0.23 24-h Indoor HI $PM_{2.5}$ = 0.37 24-h mean personal PM 8-h max O_3 = 0.01 8-h Max NO_2 = 0.27 8-h Max Personal PM = 0.94 8-h Max TEOM PM_{10} = 0.36 24-h Mean TEOM PM_{10} = 0.39 24-h Central HI PM_{10} = 0.36 24-h Central HI $PM_{2.5}$ = 0.43 24-h Outdoor HI PM_{10} = 0.34 24-h Outdoor HI $PM_{2.5}$ = 0.44 24-h Indoor HI PM_{10} = 0.29 24-h Indoor HI $PM_{2.5}$ = 0.46 24-h Mean TEOM PM_{10} 8-h max O_3 = 0.41 8-h Max NO_2 = 0.58 8-h Max Personal PM = 0.40 24-h Mean Personal PM = 0.39 8-h Max TEOM PM_{10} = 0.92 24-h Central HI PM_{10} = 0.86 24-h Central HI $PM_{2.5}$ = 0.78 24-h Outdoor HI PM_{10} = 0.79 24-h Outdoor HI $PM_{2.5}$ = 0.78 24-h Indoor HI PM_{10} = 0.36 24-h Indoor HI $PM_{2.5}$ = 0.59	Results presented graphically: Percent predicted FEV_1 was inversely associated with personal exposure to fine particles. - Inverse associations of FEV_1 with stationary-site indoor, outdoor and central-site gravimetric $PM_{2.5}$ and PM_{10}, and with hourly TEOM PM_{10}

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Delfino et al. (2006, 090745) **Period of Study:** Region 1: Aug to Mid Dec 2003. Region 2: Jul through Nov 2004 **Location:** Region 1: Riverside, CA. Region 2: Whittier, CA	**Outcome:** Fractional Concentration of Nitric Oxide in exhaled air (FENO) **Age Groups:** 9 through 18 **Study Design:** Longitudinal Panel Study **N:** 45 children **Statistical Analyses:** Linear mixed-effects models Two-stage hierarchical model Empirical Variograms Fourth-order polynomial distributed lag mixed-effects model **Covariates:** Personal temperature, Personal Rel. Humid., 10-day exposure run, Respiratory infections, Region of study, Sex, Cumulative daily use of as-needed B-agonist inhalers **Dose-response Investigated?** No **Lags Considered:** Lag 0, Lag 1, 2-day ma	**Pollutant:** PM_{10} Central Site **Averaging Time:** 24 h Riverside **Mean (SD):** 70.82 (29.36) 50th(Median): 65.96 **Range (Min, Max):** (30.75,54.05) $\mu g/m^3$ Whittier **Mean (SD):** 35.73 (16.6) 50th(Median): 34.65 **Range (Min, Max):** (5.86, 105.46) $\mu g/m^3$ **Monitoring Stations:** 48 personal nephelometers, 2 central sites	**PM Increment:** IQR increase (Riverside: 28.41 $\mu g/m^3$, Whittier 21.87 $\mu g/m^3$) Coefficient [Lower CI, Upper CI] lag: Lag = 2-day ma Stratified by Medication Use Not Taking Anti-Inflamm. Medication Central 0.76 (-1.54, 3.07) Taking Anti-Inflamm. Medication Central 0.53 (-0.83, 1.90) Inhaled Corticosteroids Central 1.28 (-0.01, 2.58) Antileukotrienes +- inhaled corticosteroids Central -2.10 (-5.33, 1.12) **Notes**: Fig of Estimated lag effect of hourly personal $PM_{2.5}$ on FENO. Fig of the Estimated lag effect of hourly personal $PM_{2.5}$ on FENO by use of medications. Fig of one- and two-pollutant models for change in FENO using 2-day Ma personal and central-site pollutant measurements.

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Desqueyroux et al. (2002, 026052) **Period of Study:** Nov 1995-Nov 1996 **Location:** Paris, France	**Outcome:** Asthma attacks **Age Groups:** Adults. **Study Design:** Panel study **N:** 60 moderate to severe adult asthmatics **Statistical Analyses:** Marginal logistic regression **Covariates:** FEV_1, smoking, allergy, oral steroid treatment, mean daily temperature, relative humidity, pollen counts, season, holiday period **Season:** winter, summer **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 1, 2, 3, 4, 5, 3-5	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** Summer: 23 (9) Winter: 28 (14) **Range (Min, Max):** Summer: 6, 63 Winter: 9, 84 **Monitoring Stations:** 7 **Copollutant:** SO_2 , NO_2, O_3	**PM Increment:** 10 µg/m^3 OR Estimate [Lower CI, Upper CI] lag: 0.87 [0.71, 1.06] lag 1 0.93 [0.80, 1.08] lag 2 1.11 [0.98, 1.26] lag 3 1.17 [1.03, 1.33] lag 4 1.16 [1.01, 1.34] lag 5 1.21 [1.01, 1.34] lag 3-5 Vs seasons alone: Winter: 1.41 [1.16, 1.71] lag 3-5 Summer: 1.03 [0.72, 1.47] lag 3-5 Vs link to explanatory factors: No link: [1.71 [1.20, 2.43] lag 3-5 Link: 1.27 [1.06, 1.52] lag 3-5 Vs occurrence of infection: Without infection: 1.52 [1.16, 2.00] lag 3-5 With infection: 1.30 [1.03, 1.65] lag 3-5 Vs baseline pulmonary function: FEV_1 >/ = 68% predicted: 1.38 [1.06, 1.79] lag 3-5 FEV <68% predicted: 1.45 [1.11, 1.90] lag 3-5 Vs smoking habits: Nonsmokers: 1.53 [1.18, 1.98] lag 3-5 Current & ex-smokers: 1.18 [0.90, 1.54] lag 3-5 Vs allergy: Non-allergic: 1.29 [0.94, 1.77] lag 3-5 Allergic: 1.49 [1.17, 1.90] lag 3-5 Vs regular oral steroid treatment: No: 1.41 [1.15, 1.73] lag 3-5 Yes: 1.41 [0.88, 2.25] lag 3-5 Multipollutant model: PM_{10} + NO_2: 1.43 [1.16, 1.76] Lag 3-5 PM_{10} + SO_2: 1.51 [1.20, 1.90] Lag 3-5 PM_{10} + O_3: 1.09 [0.71, 1.67] Lag 3-5
Reference: Diette et al. (2007, 156399) **Period of Study:** Sep 2001–Dec 2003 **Location:** East Baltimore, MD	**Outcome:** Asthma in the last 12 mo (493.x) **Age Groups:** 2 to 6 yr old **Study Design:** Prospective cohort **N:** 150 with asthma 150 without asthma **Statistical Analyses:** Student's two-tailed t-test Kruskal-Wallis test Pearson's chi square Fisher's exact test **Covariates:** Season of collection **Dose-response Investigated?** No **Statistical Package:** STATASE 8.0	**Pollutant:** PM_{10} **Averaging Time:** 72 h **50th(Median):** 43.7 **IQR:** (29-70)	**Notes**: "Pollutant concentrations in the homes of asthmatic and control children who lived in the same home for their whole life were not different compared with those who had moved at least once."

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Ebelt et al. (2005, 056907) **Period of Study:** Summer of 1998 **Location:** Vancouver, Canada	**Outcome:** spirometry **Age Groups:** Range from 54-86 yr mean age = 74 yr **Study Design:** Extended analysis of a repeated-measures panel study **N:** 16 persons with COPD **Statistical Analyses:** Earlier analysis expanded by developing mixed-effect regression models and by evaluating additional exposure indicators **Dose-response Investigated?** No **Statistical Package:** SAS V8	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** Ambient PM_{10}: 17 (6) Exposure to ambient PM_{10}: 10.3 (4.6) **Range (Min, Max):** Ambient PM_{10}: (7-36) Exposure to ambient PM_{10}: (1.5-23.8) **Monitoring Stations:** 5 **Copollutant (correlation):** Ambient $PM_{10-2.5}$: r = 0.69 Ambient $PM_{2.5}$: r = 0.78 Exposure to Ambient PM10: r = 0.71	**PM Increment:** Ambient PM_{10}: 7 (IQR) Exposure to ambient PM_{10}: 6.5 (IQR) **Notes**: Effect estimates are presented in Fig 2 and Electronic Appendix Table 1 (only available with electronic version of article) and not provided quantitatively elsewhere.
Reference: Fischer et al. (2007, 156435) **Period of Study:** 7 wk (dates not specified) **Location:** The Netherlands	**Outcome:** Respiratory Symptoms, Sore throat, Runny nose, Cold, Sick at home **Study Design:** Prospective cohort **N:** 68 **Statistical Analyses:** Linear regression model (PROC mixed) **Age Groups:** 10-11 **Lag:** 1-2 **Statistical Package:** SAS v 6.11	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 56 µg/m^3 IQ (25th, 75th): (21, 187) µg/m^3 **Copollutants:** BS NO_2 CO NO	**Increment:** 10 µg/m^3 % Increase in eNO and PM_{10} and change in spirometric lung function lag eNO and PM10 only 6.5 (0.9, 12.4) 1 7.8 (-11.3, 31.0) 2 FVC mean (SEM) 0.4 (0.5) 1 0.6 (1.6) 2 FEV_1 mean (SEM) -0.3 (0.5) 1 -2.1 (1.9) 2 PEF mean (SEM) -2.8 (3.3) 1 7.1 (12.0) 2 MMEF mean (SEM) -0.5 (1.7) 1 -2.5 (5.9) 2
Reference: Forsberg et al. (1998, 051714) **Period of Study:** Jan 1994-March 1994 **Location:** Urban and rural areas of Umea, Sweden	**Outcome:** Respiratory Symptoms, Shortness of breath Wheeze, Asthma attacks, Recent asthma, Dry cough, Doctor-diagnosed asthma, Recently treated for asthma, Early chest illness **Study Design:** Cohort panel **Statistical Analyses:** Logistic linear regression **Age Groups:** 6-12	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg Mean (SD): Urban: 13.4 µg/m3 Rural: 11.5 µg/m3 **Range (Min, Max):** Urban: (0, 40.5) µg/m3 Rural: (1.6, 29.0) µg/m3 Copollutants (correlation): BS: r = 0.73	**Increment:** 10 µg/m^3 OR between prevalence of acute respiratory symptoms and PM_{10} exposure for urban and rural children lag Urban children: Cough: 1.031 (0.957, 1.112) 0 0.997 (0.923, 1.077) 1 1.018 (0.940, 1.103): 2 1.094 (0.895, 1.338) 0-6 avg Phlegm: 0.998 (0.899, 1.108) 0 1.035 (0.928, 1.154) 1 1.121 (1.013, 1.240) 2 1.043 (0.822, 1.324) 0-6 avg Upper respiratory symptoms: 1.004 (0.949, 1.063) 0 0.975 (0.922, 1.031) 1 0.951 (0.895, 1.010) 2 0.849 (0.687, 1.050) 0-6 avg Lower respiratory symptoms: 0.984 (0.872, 1.110) 0 0.919 (0.812, 1.039) 1 0.894 (0.771, 1.036) 2 0.800 (0.617, 1.038) 0-6 avg Rural children (control) Cough: 0.997 (0.900, 1.105) 0 1.003 (0.906, 1.112) 1 0.997 (0.891, 1.116) 2 0.855 (0.655, 1.115) 0-6 avg Phlegm: 1.024 (0.880, 1.192) 0 0.995 (0.853, 1.160) 1 1.117 (0.956, 1.305) 2 1.041 (0.742, 1.459) 0-6 avg Upper respiratory symptoms: 1.093 (0.989, 1.208) 0 1.018 (0.918, 1.130) 1

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
			1.075 (0.962, 1.201) 2 1.052 (0.786, 1.407) 0-6 avg Lower respiratory symptoms: 1.022 (0.855, 1.180) 0 0.998 (0.855, 1.164) 1 1.000 (0.830, 1.206) 2 0.939 (0.703, 1.253) 0-6 avg
			OR between incidence of acute respiratory symptoms and PM_{10} exposure in urban and rural children lag
			Urban Children: Cough: 1.114 (0.886, 1.401) 0 0.891 (0.703, 1.130) 1 0.766 (0.577, 1.017) 2 0.817 (0.523, 1.276) 0-6 avg Phlegm: 0.954 (0.664, 1.371) 0 1.056 (0.744, 1.501) 1 1.416 (0.969, 2.069) 2 0.808 (0.357, 1.827) 0-6 avg Upper respiratory symptoms: 1.155 (0.965, 1.383) 0 0.788 (0.629, 0.986) 1 0.886 (0.728, 1.077) 2 0.770 (0.549, 1.081) 0-6 avg Lower respiratory symptoms: 1.060 (0.828, 1.356) 0 0.763 (0.584, 0.996) 1 0.652 (0.493, 0.863) 2 0.519 (0.306, 0.882) 0-6 avg Rural Children: Cough: 1.052 (0.767, 1.444) 0 0.753 (0.547, 1.038) 1 0.840 (0.571, 1.235) 2 0.800 (0.409, 1.565) 0-6 avg Phlegm: 1.051 (0.731, 1.509) 0 1.010 (0.693, 1.472) 1 0.998 (0.652, 1.528) 2 0.797 (0.344, 1.847) 0-6 avg Upper respiratory symptoms: 1.044 (0.813, 1.341) 0 0.810 (0.612, 1.072) 1 0.800 (0.611, 1.048) 2 0.714 (0.417, 1.220) 0-6 avg Lower respiratory symptoms: 1.079 (0.756, 1.539) 0 0.888 (0.615, 1.281) 1 0.715 (0.472, 1.083) 2 0.822 (0.395, 1.711) 0-6 avg
			OR between prevalence of medication use and PM10 exposure in urban and rural children lag
			Bronchodilator use - Urban children: 0.998 (0.951, 1.048) 0 0.999 (0.952, 1.049) 1 1.006 (0.953, 1.062) 2 0.919 (0.775, 1.090) 0-6 avg Rural children: 0.970 (0.904, 1.040) 0 0.959 (0.893, 1.030) 1 1.008 (0.927, 1.095) 2 1.087 (0.914, 1.292) 0-6 avg
			OR between incidence of medication use and PM_{10} exposure in urban and rural children lag
			Bronchodilator use - Urban children: 1.498 (0.899, 2.498) 0 1.049 (0.565, 1.947) 1 1.148 (0.674, 1.954) 2 1.787 (0.611, 5.227) 0-6 avg Rural children: 1.275 (0.702, 2.315) 0 0.924 (0.437, 1.956) 1

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
			1.005 (0.522, 1.936) 2 1.823 (0.534, 6.277) 0-6 avg
Reference: Goncalves et al. (2005, 089884) **Period of Study:** Dec 1992-Mar 1993. Dec 1992-Mar 1994 **Location:** Sao Paulo	**Outcome:** Respiratory morbidity/admissions **Age Groups:** Children <13 yr **Study Design:** Time series **Statistical Analyses:** Principal component analysis **Covariates:** Daily mean temperature, daily mean water vapor density, solar radiation **Season:** Summer **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** Lag 3	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Copollutant:** SO_2 , O_3	**PCA coefficients:** PC1, PC2, PC3: Summer 1992/1993: PM_{10}: 0.69, 0.45, 0.13 Solar Radiation: -0.04, 0.94 to -0.12 Mean Temperature: 0.62, 0.44 to -0.47 Mean Water Vapor Density: 0.73 to -0.46 to -0.26 SO_2: 0.78 to -0.03, 0.33 O_3: 0.18, 0.63, 0.37 Respiratory Mortality: 0.05 to -0.02, 0.81 Variations explained by Principal Component: PC1: 0.29 PC2: 0.27 PC3: 0.17 Summer 1993/1994: PM_{10}: 0.38, 0.80 to -0.23 Solar Radiation: 0.02, 0.09 to -0.97 Mean Temperature: 0.71, 0.40 to -0.37 Mean Water Vapor Density: 0.88, 0.25, 0.09 SO_2: 0.01, 0.92, 0.00 O_3: 0.47 to -0.06 to -0.35 Respiratory Mortality: -0.73, 0.11, 0.08 Variations explained by Principal Component: PC1: 0.31 PC2: 0.25 PC3: 0.18 **Notes**: Association between respiratory morbidity and air pollution more likely during summer with smaller contrasts in synoptic weather condition (summer 1992/93) but respiratory morbidity more related to weather variables during summer with larger contrasts (summer 1993/94).
Reference: Gordian and Choudhury (2003, 054842) **Period of Study:** 1994-Dec 1996 **Location:** Anchorage, Alaska	**Outcome:** Asthma medication among school children **Age Groups:** Elementary school children (kindergarten-6th grade) **Study Design:** Time series **Statistical Analyses:** Time series regression model **Covariates:** Day of the week, month, time trend, temperature **Season:** All seasons **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 1, 2, 7, 14, 21, 28	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 36.11 (30.46) **Range (Min, Max):** 2.96, 210.0 **Monitoring Stations:** 1	Model regression slope coefficient for PM_{10} (estimated SE) lag: 7.25 (2.88) lag 21 RR: 1.075 (1.016, 1.138) **Notes**: PM_{10} coefficients for other lags were also statistically significant but not reported.

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Harre et al. (1997, 095726) **Period of Study:** Jun 994-Aug 1994 **Location:** Christchurch, New Zealand	**Outcome:** Respiratory symptoms, Cough, Wheeze, Chest tightness, Shortness of breath, Change in sputum volume, Nose, throat, or eye irritation, PEFR **Study Design:** Prospective cohort **Statistical Analyses:** Poisson, log linear regression **Age Groups:** >55	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Copollutants:** CO SO_2 NO_2	**Increment**: 35.04 µg/m^3 **Relative Risk (Lower CI, Upper CI)** lag: Chest symptoms: 1.38 (1.07, 1.78) 1 Wheeze: 0.97 (0.75, 1.26) 1 Nebulizer Use: 0.71 (0.42, 1.18) 1 Inhaler Use: 0.94 (0.78, 1.13) 1
Reference: Hastings and Jardine (2002, 030344) **Period of Study:** 1997-1998 **Location:** Bosnia (U.S. military camps)	**Outcome:** Weekly rates of upper respiratory disease (URD), reported by the medical treatment facility in each military camp **Age Groups:** U.S. soldiers **Study Design:** Ecologic (at level of military camp) **N:** 5 camps **Statistical Analyses:** 1.Pearson correlations between weekly URD rates and weekly PM_{10} (avg and max) 2.Kruskal Wallace test to compare URD rates in the 4 exposure quartiles 3. Mann Whitney test to compare dichotomized exposure groups (above and below 50th percentile) **Dose-response Investigated?** Yes **Lags Considered:** Weekly rates of URD disease were related to avg weekly PM levels in the same week	**Pollutant:** PM_{10} **Mean (SD):** PM_{10} avg: 75.5 PM_{10} max: 92.9 **Percentiles:** PM_{10} max: 25th: 58.57 50th: 74.55 75th: 107.56 PM_{10} avg: 25th: 42.19 50th: 64.17 75th: 81.75 **Range (Min, Max):** PM_{10} avg: 25.0, 338.7 PM_{10} max: 25.0, 338.7 **Monitoring Stations:** At least 1 in each of the 5 camps	**PM max Quartiles (combining all camps):** Q1: <58.7 µg/m^3 Q2: 60.1 to <75.54 µg/m^3 Q3: 78.56 to <107.56 µg/m^3 Q4: >107.56 µg/m^3 For dichotomous analysis cutoff = 74.55 µg/m^3 PM avg Quartiles (combining all camps): Q1: <42.19 µg/m3 Q2: 42.19 to 64.17 µg/m3 Q3: 64.17 to 81.75 µg/m3 Q4: >81.75 µg/m3 For dichotomous analysis cutoff = 64.17 µg/m^3 Pearson correlation coefficients between URD rate and PM category [p-value]: PM_{10} max: quartiles of PM*URD rates All camps 0.203 [0.041] Blue Factory camp 0.277 [0.095] Comanche 0.165 [0.237] Demi 0.639 [0.123] McGovern 0.535 [0.177] Tuzla Main 0.107 [0.327] PM_{10} max: dichotomous PM*URD rates: All camps 0.283 [0.007] Blue Factory camp 0.038 [0.430] Comanche 0.282 [0.107] Demi 0.927 [0.012] McGovern 0.853 [0.033] Tuzla Main 0.155 [0.258] PM_{10} avg: quartiles of PM*URD rates: All camps 0.149 [0.101] Blue Factory camp 0.301 [0.077] Comanche 0.246 [0.141] Demi 0.437 [0.231] McGovern 0.853 [0.033] Tuzla Main 0.182 [0.222] PM_{10} avg: dichotomous PM*URD rates: All camps 0.060 [0.305] Blue Factory camp -0.075 [0.365] Comanche 0.143 [0.268] Demi N/A* McGovern N/A* Tuzla Main 0.123 [0.303] Kruskal Wallace p-value comparing URD rates across exposure quartiles: PM_{10} max All camps 0.047 Blue Factory camp 0.321 Comanche 0.556 Demi 0.165 McGovern 0.202 Tuzla Main 0.554 PM_{10} avg

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
			All camps 0.672 Blue Factory camp 0.809 Comanche 0.658 Demi 0.564 McGovern 0.157 Tuzla Main 0.891 Mann-Whitney p-value comparing URD rates between upper and lower 50th percentile of PM: PM_{10} max All camps 0.034 Blue Factory camp 0.173 Comanche 0.314 Demi 0.083 McGovern 0.401 Tuzla Main 0.481 PM_{10} avg All camps 0.824 Blue Factory camp 0.682 Comanche 0.508 Demi N/A* McGovern N/A* Tuzla Main 0.656 **Notes**: * There were no days that fell in the upper 50 percentile for PM avg in these camps -Rates of URD by PM quartiles for each camp presented in figures. Authors state, "Generally the avg URD rate increased with quartile of maximum exposure…the trend was not as clear for quartiles of PM_{10} avg exposure"

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Hong et al. (2007, 091347) **Period of Study:** Mar 23-May 2004 **Location:** School on the Dukjeok Island near Incheon City, Korea	**Outcome:** Peak expiratory flow rate (PEFR) **Age Groups:** 3rd to 6th grade (mean age = 9.6 yr) **Study Design:** Panel study **N:** 43 schoolchildren **Statistical Analyses:** Mixed linear regression **Covariates:** Age, sex, height, weight, asthma history, and passive smoking exposure at home **Dose-response Investigated?** No **Lags Considered:** 0, 1, 2, 3, 4, 5	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 35.30 (23.48) 50th (Median): 29.36 **Range (Min, Max):** (12.24-124.87) PM Component: Fe: mean = 0.208 (0.203) µg/m^3 Median = 0.112 **Range (Min, Max):** (0.061-0.806) Mn: mean = 0.008 (0.005) µg/m^3 Median = 0.007 **Range (Min, Max):** (0.000-0.019) Pb: mean = 0.051 (0.031) µg/m^3 Median = 0.051 **Range (Min, Max):** (0.011-0.155) Zn: mean = 0.021 (0.021) µg/m^3 Median = 0.013 **Range (Min, Max):** (0.006-0.112) Al: mean = 0.085 (0.100) µg/m^3 Median = 0.031 **Range (Min, Max):** (0.017-0.344) Copollutant: $PM_{2.5}$	**Effect Estimate:** Regression coefficients of morning and daily mean PEFR on PM_{10} and metal components using linear mixed-effects regression Lag 1 (PM_{10}) Morning PEFR Crude: ß = -0.00, p = 0.99 Adjusted: ß = -0.04, p = 0.37 Mean PEFR Crude: ß = 0.00, p = 0.93 Adjusted: ß = -0.05, p = 0.12 Lag 1 (logFe) Morning PEFR Crude: ß = -1.26, p = 0.31 Adjusted: ß = -3.24, p = 0.13 Mean PEFR Crude: ß = -1.20, p = 0.20 Adjusted: ß = -2.37, p = 0.15 Lag 1 (logMn) Morning PEFR Crude: ß = -4.40, p < 0.01 Adjusted: ß = -9.82, p < 0.01 Mean PEFR Crude: ß = -4.05, p < 0.01 Adjusted: ß = -8.44, p < 0.01 Lag 1 (logPb) Morning PEFR Crude: ß = -6.79, p < 0.01 Adjusted: ß = -6.83, p < 0.01 Mean PEFR Crude: ß = -6.23, p < 0.01 Adjusted: ß = -6.37, p < 0.01 Lag 1 (logZn) Morning PEFR Crude: ß = -0.55, p = 0.71 Adjusted: ß = -0.98, p = 0.59 Mean PEFR Crude: ß = 1.33, p = 0.24 Adjusted: ß = 1.53, p = 0.28 Lag1 (logAl) Morning PEFR Crude: ß = -0.58, p = 0.57 Adjusted: ß = -2.22, p = 0.25 Mean PEFR Crude: ß = -0.59, p = 0.45 Adjusted: ß = -1.48, p = 0.32 Regression coefficients of morning and daily mean PEFR on metal components of PM_{10} and GSTM1 and GSTT1 genotype using linear mixed-effects regression Lag 1 (logPb) Morning PEFR: ß = -7.26, p < 0.01 Mean PEFR: ß = -6.43, p < 0.01 GSTM1 Morning PEFR: ß = 21.19, p = 0.23 Mean PEFR: ß = 20.09, p = 0.25 Lag 1 (logMn) Morning PEFR: ß = -10.31, p < 0.01 Mean PEFR: ß = -8.66, p < 0.01 GSTM1 Morning PEFR: ß = 21.02, p = 0.23 Mean PEFR: ß = 19.84, p = 0.25 Lag 1 (logPb) Morning PEFR: ß = -7.26, p < 0.01 Mean PEFR: ß = -6.43, p < 0.01 GSTT1 Morning PEFR: ß = 2.07, p = 0.90 Mean PEFR: ß = -2.39, p < 0.88 Lag 1 (logMn) Morning PEFR: ß = -10.32, p < 0.01 Mean PEFR: ß = -8.67, p < 0.01 GSTT1 Morning PEFR: ß = 2.02, p = 0.90 Mean PEFR: ß = 2.33, p = 0.88

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Hwang et al. (2006, 088971) **Period of Study:** 2001 **Location:** Taiwan	**Outcome:** Allergic rhinitis **Study Design:** Cross-sectional **Statistical Analyses:** Two-stage hierarchical models **Age Groups:** 6-15 yr	**Pollutant:** PM_{10} **Averaging Time:** 1-h avg **Mean (SD):** 55.58 (16.57) **Range (Min, Max):** (29.36, 99.58) **Copollutants (correlation):** CO: r = 0.27 NO_X: r = 0.34 O_3: r = 0.28 SO_2: r = 0.58	**Increment:** 10 µg/m^3 **Odds Ratio (Lower CI, Upper CI)** lag: PM_{10} alone: 1.00 (0.99, 1.02) , PM_{10}: 0.99 (0.97, 1.00) CO, PM_{10}: 1.00 (0.99, 1.01) O_3, PM_{10}: 1.00 (0.99, 1.02) Gender Male: 1.02 (0.99, 1.04) Female: 0.99 (0.97, 1.02) Parental atopy* Yes: 1.00 (0.98, 1.03) No: 1.01 (0.99, 1.03) Parental education <6 yr: 1.05 (0.96, 1.14) 6-8 yr: 1.03 (0.98, 1.07) 9-11 yr: 1.00 (0.98, 1.03) 12+ yr: 0.99 (0.97, 1.02) Environmental tobacco smoke Yes: 1.01 (0.99, 1.03) No: 1.00 (0.98, 1.03) Visible mold** Yes: 1.02 (0.99, 1.06) No: 1.00 (0.98, 1.02) * Parental atopy was a measure of genetic predisposition and was defined as the father or the mother of the index child ever having been diagnosed as having asthma, allergic rhinitis, or atopic eczema. ** Visible mold found in the home.
Reference: Jalaludin et al. (2004, 056595) **Period of Study:** Feb 1994-Dec 1994 **Location:** Western and southwestern Sydney, Australia	**Outcome:** Respiratory symptoms, Wheeze, Dry cough, Wet cough **Study Design:** Longitudinal study panel **Statistical Analyses:** Logistic regression model (GEE) **Age Groups:** 9-11 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 22.8 (13.8) **IQ Range (25th,75th):** (12.00, 122.8) **Copollutants (correlation):** O_3: r = 0.13 NO_2: r = 0.26	**Increment:** 10 µg/m^3 **Odds Ratio (Lower CI, Upper CI)** **Lag** Wheeze 1.01 (0.99, 1.03) 0 1.01 (0.97, 1.04) 1 0.99 (0.96, 1.03) 2 1.02 (0.98, 1.06) 0-2 avg 1.04 (0.99, 1.10) 0-5 avg Dry Cough 1.00 (0.98, 1.03) 0 1.00 (0.97, 1.03) 1 1.00 (0.97, 1.02) 2 1.00 (0.97, 1.03) 0-2 avg 1.03 (0.98, 1.08) 0-5 avg Wet Cough 1.01 (0.99, 1.04) 0 0.99 (0.97, 1.01) 1 1.00 (0.97, 1.03) 2 0.99 (0.96, 1.02) 0-2 avg 0.99 (0.94, 1.04) 0-5 avg Inhaled B2-agonist Use 0.99 (0.98, 1.01) 0 1.00 (0.98, 1.03) 1 0.99 (0.97, 1.01) 2 1.00 (0.97, 1.02) 0-2 avg 1.02 (0.98, 1.06) 0-5 avg Inhaled Corticosteroid Use 1.00 (0.99, 1.01) 0 1.00 (0.99, 1.02) 1 1.00 (0.99, 1.02) 2 1.00 (0.98, 1.02) 0-2 avg 1.00 (0.97, 1.02) 0-5 avg Doctor Visit for Asthma 1.11 (1.04, 1.19) 0 1.10 (1.02, 1.19) 1 1.15 (1.06, 1.24) 2 1.11 (1.03, 1.20) 0-2 avg 1.14 (0.98, 1.31) 0-5 avg **OR for respiratory symptoms and PM10 exposure by different groups**

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
			All children Wheeze: 1.01 (0.99, 1.04) Dry Cough: 1.00 (0.97, 1.02) Wet Cough: 1.01 (0.98, 1.04) Inhaled B2-agonist Use: 1.00 (0.98, 1.02) Inhaled Corticosteroid Use: 0.99 (0.98, 1.01) Doctor Visit for asthma: 1.11 (1.03, 1.19) Group 1* Wheeze: 1.01 (0.98, 1.04) Dry Cough: 0.97 (0.94, 0.99) Wet Cough: 1.00 (0.97, 1.03) Inhaled B2-agonist use: 1.00 (0.98, 1.02) Inhaled Corticosteroid Use: 1.00 (0.98, 1.01) Doctor Visit for asthma: 1.09 (0.98, 1.21) Group 2** Wheeze: 1.01 (0.97, 1.05) Dry Cough: 1.02 (0.98, 1.06) Wet Cough: 1.01 (0.96, 1.06) Inhaled B2-agonist use: 0.99 (0.94, 1.05) Inhaled Corticosteroid Use: 0.99 (0.97, 1.01) Doctor Visit for asthma: 1.12 (1.02, 1.23) Group 3*** Wheeze: 1.08 (0.90, 1.31) Dry Cough: 1.01 (0.91, 1.11) Wet Cough: 1.02 (0.94, 1.11) Inhaled B2-agonist use: 0.98 (0.84, 1.11) Inhaled Corticosteroid Use: 1.27 (1.08, 1.49) Doctor Visit for asthma: NR *Group 1 consists of children with a history of wheeze in the past 12 mo, positive histamine challenge, and doctor diagnosed asthma. **Group 2 consists of children with a history of wheeze in the past 12 mo and doctor diagnosed asthma. ***Group 3 consists of children only with a history y of wheeze in the past 12 mo.

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Jansen, et al. (2005, 082236) **Period of Study:** 1987-2000 **Location:** Seattle, WA	**Outcome:** FENO: fractional exhaled nitrogen oxide, Spirometry, Blood pressure, SaO_2: oxygen saturation, Pulse rate **Age Groups:** 60-86 yr old **Study Design:** Short-term cross-sectional case series **N:** 16 subjects diagnosed with COPD, asthma, or both **Statistical Analyses:** Linear mixed effects model with random intercepts **Covariates:** Age, relative humidity, temperature, medication use **Season:** winter 2002-2003 **Dose-response Investigated?** No **Statistical Package:** STATA	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** Fixed-site Monitor: 18.0 All Subjects (N = 16) Indoor, home: 11.93 Outdoor, home: 13.47 Personal: 23.34 Asthmatic Subjects (N = 7) Indoor, home: 12.54 Outdoor, home: 11.86 Personal: 26.88 COPD Subjects (N = 9) Indoor, home: 11.45 Outdoor, home: 14.76 Personal: 19.91 **Range (Min, Max):** Fixed-site Monitor 2.5, 51 **IQR:** All Subjects Indoor, home: 6.93 Outdoor, home: 9.53 Personal: 20.72 Asthmatic Subjects Indoor, home: 10.19 Outdoor, home: 8.77 Personal: 20.08 COPD Subjects Indoor, home: 4.56 Outdoor, home: 6.14 Personal: 19.94	**PM Increment:** 10 $\mu g/m^3$ Slope [95% CI]: dependence of FENO concentration [ppb] on PM_{10} Asthmatic Subjects Indoor, home: 3.81 [-0.86: 8.50] Outdoor, home: 5.87 [2.87: 8.88]* Personal: 0.66 [-0.56: 1.88] COPD Subjects Indoor, home: 2.19 [-3.48: 7.87] Outdoor, home: 4.45 [-1.11: 10.01] Personal: 0.17 [-1.61: 1.96] Results indicate that FENO may be a more sensitive biomarker of PM exposure than other traditional health endpoints.

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Johnston, et al. (2006, 091386) **Period of Study:** 7 mo (Apr 7-Nov 7, 2004) **Location:** Darwin, Australia	**Outcome:** Asthma symptoms **Age Groups:** All ages **Study Design:** Time-series **N:** 251 people (130 adults, 121 children **Statistical Analyses:** Logistic regression model **Covariates:** Minimum air temperature, doctor visits for influenza and the prevalence of asthma symptoms and, the fungal spore count and both onset of asthma symptoms and commencement of reliever medication **Season:** "Dry season"-specific months NR, note Southern Hemisphere **Dose-response Investigated?** No **Statistical Package:** STATA8 **Lags Considered:** 0-5 days	**Pollutant:** PM_{10} **Averaging Time:** Daily **Mean (SD):** 20 (6.4) **Range (Min, Max):** 2.6-43.3 **PM Component:** Vegetation fire smoke (95%) and motor vehicle emissions (5%) **Monitoring Stations:** 1 **Correlation:** $PM_{2.5}$: r = 0.90	**PM Increment:** 10 µg/m^3 **RR Estimate [Lower CI, Upper CI]** Symptoms attributable to asthma Overall:1.010 (0.98,1.04) Adults:1.027 (0.987,1.068) Children:0.930 (0.966, 1.060) Using preventer: 1.022 (0.985, 1.060) Became symptomatic Overall: 1.240 (1.106,1.39) Adults: 1.277 (1.084,1.504) Children: 1.247 (1.058,1.468) Using preventer:1.317 (1.124,1.543) Used Reliever Overall: 1.010 (0.99, 1.04) Adults: 1.026 (0.990, 1.063) Children: 1.006 (0.960,1.055) Using preventer:1.035 (1.004,1.060) Commenced Reliever Overall: 1.132 (0.99, 1.29) Adults: 1.199 (0.994, 1.446) Children: 1.093 (0.906,1.319) Using preventer:1.194 (0.996, 1.432) Commenced Oral Steroids Overall: 1.540 (1.01, 2.34) Adults: 1.752 (1.008, 3.045) Children: 1.292 (0.682, 2.448) Using preventer:1.430 (0.888, 2.304) Asthma Attack Overall: 1.030 (0.95, 1.12) Adults: 1.08 (0.976, 1.202) Children: 0.861 (0.710, 1.044) Using preventer:1.051 (0.939,1.175) Exercise induced asthma Overall: 0.980 (0.92, 1.05) Adults: 0.988 (0.902, 1.081) Children: 0.972 (0.844,1.119) Using preventer:1.026 (0.928,1.134) Saw a health professional for asthma Overall: 1.030 (0.85, 1.26) Adults: 1.064 (0.794, 1.424) Children: 0.998 (0.749,1.328) Using preventer:0.924 (0.731, 1.169) Missed school or work due to asthma Overall: 1.102 (0.941, 1.290) Adults: 1.135 (0.897, 1.435) Children: 1.073 (0.862,1.333) Using preventer:1.025 (0.857,1.228) Mean daily number of asthma symptoms Overall: 1.020 (1.001,1.031) Adults: 1.027 (1.005,1.049) Children: 1.016 (0.986,1.047) Using preventer:1.034 (1.011,1.058) Mean Daily number of applications of reliever Overall: 1.020 (1.00,1.030) Adults: 1.032 (1.008, 1.057) Children: 1.002 (0.969,1.034) Using preventer:1.022 (1.001,1.043)

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Just et al. (2002, 035429) **Period of Study:**Apr 1996-Jun 1996 **Location:** Paris, France	**Outcome:** Incident and prevalent episodes of asthma attacks, nocturnal cough, wheeze, symptoms of irritation, respiratory infections, supplementary use of β2-agonists, Z-transformed peak expiratory flow (PEF), daily PEF variability **Age Groups:** 7-15 yr old **Study Design:** Cohort **N:** 82 children **Statistical Analyses:** Linear regression, logistic regression, GEE **Covariates:** Effects of time trend, day of the week, weather, pollen levels **Season:** Spring/summer **Lags Considered:** 0, 0-2 mean, 0-4 mean	**Pollutant:** PM_{10} **Averaging Time:** Daily **Mean (SD):** 23.5 (8.4) **Range (Min, Max):** 9.0, 44.0 **Monitoring Stations:** 5 **Copollutant (correlation):** BS: 0.59 SO_2: 0.70 NO_2: 0.54 O_3: 0.21 Temp: 0.04 Humid: -0.41	**PM Increment:** 10 μg/m^3 for binary responses data (results that use odds ratios [ORs]) **Incident episodes of** 1) Asthma a) lag 0: 1.06 (0.61, 1.83) b) 0-2 mean: 1.09 (0.48, 2.49) c) 0-4 mean: 1.07 (0.44, 2.65) 2) Nocturnal cough a) lag 0: 1.10 (0.88, 1.37) b) 0-2 mean: 1.03 (0.77, 1.37) c) 0-4 mean: 1.11 (0.86, 1.42) 3) Respiratory infections a) lag 0: 0.64 (0.35, 1.15) b) 0-2 mean: 0.74 (0.38, 1.43) c) 0-4 mean: 0.99 (0.58, 1.68) **Prevalent episodes of** 1) Asthma a) lag 0: 1.07 (0.72, 1.59) b) 0-2 mean: 1.18 (0.64, 2.17) c) 0-4 mean: 1.16 (0.63, 2.13) 2) Nocturnal cough a) lag 0: 1.05 (0.83, 1.34) b) 0-2 mean: 1.10 (0.81, 1.50) c) 0-4 mean: 1.09 (0.79, 1.52) 3) Respiratory infections a) lag 0: 1.17 (0.68, 2.03) b) 0-2 mean: 1.31 (0.51, 3.36) c) 0-4 mean: 1.71 (0.71, 4.12) 4) Eye irritation a) lag 0: 1.18 (1.01, 1.39) b) 0-2 mean: 1.28 (1.03, 1.59) c) 0-4 mean: 1.42 (1.12, 1.80) **Analysis restricted to days with no steroid use:** **Incident episodes of** 1) Eye irritation a) lag 0: 1.07 (0.66, 1.71) b) 0-2 mean: 0.83 (0.45, 1.53) c) 0-4 mean: 0.92 (0.46, 1.83) 2) Throat irritation a) lag 0: 1.33 (0.66, 2.69) b) 0-2 mean: 1.28 (0.58, 2.80) c) 0-4 mean: 1.06 (0.38, 2.95) 3) Nose irritation a) lag 0: 0.74 (0.48, 1.13) b) 0-2 mean: 0.76 (0.42, 1.36) c) 0-4 mean: 0.96 (0.53, 1.73) **Prevalent episodes of** 1) Eye irritation a) lag 0: 1.20 (0.88, 1.65) b) 0-2 mean: 1.71 (0.97, 3.01) c) 0-4 mean: 1.97 (1.03, 3.76) 2) Throat irritation a) lag 0: 1.23 (0.83, 1.82) b) 0-2 mean: 1.08 (0.68, 1.73) c) 0-4 mean: 0.91 (0.47, 1.73) 3) Nose irritation a) lag 0: 1.20 (0.91, 1.58) b) 0-2 mean: 1.09 (0.78, 1.52) c) 0-4 mean: 1.09 (0.73, 1.61) **Notes:** The authors noted that incident or prevalent wheeze was not correlated with levels of any type of pollutant. Also, they state no relationship was observed between PEF variables and levels of PM. The authors also note that in a multipollutant model assessing independent effects of PM and O_3 on prevalent episodes of eye irritation (mean 0-4), the PM parameter decreased and was not significant ($p = 0.19$).

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Kulkarni et al. (2006, 089257) **Period of Study:** Nov 2002-Dec 2003 **Location:** Leicester, United Kingdom	**Outcome:** Lung function by spirometry: FVC, FEV_1, FEV_1: FVC, FEF_{25-75} **Age Groups:** 8-15 yr **Study Design:** Cross-sectional **N:** 114 children, 64 provided sputum for assessment of carbon content of macrophages. **Statistical Analyses:** Linear regressions, Spearman rank correlations. Mann-Whitney, Chi-square and unpaired t tests were used to compare results between asthmatic and non asthmatic children **Covariates:** BMI, sex, exercise, traffic PM_{10} **Dose-response Investigated?** Yes **Statistical Package:** SPSS	**Pollutant:** Primary PM_{10} ($\mu g/m^3$) concentration was modeled, and was considered a covariate for carbon content of macrophages. Carbon content of alveolar macrophages was the primary variable of interest. **Averaging Time:** 1 yr 50th(Median): Children without asthma, 1.21 Children with asthma, 1.81 **Range (Min, Max):** Children without asthma, 0.10, 2.17 Children with asthma, 0.17, 2.13 **PM Component:** Carbon content in alveolar macrophages **Monitoring Stations:** NR. **Copollutant (correlation):** Vs carbon content in macrophages (increment, coefficient range]) -1.0 $\mu g/m^3$, 0.1 [0.01-0.18]	**PM Increment:** 1.0 $\mu g/m^3$ **% Change [Lower CI, Upper CI]:** Single pollutant model: FEV_1: -4.3 [-8.5, 0.2] p = 0.04 R2 = 0.06 Single pollutant model: FVC: -1.2 [-5.6, 3.2] p = 0.59 R2 = 0.005 Single pollutant model: FEF_{25-75}: -8.6 [-17.3, 0.1] p = 0.05 R2 = 0.06 2 pollutant model with Macrophage Carbon: FEV_1: PM_{10} -2.9 [-6.9, 1.2] p = 0.17 FVC: PM_{10} 0.1 [-4.4, 4.6] p = 0.96 FEF_{25-75}: PM_{10} -5.5 [-14.2, 3.1] p = 0.21
Reference: Kuo, et al. (2002, 036310) **Period of Study:** 1-yr period (yr not specified) **Location:** Central Taiwan	**Outcome:** Asthma (yes/no) **Age Groups:** 13-16 yr **Study Design:** Cohort **N:** 12,926 total children 775 asthmatic children 8 junior high schools **Statistical Analyses:** Pearson correlation coefficients Logistic regression **Covariates:** Gender, age, residential area, level of parental education, number cigarettes smoked by family members, incense burning in the home, frequency of physical activities **Dose-response Investigated?** No **Statistical Package:** SAS 6.12 **Lags Considered:** Monthly avg at each school	**Pollutant:** PM_{10} **Averaging Time:** 1 h **Mean (SD):** School A: 59.7 School B: 65.3 School C: 84.3 School D: 59.2 School E: 75.3 School F: 60.2 School G: 54.1 School H: 69.0 **Monitoring Stations:** 8 (1 for each school)	**PM Increment:** Dichotomized annual avg: <65.9 $\mu g/m^3$ ≥ 65.9 $\mu g/m^3$ **OR Estimate [Lower CI, Upper CI] lag:** Crude (outcome = asthma, yes/no) <65.9 $\mu g/m^3$: 1 (ref) ≥ 65.9 $\mu g/m^3$: 0.837 [NR] Adjusted (outcome = asthma, yes/no) <65.9 $\mu g/m^3$: 1 (ref) ≥ 65.9 $\mu g/m^3$: 0.947 [0.640, 1.401] **Notes:** Asthma prevalence was highest in urban areas and lowest in rural areas Pearson correlation between annual PM levels at each school and asthma prevalence at each school: 0.214 (p > 0.05)
Reference: Lagorio et al. (2006, 089800) **Period of Study:** May 1999-Jun 1999 Jan 1999-Dec 1999 **Location:** Rome, Italy	**Outcome:** Lung function of subjects (FVC and FEV_1) with COPD, Asthma **Age Groups:** COPD: 50 to 80 yr Asthma: 18 to 64 yr **Study Design**: Time series panel **N:** COPD N = 11; Asthma N = 11 **Statistical Analyses:** Non-parametric Spearman correlation GEE **Covariates:** COPD and IHD: daily mean temperature, season variable (spring or winter), relative humidity, day of week Asthma: season variable, temperature, humidity, and β-2-agonist use **Season:** Spring and winter **Dose-response Investigated?** Yes **Statistical Package:** STATA **Lags Considered:** 1-3 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** Overall: 42.8 (21.8) Spring: 36.9 (10.8) Winter: 49.0 (28.1) **Range (Min, Max):** (7.9, 123) **PM Component:** NR **Monitoring Stations**: Two fixed sites: (Villa Ada and Istituto superior di Sanita) **Copollutant (correlation):** NO_2 r = 0.45 O_3 r = -0.36 CO r = 0.55 SO_2 r = 0.21 $PM_{10-2.5}$ r = 0.61 $PM_{2.5}$ r = 0.93	**PM Increment:** 1 $\mu g/m^3$ They observed negative association between ambient PM_{10} and respiratory function (FVC and FEV_1) in the COPD panel. The effect on FVC was seen at lag 24 h, 48 h, and 72 h. The effect on FEV_1 was evident at lag 72 h. There was no statistically significant effect of PM_{10} on FVC and FEV_1 in the asthmatic and IHD panels. β **Coefficient (SE)** **COPD** FVC(%) 24 h -0.66 (0.30) 48-h -0.75 (0.35) 72-h -0.94 (0.47) FEV_1(%) 24 h -0.37 (0.27) 48-h -0.58 (0.31) 72-h -0.87 (0.43) **Asthma** FVC(%) 24 h -0.12 (0.24) 48-h -0.09 (0.29) 72-h -0.08 (0.36) FEV_1(%) 24 h -0.28 (0.28) 48-h -0.40 (0.34) 72-h -0.40 (0.43)

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Lee, et al. (2007, 093042) **Period of Study:** 2000-2001 **Location:** South-Western Seoul Metropolitan area, Seoul, South Korea	**Outcome:** PEFR (peak expiratory flow rate), lower respiratory symptoms (cold, cough, wheeze) **Age Groups:** 61-89 yr (77.8 mean age) **Study Design:** Longitudinal panel survey **N:** 61 adults **Statistical Analyses:** Logistic regression model **Covariates:** Temperature (Celsius), relative humidity, age, season **Dose-response Investigated?** No **Statistical Package:** SAS 8.0 **Lags Considered:** 0-4 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD)**: 71.40 (30.69) Percentiles: 25th: 43.47 50th(Median): 74.92 75th: 87.54 **Range (Min, Max):** 26.23, 148.34 **Monitoring Stations:** 2	**PM Increment:** 10 µg/m^3 **Effect Estimate [Lower CI, Upper CI] lag:** PEFR (peak expiratory flow rate) -0.39 (-0.63 to -0.14) 1 day relative odds of a lower respiratory symptom (cold, cough, wheeze) 1.015 (0.900,1.144) 1 day
Reference: Lewis, et al. (2005, 081079) **Period of Study:** Winter 2001-spring 2002 **Location:** Detroit, Michigan, USA	**Outcome**: Poorer lung function (increased diurnal variability and decreased forced expiratory volume) **Age Groups:** 7-11 yr **Study Design:** longitudinal cohort study **N:** 86 children **Statistical Analyses:** descriptive statistics and bivariate analyses of exposures, multivariable regression models that included interaction terms between exposure measures and CS use or, alternatively, presence of a URI, multivariate analog of linear regression. **Covariates:** sex, home location, annual family income, presence of one or more smokers in household, race, season (entered as dummy variables), and parameters to account for intervention group effect. **Season:** Winter 2001 (Feb 10-23), spring 2001 (May 5-18), summer 2001 (Jul 14-27), fall 2001 (Sep 22-Oct 5), winter 2002 (Jan 18-31), and spring 2002 (May 18-31). **Dose-response Investigated?** No **Lags Considered:** 1-2 days 3-5 days	**Pollutant:** PM_{10} **Averaging Time:** 2 wk **Mean (SD):** Eastside 23.0 (13.5) Southwest 28.2 (16.1) **Range (Min, Max):** 2.9, 70.9 **PM Component:** ("likely" in southwest site) carbon and diesel emissions **Monitoring Stations:** 2 **Copollutant:** $PM_{2.5}$ 0.93 O_3 Daily mean 0.59 O_3 8-h peak 0.57	**PM Increment:** 19.1 µg/m^3 **Lung function among children reporting use of maintenance CSs** Diurnal variability FEV_1 Lag 1: 1.53 [-0.85, 3.90] Lag 1: 2.94 [-1.07, 6.96] $PM_{10} + O_3$ Lag 2: 5.32 [0.32, 10.33] Lag 2: 13.73 [8.23, 19.23] $PM_{10} + O_3$ Lag 3-5: 1.46 [-2.21,5.13] Lag 3-5: 3.30 [0.58, 6.02] $PM_{10} + O_3$ Lowest daily value FEV_1 Lag 1: -0.28 [-2.34, 1.77] Lag 1: -6.25 [-11.15 to -1.36] $PM_{10} + O_3$ Lag 2: -2.21 [-3.97 to -0.46] Lag 2: -5.97 [-11.06 to -0.87] $PM_{10} + O_3$ Lag 3-5: -2.58 [-7.65, 2.49] Lag 3-5: 1.98 [-0.38, 4.33] $PM_{10} + O_3$ **Lung function among children reporting presence of URI on day of lung function assessment** Diurnal variability FEV_1 Lag 1: 3.51 [-4.52,11.55] Lag 1: 3.21 [-1.28,7.71] $PM_{10} + O_3$ Lag 2: 1.12 [-4.62, 6.86] Lag 2: 5.40 [-0.82, 11.62] $PM_{10} + O_3$ Lag 3-5: 3.90 [0.34, 7.47] Lag 3-5: 6.27 [0.07, 12.47] $PM_{10} + O_3$ Lowest daily value FEV_1 Lag 1: -2.72 [-9.47, 4.03] Lag 1: -13.11 [-21.59 to -4.62] $PM_{10} + O_3$ Lag 2: 0.24 [-5.10, 4.63] Lag 2: -3.32 [-6.83, 0.18] $PM_{10} + O_3$ Lag 3-5: -4.48 [-8.36, 0.60] Lag 3-5: -3.17 [-5.82 to -0.51] $PM_{10} + O_3$

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Mar et al. (2004, 057309) **Period of Study:** 1997-1999 **Location:** Spokane, Washington	**Outcome:** Respiratory symptoms **Age Groups:** Adults: Ages 20-51 yr Children: Ages 7-12 yr **Study Design:** Time-series **N:** 25 people **Statistical Analyses:** Logistic regression **Covariates:** Temperature, relative humidity, day of-the-wk **Statistical Package:** STATA 6 **Lags Considered:** 0-2 days	**Pollutant:** PM_{10} **Mean (SD):** 1997: 24.5 (18.5) 1998: 20.6 (12.3) 1999: 16.8 (8.0) **Monitoring Stations:** 1 station **Copollutant (correlation):** PM_{10} PM1: r = 0.48 $PM_{2.5}$: r = 0.61 $PM_{10-2.5}$: r = 0.93	**PM Increment:** 10 µg/m^3 **OR Estimate [Lower CI, Upper CI]** **lag:** **Adult Respiratory symptoms:** Wheeze: 1.01[0.93, 1.09] lag 0 0.98[0.91, 1.06] lag 1 0.99[0.92, 1.06] lag 2 Breath: 1.02[0.96, 1.08] lag 0 1.01[0.97, 1.06] lag 1 1.02[0.97, 1.06] lag 2 Cough: 0.96[0.88, 1.05] lag 0 0.97[0.90, 1.04] lag 1 0.98[0.92, 1.05] lag 2 Sputum: 1.01[0.92, 1.12] lag 0 0.99[0.91, 1.08] lag 1 1.00[0.93, 1.08] lag 2 Runny Nose: 0.98[0.93, 1.04] lag 0 0.97[0.93, 1.02] lag 1; 0.97[0.94, 1.01] lag 2 Eye Irritation: 0.97[0.87, 1.08] lag 0 0.97[0.88, 1.06] lag 1 0.97[0.91, 1.04] lag 2 Lower Symptoms: 0.96[0.91, 1.02] lag 0 0.95[0.89, 1.00] lag 1 0.95[0.90, 1.00] lag 2 Any Symptoms: 0.97[0.93, 1.02] lag 0 0.96[0.91, 1.00] lag 1 0.95[0.91, 0.99] lag 2 **Children Respiratory symptoms**: Wheeze: 0.92[0.71, 1.18] lag 0 0.89[0.64, 1.24] lag 1 0.95[0.69, 1.31] lag 2 Breath: 1.04[0.95, 1.15] lag 0 1.04[0.95, 1.15] lag 1 1.06[0.95, 1.19] lag 2 Cough: 1.09[1.02, 1.16] lag 0 1.08[1.02, 1.14] lag 1 1.10[1.02, 1.18] lag 2 Sputum: 1.08[0.98, 1.17] lag 0 1.07[0.98, 1.17] lag 1 1.07[0.98, 1.16] lag 2 Runny Nose: 1.08[1.00, 1.16] lag 0 1.08[1.02, 1.15] lag 1 1.08[1.02, 1.14] lag 2 Eye Irritation: 1.06[0.74, 1.51] lag 0 0.94[0.70, 1.26] lag 1 0.99[0.88, 1.12]lag 2 Lower Symptoms: 1.07[1.00, 1.14] lag 0 1.06[0.98, 1.15] lag 1 1.07[0.95, 1.19] lag 2 Any Symptoms: 1.07[1.02, 1.11] lag 0 1.09[1.03, 1.15] lag 1 1.10[1.03, 1.17] lag 2

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Mar et al. (2005, 087566) **Period of Study:** 1999-2001 **Location:** Seattle, Washington	**Outcome:** Pulmonary function (arterial oxygen saturation) and cardiac function (heart rate and blood pressure) **Study Design:** Time series **N:** 88 **Statistical Analyses:** Linear logistic regression **Age Groups:** >57	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI)** **Lag** Indoor Systolic: 0.92 (-0.95, 2.78) 0 Diastolic: 0.63 (-0.29, 1.56) 0 Outdoor Systolic: -0.10 (-1.37, 1.18) 0 Diastolic: -0.03 (-0.79, 0.73) 0 Nephelometer Systolic: 0.35 (-0.91, 1.61) 0 Diastolic: -0.12 (-0.91, 0.67) 0 **% Increase between heart rate and PM10 exposure for people >57** PM_{10} Indoor: 0.02 (-0.54, 0.58) 0 Outdoor: -0.48 (-1.03, 0.06) 0 Nephelometer: -0.31 (-0.76, 0.14) 0
Reference: McCormack et al. (2009, 199833) **Period of Study:** Sep 2001-Apr 2004 **Location:** East Baltimore, Maryland	**Outcome:** Asthma symptoms **Study Design:** Panel **Statistical Analysis:** Chi-square, Student t-test, Negative binomial regression models with GEE, Logistic regression with GEE **Statistical Package:** StataSE **Age Groups:** Asthmatic children aged 2-6 yr	**Pollutant:** $PM_{10-2.5}$, $PM_{2.5}$ **Averaging Time:** 3 days **Mean (SD) Unit:** $PM_{10-2.5}$: 17.4 ± 21.2 µg/m^3 $PM_{2.5}$: 40.3 ± 35.4 µg/m^3 **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **Relative Risk (Min CI, Max CI) Lag** Bivariate Models, $PM_{10-2.5}$ Cough, wheezing, chest tightness: 1.05 (0.99-1.10), p = 0.08 Slow down: 1.08 (1.03-1.13). p < 0.01 Symptoms with running: 1.03 (0.97-1.09). p = 0.39 Nocturnal symptoms: 1.06 (1.01-1.11), p = 0.03 Limited speech: 1.11 (1.05-1.18), p < 0.01 Rescue medication use: 1.06 (1.02-1.11), p < 0.01 Bivariate Models, $PM_{2.5}$ Cough, wheezing, chest tightness: 1.01 (0.98-1.05), p = 0.41 Slow down: 1.00 (0.97-1.04), p = 0.85 Symptoms with running: 1.04 (1.01-1.07), p = 0.14 Nocturnal symptoms: 1.02 (0.98-1.05), p = 0.37 Limited speech: 1.01 (0.95-1.07), p = 0.33 Rescue medication use: 1.03 (1.00-1.60), p = 0.06 Multivariate Models, $PM_{10-2.5}$ Cough, wheezing, chest tightness: 1 .06 (1.01-1.12), p = 0.02 Slow down: 1.08 (1.02-1.14), p = 0.01 Symptoms with running: 1.00 (0.94-1.08), p = 0.81 Nocturnal symptoms: 1.08 (1.01-1.14), p = 0.02 Limited speech: 1.11 (1.03-1.19), p < 0.01 Rescue medication use: 1.06 (1.01-1.10), p = 0.02 Multivariate Models, $PM_{2.5}$ Cough, wheezing, chest tightness: 1.03 (0.99-1.07), p = 0.18 Slow down: 1.04 (1.00-1.09), p = 0.06 Symptoms with running: 1.07 (1.02-1.11), p < 0.01 Nocturnal symptoms: 1.06 (1.01-1.10), p = 0.01 Limited speech: 1.07 (1.00-1.14), p = 0.04 Rescue medication use: 1.04 (1.01-1.08), p = 0.04

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Mortimer et al. (2008, 187280) **Period of Study:** 1989-2000 **Location:** Joaquin Valley, California	**Outcome:** Respiratory Symptoms, Decreased lung function **Study Design:** Time series **Statistical Analyses:** Deletion/Substitution/ Addition algorithm (GEE) Logistic linear regression **Age Groups:** 6-11	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Copollutants (correlation):** CO: r = 0.05 NO_2: r = 0.30 O_3: r = 0.39	**Increment:** NR β (SE): **FVC:** PM_{10} (age 0-3 yr): 0.0121 (0.0037) FEV_1**:** PM_{10} (age 0-3 yr): 0.0102 (0.0034) **PEF:** PM_{10} (Mother smoked during pregnancy): -0.0102 (0.0039)
Reference: Mortimer et al. (2002, 030281) **Period of Study:** Jun-Aug 1993 **Location:** Eight urban areas of the U.S.: Bronx and East Harlem, NY Baltimore, MD Washington, DC Detroit, MI Cleveland, OH Chicago, IL and St. Louis, MO.	**Outcome:** peak expiratory flow rate (PEFR) and symptoms **Age Groups:** 4-9 yr **Study Design:** Cohort study **N:** 846 children with a history of asthma **Statistical Analyses:** Mixed linear models and GEE **Covariates:** Day of study, previous 12-h mean temperature, urban area, diary number, rain in the past 24 h **Season:** Summer **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 0, 1, 2, 3, 4, 5, 6, 1-5 avg, 1-4 avg, 0-4 avg, 0-3 avg	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 53 **Monitoring Stations:** NR **Copollutant (correlation):** 8-h avg O_3: r = 0.51	**PM Increment:** 20 µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** (RR estimates are odds ratios for incidence of morning asthma symptoms using the avg of lag 1-2) 3 urban areas (DE, CL, CH) Single pollutant: OR = 1.26 (1.00-1.59) O_3+PM_{10}: OR = 1.25 (0.97-1.61) O_3+SO_2 +NO_2+PM_{10}: OR = 1.14 (0.80-1.48)
Reference: Moshammer and Neuberger (2003, 041956) **Period of Study:** 2000-2001 **Location:** Linz, Austria	**Outcome:** Lung Function: FVC, FEV_1, MEF_{25}, MEF_{50}, MEF_{75}, PEF, LQ Signal, PAS Signal **Age Groups:** Ages 7 to 10 **Study Design:** Case-crossover **N:** 161 children 1898-2120 "half-h means" **Statistical Analyses:** Correlations Regression Analysis **Covariates:** Morning, evening, night **Season:** Spring, summer, winter, fall **Dose-response Investigated?** No	**Pollutant:** PM_{10} **Averaging Time:** 8 h Daily Means **Mean (SD):** 23.13 (20.08) **Range (Min, Max):** (NR, 190.79) **Monitoring Stations:** 1 **Copollutant (correlation):** LQ = 0.751 PAS = 0.406	**Notes:** "Acute effects of 'active particle surface' as measured by diffusion charging were found on pulmonary function (FVC, FEV_1, MEF_{50}) of elementary school children and on asthma-like symptoms of children who had been classified as sensitive."
Reference: Moshammer et al. (2006, 090771) **Period of Study:** 2000-2001 **Location:** Linz, Austria	**Outcome:** Respiratory symptoms and decreased lung function **Age Groups:** Children ages 7-10 **Study Design:** Time-series **N:** 163 children **Statistical Analyses:** GEE model **Covariates:** Sex, age, height, weight **Dose-response Investigated?** NR **Statistical Package:** NR **Lags Considered:** 1	**Pollutant:** PM_{10} **Averaging Time:** 8 h **Mean (SD):** Maximum 24 h: 76.39 **Annual avg:** 19.06 **Percentiles:** 8-h mean 25th: 14.39 8-h mean 50th(Median): 24.85 8-h mean 75th: 38.82 **Monitoring Stations:** 1 station **Copollutant (correlation):** PM_1: r = 0.91 $PM_{2.5}$: r = 0.93 NO_2: r = 0.62	**PM Increment:** 10 µg/m^3 **% change in Lung Function per 10 µg/m3** FEV: 0.11 FVC: 0.06 $FEV_{0.5}$: -0.19 MEF_{75}%: -0.30 MEF_{50}%: -0.36 MEF_{25}%: 0.41 PEF: 0.22 **% change in Lung Function per IQR** FEV: -0.27 FVC: -0.07 $FEV_{0.5}$: -0.47 MEF_{75}%: -0.74 MEF_{50}%: -0.86 MEF_{25}%: 0.98 PEF: -0.54

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Neuberger et al. (2004, 093249) **Period of Study:** Sep 1999-Mar 2000 **Location:** Vienna, Austria	**Outcome:** Ratio measure: Time to peak tidal expiratory flow divided by total expiration time (i.e., tidal lung function, a surrogate for bronchial obstruction) **Age Groups:** 3.0-5.9 yr (preschool children) **Study Design:** Longitudinal prospective cohort **N:** 56 children **Statistical Analyses:** Mixed models linear regression, with autoregressive correlation structure **Covariates:** Age, sex, respiratory rate, phase angle, temperature, kindergarten, parental education, observer (also in sensitivity analyses: height, weight, cold/sneeze on same day, heating with fossil fuels, hair cotinine, number of tidal slopes used to measure tidal lung function) **Dose-response Investigated?** No **Statistical Package:** SAS 8.0 **Lags Considered:** 0	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Copollutant (correlation):** $PM_{2.5}$ (r = 0.94) in Vienna	**PM Increment:** Interquartile range (NR) Change in mean associated with an IQR increase in PM (p-value) lag -1.067 (0.241) lag 0
Reference: Neuberger et al. (2004, 093249) **Period of Study:** Oct. 2000-May 2001 **Location:** Linz, Austria	**Outcome:** Forced oscillatory resistance (at zero Hz), FVC, FEV_1, MEF_{25}, MEF_{50}, MEF_{75}, PEF **Age Groups:** 7-10 yr **Study Design:** Longitudinal prospective cohort **N:** 164 children **Statistical Analyses:** Mixed models linear regression with autoregressive correlation structure **Covariates:** sex, time and individual **Season:** Oct-May **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 0-7	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Monitoring Stations:** 1	**PM Increment:** 1 µg/m^3 **Notes:** No significant associations between PM_{10} and the metrics of lung function were reported. The authors state they only reported significant associations, so results are assumed to be null.
Reference: Odajima et al. (2008, 192005) **Period of Study:** Apr 2003-Mar 2004 **Location:** Fukuoka, Japan	**Outcome:** PEF **Study Design:** Panel/Field **Statistical Analysis:** GEE **Statistical Package:** SAS **Covariates:** Age, sex, growth index, temperature, NO_2, O_3 **Age Groups:** Asthmatic children, 4-11 yr old	**Pollutant:** PM_{10} **Averaging Time:** 3 h **Mean (SD) Unit:** Warmer months, 5-8 am SPM: 40.7 µg/m^3 NO_2: 15.2 ppb O_3: 17.7 ppb Warmer months, 7-10pm SPM: 41.5 µg/m^3 NO_2: 20.0 ppb O_3: 28.1 ppb Colder months, 5-8am SPM: 32.6 µg/m^3 NO_2: 20.5 ppb O_3: 17.5 ppb Colder months, 7-10pm SPM: 34.7 µg/m^3 NO_2: 28.0 ppb O_3: 19.4 ppb **Range (Min, Max):**	**Increment:** 10 µg/m^3 **Relative Risk (Min CI, Max CI)** **Lag** Apr-Sep, morning sample, multi-pollutant:: SPM, 5am-8am: -0.6 (-1.228, 0.028) SPM, 2am-5am: -0.78 (-1.399, -0.161) SPM, 11pm-2am: -0.612 (-1.180, -0.045) SPM, 8pm-11am: -0.732 (-1.318, -0.145) O_3, 5am-8am: -0.575 (-1.569, 0.419) O_3, 2am-5am: -0.052 (-0.997, 0.893) O_3, 11pm-2am: -0.305 (-1.269, 0.658) O_3, 8pm-11am: -0.416 (-1.283, 0.451) NO_2, 5am-8am: -0.3 (-2.246, 1.645) NO_2, 2am-5am: 0.265 (-1.354, 1.885) NO_2, 11pm-2am: -0.187 (-1.447, 1.073) NO_2, 8pm-11am: 0.432 (-0.689, 1.553) Single-pollutant model: SPM, 5am-8am: -0.67 (-1.236, -0.104) SPM, 2am-5am: -0.761 (-1.328, -0.194) SPM, 11pm-2am: -0.661 (-1.159, -

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
		Warmer months, 5-8am SPM: (11.0, 126.0) NO_2: (1.3, 44.7) O_3: (0.3, 52.3) Warmer months, 7-10pm SPM: (8.3, 191.3) NO_2: (3.0, 51.3) O_3: (1.3, 71.3) Colder months, 5-8am SPM: (9.0, 160.0) NO_2: (1.3, 44.0) O_3: (0.6, 48.7) Colder months, 7-10pm SPM: (10.3, 131.0) NO_2: (3.6, 49.0) O_3: (1.0, 60.0) **Copollutant (correlation):** Warmer months (24-h mean): O_3: r = 0.32 NO_2: r = 0.30 Colder months (24-h mean): O_3: r = -0.02 NO_2: r = 0.45	0.163) SPM, 8pm-11am: -0.714 (-1.212, -0.215) Evening sample, multi-pollutant model SPM, 7pm-10pm: -0.449 (-1.071, 0.174) SPM, 4pm-7pm: -0.434 (-1.122, 0.254) SPM, 1pm-4pm: -0.415 (-1.015, 0.184) SPM, 10am-1pm: -0.522 (-1.199, 0.155) O_3, 7pm-10pm: -0.22 (-1.171, 0.731) O_3, 4pm-7pm: -0.118 (-0.809, 0.574) O_3, 1pm-4pm: -1.086 (-0.888, 0.516) O_3, 10am-1pm: -0.315 (-1.123, 0.493) NO_2, 7pm-10pm: 0.296 (-0.806, 1.397) NO_2, 4pm-7pm: 0.220 (-0.818, 1.258) NO_2, 1pm-4pm: 0.438 (-0.568, 1.444) NO_2, 10am-1pm: 0.536 (-0.546, 1.617) Single-pollutant model: SPM, 7pm-10pm: -0.449 (-0.956, 0.058) SPM, 4pm-7pm: -0.449 (-1.029, 0.131) SPM, 1pm-4pm: -0.414 (-0.943, 0.115) SPM, 10am-1pm: -0.486 (-1.051, 0.079) Oct-Mar, morning sample, multi-pollutant:: SPM, 5am-8am: 0.290 (-0.279, 0.859) SPM, 2am-5am: 0.431 (-0.173, 1.036) SPM, 11pm-2am: 0.304 (-0.311, 0.919) SPM, 8pm-11am: 0.010 (-0.523, 0.543) O_3, 5am-8am: -0.415 (-1.568, 0.738) O_3, 2am-5am: -0.046 (-1.245, 1.153) O_3, 11pm-2am: 0.004 (-1.265, 1.273) O_3, 8pm-11am: -0.470 (-2.017, 1.077) NO_2, 5am-8am: -0.319 (-2.269, 1.631) NO_2, 2am-5am: 0.262 (-1.777, 2.300) NO_2, 11pm-2am: 0.609 (-1.132, 2.350) NO_2, 8pm-11am: 0.155 (-1.545, 1.856) Single-pollutant model: SPM, 5am-8am: 0.308 (-0.189, 0.805) SPM, 2am-5am: 0.485 (-0.026, 0.996) SPM, 11pm-2am: 0.486 (-0.049, 1.022) SPM, 8pm-11am: 0.100 (-0.414, 0.613) Evening Sample, Multi-pollutant Model SPM, 7pm-10pm: 0.059 (-0.397, 0.515) SPM, 4pm-7pm: 0.360 (-0.093, 0.812) SPM, 1pm-4pm: 0.357 (-0.157, 0.871) SPM, 10am-1pm: 0.169 (-0.394, 0.731) O_3, 7pm-10pm: -0.656 (-2.394, 1.083) O_3, 4pm-7pm: 0.046 (-1.140, 1.232) O_3, 1pm-4pm: 0.164 (-1.038, 1.365) O_3, 10am-1pm: 0.665 (-0.613, 1.942) NO_2, 7pm-10pm: -0.415 (-2.444, 1.613) NO_2, 4pm-7pm: -0.144 (-1.490, 1.202) NO_2, 1pm-4pm: -0.181 (-1.821, 1.459) NO_2, 10am-1pm: 0.194 (-1.503, 1.890) Single-pollutant model : SPM, 7pm-10pm: 0.071 (-0.388, 0.529) SPM, 4pm-7pm: 0.318 (-0.123, 0.758) SPM, 1pm-4pm: 0.317 (-0.171, 0.804) SPM, 10am-1pm: 0.112 (-0.412, 0.636)

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Peacock et al. (2003, 042026) **Period of Study:** Nov 1996-Feb 1997 **Location:** Southern England	**Outcome:** Reduced peak expiratory flow rate (PEFR) **Age Groups:** 7-13 yr **Study Design:** Time-series **N:** 179 **Statistical Analyses:** GEE, multiple regression **Covariates:** Day of the week, 24-h mean outside temperature. **Season:** Winter **Dose-response Investigated?** No **Statistical Package:** STATA **Lags Considered:** Same day, lag 1, lag 2, 5-day ma	**Pollutant:** PM_{10} **Averaging Time:** Daily **Mean (SD):** Rural (nationally validated) 21.2 (11.3) Rural (locally validated) 18.7 (11.3) Urban 1 18.4 (9.8) Urban 2 22.7 (10.6) **Percentiles:** 10th Rural (nationally validated) 11.0 Rural (locally validated) 9.0 Urban 1 10.5 Urban 2 12.5 90th Rural (nationally validated) 33.0 Rural (locally validated) 32.5 Urban 1 32.0 Urban 2 36.0 **Range (Min, Max):** Rural (nationally validated) 7.0, 82.0 Rural (locally validated) 6.6, 87.9 Urban 1 4.7, 62.8 Urban 2 6.7, 63.7 **Monitoring Stations:** 3 **Copollutants:** NO_2 O_3 SO_2 SO_4^{2-}	**Increment:** 10 µg/m^3 **Odds Ratio (Lower CI, Upper CI)** **Lag** **Change in PEFR** Community -0.04 (-0.11, 0.03) 0 0.03 (-0.04, 0.05) 1 -0.01 (-0.07, 0.05) 2 -0.10 (-0.25, 0.05) 0-4 avg Local -0.01 (-0.06, 0.03) 0 0.04 (0.01, 0.08) 1 0.01 (-0.04, 0.05) 2 0.04 (-0.05, 0.13) 0-4 avg **20% decrease in PEFR** All children 1.012 (0.992, 1.031) 0 1.016 (0.995, 1.036) 1 1.013 (1.000, 1.025) 2 1.037 (0.992, 1.084) 0-4 avg Wheezy Children Only 1.016 (0.986, 1.047) 0 1.030 (1.001, 1.060) 1 1.018 (0.995, 1.041) 2 1.114 (1.057, 1.174) 0-4 avg
Reference: Peled, et al. (2005, 156015) **Period of Study:** 5-6 wk between Mar-Jun 1999 and Sep-Dec 1999. **Location:** Ashdod, Ashkelon and Sderot, Israel	**Outcome:** Reduced peak expiratory flow (PEF) **Age Groups:** 7-10 yr **Study Design:** Nested cohort study **N:** 285 **Statistical Analyses:** Time series analysis, generalized linear model, GEE, one-way ANOVA **Covariates:** seasonal changes, meteorological conditions and personal physiological, clinical and socioeconomic measurements **Season:** Spring, fall **Dose-response Investigated?** No **Statistical Package:** STATA	**Pollutant:** PM_{10} **Averaging Time:** Daily **Mean:** Ashkelon: 67.1 Sderot: 52.9 Ashdod: 31.0 **PM Component:** Local industrial emissions, desert dust, vehicle emissions and emissions from two electric power plants **Monitoring Stations:** 6 **Copollutant:** $PM_{2.5}$	**PM Increment:** 1 µg/m^3 β **coefficient (SE) [95% CI]** Sderot: PM_{10} MAX: -0.34 (0.41) [-1.16, 0.46] PM_{10} MAX x sin(ω2 day): 0.84 (0.22) [0.405, 1.28] PM_{10} MAX x cos (ω1 day): -1.61 (0.41) [-2.43, 0.79] PM_{10} MAX x sin (ω1 day): 0.44 (0.120) [-0.68-0.21] In Sderot, an interaction between PM_{10} and the sequential day were significantly associated with PEF.
Reference: Pitard, et al. (2004, 087433) **Period of Study:** 732 days (Jul 1998-Jun 2000) **Location:** City of Rouen, France	**Outcome:** Respiratory drug sales **Age Groups:** 0-14, 15-64, 65-74, over 75 yr **Study Design:** Ecological time-series **N:** 106,592 **Statistical Analyses:** Generalized additive model **Covariates:** Days of the weeks, trend, seasonal variations, influenza epidemics, meteorological variables, holidays **Dose-response Investigated?** No **Statistical Package:** S-plus **Lags Considered:** 0 to 10 days	**Pollutant:** PM_{10} **Averaging Time:** Daily **Mean (SD):** 16.7 (13.3) **Percentiles:** 25th: 8.00 50th(Median): 13.0 75th: 20 **Range (Min, Max):** 2.00, 126 **Monitoring Stations:** 2 **Copollutant (correlation):** SO_2 (0.39) NO_2 (0.61)	**PM Increment:** 10 µg/m^3 Percent increase in sales of anti-asthmatics and bronchodilators (Lower CI, Upper CI) lag: 6.2 (2.4, 10.1) lag 10 days Percent increase in sales of cough and cold preparation for children under 15 yr of age (Lower CI, Upper CI) lag: 9.2 (5.9, 12.6) 10 days

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Preutthipan et al. (2004, 055598) **Period of Study:** 31 days (school days) from Jan−Feb 1999 **Location:** Mae Pra Fatima School, central Bangkok, Thailand	**Outcome:** Decreases in peak expiratory flow rates (PEFR), respiratory symptoms including wheeze, shortness of breath, runny/stuffed nose, sneezing, cough, phlegm, and sore throat **Age Groups:** Third to ninth grade **Study Design:** Time- Series **N:** 133 children (93 asthmatics, 40 nonasthmatics) **Statistical Analyses:** For continuous data, an unpaired t-test or Mann-Whitney U test was used. For categorical data, the chi-square test or Fisher's exact test was used. One-way analysis of covariance (ANCOVA) was used to compare avg daily reported respiratory symptoms, diurnal PEFR variability, and the prevalence of PEFR decrements between groups of days. **Covariates:** Age, sex, weight, height, parents smoking, person smoking in home, daily number of household cigarettes, air-conditioned bedroom, fuel used for cooking (charcoal, gas), distance from home to main road **Dose-response Investigated?** No **Lags Considered:** Up to 5 days	**Pollutant:** PM_{10} **Averaging Time:** Daily **Mean (SD):** 111.0 (39) **Range (Min, Max):** 46, 201 **Monitoring Stations:** 1 **Copollutant:** SO_2 CO O_3	**PM Increment:** Authors classified exposure according to High and Low PM_{10} days: High = >120 µg/m^3 Low = <120 µg/m^3 Daily reported respiratory symptoms and diurnal PEFR variability as classified by concurrent days with high vs.. low PM_{10} Mean % reporting (SEM) Asthmatics: High PM_{10} Wheeze/shortness of breath = 21.3 (1.4) Runny/stuffed nose or sneezing = 42.3 (1.8) Cough = 59.9 (1.9) Phlegm = 60.5 (2.3) Sore throat = 23.7 (1.5) Any respiratory symptoms = 72.2 (3.2) Diurnal PEFR variability = 3.0 (0.4) Asthmatics: Low PM_{10} Wheeze/shortness of breath = 19.3 (1.3) Runny/stuffed nose or sneezing = 35.8 (1.6) Cough = 59.1 (1.6) Phlegm = 58.6 (2.0) Sore throat = 21.0 (1.4) Any respiratory symptoms = 63.8 (2.8) Diurnal PEFR variability = 2.8 (0.3) Nonasthmatics: High PM_{10} Wheeze/shortness of breath = 11.7 (1.4) Runny/stuffed nose or sneezing = 40.9 (2.5) Cough = 50.4 (2.6) Phlegm = 50.2 (2.5) Sore throat = 27.1 (1.7) Any respiratory symptoms = 67.8 (3.7) Diurnal PEFR variability = 2.4 (0.4) Nonasthmatics: Low PM_{10} Wheeze/shortness of breath = 9.3 (1.2) Runny/stuffed nose or sneezing = 33.1 (2.2) Cough = 54.0 (2.2) Phlegm = 49.9 (2.2) Sore throat = 23.9 (1.5) Any respiratory symptoms = 56.4 (3.2) Diurnal PEFR variability = 2.1 (0.4) **Notes:** None of the daily reported respiratory symptoms had significant direct correlations with daily PM_{10} levels, according to the authors.

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Rabinovitch et al. (2004, 096753) **Periods of Study:** Nov 1999-Mar 2000 Nov 2000-Mar 2001 Nov 2001-Mar 2002 **Location:** Denver, Colorado	**Outcome:** Respiratory symptoms, Asthma symptoms (cough and wheeze), Upper respiratory symptoms **Study Design:** Time-series panel **Statistical Analyses:** Logistic linear regression **Age Groups:** 6-12	**Pollutants:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 28.1 (13.2) **Range (Min, Max):** (6.0, 102.0) **Copollutant:** CO NO_2 SO_2 O_3	**Increment:** 1 µg/m^3 β (SE) AM: -0.010 (0.008) PM: -0.011 (0.010) **Odds Ratio (Lower CI, Upper CI)** **Lag** 1.016 (0.911, 1.133) 0-3 avg. OR for respiratory symptoms and PM_{10} exposure for children age 6-12 Asthma exacerbation: 1.00 (0.75, 1.25) 0-3 avg Medication: 0.85 (0.75, 0.95) 0-3 avg Previous night's symptoms: 1.10 (1.00, 1.20) 0-3 avg Current day's symptoms: 1.00 (0.90, 1.10) 0-3 avg **% Increase (Lower CI, Upper CI)** **Lag** % Increase in FEV_1 or PEF and PM_{10} exposure for children age 6-12 AM FEV_1: -0.01 (-0.02, 0.01) 0-3 avg PM FEV_1: -0.02 (-0.03, 0.02) 0-3 avg AM PEF: -0.025 (-0.035, 0.02) 0-3 avg PM PEF: 0.00 (-0.03, 0.03) 0-3 avg.
Reference: Renzetti et al. (2009, 199834) **Period of Study:** Jun 2006-Jul 2006 **Location:** Pescara and Ovindoli, Italy	**Outcome:** Airway inflammation and function **Study Design:** Panel **Covariates:** NR **Statistical Analysis:** Student T-test, Pearson's correlation coefficients **Statistical Package:** StatView **Age Groups:** Children, mean age 9.9 yr	**Pollutant:** PM_{10} **Averaging Time:** Daily **Mean (SD) Unit:** Urban: 56.9 ± 13.1 µg/m^3 Rural: 13.8 ± 5.6 µg/m^3 **Copollutant (correlation):** NR	All results are presented in Fig format.

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Rojas-Martinez et al. (2007, 091064) **Period of Study:** 1996-1999 **Location:** Mexico City, Mexico	**Outcome:** Lung function: FEV_1, FVC, $FEF_{25-75\%}$ **Age Groups:** Children 8 yr old at time of cohort recruitment **Study Design:** School-based "dynamic" cohort study **N:** 3170 children 14,545 observations **Statistical Analyses:** Three-level generalized linear mixed models with unstructured variance-covariance matrix **Covariates:** Age, body mass index, height, height by age, weekday spent outdoors, environmental tobacco smoke, previous-day mean air pollutant concentration, time since first test **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 0-1 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h, 6 mo **Mean (SD):** 24-h averaging Tlalnepantla: 66.7 (35.6) Xalostoc: 96.7 (49.4) Merced: 79.3 (40.8) Pedregal: 53.4 (31.9) Cerro de la Estrella: 69.6 (35.3) 6-mo averaging **Mean:** 75.6 **Percentiles:** 6-mo averaging 25th: 55.8 50th(Median): 67.5 75th: 92.2 **Monitoring Stations:** 5 sites for PM_{10}, 10 for other pollutants **Copollutant:** O_3 NO_2	**PM Increment:** IQR PM_{10}, 6-LC: 36.4 **GIRLS** **One-pollutant model** FVC: -39 [-47: -31] FEV: -29 [-36: -21] $FEF_{25-75\%}$: -17 [-36: 1] FEV_1/FVC: 0.12 [0.07: 0.17] **Two-pollutant model** PM_{10}, 6-LC & O_3 FVC: -30 [-39: -22] FEV: -24 [-31: -16] $FEF_{25-75\%}$: -9 [-26: 9] FEV_1/FVC: 0.10 [0.06: 0.15] PM_{10}, 6-LC & NO_2 FVC: -21 [-30: -13] FEV: -17 [-25: -8] $FEF_{25-75\%}$: -23 [-43: -4] FEV_1/FVC: 0.07 [0.02: 0.13] **Multipollutant model** PM_{10}, 6-LC, O_3, & NO_2 FVC: -14 [-23: -5] FEV: -11 [-20: -3] FEF25-75%: -7 [-27: 12] FEV_1/FVC: 0.08 [0.03: 0.13] **BOYS** **One-pollutant model** FVC: -33 [-41: -25] FEV: -27 [-34: -19] $FEF_{25-75\%}$: -18 [-34: -2] FEV_1/FVC: 0.04 [-0.01: 0.09] **Two-pollutant model** PM_{10}, 6-LC & O_3 FVC: -28 [-36: -19] FEV: -22 [-30: -15] $FEF_{25-75\%}$: -10 [-27: 7] FEV_1/FVC: 0.04 [-0.01: 0.09] PM_{10}, 6-LC & NO_2 FVC: -16 [-26: -7] FEV: -19 [-27: -10] $FEF_{25-75\%}$: -26 [-44: -9] FEV_1/FVC: 0.005 [-0.06: 0.05] **Multipollutant model** PM_{10}, 6-LC, O_3, & NO_2 FVC: -12 [-22: -3] FEV: -15 [-23: -6] $FEF_{25-75\%}$: -12 [-30: 6] FEV_1/FVC: -0.002 [-0.06: 0.05] Long-term exposure to O_3, PM_{10}, and NO_2 is associated with decrements in FVC and FEV_1 growth in Mexico City schoolchildren. In a multipollutant model, PM_{10} (-12%), O_3 (-9%), and NO_2 (-41%) each contribute independently and statistically significantly to diminished FVC growth. For FEV_1, however, the multipollutant model indicates that only PM_{10} (-15%) and NO_2 (-25%) each contribute independently and statistically significantly to diminished FEV_1 growth.

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Sahsuvaroglu et al. (2009, 190983) **Period of Study:** 1994-1995 **Location:** Hamilton, Canada	**Outcome:** Asthma symptoms **Study Design:** Panel **Covariates:** Neighborhood income, dwelling value, state of housing, deprivation index, smoking **Statistical Analysis:** Logistic regressions **Statistical Package:** SPSS **N:** 6388 **Age Groups:** Children in grades 1 and 8	**Pollutant:** PM_{10} **Averaging Time:** 3-yr avg **Avg:** All Subjects: 20.90 µg/m^3 Boys: 20.88 µg/m^3 Girls: 20.92 µg/m^3 **Range:** All Subjects: 26.98 Boys: 26.98 Girls: 20.10 **Copollutant (correlation):** NO_XTheissen: 0.083 SO_2Theissen: -0.021 O_3Theissen: -0.251 NO_2Kriged: 0.126 NO_2LUR: 0.072	**Increment:** NR **Odds Ratio (95%CI) for copollutant model PM10Spline and NO2LUR** All Girls: 1.063 (0.969-1.666) Older Girls: 1.058 (0.918-1.219) **Odds Ratio (95%CI) for copollutant model PM10Spline and NO2LUR, SO2Theissen and O3Theissen** All Girls: 1.045 (0.943-1.158) Older Girls: 1.044 (0.891-1.225) **Regression coefficients (95%CI) between non-allergic asthma and PM10Spline exposure** All Children: 1.043 (0.996-1.092) Younger Children: 1.011 (0.929-1.100) Older Children: 1.073 (1.013-1.136) All Girls: 1.069 (0.999-1.144) All Boys: 1.024 (0.962-1.091) Younger Girls: 1.065 (0.943-1.203) Younger Boys: 0.962 (0.853-1.085) Older Girls: 1.072 (0.984-1.169) Older Boys: 1.075 (0.995-1.160)
Reference: Sanchez-Carrillo et al. (2003, 098428) **Period of Study:** 1996-1997 **Location:** metropolitan Mexico City, Mexico	**Outcome:** Upper respiratory symptom indicator (wet cough, sore throat, hoarseness, nose dryness, and head cold); Lower respiratory symptom indicator (dry cough, lack of air, and chest sounds); and Ocular symptom indicator (eye irritation, eye itch, eye burning, teary eyes, red eyes, and eye infection) **Age Groups:** All ages **Study Design:** Cohort **N:** 151,418 interviews **Statistical Analyses:** Logistic regression models **Covariates:** Sex, age, education, cigarette smoking, season, emergency episode mass media report, temperature, and relative humidity **Dose-response Investigated?** Yes **Statistical Package:** NR **Lags Considered:** 1	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** Northeast: 132 (52) Northwest: 87 (46) Central: 85 (37) Southeast: 79 (35) Southwest: 55 (28) **Range (Min, Max):** Northeast: (34-269) Northwest: (10-275) Central: (9-319) Southeast: (14-225) Southwest: (12-264) **Monitoring Stations**: Up to 32 **Copollutant (correlation):** O_3: r = 0.067 O_3 8: 00-18: 00 h: r = 0.075 SO_2: r = 0.265 NO_2: r = 0.265	**Effect Estimate [Lower CI, Upper CI]:** PM_{10} quartiles: 10.04-52.62 (ref) 52.63-73.58 Upper respiratory indicator: 1.02 (0.99-1.06) Lower respiratory indicator: 1.04 (0.99-1.09) Ocular indicator: 0.99 (0.95-1.03) 73.59-101.91 Upper respiratory indicator: 1.07 (1.03-1.10) Lower respiratory indicator: 1.09 (1.04-1.14) Ocular indicator: 0.89 (0.86-0.92)101.92-318.80 Upper respiratory indicator: 0.93 (0.90-0.97) Lower respiratory indicator: 1.03 (0.98-1.08) Ocular indicator: 0.84 (0.81-0.87) **Northeast -** 2nd quartile Upper respiratory indicator: 0.354 (0.112-1.222) Lower respiratory indicator: 0.215 (0.040-1.160) Ocular indicator: 1.080 (0.915-1.274) 3rd quartile Upper respiratory indicator: 0.118 (0.039-0.356) Lower respiratory indicator: 0.126 (0.023-0.690) Ocular indicator: 1.228 (0.720-2.095) 4th quartile Upper respiratory indicator: 0.095 (0.034-0.267) Lower respiratory indicator: 0.119 (0.026-0.549) Ocular indicator: 0.878 (0.619-1.246) **Northwest -** 2nd quartile Upper respiratory indicator: 0.990 (0.898-1.090) Lower respiratory indicator: 1.246 (1.087-1.429) Ocular indicator: 1.218 (0.808-1.834) 3rd quartile Upper respiratory indicator: 1.133 (0.974-1.317) Lower respiratory indicator: 1.202 (1.044-1.385) Ocular indicator: 0.345 (0.125-0.951) 4th quartile Upper respiratory indicator:

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
			1.019 (0.904-1.149) Lower respiratory indicator: 1.344 (1.137-1.589) Ocular indicator: 1.949 (1.416-2.683) **Central -** 2nd quartile Upper respiratory indicator: 1.088 (1.002-1.183) Lower respiratory indicator: 1.046 (0.930-1.176) Ocular indicator: 1.220 (1.115-1.335) 3rd quartile Upper respiratory indicator: 1.054 (0.977-1.137) Lower respiratory indicator: 1.055 (0.948-1.175) Ocular indicator: 1.049 (0.965-1.142) 4th quartile Upper respiratory indicator: 0.899 (0.826-0.979) Lower respiratory indicator: 0.952 (0.845-1.073) Ocular indicator: 0.875 (0.796-0.963) **Southeast -** 2nd quartile Upper respiratory indicator: 0.778 (0.575-1.052) Lower respiratory indicator: 1.047 (0.916-1.196) Ocular indicator: 0.460 (0.299-0.708) 3rd quartile Upper respiratory indicator: 1.297 (1.127-1.491) Lower respiratory indicator: 1.391 (1.131-1.711) Ocular indicator: 0.474 (0.314-0.715) 4th quartile Upper respiratory indicator: 0.893 (0.812-0.983) Lower respiratory indicator: 0.937 (0.818-1.073) Ocular indicator: 0.314 (0.182-0.542) **Southwest -** 2nd quartile Upper respiratory indicator: 0.987 (0.913-1.066) Lower respiratory indicator: 2.181 (1.177-4.040) Ocular indicator: 1.026 (0.928-1.135) 3rd quartile Upper respiratory indicator: 0.673 (0.673-1.886) Lower respiratory indicator: 0.899 (0.790-1.024) Ocular indicator: 1.017 (0.862-1.200) 4th quartile Upper respiratory indicator: 0.524 (0.524-1.787) Lower respiratory indicator: 4.346 (0.917-20.606) Ocular indicator: 0.187 (0.090-0.387)

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Schildcrout et al. (2006, 089812) **Period of Study:** Nov 1993-Sep 1995 **Location:** Albuquerque, New Mexico Baltimore, Maryland Boston, Massachusetts Denver, Colorado San Diego, California Seattle, Washington St. Louis, Missouri Toronto, Ontario, Canada	**Outcome:** Asthma Symptoms, Rescue Inhaler Uses **Age Groups:** 5-12 yr **Study Design:** Meta-analysis of CAMP **N:** 990 children **Statistical Analyses:** "Working independence covariance structure" Logistic Regression Poisson Regression "GEE Procedure" **Covariates:** Season, age, race-ethnicity, annual family income, day of the week **Dose-response Investigated?** **Statistical Package:** SAS 8.2 R **Lags Considered:** 0 day lag, 1 day lag, 2 day lag, 3-day moving sum	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg Seattle: Daily Albuquerque: Daily Baltimore: 50% of study days measured Boston: 23% of study days measured Denver: 37% of study days measured San Diego: 24% of study days measured St. Louis: 19% of study days measured Toronto: 47% of study days measured **Percentiles:** 10th: 6.8-14.0 25th: 12.0-22.4 50th(Median): 17.7-32.4 75th: 26.2-42.7 90th: 32.5-53.9 **Monitoring Stations:** 1-12 **Copollutant (correlation):** NO_2 r = 0.26-0.64 SO_2 r = 0.31-0.65 O_3 r = 0.03-0.73 CO r = 0.24-0.88	**PM Increment:** 25 µg/m^3 **One-pollutant model** Asthma Symptoms: 1.02 [0.94, 1.11] 0 1.01 [0.97, 1.06] 1 1.02 [0.98, 1.07] 2 1.01 [0.98, 1.05] 3-day moving sum Rescue Inhaler Uses: [0.97, 1.05] 0 [0.97, 1.05] 1 1.00 [0.97, 1.03] 2 1.01 [0.98, 1.03] 3-day moving sum **Two-pollutant model** Asthma Symptoms: CO-PM_{10} 1.08 [1.01, 1.15] 0 1.06 [0.99, 1.14] 1 1.08 [1.02, 1.14] 2 1.05 [1.01, 1.08] 3-day moving sum NO_2^- PM_{10} 1.06 [0.99, 1.13] 0 1.04 [0.97, 1.11] 1 1.08 [1.02, 1.15] 2 1.04 [1.00, 1.07] 3-day moving sum SO_2-PM_{10} 1.05 [0.98, 1.13]; 0 1.04 [0.96, 1.14] 1 1.05 [0.98, 1.12] 2 1.04 [0.99, 1.08] 3-day moving sum Rescue Inhaler Uses: CO-PM_{10} 1.06 [0.99, 1.13] 0 1.05 [0.99, 1.11] 1; 1.05 [1.01, 1.09] 2 1.03 [1.00, 1.07] 3-day moving sum NO_2^- PM_{10} 1.03 [0.97, 1.08] 0 1.03 [0.98, 1.08] 1 1.04 [1.00, 1.09] 2 1.02 [1.00, 1.05] 3-day moving sum SO_2-PM_{10} 1.01 [0.95, 1.07] 0 1.02 [0.97, 1.07] 1 1.03 [0.98, 1.09] 2 1.02 [0.98, 1.05] 3-day moving sum

[1]All units expressed in µg/m^3 unless otherwise specified.

Table E-10. Short-term exposure - respiratory morbidity outcomes - $PM_{10-2.5}$.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Aekplakorn et al. (2003, 089908) **Period of Study:** 107 days, Oct 1997-Jan 1998 **Location:** Mae Mo district, Lampang Province, north Thailand	**Outcome:** Upper respiratory symptoms, lower respiratory symptoms, cough **Age Groups**: 6-14 yr **Study Design:** Logistic regression **N:** 98 asthmatic school children **Statistical Analyses:** Generalized Estimating Equations, stratified analysis, PROC GENMOD **Covariates:** Temperature and relative humidity **Season**: Winter **Dose-response Investigated?** No **Statistical Package**: SAS v 8.1	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** Daily **Mean (SD):** NR **Range (Min, Max):** NR **Monitoring Stations**: 3 **Copollutant**: PM_{10}, SO_2	**PM Increment:** 10 µg/m^3 **Odds Ratios [Lower CI, Upper CI] lag:** Asthmatics: URS: 1.04 (0.93, 1.17) lag 0 LRS: 1.09 (0.95, 1.26) lag 0 Cough: 1.08 (0.96, 1.21) lag 0 Non-Asthmatics: URS: 1.05 (0.99, 1.19) lag 0 LRS: 0.90 (0.72, 1.11) lag 0 Cough: 0.95 (0.81, 1.11) lag 0

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Bourotte et al. (2007, 150040) **Period of Study:** May 2002-Jul 2002 **Location:** Sao Paulo, Brazil	**Outcome:** Peak expiratory flow (PEF) **Age Groups**: Avg age 39.8 ± 12.3 yr **Study Design:** Cross-sectional **N:** 33 patients **Statistical Analyses:** Linear mixed-effects model **Covariates:** Gender, Age, BMI, Air Pollutants, Ambient temperature, Relative Humidity **Season:** Winter **Dose-response Investigated?** No **Statistical Package**: S-plus **Lags Considered:** 2-day lag, 3-day lag	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** 21.7 (12.9) µg/m^3 **Range (Min, Max):** (4.13, 62.0) **Components:** Na^+ K^+ $Mg2^+$ $Ca2^+$ Finf Cl- NO_3^- SO_4^{2-} **Monitoring Stations**: 1	**PM Increment:** NR **Effect [Lower CI, Upper CI] lag:** Morning PEF Na^+ concurrent day = -0.454 (-1.605, 0.697) Na^+ 2-day lag = -0.907 (-2.288, 0.474) Na^+ 3-day lag = -1.361 (-2.972, 0.251) K^+ concurrent day = 1.685 (-0.492, 3.862) K^+ 2-day lag = 1.838 (-1.272, 4.984) K^+ 3-day lag = 2.604 (-0.812, 6.025) Mg_2^+ concurrent day = 2.265* (-0.427, 4.956) Mg_2^+ 2-day lag = 1.271 (-1.869, 4.410) Mg_2^+ 3-day lag = 0.939 (-2.425, 4.303) Ca_2^+ concurrent day = 5.491* (2.558, 8.424) Ca_2^+ 2-day lag = 6.358* (2.251, 10.465) Ca_2^+ 3-day lag = 6.069 (1.962, 10.176) F_{inf} concurrent day = 1.572 (-0.792, 3.935) F_{inf} 2-day lag = 1.630 (-1.679, 4.939) F_{inf} 3-day lag = 2.736* (-1.754, 7.226) Cl^- concurrent day = -0.951 (-2.238, 0.336) Cl^- 2-day lag = -1.871 (-3.242 to -0.4997) Cl^- 3-day lag = -2.286* (-3.934 to -0.638)\ NO_3^- concurrent day = 4.195* (-0.063, 8.452) NO_3^- 2-day lag = 6.292* (2.034, 10.55) $NO_{3_2}^-$ 3-day lag = 7.341* (3.083, 11.60) $SO_{4_2}^{2-}$ concurrent day = 3.528 (-0.053, 7.110) $SO_{4_2}^{2-}$ 2-day lag = 4.411* (0.829, 7.991)| SO_4^{2-} 3-day lag = 6.175* (2.593, 9.756) Evening PEF Na^+ concurrent day = -0.680 (-1.831, 0.471) Na^+ 2-day lag = -1.90 (-3.316 to -0.494) Na^+ 3-day lag = -2.336* (-3.878 to -0.794) K^+ concurrent day = 0.613 (-1.564, 2.790) K^+ 2-day lag = 0.613 (-2.497, 3.723) K^+ 3-day lag = 0.000 (-3.421, 3.421)| Mg_2+ concurrent day = -0.718 (-3.522, 2.085) Mg_2+ 2-day lag = -1.933 (-5.073, 1.206) Mg_2+ 3-day lag = -3.591 (-7.056 to -0.126) Ca_2+ concurrent day = 2.312* (-1.208, 5.832) Ca_2+ 2-day lag = 2.023 (-2.084, 6.130) Ca_2+ 3-day lag = 0.578 (-3.530, 4.685) F_{inf} concurrent day = -1.281 (-3.644, 1.083) F_{inf} 2-day lag = -2.503 (-5.930, 0.924) F_{inf} 3-day lag = -4.540 (-9.149, 0.068) Cl^- concurrent day = -0.317 (-1.604, 0.970) Cl^- 2-day lag = -1.268 (-2.556, 0.019) Cl^- 3-day lag = -1.902 (-3.589 to -0.216) NO_3^- concurrent day = 3.146 (-1.112, 7.404) NO_3^- 2-day lag = 3.146 (-1.112, 7.404) $NO_{3_2}^-$ 3-day lag = 1.049 (-3.209, 5.306) $SO_{4_2}^{2-}$ concurrent day = 1.764 (-1.817, 5.346) $SO_{4_2}^{2-}$ 2-day lag = 2.646 (-0.935, 6.228) SO_4^{2-} 3-day lag = 1.764 (-1.817, 5.346)
Reference: Ebelt et al. (2005, 056907) **Period of Study:** Summer of 1998 **Location:** Vancouver, Canada	**Outcome:** Spirometry **Age Groups**: Range from 54-86 yr Mean age= 74 yr **Study Design:** Extended analysis of a repeated-measures panel study **N:** 16 persons with COPD **Statistical Analyses:** Earlier analysis expanded by developing mixed-effect regression models and by evaluating additional exposure indicators **Dose-response Investigated?** No **Statistical Package**: SAS V8	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 24 h **Mean (SD):** Ambient $PM_{10-2.5}$: 5.6 (3.0) Exposure to ambient $PM_{10-2.5}$: 2.4 (1.7) **Range (Min, Max):** Ambient $PM_{10-2.5}$: (-1.2-11.9) Exposure to ambient $PM_{10-2.5}$: (-0.4-7.2) **Monitoring Stations**: 5 **Copollutant (correlation):** Ambient PM_{10}: r= 0.69 Ambient $PM_{2.5}$: r= 0.15 Nonsulfate Ambient $PM_{2.5}$: r= 0.14 Exposure to Ambient $PM_{10-2.5}$: r= 0.73	**PM Increment:** Ambient $PM_{10-2.5}$: 4.5 (IQR) Exposure to ambient $PM_{10-2.5}$: 2.4 (IQR) **Notes:** Effect estimates are presented in Fig 2 and Electronic Appendix Table 1 (only available with electronic version of article) and not provided quantitatively elsewhere.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Lagorio et al.(2006, 089800) **Period of Study:** May 1999-June 1999 and Nov 1999-Dec 1999 **Location:** Rome, Italy	**Outcome:** Lung function of subjects (FVC and FEV_1) with COPD, Asthma **Age Groups**: COPD 50-80 yr Asthma 18-64 yr **Study Design:** Time series **N:** COPD N = 11; Asthma N = 11 **Statistical Analyses:** Non-parametric Spearman correlation GEE **Covariates:** COPD: daily mean temperature, season variable (spring or winter), relative humidity, day of week Asthma: season variable, temperature, humidity, and □-2-agonist use **Season:** Spring and winter **Dose-response Investigated?** Yes **Statistical Package**: STATA **Lags Considered:** 1-3 days	**PM Size:** $PM_{10-2.5}$ **Averaging Time:** 24 h **Mean (SD):** Overall: 15.6 (7.2) Spring: 18.7 (7.4) Winter: 12.3 (5.4) **Range (Min, Max):** (3.4, 39.6) **PM Component:** Cd: 0.46±0.40 ng/m^3 Cr: 1.9±1.7 ng/m^3 Fe: 283±167 ng/m^3 Ni: 4.8±6.5 ng/m^3 Pb: 30.6±19.0 ng/m^3 Pt: 5.0±8.6 pg/m^3 V: 1.8±1.4 ng/m^3 Zn: 45.8±33.1 ng/m^3 **Monitoring Stations**: Two fixed sites: (Villa Ada and Istituto superior di Sanita) **Copollutant (correlation):** NO_2 r = 0.51 O_3 r = 0.31 CO r = -0.09 SO_2 r = -0.16 PM_{10} r = 0.61 $PM_{2.5}$ r = 0.34	**PM Increment:** 1 µg/m^3 They observed no statistically significant effect of $PM_{10-2.5}$ on FVC and FEV_1 on any of the panels (COPD, Asthma). β Coefficient (SE) COPD FVC(%) 24 h -1.32 (1.06)^I 48-h -1.46 (1.31) 72-h -1.38 (1.53) FEV_1(%) 24 h -0.59 (0.95) 48-h -1.01 (1.19) 72-h -0.90 (1.42) Asthma FVC(%) 24 h -0.17 (0.75) 48-h -0.36 (0.91) 72-h -0.24 (1.07) FEV_1(%) 24 h -0.67 (0.89) 48-h -1.19 (1.07) 72-h -0.51 (1.26)
Reference: Laurent et al. (2008, 156672) **Period of Study:** Dec 2003-Dec 2004 **Location:** Strasbourg, France	**Outcome:** Sales of short acting β-agonists **Study Design:** Case-crossover **Covariates:** NR **Statistical Analysis:** Conditional logistic regression **Age Groups:** 0-39 yr	**Pollutant:** PM_{10} **Averaging Time:** NR **Mean (SD) Unit:** 20.8 (10.2) µg/m^3 **Range (Min, Max):** NR **Copollutant (correlation):** NO_2, O_3, correlations NR	**Increment:** 10 µg/m^3 **Percent Increase in Short Acting β-agonists sold** Per increment increase in ambient PM_{10} at lags 4-7, a 7.5% increase (95% CI: 4-11.2%) was seen in SABA sales. All other results were given in Fig 1 and 2
Reference: Tang et al. (2007, 091269) **Period of Study:** Dec 2003-Feb 2005 **Location:** Sin-Chung City, Taipei County, Taiwan	**Outcome:** Peak expiratory flow rate (PEFR) of asthmatic children **Age Groups**: 6-12 yr **Study Design:** Panel study **N:** 30 children **Statistical Analyses:** Linear mixed-effect models were used to estimate the effect of PM exposure on PEFR **Covariates:** Gender, age, BMI, history of respiratory or atopic disease in family, SHS, acute asthmatic exacerbation in past 12 mo, ambient temperature and relative humidity, presence of indoor pollutants, and presence of outdoor pollutants, **Dose-response Investigated?** yes **Statistical Package**: S-Plus 2000 **Lags Considered:** 0-2	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 1 h **Mean (SD):** Personal: 17.8 (19.6) Ambient: 17.0 (10.6) **Range (Min, Max):** Personal: 0.3-195.7 Ambient: 0.1-80.2 **Monitoring Stations**: 1	**PM Increment:** 15.9 µg/m^3 RR Estimate [Lower CI, Upper CI] lag: Change in morning PEFR: -20.55 (-45.83, 4.73) lag 0 -39.05 (-104.16 , 26.06) lag 1 -39.56 (-79.56, 0.44) lag 2 -37.15 (-105.01, 30.7) 2-day mean -35.47 (-27.32, 56.38) 3-day mean Change in evening PEFR: -1.68 (-19.13, 15.78) lag 0 1.59 (-14.32, 17.5) lag 1 0.86 (-30.84, 32.57) lag 2 5.97 (-15.57, 27.5) 2-day mean 29.75 (-1.69, 61.18) 3-day mean

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Trenga et al., (2006, 155209) **Period of Study:** 1999-2002 **Location:** Seattle, WA	**Outcome**: Lung function: FEV_1, PEF, MMEF (maximal midexpiratory flow assessed only for children) **Age Groups**: Adults (56-89-yr-old) healthy & with COPD Asthmatic children 6-13-yr-old **Study Design:** Adult and pediatric panel study over 3 yr with 1 monitoring period ("session") per yr **N:** 57 adults (33 healthy, 24 with COPD) = 692 subject-days = 207 study-days 17 asthmatic children = 319 subject-days = 98 study-days **Statistical Analyses:** Mixed effects, longitudinal regression models, with the effects of pollutant decomposed into each subject's a) overall mean b) Difference between their session-specific mean and overall mean c) Difference between their daily values and session-specific mean **Covariates:** Gender, age, ventral site temperature and relative humidity, CO, NO_2 **Season:** NR **Dose-response Investigated?** No **Statistical Package**: SAS **Lags Considered:** 0-1 days	**Pollutant:** $PM_{10-2.5}$ (coarse) **Averaging Time:** 24 h **Percentiles:** Subject-specific exposure PM_{10}-$PM_{2.5}$ Outdoor 25th: 3.3 50th (Median): 4.7 75th: 6.9 Adults Outdoor 25th: 3.3 50th (Median): 5.0 75th: 7.1 **Range (Min, Max):** Subject-specific exposure Children Outdoor (0.0, 25.3) Adults Outdoor (0.0, 25.7) **Monitoring Stations**: 2 Also subject-specific local outdoors (i.e., at each home), indoor, and personal **Copollutant (correlation):** CO NO_2 $PM_{2.5}$	**PM Increment:** 10 µg/m^3 **Adult** Outdoor Home PM_{10}-$PM_{2.5}$ FEV_1 Overall: Lag 0 -27.9 [-87.5: 31.8] Lag 1 47.1 [-5.1: 99.4] No-COPD: Lag 0 -49.2 [-22.3: 23.9] Lag 1 74.3 [6.8: 141.8] COPD: Lag 0 7.3 [-84.7: 99.4] Lag 1 11.5 [-65.4: 88.3] PEF Overall: Lag 0 5.3 [-5.1: 15.7] Lag 1 -2.5 [-11.6: 6.5] No-COPD: Lag 0 5.1 [-7.7: 17.8] Lag 1 -5.8 [-17.5: 5.9] COPD: Lag 0 5.7 [-10.3: 21.6] Lag 1 1.7 [-11.5: 14.9] **Pediatric** FEV_1 Outdoor Home PM_{10}-$PM_{2.5}$ Overall Lag 0 -7.43 [-69.41: 54.55] Lag 1 -25.61 [-88.16: 36.94] No Anti-inflam. Medication Lag 0 -63.87 [-199.58: 71.84] Lag 1 -96.48 [-232.48: 39.52] Anti-inflam. Medication Lag 0 6.57 [-96.90: 110.04] Lag 1 -8.63 [-217.39: 200.14] PEF Outdoor Home PM_{10}-$PM_{2.5}$ Overall Lag 0 4.53 [-6.60: 15.67] Lag 1 -3.35 [-14.31: 7.62] No Anti-inflam. Medication Lag 0 2.05 [-22.36: 26.45] Lag 1 -6.56 [-30.90: 17.78] Anti-inflam. Medication Lag 0 5.15 [-7.90: 18.19] Lag 1 -2.58 [-15.35: 10.19] MMEF Outdoor Home PM_{10}-$PM_{2.5}$ Overall Lag 0 -0.01 [-7.29: 7.28] Lag 1 -2.07 [-9.25: 5.12] No Anti-inflam. Medication Lag 0-7.14 [-23.16: 8.87] Lag 1 -14.39 [-30.11: 1.32] Anti-inflam. Medication Lag 0 1.76 [-6.78: 10.30] Lag 1 0.89 [-7.56: 9.33]

[1]All units expressed in µg/m^3 unless otherwise specified.

Table E-11. Short-term exposure - respiratory morbidity outcomes - $PM_{2.5}$ (including components/sources).

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Adamkiewicz et al. (2004, 087925) **Period of Study:** Aug-Dec 2000 **Location:** Steubenville, Ohio	**Outcome:** FENO **Age Groups**: Ranged 53.5-90.6 yr **Study Design:** Prospective cohort **N:** Total of 294 breaths from 29 subjects **Statistical Analyses:** Fixed effect models, ANOVA, GLM procedure **Covariates:** Subject, week of study, day of the week, h of the day, ambient barometric pressure, temperature, and relative humidity **Dose-response Investigated?** No **Statistical Package**: SAS **Lags Considered:** Hourly lags, 0-48 h	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 1 h **Mean (SD):** 19.5 **Percentiles:** 25th: 7.6 75th: 25.5 **Range (Min, Max):** NR, 105.8 **Monitoring Stations**: 1 **Averaging Time:** 24 h **Mean (SD):** 19.7 **Percentiles:** 25th: 9.7 75th: 27.4 **Range (Min, Max):** NR, 57.8 **Monitoring Stations**: 1 **Copollutant (correlation):** Ambient NO Indoor NO NO_2 O_3 SO_2	**PM Increment:** 17.9 µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** 1-h Single pollutant models: 0.36 (0.58-2.14) **PM Increment:** 17.7 Effect Estimate [Lower CI, Upper CI]: 24-h ma: 1.45 (0.33-2.57) Multipollutant models for $PM_{2.5}$, ambient NO and room NO and estimated change in FENO (ppb) for an IQR in pollutant measure Model 1 1.95 (0.47-3.43) Model 2 1.38 (0.26-2.51) Model 4 1.97 (0.48-3.46) **Notes:** Association of FENO with $PM_{2.5}$ at different lags presented in Fig 1 are not presented quantitatively elsewhere.
Reference: Adar et al. (2007, 098635) **Period of Study:** Mar-Jun 2002 **Location:** St. Louis, MO	**Outcome:** FENO **Age Groups**: 60+ **Study Design:** Panel Study **N:** 44 non-smoking seniors **Statistical Analyses:** Mixed models containing random subject effects **Covariates:** Day of week, trip type, FENO collection device, current illness, use of vitamins, antihistamines, statins, steroids, and asthma medications, temperature, pollen, mold, NO concentration in testing room **Statistical Package**: SAS **Lags Considered:** 0	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** Pretrip: 14.8 Post-trip: 16.5 **Percentiles:** 25th (pretrip): 11.2 75th (pretrip): 20.1 25th (post-trip): 11.7 75th (post-trip): 21.6 **Monitoring Stations**: 1 **Copollutant (correlation):** BC CO NO_2 SO_2 O_3	**PM Increment:** 9.8 µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** Pre-trip % change: 21.9 (6.7, 39.4) Post-trip % change: -4.7 (-17.1, 9.6)
Reference: Aekplakorn et al. (2003, 089908) **Period of Study:** 107 days, from Oct 1997-Jan 1998 **Location:** Mae Mo district, Lampang Province, north Thailand	**Outcome:** Upper respiratory symptoms, lower respiratory symptoms, cough **Age Groups**: 6-14 yr old **Study Design:** Logistic regression **N:** 98 asthmatic school children **Statistical Analyses:** Generalized Estimating Equations, stratified analysis, PROC GENMOD **Covariates:** Temperature and relative humidity **Season:** Winter **Dose-response Investigated?** No **Statistical Package**: SAS v 8.1	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily **Mean (SD):** Sob Pad station: 24.77 Sob Mo station: 24.89 Hua Fai station: 26.27 **Range (Min, Max):** Sob Pad: 4.52, 24.77 Sob Mo: 3.13, 24.89 Hua Fai: 3.67, 26.27 **Monitoring Stations**: 3 **Copollutant:** PM_{10} SO_2	**PM Increment:** 10 µg/m^3 **Odds Ratios [Lower CI, Upper CI] lag:** Asthmatics: URS: 1.04 (0.99, 1.09) lag 0 LRS: 1.05 (0.98, 1.2) lag 0 Cough: 1.05 (0.99, 1.10) lag 0 Non-Asthmatics: URS: 1.03 (0.96, 1.09) lag 0 LRS: 1.02 (0.93, 1.10) lag 0 Cough: 1.00 (0.93, 1.07) lag 0 **PM_{10} + SO_2** Asthmatics: URS: 1.04 (0.99, 1.10) lag 0 LRS: 1.05 (0.98, 1.10) lag 0 Cough: 1.05 (0.99, 1.11) lag 0 Non-Asthmatics: URS: 1.03 (0.97, 1.09) lag 0 LRS: 1.02 (0.93, 1.11) lag 0 Cough: 1.00 (0.93, 1.07) lag 0

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Allen et al. (2008, 156208) **Period of Study:** 1999-2002 (additional PM composition data collected Dec 2000 and May 2001) **Location:** Seattle, USA	**Outcome:** Daily changes in exhaled nitric oxide (FENO) and 4 lung function measures, midexpiratory flow (MEF), peak expiratory flow (PEF), forced expiratory volume in 1 second (FEV_1), and forced vital capacity (FVC) **Age Groups:** 6-13 yr **Study Design:** Panel study **N:** 19 children with asthma **Statistical Analyses:** Linear mixed effects model with random intercept to test for within participant associations **Covariates:** Temperature, relative humidity, BMI, age, and, in the case of FENO, ambient NO measured at a centrally located monitoring site Models also included a term for within-participant, within-session effects, and a term for participant between-session effects **Effect modification**: Decided a priori to include interaction term for $PM_{2.5}$ exposure and inhaled corticosteroids	**Pollutant:** $PM_{2.5}$ **Mean (SD):** 11.23 (6.48) **Range (Min, Max):** 2.76-40.38 25th: 6.38 75th: 14.73 **Copollutant (correlation):** Ambient LAC* r=0.83 Ambient LG**r=0.84 Personal $PM_{2.5}$: r=0.34 Personal LAC: r=0.54 Ambient-generated $PM_{2.5}$: r=0.87 Nonambient-generated $PM_{2.5}$: r=-0.06 * LAC Light-absorbing carbon ** LG: Leroglucosan (a marker of wood smoke)	Health effect estimates presented in graphic form (Fig 1). Summary from text is as follows: Personal LAC, personal $PM_{2.5}$, and ambient-generated $PM_{2.5}$ were associated with ($p < 0.05$) and ambient $PM_{2.5}$ was marginally associated ($p=0.09$) with increased FENO. Neither of the ambient combustion markers (LAC, LG) nor nonambient-generated $PM_{2.5}$ was associated with FENO changes. All of the ambient concentrations were associated with decrements in PEF and MEF while ambient-generated $PM_{2.5}$ was marginally associated ($p < 0.10$). Only ambient LG was associated with a decrease in FEV_1 and there were no associations between exposure metrics and FVC.
Reference: Barraza-Villarreal et al.(2008, 156254) **Period of Study:** Jun 2003-Jun 2005 **Location:** Mexico City	**Outcome:** Respiratory Symptoms, Coughing, Wheezing, Airway inflammation, Asthma **Study Design:** Prospective cohort **Statistical Analyses:** Bivarate analysis **Age Groups**: 6-14	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Maximum 8-h avg **Mean (SD) unit:** 28.9 (2.8) **Range (Min, Max):** (4.2, 102.8) **Copollutants (correlation):** O_3 NO_2	**Increment:** 17.5 µg/m^3 **% Increase (Lower CI, Upper CI)** **lag:** **Asthmatic children** Inflammatory Marker: FENO: 1.08 (1.01, 1.16) 0 IL-8: 1.08 (0.98, 1.19) 0 ph_EBC: -0.03 (-0.09, 0.03) 0 Lung Function: FEV_1: -16.0 (-31.0 to -0.13) 0-4 avg FVC: -23.0 (-42.0 to -5.21) 0-4 avg FEV25-75: -11.0 (-42.0, 20.3) 0-4 avg **Nonasthmatic children** Inflammatory Marker: FENO: 0.89 (0.78, 1.01) 0 IL-8: 1.16 (1.00, 1.36) 0; ph_EBC: -0.05 (-0.14, 0.04) 0 Lung Function: FEV_1: -21.0 (-42.3, 0.38) 0-4 avg FVC: -29.0 (-52.8 to -4.35) 0-4 avg FEV_{25-75}: -20.0 (-69.0, 29.0) 0-4 avg **All children age 6-14** Respiratory Symptom: Cough: 1.11 (1.06, 1.17) Wheezing: 1.06 (0.99, 1.13)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Bennett et al. (2007, 156268) **Period of Study:** 1992-2005 **Location:** Melbourne, Australia	**Outcome:** Adverse respiratory symptoms (wheeze, shortness of breath on waking, cough in the morning, phlegm in the morning, cough with phlegm in the morning, asthma attack) **Age Groups**: All ages with a mean of 37.2 yr **Study Design:** Cohort study **N:** 1446 persons **Statistical Analyses:** Logistic regression models **Covariates:** Age, gender, current smoking status, medication use (ß2-agonist and inhaled steroid), atopy **Dose-response Investigated?** No **Statistical Package**: STATA statistical software, version 9 (Statcorp, 2005)	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** 6.8 **Range (Min, Max):** (1.8-73.3) **Monitoring Stations**: 1	**PM Increment:** 1 µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** Within-person (longitudinal effects) Wheeze: OR=1.08 (0.79-1.48) SOB on waking: OR=1.34 (0.84-2.16) Cough in the morning: OR=0.74 (0.47-1.15) Phlegm in the morning: OR=1.55 (0.95-2.53) Cough w/ phlegm morning: OR=1.28 (0.70-2.33) Asthma attack: OR=0.91 (0.55-1.49) Between-person (cross-sectional) effects Wheeze: OR=1.32 (0.82-2.10) SOB on waking: OR=1.29 (0.46-3.60) Cough in the morning: OR=0.21 (0.07-0.62) Phlegm in the morning: OR=0.49 (0.16-1.44) Cough w/ phlegm morning: OR=0.28 (0.08-0.97) Asthma attack: OR=0.52 (0.17-1.59)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Bourotte et al. (2007, 150040) **Period of Study:** May 2002-Jul 2002 **Location:** Sao Paulo, Brazil	**Outcome:** Peak expiratory flow (PEF) **Age Groups**: Avg age 39.8 ± 12.3 yr **Study Design:** Cross-sectional **N:** 33 patients **Statistical Analyses:** Linear mixed-effects model **Covariates:** Gender, Age, BMI, Air Pollutants, Ambient temperature, Relative Humidity **Season:** Winter **Dose-response Investigated?** No **Statistical Package**: S-plus **Lags Considered:** 2-day lag, 3-day lag	**Pollutant:** $PM_{2.5}$ (Fine) **Averaging Time:** 24 h **Mean (SD):** 11.9 (5.12) **Range (Min, Max):** (2.82, 26.6) **Components:** K^+ Mg_2^+ Ca_2^+ F_{inf} Cl^- NO_3^- SO_4^{2-} **Monitoring Stations**: 1	**PM Increment:** NR **Effect [Lower CI, Upper CI] lag:** **Morning PEF** Na^+ concurrent day = -0.409 (-2.485, 1.667) Na^+ 2-day lag = -0.818 (-4.139, 2.503) Na^+ 3-day lag = -0.205 (-4.356, 3.974) K^+ concurrent day = -0.211 (-2.778, 2.357) K^+ 2-day lag = -0.843 (-4.695, 3.008) K^+ 3-day lag = 0.843 (-4.292, 5.978) Mg_2^+ concurrent day = -1.750 (-5.302, 1.802) Mg_2^+ 2-day lag = -5.016 (-10.79, 0.762) Mg_2^+ 3-day lag = -3.850 (-10.15, 2.449) Ca_2^+ concurrent day = 3.192* (-0.599, 6.943) Ca_2^+ 2-day lag = 5.880 (1.105, 10.65) Ca_2^+ 3-day lag = 7.560* (2.103, 13.02) F_{inf} concurrent day = 2.218* (-0.033, 4.470) F_{inf} 2-day lag = 3.697* (1.446, 5.949) Fl_{nf} 3-day lag =4.067* (1.065, 7.069) Cl^- concurrent day = -1.010 (-3.469, 1.450) Cl^- 2-day lag = -1.615 (-5.714, 2.483) Cl^- 3-day lag = -1.615 (-6.534, 3.303) NO_3^- concurrent day = 3.144 (0.409, 5.878) NO_3^- 2-day lag = 3.593 (0.858, 6.328) NO_3^- 3-day lag = 4.491 (1.756, 7.226) SO_4^{2-} concurrent day = 2.210 (-0.032, 4.272) SO_4^{2-} 2-day lag = 3.180 (1.028, 5.332) SO_4^{2-} 3-day lag = 3.180 (1.028, 5.332) **Evening PEF** Na^+ concurrent day = -1.636 (-3.712, 0.440) Na^+ 2-day lag = -0.205 (-3.256, 3.117) Na^+ 3-day lag = -1.023 (-5.174, 3.129) K^+ concurrent day = -1.897 (-4.465, 0.670) K^+ 2-day lag = -1.686 (-5.966, 2.592) K^+ 3-day lag = -1.054 (-6.189, 4.081) Mg_2^+ concurrent day = -2.753 (-6.400, 0.894) Mg_2^+ 2-day lag = -2.567 (-8.534, 3.401) Mg_2^+ 3-day lag = -4.876 (-11.36, 1.612) Ca_2^+ concurrent day = 2.184 (-1.567, 5.935) Ca_2^+2-day lag = 5.040 (0.265, 9.815) Ca_2^+ 3-day lag = 5.040 (-0.417, 10.50) F_{inf} f concurrent day = 1.479 (-0.773, 3.730) F_{inf} 2-day lag = 1.819 (-0.403, 4.100) F_{inf} 3-day lag = 2.958 (-0.044, 5.960) Cl^- concurrent day = -0.404 (-2.863, 2.055) Cl^- 2-day lag = 0.000 (-4.099, 4.099) Cl^- 3-day lag =0.202 (-4.716, 5.120) NO_3^- concurrent day = 1.796 (-0.939, 4.531) NO_3^- 2-day lag = 2.695 (-0.040, 5.430) NO_3^- 3-day lag = 3.144 (0.409, 5.878) SO_4^{2-} concurrent day = 2.120 (-0.032, 4.272) SO_4^{2-} 2-day lag = 2.120 (-0.032, 4.272) SO_4^{2-} 3-day lag =2.120 (-0.032, 4.272)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: de Hartog et al. (2003, 001061) **Period of Study:** Winter of 1998-1999 (in Amsterdam, from Nov 1998-Jun 1999; in Erfurt, from Oct 1998-Apr 1999; and in Helsinki, from Nov 1998-Apr 1999.) **Location:** Amsterdam, the Netherlands Erfurt, Germany and Helsinki, Finland	**Outcome:** Respiratory symptoms **Age Groups**: ≥ 50 yr **Study Design: C**ohort **N:** 131 subjects with history of coronary heart disease **Statistical Analyses:** Logistic regression **Covariates:** Ambient temperature, relative humidity, atmospheric pressure, incidence of influenza-like illness **Season**: Winter **Dose-response Investigated?** No **Statistical Package**: S-PLUS 2000 **Lags Considered:** 0-, 1-, 2-, 3-, and 5-day avg	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** Amsterdam, the Netherlands: 20.0 Erfurt, Germany: 23.4 Helsinki, Finland: 12.8 **Range (Min, Max):** Amsterdam, the Netherlands: (3.8-82.2) Erfurt, Germany: (4.5-118.1) Helsinki, Finland: (3.1-39.8) Unit (i.e. $\mu g/m^3$): $\mu g/m^3$ **Monitoring Stations**: 1 **Copollutant:** PM_{10} NC0.01-0.1 CO NO_2 SO_2	**PM Increment:** 10 $\mu g/m^3$ **Effect Estimate [Lower CI, Upper CI]:** Association of air pollution and incidence of symptoms in three panels of elderly subjects **Lag 0** Chest pain w/ physical exertion: 1.04 (0.96-1.13) Shortness of breath: 1.04 (0.96-1.12) Awakened, breathing problems: NA Avoidance of activities: 1.04 (0.96-1.14) Phlegm: 1.03 (0.93-1.13) **Lag 1** Chest pain w/ physical exertion: 1.01 (0.93-1.09) Shortness of breath: 1.06 (0.99-1.14) Awakened, breathing problems: 1.09 (1.00-1.20) Avoidance of activities: 1.03 (0.95-1.12) Phlegm: 1.10 (1.01-1.19) **Lag 2** Chest pain w/ physical exertion: 0.98 (0.90-1.05) Shortness of breath: 1.05 (0.98-1.12) Awakened, breathing problems: 1.04 (0.95-1.14) Avoidance of activities: 1.05 (0.97-1.14) Phlegm: 1.08 (1.00-1.18) **Lag 3** Chest pain w/ physical exertion: 1.00 (0.93-1.08) Shortness of breath: 1.08 (1.01-1.15) Awakened, breathing problems: 0.99 (0.91-1.08) Avoidance of activities: 1.06 (0.98-1.14) Phlegm: 1.10 (1.01-1.19) **5-day** Chest pain w/ physical exertion: 1.02 (0.91-1.13) Shortness of breath: 1.12 (1.02-1.24) Awakened, breathing problems: 1.03 (0.90-1.18) Avoidance of activities: OR= 1.09 (0.97-1.22) Phlegm: OR= 1.16 (1.03-1.32)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Delfino et al. (2004, 056897) **Period of Study:** Sep-Oct 1999 Apr-Jun 2000 **Location:** Alpine, California	**Outcome**: FEV_1 **Age Groups**: 9-19 yr old **Study Design:** Panel study **N:** 24 children **Statistical Analyses:** GLM Akaike's information criterion and Bayesian information criterion **Covariates:** Day of wk, personal temperature and relative humidity, time of FEV_1 maneuver (morning, afternoon, or evening), Season (fall 1999 or spring 2000), As-needed medication use, Presence or absence of upper or lower respiratory infections **Season:** Spring, fall **Dose-response Investigated?** No **Statistical Package**: SAS **Lags Considered:** 0-4	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg 1-h max personal PM last 24 h **Mean (SD):** 151.0 (12.03) 90th: 292.4 **Range (Min, Max):** (9.1, 996.8) Mean personal PM last 24 h **Mean (SD):** 37.9 (19.9) 90th: 65.1 **Range (Min, Max):** 3.9, 113.8 Home stationary-site PM 24-h Mean indoor $PM_{2.5}$ **Mean (SD):** 12.1 (5.4) 90th: 20.2 **Range (Min, Max):** 2.8, 35.3 24-h Mean outdoor $PM_{2.5}$ **Mean (SD):** 11.0 (5.4) 90th: 18.4 **Range (Min, Max):** 1.8, 31.0 Central outdoor stationary-site PM 24-h Mean $PM_{2.5}$ **Mean (SD):** 10.3 (5.6) 90th: 18.4 **Range (Min, Max):** 1.7, 29.1 **Copollutant (correlation):** 24-h Central HI $PM_{2.5}$ 8-h max O_3 = 0.24 8-h Max NO_2 = 0.73 8-h Max Personal PM = 0.38 24-h Mean Personal PM = 0.43 8-h Max TEOM PM_{10} = 0.71 24-h Mean TEOM PM_{10} = 0.78 24-h Central HI PM_{10} = 0.90 24-h Outdoor HI $PM_{2.5}$ = 0.89 24-h Outdoor HI PM_{10} = 0.72 24-h Indoor HI PM_{10} = 0.40 24-h Indoor HI $PM_{2.5}$ = 0.73	Results presented graphically; % predicted FEV_1 was inversely associated with personal exposure to fine particles. Inverse associations of FEV_1 with stationary-site indoor, outdoor and central-site gravimetric $PM_{2.5}$ and PM_{10}, and with hourly TEOM PM_{10}

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Delfino et al. (2006, 090745) **Period of Study:** Region 1: Aug-Mid Dec 2003. Region 2: Jul-Nov 2004 **Location:** Region 1: Riverside, CA. Region 2: Whittier, CA	**Outcome:** Fractional Concentration of Nitric Oxide in exhaled air (FENO) **Age Groups**: 9 through 18 **Study Design:** Longitudinal Panel Study **N:** 45 children Riverside children 32 Whittier children **Statistical Analyses:** Linear mixed-effects models Two-stage hierarchical model Empirical Variograms Fourth-order polynomial distributed lag mixed-effects model **Covariates:** Personal temperature, Personal Rel. Humid., 10-day exposure run, Respiratory infections, Region of study, Sex, Cumulative daily use of as-needed B-agonist inhalers **Dose-response Investigated?** No **Lags Considered:** 0, 1, 2, MA day	**Pollutant**: $PM_{2.5}$ **Personal Exposure** **Averaging Time:** 24 h **Riverside** **Mean (SD):** 32.78 (21.84) 50th(Median): 28.14 **Range (Min, Max):** 7.27, 98.43 **Whittier** **Mean (SD):** 36.2 (25.46) 50th(Median): 29.07 **Range (Min, Max):** 7.55, 197.05 **Personal Exposure** **Averaging Time:** 1 h **Riverside** **Mean (SD):** 97.94 (70.29) 50th(Median): 83.7 **Range (Min, Max):** 14.9, 431.8 **Whittier** **Mean (SD):** 93.63 (75.19) 50th(Median): 71.95 **Range (Min, Max):** 5.8, 572.9 **Personal Exposure** **Averaging Time:** 8 h **Riverside** **Mean (SD):** 47.21 (30.9) 50th(Median): 38.5 **Range (Min, Max):** 8.9, 132.1 **Whittier** **Mean (SD):** 51.75 (36.88) 50th(Median): 40.15 **Range (Min, Max):** 8.7, 254.1 **Central Site** **Averaging Time:** 24 h **Riverside** **Mean (SD):** 36.63 (23.46) 50th(Median): 29.26 **Range (Min, Max):** (9.52, 87.22) **Whittier** **Mean (SD):** 18 (12.14) 50th(Median): 16.3 **Range (Min, Max):** 2.7, 77.09 **Monitoring Stations**: 48 personal nephelometers 2 central sites **Copollutant (correlation):** **Personal** 24-h personal $PM_{2.5}$ 1.00 24-h personal EC 0.18 24-h personal OC 0.15 24-h personal NO_2 0.33 24-h central $PM_{2.5}$ 0.64 24-h central EC 0.12 24-h central OC 0.21 24-h central NO_2 0.22 **Central** 24-h personal $PM_{2.5}$ 0.64 24-h personal EC 0.00 24-h personal OC -0.11 24-h personal NO_2 0.12 24-h central $PM_{2.5}$ 1.00 24-h central EC 0.55 24-h central OC 0.66 24-h central NO_2 0.25	**PM Increment:** IQR increase (Riverside: 28.41 µg/m^3, Whittier 21.87 µg/m^3) **Coefficient [Lower CI, Upper CI]** **lag:** Mixed-model estimates of the association between personal and central-site air pollutant exposure and FENO Lag 0 Personal 0.42 (-0.15, 0.99) Central 0.03 (-0.68, 0.74) Lag 1 Personal 0.51 (-0.10, 1.12) Central 0.44 (-0.28, 1.16) 2-day ma Personal 1.01 (0.14, 1.88) Central 0.52 (-0.43, 1.47) Stratified by Medication Use Lag = 2-day ma Not Taking Anti-Inflamm. Medication Personal 1.11 (-1.39, 3.60) Central 0.44 (-1.65, 2.53) Taking Anti-Inflamm. Medication Personal 1.01 (0.19, 1.84) Central 0.55 (-0.47, 1.57) Inhaled Corticosteroids Personal 1.58 (0.72, 2.43) Central 1.16 (0.11, 2.20) Antileukotrienes +- inhaled corticosteroids Personal -0.89 (-2.73, 0.95) Central -0.75 (-2.83, 1.32) **Notes:** Fig of Estimated lag effect of hourly personal $PM_{2.5}$ on FENO. Fig of the Estimated lag effect of hourly personal $PM_{2.5}$ on FENO by use of medications. Fig of one- and two-pollutant models for change in FENO using 2-day Ma personal and central-site pollutant measurements.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Delfino et al. (2006, 090745) **Period of Study:** Region 1: Aug-Mid Dec 2003. Region 2: Jul-Nov 2004 **Location:** Region 1: Riverside, CA. Region 2: Whittier, CA	**Outcome:** Fractional Concentration of Nitric Oxide in exhaled air (FENO) **Age Groups**: 9 through 18 **Study Design:** Longitudinal Panel Study **N:** 45 children **Statistical Analyses:** Linear mixed-effects models Two-stage hierarchical model Empirical Variograms Fourth-order polynomial distributed lag mixed-effects model **Covariates:** Personal temperature, personal rel. humid., 10-day exposure run, respiratory infections, region of study, sex, cumulative daily use of as-needed B-agonist inhalers **Dose-response Investigated?** No **Lags Considered:** Lag 0, Lag 1, 2-day ma	**Pollutant:** $PM_{2.5}$ **PM Component:** EC **Personal Exposure** **Averaging Time:** 24 h Riverside **Mean (SD):** 0.42 (0.69) 50th(Median): 0.34 µg/m^3 **Range (Min, Max):** 0.01, 6.94 Whittier **Mean (SD):** 0.78 (1.42) 50th(Median): 0.47 **Range (Min, Max):** 0, 17.2 **Central Site** **Averaging Time:** 24 h Riverside **Mean (SD):** 1.61 (0.78) 50th(Median): 1.35 **Range (Min, Max):** 0.52, 3.64 Whittier **Mean (SD):** 0.71 (0.43) 50th(Median): 0.63 **Range (Min, Max):** 0.14, 2.95 **Monitoring Stations**: 48 personal nephelometers, 2 central sites **Copollutant (correlation):** **Personal** 24-h personal $PM_{2.5}$ 0.18 24-h personal EC 1.00 24-h personal OC 0.41 24-h personal NO_2 0.0.21 24-h central $PM_{2.5}$ 0.00 24-h central EC 0.04 24-h central OC -0.01 24-h central NO_2 0.23 **Central** 24-h personal $PM_{2.5}$ 0.12 24-h personal EC 0.04 24-h personal OC 0.03 24-h personal NO_2 0.19 24-h central $PM_{2.5}$ 0.55 24-h central EC 1.00 24-h central OC 0.87 24-h central NO_2 0.70	**PM Increment:** IQR increase (Riverside: 28.41 µg/m^3, Whittier 21.87 µg/m^3) **Coefficient [Lower CI, Upper CI] lag:** Mixed-model estimates of the association between personal and central-site air pollutant exposure and FENO Lag 0 Personal 0.29 (0.10, 0.48) Central 0.10 (-0.65, 0.85) Lag 1 Personal -0.01 (-0.23, 0.21) Central 0.99 (0.27, 1.71) 2-day ma Personal 0.72 (0.32, 1.12) Central 1.38 (0.15, 2.61) Stratified by Medication Use Lag = 2-day ma Not Taking Anti-Inflamm. Medication Personal 0.84 (0.08, 1.60) Central 1.02 (-2.55, 4.60) Taking Anti-Inflamm. Medication Personal 0.71 (0.28, 1.15) Central 1.42 (0.25, 2.60) Inhaled Corticosteroids Personal 0.67 (0.28, 1.07) Central 1.28 (0.07, 2.49) Antileukotrienes +- inhaled corticosteroids Personal 0.03 (-3.29, 3.35) Central 1.15 (-1.58, 3.88) **Notes:** Fig of Estimated lag effect of hourly personal $PM_{2.5}$ on FENO. Fig of the estimated lag effect of hourly personal $PM_{2.5}$ on FENO by use of medications. Fig of one- and two-pollutant models for change in FENO using 2-day Ma personal and central-site pollutant measurements.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Delfino et al. (2006, 090745) **Period of Study:** Region 1: Aug-Mid Dec 2003. Region 2: Jul through Nov 2004 **Location:** Region 1: Riverside, CA. Region 2: Whittier, CA	**Outcome:** Fractional Concentration of Nitric Oxide in exhaled air (FENO) **Age Groups**: 9 through 18 **Study Design:** Longitudinal Panel Study **N:** 45 children **Statistical Analyses:** Linear mixed-effects models Two-stage hierarchical model Empirical Variograms Fourth-order polynomial distributed lag mixed-effects model **Covariates:** Personal temperature, personal rel. humid., 10-day exposure run, respiratory infections, region of study, sex, cumulative daily use of as-needed B-agonist inhalers **Dose-response Investigated?** No **Lags Considered:** Lag 0, Lag 1, 2-day ma	**Pollutant:** $PM_{2.5}$ **PM Component:** OC **Personal Exposure** **Averaging Time:** 24 h Riverside **Mean (SD):** 5.63 (2.59) 50th(Median): 4.98 **Range (Min, Max):** 1.94, 12.38 Whittier **Mean (SD):** 6.81 (3.45) 50th(Median): 6.43 **Range (Min, Max):** 2.18, 31.5 **Central Site** **Averaging Time:** 24 h Riverside **Mean (SD):** 6.88 (1.86) **Percentiles:** 50th Median: 6.07 **Range (Min, Max):** 4.11, 11.62 Whittier **Mean (SD):** 3.93 (1.49) 50th(Median): 3.76 **Range (Min, Max):** 1.64, 8.82 **Monitoring Stations**: 48 personal nephelometers, 2 central sites **Copollutant (correlation):** **Personal** 24-h personal $PM_{2.5}$ 0.15 24-h personal EC 0.41 24-h personal OC 1.00 24-h personal NO_2 0.20 24-h central $PM_{2.5}$ -0.11 24-h central EC 0.03 24-h central OC -0.02 24-h central NO_2 0.21 **Central** 24-h personal $PM_{2.5}$ 0.21 24-h personal EC -0.01 24-h personal OC -0.02 24-h personal NO_2 0.17 24-h central $PM_{2.5}$ 0.66 24-h central EC 0.87 24-h central OC 1.00 24-h central NO_2 0.62	**PM Increment:** IQR increase (Riverside: 28.41 µg/m^3, Whittier 21.87 µg/m^3) Mixed-model estimates of the association between personal and central-site air pollutant exposure and FENO Lag 0 Personal 0.51 (-0.28, 1.30) Central 0.93 (-0.20, 2.06) Lag 1 Personal 0.13 (-0.77, 1.03) Central0.51 (-0.64, 1.66) 2-day ma Personal 0.94 (-0.47, 2.35) Central 1.6 (-0.17, 3.37) Stratified by Medication Use Lag = 2-day ma. Not Taking Anti-Inflamm. Medication Personal 0.88 (-1.62, 3.38) Central 0.36 (-4.07, 4.79) Taking Anti-Inflamm. Medication Personal 0.87 (-0.79, 2.53) Central 2.05 (0.24, 3.86) Inhaled Corticosteroids Personal 2.47 (0.30, 4.64) Central 1.96 (0.14, 3.78) Antileukotrienes +- inhaled corticosteroids Personal 0.52 (-1.99, 3.02) Central 1.29 (-2.58, 5.15) **Notes:** Fig of Estimated lag effect of hourly personal $PM_{2.5}$ on FENO. Fig of the Estimated lag effect of hourly personal $PM_{2.5}$ on FENO by use of medications. Fig of one- and two-pollutant models for change in FENO using 2-day Ma personal and central-site pollutant measurements

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Dubowsky et al. (2006, 088750) **Period of Study:** Mar 2002–Jun 2002 **Location:** St. Louis, Missouri	**Outcome:** Chronic inflammation, Diabetes, Obesity, Hypertension, Cardiac Risk **Study Design:** Prospective Cohort **Statistical Analyses:** Poisson, LOESS **Age Groups**: ≥ 60	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD) unit:** 16 (6.0) **Range (Min, Max):** 6.5, 28 **Copollutants:** BC CO NO_2 SO_2 O_3	**Increment:** 5.4 µg/m^3 **% Increase (Lower CI, Upper CI)** **Lag** % increase in inflammatory response and exposure to $PM_{2.5}$ in people ≥ 60 Inflammatory Marker: IL-6: -8 (-16, 8) 1: -6 (-10, 5) 2: -5 (-11, 6) 3: -3 (-9, 6) 4: -4 (-12, 10) 5: -5 (-13, 8) 6: -6 (-14, 9) 7 CRP: -2 (-22, 15) 1: 3 (-8, 17) 2: 4 (-9, 20) 3: 9 (-4, 27) 4: 11 (-5, 35) 5: 8 (-9, 29) 6: 5 (-12, 26) 7 WBC: 0 (-2, 4) 1: 1 (-1, 2) 2: 2 (-1, 3) 3: 1 (-2, 5) 4: 3 (-1, 10) 5: 5 (0, 12) 6: 8 (0, 14) 7 % Increase in inflammatory responses and exposure to ambient $PM_{2.5}$ concentrations in people ≥ 60 Inflammatory Marker: CRP All conditions*: 14 (-5.4, 37) 0-5 avg 3 conditions met*: 81 (21, 172) 0-5 avg 2 conditions met*: 11 (-7.3, 33) 0-5 avg IL-6 All conditions*: -2.1 (-13, 11) 0-5 avg 3 conditions met*: 23 (-5.3, 59) 0-5 avg 2 conditions met*: -3.1 (-14, 9.7) 0-5 avg WBC All conditions*: 3.4 (-1.8, 8.9) 0-5 avg 3 conditions met*: 0.4 (-8.8, 11) 0-5 avg 2 conditions met*: 3.6 (-1.7, 9.1) 0-5 avg * All conditions met means model is adjusted for sex, obesity, diabetes, smoking history, ambient and microenvironmental apparent temperature, mold, pollen, trip, h, and vitamins. Three conditions met means model is adjusted for three of the variables. Two conditions met means model is adjusted for 2 of the variables.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ebelt et al. (2005, 056907) **Period of Study:** Summer of 1998 **Location:** Vancouver, Canada	**Outcome:** spirometry, **Age Groups**: range from 54-86 yr Mean age= 74 yr **Study Design:** extended analysis of a repeated-measures panel study **N:** 16 persons with COPD **Statistical Analyses:** Earlier analysis expanded by developing mixed-effect regression models and by evaluating additional exposure indicators **Dose-response Investigated?** No **Statistical Package**: SAS V8	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** Ambient $PM_{2.5}$: 11.4 (4.6) Exposure to ambient $PM_{2.5}$: 7.9 (3.7) Nonsulfate ambient $PM_{2.5}$: 9.3 (3.7) Exposure to nonsulfate ambient $PM_{2.5}$: 6.5 (3.0) Total exposure to $PM_{2.5}$: 18.5 (14.9) Exposure to nonambient $PM_{2.5}$: 10.6 (14.5) **Range (Min, Max):** Ambient $PM_{2.5}$: (4.2-28.7) Exposure to ambient $PM_{2.5}$: (0.9-21.3) Nonsulfate ambient $PM_{2.5}$: (3.3-23.3) Exposure to nonsulfate ambient $PM_{2.5}$: (0.7-16.9) Total exposure to $PM_{2.5}$: (2.2-90.9) Exposure to nonambient $PM_{2.5}$: (-2.6-85.0) **Monitoring Stations**: 5 **Copollutant (correlation):** Ambient PM_{10}: r= 0.78 Ambient $PM_{10-2.5}$: r= 0.15 Ambient Sulfate- 0.82 Nonsufate Ambient $PM_{2.5}$: r= 0.98	**PM Increment:** Ambient $PM_{2.5}$: 5.8 (IQR) Exposure to ambient $PM_{2.5}$: 4.4 (IQR) Nonsulfate ambient $PM_{2.5}$: 4.2 (IQR) Exposure to nonsulfate ambient $PM_{2.5}$: 3.4 (IQR) Total exposure to $PM_{2.5}$: 10.1 (IQR) Exposure to nonambient $PM_{2.5}$: 8.9 (IQR) **Notes:** Effect estimates are presented in Fig 2 and Electronic Appendix Table 1 (only available with electronic version of article) and not provided quantitatively elsewhere.
Reference: Ebelt et al. (2005, 056907) **Period of Study:** Summer of 1998 **Location:** Vancouver, Canada	**Outcome:** spirometry **Age Groups**: Range from 54-86 yr Mean age= 74 yr **Study Design:** extended analysis of a repeated-measures panel study **N:** 16 persons with COPD **Statistical Analyses:** Earlier analysis expanded by developing mixed-effect regression models and by evaluating additional exposure indicators **Dose-response Investigated?** No **Statistical Package**: SAS V8	**Pollutant:** Sulfate (SO_4) **Averaging Time:** 24 h **Mean (SD):** Ambient Sulfate: 2.0 (1.1) Exposure to Ambient Sulfate: 0.2 (4.7) **Range (Min, Max):** Ambient Sulfate: (0.4-5.4) Exposure to ambient Sulfate: (0.2-4.7) **Monitoring Stations**: 5 **Copollutant (correlation):** Ambient $PM_{2.5}$: r= 0.82 Nonsulfate Ambient $PM_{2.5}$: r= 0.74 Exposure to Ambient Sulfate: r= 0.82	**PM Increment:** Ambient Sulfate: 1.5 (IQR) Exposure to Ambient Sulfate: 0.9 (IQR) **Notes:** Effect estimates are presented in Fig 2 and Electronic Appendix Table 1 (only available with electronic version of article) and not provided quantitatively elsewhere.
Reference: Ferdinands et al. (2008, 156433) **Period of Study:** Aug 2004 **Location:** Atlanta, Georgia	**Outcome:** Respiratory Symptoms, airway inflammation **Study Design:** Prospective cohort **Statistical Analyses:** Pearson Correlation Analysis **Age Groups**: 14-18	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD) unit:** 27.2 (11.9) **Range (Min, Max):** 21.7, 34.7 **Copollutants (correlation):** O_3: r= 0.8-0.9	The study presents results qualitatively not quantitatively.
Reference: Gent et al. (2003, 052885) **Period of Study:** Apr-Sep 2001 **Location:** Connecticut Springfield, MA	**Outcome:** Respiratory symptoms including: Wheeze, persistent cough, chest tightness, shortness of breath **Age Groups**: Infants **Study Design:** 1-yr prospective cohort study **N:** 1002 infants 17160 observations **Statistical Analyses:** Logistic regression analysis GEEs Tests for linear trend Test for goodness of fit Hosmer-Lemeshow statistic for regression	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** 13.1 (7.9) **Percentiles**: 20th: 6.9 40th: 9.0 50th(Median): 10.3 60th: 12.1 80th: 19.0 **Range (Min, Max):** 3.7, 44.2 **Monitoring Stations**: 4 sites **Copollutant (correlation):** Temperature: 0.58	**PM Increment:** 12 $\mu g/m^3$ same day 19 $\mu g/m^3$ previous day **Model 5 (same day)** **Wheeze** <6.9 = 1.00 6.9-8.9 = 0.95 (0.83, 1.10) 9.0-12.0 = 1.04 (0.89, 1.20) 12.1-18.9 = 1.05 (0.92, 1.20) ≥ 19.0 = 0.93 (0.78, 1.11) **Persistent Cough** <6.9 =1.00 6.9-8.9 = 0.95 (0.87, 1.04) 9.0-12.0 = 0.96 (0.87, 1.06) 12.1-18.9 = 1.00 (0.91, 1.09) ≥ 19.0 = 0.95 (0.83, 1.09) **Chest Tightness** <6.9 = 1.00 6.9-8.9 = 1.01 (0.86, 1.19) 9.0-12.0 = 1.06 (0.89, 1.26) 12.1-18.9 = 1.24 (1.06, 1.45) ≥ 19.0 = 1.05 (0.84, 1.33) **Shortness of Breath** <6.9 = 1.00 6.9-8.9 = 1.01 (0.87, 1.17) 9.0-12.0 = 1.03 (0.87, 1.22)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
	Covariates: Temperature **Dose-response Investigated?** No **Statistical Package**: SAS **Lags Considered:** 1-day lag		12.1-18.9 = 1.07 (0.91, 1.25) ≥ 19.0 = 1.03 (0.83, 1.28) **Bronchodilator** <6.9 = 1.00 6.9-8.9 = 1.04 (0.99, 1.09) 9.0-12.0 = 1.02 (0.96, 1.08) 12.1-18.9 = 1.04 (0.99, 1.09) ≥ 19.0 = 1.02 (0.97, 1.08) **Model 6 (previous day)** **Wheeze** <6.9 = 1.00 6.9-8.9 = 1.06 (0.95, 1.20) 9.0-12.0 = 1.09 (0.94, 1.28) 12.1-18.9 = 1.03 (0.89, 1.19) ≥ 19.0 = 1.14 (0.97, 1.34) **Persistent Cough** <6.9 =1.00 6.9-8.9 = 1.04 (0.94, 1.14) 9.0-12.0 = 1.05 (0.94, 1.17) 12.1-18.9 = 1.03 (0.94, 1.14) ≥ 19.0 = 1.12 (1.02 1.24) **Chest Tightness** <6.9 = 1.00 6.9-8.9 = 1.03 (0.87, 1.23) 9.0-12.0 = 1.04 (0.85, 1.27) 12.1-18.9 = 1.00 (0.84, 1.19) ≥ 19.0 = 1.21 (1.00, 1.46) **Shortness of Breath** <6.9 = 1.00 6.9-8.9 = 1.00 (0.84, 1.19) 9.0-12.0 = 1.09 (0.90, 1.31) 12.1-18.9 = 1.09 (0.90, 1.31) ≥ 19.0 = 1.26 (1.02, 1.54) **Bronchodilator** <6.9 = 1.00 6.9-8.9 = 0.98 (0.94, 1.03) 9.0-12.0 = 0.99 (0.95, 1.03) 12.1-18.9 = 0.97 (0.94, 1.01) ≥ 19.0 = 0.99 (0.95, 1.04) $PM_{2.5}$ + O_3: **Medication Users: Same-day** **Wheeze** <6.9 = 1.00 6.9-8.9 = 0.89 (0.75, 1.29) 9.0-12.0 = 1.02 (0.87, 1.19) 12.1-18.9 = 0.94 (0.77, 1.15) ≥ 19.0 = 0.83 (0.65, 1.06) **Persistent Cough** <6.9 = 1.00 6.9-8.9 = 0.95 (0.84, 1.06) 9.0-12.0 = 0.97 (0.86, 1.10) 12.1-18.9 = 0.94 (0.77, 1.15) ≥ 19.0 = 0.83 (0.65, 1.06) **Chest Tightness** <6.9 = 1.00 6.9-8.9 = 0.90 (0.74, 1.09) 9.0-12.0 = 0.97 (0.79, 1.18) 12.1-18.9 = 0.97 (0.76, 1.25) ≥ 19.0 = 0.76 (0.54, 1.05) **Shortness of Breath** <6.9 = 1.00 6.9-8.9 = 0.95 (0.80, 1.12) 9.0-12.0 = 1.00 (0.82, 1.21) 12.1-18.9 = 0.90 (0.73, 1.12) ≥ 19.0 = 0.87 (0.65, 1.17) **Bronchodilator** <6.9 = 1.00 6.9-8.9 = 1.03 (0.98, 1.08) 9.0-12.0 = 1.01 (0.96, 1.07) 12.1-18.9 = 1.02 (0.95, 1.08) ≥ 19.0 = 0.99 (0.91, 1.07) **Previous Day** **Wheeze** <6.9 = 1.00 6.9-8.9 = 1.03 (0.89, 1.18) 9.0-12.0 = 1.05 (0.88, 1.24) 12.1-18.9 = 0.98 (0.82, 1.17) ≥ 19.0 = 1.05 (0.85, 1.29) **Persistent Cough** <6.9 = 1.00 6.9-8.9 = 0.99 (0.89, 1.11) 9.0-12.0 = 0.98 (0.86, 1.10) 12.1-18.9 = 0.95 (0.83, 1.10) ≥ 19.0 = 1.00 (0.88, 1.15) **Chest Tightness** <6.9 = 1.00 6.9-8.9 = 0.89 (0.72, 1.10) 9.0-12.0 = 0.90 (0.70, 1.16) 12.1-18.9 = 0.81 (0.63, 1.03) ≥ 19.0 = 0.91 (0.71, 1.17) **Shortness of Breath** <6.9 = 1.00 6.9-8.9 = 0.96 (0.78, 1.18)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			9.0-12.0 = 1.00 (0.81, 1.25) 12.1-18.9 = 0.96 (0.74, 1.24) ≥ 19.0 = 1.20 (0.94, 1.52) **Bronchodilator** <6.9 = 1.00 6.9-8.9 = 0.99 (0.94, 1.04) 9.0-12.0 = 0.97 (0.93, 1.02) 12.1-18.9 = 0.96 (0.91, 1.02) ≥ 19.0 = 0.97 (0.89, 1.04) $PM_{2.5}$ + O_3: **Non-users: Same-day** **Wheeze** <6.9 = 1.00 6.9-8.9 = 0.92 (0.72, 1.17) 9.0-12.0 = 1.08 (0.85, 1.36) 12.1-18.9 = 0.94 (0.73, 1.22) ≥ 19.0 = 1.15 (0.75, 1.75) **Persistent Cough** <6.9 = 1.00 6.9-8.9 = 0.96 (0.83, 1.12) 9.0-12.0 = 1.02 (0.89, 1.18) 12.1-18.9 = 0.93 (0.78, 1.12) ≥ 19.0 = 1.07 (0.85, 1.34) **Chest Tightness** <6.9 = 1.00 6.9-8.9 = 0.84 (0.54, 1.31) 9.0-12.0 = 1.09 (0.74, 1.61) 12.1-18.9 = 0.78 (0.47, 1.30) ≥ 19.0 = 0.71 (0.36, 1.39) **Shortness of Breath** <6.9 = 1.00 6.9-8.9 = 0.61 (0.39, 0.95) 9.0-12.0 = 1.13 (0.85, 1.50) 12.1-18.9 = 0.72 (0.42, 1.23) ≥ 19.0 = 1.17 (0.72, 1.90) **Bronchodilator Use:** <6.9 = 1.00 6.9-8.9 = 0.95 (0.78, 1.15) 9.0-12.0 = 0.95 (0.78, 1.16) 12.1-18.9 = 0.85 (0.69, 1.06) ≥ 19.0 = 0.99 (0.76, 1.30) **Previous-day** **Wheeze** <6.9 = 1.00 6.9-8.9 = 1.01 (0.78, 1.31) 9.0-12.0 = 1.15 (0.88, 1.51) 12.1-18.9 = 1.08 (0.78, 1.51) ≥ 19.0 = 1.18 (0.71, 1.97) **Persistent Cough** <6.9 = 1.00 6.9-8.9 = 1.07 (0.94, 1.22) 9.0-12.0 = 1.13 (0.97, 1.32) 12.1-18.9 = 1.03 (0.87, 1.22) ≥ 19.0 = 1.14 (0.88, 1.46) **Chest Tightness** <6.9 = 1.00 6.9-8.9 = 1.44 (0.90, 2.30) 9.0-12.0 = 1.50 (0.97, 2.33) 12.1-18.9 = 1.56 (0.91, 2.66) ≥ 19.0 = 1.76 (0.83, 3.73) **Shortness of Breath** <6.9 = 1.00 6.9-8.9 = 0.99 (0.75, 1.30) 9.0-12.0 = 1.30 (0.88, 1.91) 12.1-18.9 = 0.84 (0.57, 1.24) ≥ 19.0 = 1.48 (0.94, 2.34) **Bronchodilator Use** <6.9 = 1.00 6.9-8.9 = 1.05 (0.85, 1.34) 9.0-12.0 = 1.28 (1.01, 1.62) 12.1-18.9 = 1.05 (0.80, 1.37) ≥ 19.0 = 1.19 (0.83, 1.71) **Notes:** Line graphs of daily levels of O_3 and $PM_{2.5}$ and daily temperature with daily prevalence of respiratory symptoms for users of asthma maintenance medication
Reference: Gent et al, (2009, 180399) **Period of Study:** 2000-2003 **Location:** New Haven County CT	**Outcome:** Increased asthma symptoms and medication use **Study Design:** Panel **Covariates:** Season, day of the week, date **Statistical Analysis:** Logistic regression **Statistical Package:** SAS	**Pollutant:** $PM_{2.5}$ and components **Averaging Time:** Daily **Mean:** (estimated sources, µg/m^3) Motor Vehicle: 6.6 Road Dust: 2.3 Sulfur: 5.5	**Odds Ratio and p-value for sources and components of $PM_{2.5}$.** **Lags are 0, 1 or 2 days, and the mean of days 0-2 (L02).** Source: Motor Vehicle EC, Increment = 1000 ng/m^3 Wheeze L0: 1.04, p = 0.04 L1: 1.01, p = 0.70

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
	Age Groups: Children aged 4-12	Biomass Burning: 0.9 Oil: 0.8 Sea Salt: 0.5 **Range (Min, Max):** NR **Copollutant (correlation):** NR	L2: 1.00, p = 0.99 L02: 1.07, p = 0.06 Persistent Cough L0: 1.01, p = 0.42 L1: 1.01, p = 0.38 L2: 0.99, p = 0.44 L02: 1.03, p = 0.23 Shortness of Breath L0: 1.06, p = 0.001 L1: 1.01, p = 0.65 L2: 1.01, p = 0.63 L02: 1.12, p = 0.01 Chest Tightness L0: 1.03, p = 0.20 L1: 1.02, p = 0.24 L2: 1.01, p = 0.59 L02: 1.10, p = 0.04 Inhaler Use L0: 1.01, p = 0.15 L1: 1.00, p = 0.72 L2: 1.00, p = 0.75 L02: 1.02, p = 0.40 Zn, Increment = 10 ng/m^3 Wheeze L0: 1.00, p = 0.69 L1: 0.99, p = 0.54 L2: 1.00, p = 0.89 L02: 1.00, p = 0.98 Persistent Cough L0: 1.00, p = 0.60 L1: 1.00, p = 0.77 L2: 0.99, p = 0.24 L02: 1.00, p = 0.94 Shortness of Breath L0: 1.02, p = 0.001 L1: 1.00, p = 0.57 L2: 1.01, p = 0.49 L02: 1.04, p = 0.06 Chest Tightness L0: 1.00, p = 0.72 L1: 1.00, p = 0.96 L2: 1.01, p = 0.38 L02: 1.03, p = 0.13 Inhaler Use L0: 1.00, p = 0.41 L1: 1.00, p = 0.44 L2: 1.00, p = 0.52 L02: 1.01, p = 0.53 Pb, Increment = 5 ng/m^3 Wheeze L0: 1.02, p = 0.31 L1: 1.00, p = 0.91 L2: 1.01, p = 0.62 L02: 1.07, p = 0.13 Persistent Cough L0: 1.02, p = 0.25 L1: 1.00, p = 0.88 L2: 1.00, p = 0.87 L02: 1.05, p = 0.12 Shortness of Breath L0: 1.03, p = 0.11 L1: 0.98, p = 0.51 L2: 1.03, p = 0.05 L02: 1.12, p = 0.01 Chest Tightness L0: 1.02, p = 0.31 L1: 0.99, p = 0.79 L2: 1.03, p = 0.13 L02: 1.10, p = 0.02 Inhaler Use L0: 1.01, p = 0.06 L1: 0.98, p = 0.11 L2: 1.02, p = 0.04 L02: 1.04, p = 0.10 Cu, Increment = 5 ng/m^3 Wheeze

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			L0: 1.01, p = 0.59 L1: 0.99, p = 0.55 L2: 0.99, p = 0.82 L02: 1.02, p = 0.67 Persistent Cough L0: 1.02, p = 0.13 L1: 1.02, p = 0.21 L2: 0.98, p = 0.26 L02: 1.05, p = 0.04 Shortness of Breath L0: 1.06, p = 0.01 L1: 1.01, p = 0.74 L2: 0.96, p = 0.10 L02: 1.06, p = 0.21 Chest Tightness L0: 10.3, p = 0.23 L1: 1.02, p = 0.42 L2: 0.97, p = 0.17 L02: 1.04, p = 0.39 Inhaler Use L0: 1.01, p = 0.22 L1: 0.99, p = 0.37 L2: 1.00, p = 0.70 L02: 1.01, p = 0.46 Se, Increment = 1 ng/m^3 Wheeze L0: 1.00, p = 0.97 L1: 0.99, p = 0.52 L2: 1.00, p = 0.91 L02: 1.02, p = 0.71 Persistent Cough L0: 1.00, p = 0.84 L1: 0.99, p = 0.32 L2: 1.00, p = 0.93 L02: 0.98, p = 0.43 Shortness of Breath L0: 1.02, p = 0.40 L1: 0.97, p = 0.10 L2: 1.01, p = 0.55 L02: 1.02, p = 0.67 Chest Tightness L0: 1.00, p = 0.79 L1: 0.97, p = 0.13 L2: 1.01, p = 0.72 L02: 0.98, p = 0.61 Inhaler Use L0: 0.99, p = 0.20 L1: 1.01, p = 0.02 L2: 0.99, p = 0.32 L02: 0.99, p = 0.75 Source: Road Dust Si, Increment = 100 ng/m^3 Wheeze L0: 1.03, p = 0.03 L1: 1.00, p = 0.99 L2: 1.02, p = 0.26 L02: 1.07, p = 0.04 Persistent Cough L0: 1.02, p = 0.01 L1: 1.00, p = 0.78 L2: 1.01, p = 0.60 L02: 1.05, p = 0.02 Shortness of Breat1.04, p = 0.01h L0: 1.04, p = 0.01 L1: 1.01, p = 0.60 L2: 1.01, p = 0.63 L02: 1.08, p = 0.02 Chest Tightness L0: 1.02, p = 0.20 L1: 1.02, p = 0.17 L2: 1.00, p = 0.88 L02: 1.06, p = 0.10 Inhaler Use L0: 1.02, p = 0.004 L1: 0.99, p = 0.18 L2: 1.01, p = 0.45

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			L02: 1.03, p = 0.09 Fe, Increment = 100 ng/m^3 Wheeze L0: 1.04, p = 0.02 L1: 1.00, p = 0.80 L2: 1.00, p = 0.87 L02: 1.07, p = 0.05 Persistent Cough L0: 1.02, p = 0.06 L1: 1.01, p = 0.52 L2: 0.99, p = 0.52 L02: 1.04, p = 0.04 Shortness of Breath L0: 1.06, p = 0.002 L1: 1.01, p = 0.65 L2: 0.98, p = 0.27 L02: 1.08, p = 0.04 Chest Tightness L0: 1.01, p = 0.47 L1: 1.02, p = 0.22 L2: 0.98, p = 0.35 L02: 1.05, p = 0.21 Inhaler Use L0: 1.02, p = 0.004 L1: 0.99, p = 0.44 L2: 1.00, p = 0.91 L02: 1.03, p = 0.08 Al, Increment = 50 ng/m^3 Wheeze L0: 1.02, p = 0.17 L1: 1.01, p = 0.73 L2: 1.02, p = 0.30 L02: 1.07, p = 0.03 Persistent Cough L0: 1.03, p = 0.001 L1: 1.00, p = 0.96 L2: 1.00, p = 0.68 L02: 1.06, p = 0.01 Shortness of Breath L0: 1.05, p = 0.002 L1: 1.01, p = 0.63 L2: 1.01, p = 0.59 L02: 1.09, p = 0.004 Chest Tightness L0: 1.02, p = 0.21 L1: 1.02, p = 0.18 L2: 1.00, p = 0.94 L02: 1.07, p = 0.04 Inhaler Use L0: 1.02, p = 0.02 L1: 0.99, p = 0.27 L2: 1.01, p = 0.50 L02: 1.02, p = 0.11 Ca, Increment = 50 ng/m^3 Wheeze L0: 1.07, p = 0.02 L1: 1.00, p = 0.97 L2: 1.01, p = 0.74 L02: 1.14, p = 0.04 Persistent Cough L0: 1.05, p = 0.01 L1: 0.99, p = 0.64 L2: 1.00, p = 0.90 L02: 1.09, p = 0.03 Shortness of Breath L0: 1.10, p = 0.002 L1: 1.02, p = 0.66 L2: 1.00, p = 0.89 L02: 1.18, p = 0.01 Chest Tightness L0: 1.04, p = 0.26 L1: 1.03, p = 0.43 L2: 1.00, p = 0.93 L02: 1.14, p = 0.07 Inhaler Use L0: 1.04, p = 0.01

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			L1: 0.97, p = 0.06 L2: 1.01, p = 0.44 L02: 1.04, p = 0.17 Ba, Increment = 10 ng/m^3 Wheeze L0: 0.99, p = 0.57 L1: 1.00, p = 0.92 L2: 0.99, p = 0.48 L02: 0.99, p = 0.81 Persistent Cough L0: 1.00, p = 0.83 L1: 1.01, p = 0.38 L2: 0.99, p = 0.32 L02: 1.00, p = 0.81 Shortness of Breath L0: 1.04, p = 0.02 L1: 1.00, p = 0.96 L2: 0.96, p = 0.05 L02: 1.03, p = 0.38 Chest Tightness L0: 1.01, p = 0.63 L1: 1.00, p = 0.88 L2: 0.98, p = 0.30 L02: 1.02, p = 0.51 Inhaler Use L0: 1.01, p = 0.08 L1: 0.99, p = 0.19 L2: 1.00, p = 0.92 L02: 1.01, p = 0.36 Ti, Increment = 5 ng/m^3 Wheeze L0: 1.00, p = 0.59 L1: 0.99, p = 0.49 L2: 1.01, p = 0.34 L02: 1.01, p = 0.56 Persistent Cough L0: 1.00, p = 0.57 L1: 1.00, p = 0.55 L2: 1.00, p = 0.30 L02: 1.01, p = 0.29 Shortness of Breath L0: 1.01, p = 0.01 L1: 1.00, p = 0.56 L2: 1.00, p = 0.60 L02: 1.03, p = 0.05 Chest Tightness L0: 1.00, p = 0.34 L1: 1.00, p = 0.55 L2: 0.99, p = 0.49 L02: 1.01, p = 0.52 Inhaler Use L0: 1.00, p = 0.72 L1: 1.00, p = 0.30 L2: 1.00, p = 0.67 L02: 1.00, p = 0.66 Source: Sulfur S, Increment = 1000 ng/m^3 Wheeze L0: 0.98, p = 0.43 L1: 0.99, p = 0.62 L2: 1.02, p = 0.29 L02: 1.00, p = 0.99 Persistent Cough L0: 1.00, p = 0.84 L1: 1.00, p = 0.69 L2: 1.02, p = 0.21 L02: 1.02, p = 0.27 Shortness of Breath L0: 1.01, p = 0.63 L1: 0.99, p = 0.71 L2: 1.01, p = 0.55 L02: 1.01, p = 0.79 Chest Tightness L0: 0.99, p = 0.80 L1: 1.01, p = 0.62

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			L2: 1.01, p = 0.81 L02: 1.02, p = 0.68 Inhaler Use L0: 0.99, p = 0.13 L1: 1.00, p = 0.81 L2: 1.02, p = 0.04 L02: 1.00, p = 0.81 P, Increment = 50 ng/m^3 Wheeze L0: 0.98, p = 0.39 L1: 0.98, p = 0.48 L2: 1.02, p = 0.38 L02: 0.99, p = 0.89 Persistent Cough L0: 1.00, p = 0.75 L1: 0.99, p = 0.69 L2: 1.01, p = 0.38 L02: 1.03, p = 0.30 Shortness of Breath L0: 1.01, p = 0.61 L1: 0.99, p = 0.71 L2: 1.01, p = 0.67 L02: 1.01, p = 0.78 Chest Tightness L0: 1.00, p = 0.88 L1: 1.01, p = 0.72 L2: 1.00, p = 0.87 L02: 1.02, p = 0.67 Inhaler Use L0: 0.98, p = 0.15 L1: 1.00, p = 0.83 L2: 1.01, p = 0.11 L02: 1.00, p = 0.99 Source: Biomass Burning K, Increment = 50 ng/m^3 Wheeze L0: 0.98, p = 0.06 L1: 0.99, p = 0.43 L2: 1.00, p = 0.85 L02: 0.96, p = 0.04 Persistent Cough L0: 1.00, p = 0.64 L1: 1.00, p = 0.83 L2: 1.00, p = 0.46 L02: 1.00, p = 0.86 Shortness of Breath L0: 1.01, p = 0.01 L1: 0.98, p = 0.09 L2: 1.00, p = 0.38 L02: 1.00, p = 0.79 Chest Tightness L0: 1.00, p = 0.02 L1: 0.99, p = 0.24 L2: 0.98, p = 0.07 L02: 0.99, p = 0.67 Inhaler Use L0: 1.00, p = 0.68 L1: 0.99, p = 0.05 L2: 1.00, p = 0.59 L02: 0.99, p = 0.28 Source: Oil V, Increment = 10 ng/m^3 Wheeze L0: 0.99, p = 0.73 L1: 0.96, p = 0.03 L2: 0.99, p = 0.56 L02: 0.93, p = 0.04 Persistent Cough L0: 1.01, p = 0.56 L1: 0.99, p = 0.24 L2: 0.98, p = 0.01 L02: 0.96, p = 0.05 Shortness of Breath L0: 1.01, p = 0.46 L1: 0.98, p = 0.24

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			L2: 1.00, p = 0.83 L02: 0.98, p = 0.58 Chest Tightness L0: 0.99, p = 0.71 L1: 0.98, p = 0.32 L2: 0.98, p = 0.23 L02: 0.94, p = 0.12 Inhaler Use L0: 0.98, p = 0.12 L1: 1.00, p = 0.68 L2: 0.99, p = 0.22 L02: 0.96, p = 0.03 Ni, Increment = 5 ng/m^3 Wheeze L0: 1.01, p = 0.59 L1: 0.97, p = 0.09 L2: 1.00, p = 0.76 L02: 0.99, p = 0.72 Persistent Cough L0: 1.01, p = 0.21 L1: 0.99, p = 0.57 L2: 0.99, p = 0.23 L02: 1.00, p = 0.99 Shortness of Breath L0: 1.04, p = 0.05 L1: 0.98, p = 0.36 L2: 1.00, p = 0.81 L02: 1.04, p = 0.32 Chest Tightness L0: 1.01, p = 0.58 L1: 1.00, p = 0.89 L2: 0.98, p = 0.27 L02: 1.01, p = 0.84 Inhaler Use L0: 1.01, p = 0.48 L1: 1.00, p = 0.83 L2: 0.99, p = 0.51 L02: 1.01, p = 0.48 Source: Sea Salt Na, Increment = 100 ng/m^3 Wheeze L0: 0.98, p = 0.23 L1: 1.00, p = 0.80 L2: 1.00, p = 0.88 L02: 0.97, p = 0.29 Persistent Cough L0: 1.00, p = 0.58 L1: 0.99, p = 0.19 L2: 1.00, p = 0.61 L02: 0.98, p = 0.21 Shortness of Breath L0: 1.00, p = 0.94 L1: 0.99, p = 0.46 L2: 1.01, p = 0.63 L02: 0.99, p = 0.74 Chest Tightness L0: 0.99, p = 0.43 L1: 0.99, p = 0.75 L2: 1.00, p = 0.88 L02: 0.98, p = 0.61 Inhaler Use L0: 0.99, p = 0.35 L1: 1.00, p = 0.61 L2: 1.00, p = 0.85 L02: 0.99, p = 0.37 Cl, Increment = 10 ng/m^3 Wheeze L0: 1.00, p = 0.89 L1: 1.00, p = 0.88 L2: 1.00, p = 0.38 L02: 1.00, p = 0.81 Persistent Cough L0: 1.00, p = 0.31 L1: 1.00, p = 0.31 L2: 1.00, p = 0.51

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			L02: 1.00, p = 0.06 Shortness of Breath L0: 1.00, p = 0.89 L1: 1.00, p = 0.94 L2: 1.00, p = 0.70 L02: 1.00, p = 0.80 Chest Tightness L0: 1.00, p = 0.24 L1: 1.00, p = 0.28 L2: 1.00, p = 0.52 L02: 1.00, p = 0.65 Inhaler Use L0: 1.00, p = 0.69 L1: 1.00, p = 0.52 L2: 1.00, p = 0.51 L02: 1.00, p = 0.83 **Odds Ratio (95%CI) from repeated measures logistic regression models of respiratory symptoms and daily source concentrations of $PM_{2.5}$.** Lag 0 Model Wheeze, p = 0.23 Motor Vehicle: 1.05 (0.99-1.10) Road Dust: 1.10 (1.01-1.19) Sulfur: 0.97 (0.94-1.00) Biomass Burning: 0.80 (0.66-0.98) Oil: 1.02 (0.86-1.20) Sea Salt: 0.96 (0.86-1.07) Persistent Cough, p < 0.001 Motor Vehicle: 1.02 (0.99-1.04) Road Dust: 1.06 (1.01-1.11) Sulfur: 1.00 (0.98-1.01) Biomass Burning: 0.97 (0.92-1.03) Oil: 1.02 (0.95-1.10) Sea Salt: 0.99 (0.92-1.07) Shortness of Breath, p < 0.001 Motor Vehicle: 1.06 (1.01-1.11) Road Dust: 1.12 (1.02-1.22) Sulfur: 0.98 (0.94-1.02) Biomass Burning: 1.05 (0.95-1.17) Oil: 1.07 (0.92-1.26) Sea Salt: 1.01 (0.92-1.12) Chest Tightness, p < 0.001 Motor Vehicle: 1.02 (0.97-1.08) Road Dust: 1.04 (0.95-1.15) Sulfur: 0.99 (0.94-1.03) Biomass Burning: 1.06 (0.95-1.18) Oil: 0.99 (0.82-1.18) Sea Salt: 0.95 (0.84-1.08) Inhaler Use, p < 0.001 Motor Vehicle: 1.02 (1.00-1.05) Road Dust: 1.06 (1.02-1.11) Sulfur: 0.98 (0.97-1.00) Biomass Burning: 1.00 (0.96-1.03) Oil: 0.98 (0.91-1.05) Sea Salt: 0.99 (0.94-1.04) Lag 02 Model Wheeze, p = 0.86 Motor Vehicle: 1.10 (1.01-1.19) Road Dust: 1.26 (1.05-1.51) Sulfur: 0.98 (0.92-1.04) Biomass Burning: 0.64 (0.46-0.88) Oil: 0.80 (0.56-1.08) Sea Salt: 0.91 (0.82-1.16) Persistent Cough, p < 0.001 Motor Vehicle: 1.03 (0.98-1.09) Road Dust: 1.16 (1.02-1.32) Sulfur: 1.01 (0.98-1.05) Biomass Burning: 0.93 (0.81-1.06) Oil: 0.84 (0.71-1.00) Sea Salt: 0.88 (0.77-1.01)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Shortness of Breath, p = 0.006 Motor Vehicle: 1.12 (1.01-1.24) Road Dust: 1.28 (1.05-1.55) Sulfur: 0.97 (0.90-1.04) Biomass Burning: 0.78 (0.52-1.18) Oil: 0.94 (0.69-1.29) Sea Salt: 1.01 (0.79-1.29) Chest Tightness, p = 0.39 Motor Vehicle: 1.08 (0.98-1.20) Road Dust: 1.20 (0.97-1.49) Sulfur: 1.00 (0.92-1.08) Biomass Burning: 0.87 (0.62-1.22) Oil: 0.80 (0.58-1.10) Sea Salt: 0.95 (0.71-1.27) Inhaler Use, p < 0.001 Motor Vehicle: 1.03 (0.98-1.08) Road Dust: 1.09 (1.00-1.19) Sulfur: 1.00 (0.97-1.03) Biomass Burning: 0.95 (0.87-1.04) Oil: 0.92 (0.81-1.05) Sea Salt: 0.97 (0.88-1.07) **Odds Ratio (95%CI) from repeated measures logistic regression models of respiratory symptoms and daily source concentrations of $PM_{2.5}$ when copollutants are included.** Wheeze Motor Vehicle NO_2: 1.03 (0.98-1.08) CO: 1.05 (0.99-1.11) SO_2: 1.04 (0.99-1.09) O_3: 1.06 (0.97-1.16) Road Dust NO_2: 1.11 (1.02-1.20) CO: 1.10 (1.01-1.19) SO_2: 1.10 (1.01-1.19) O_3: 1.11 (1.01-1.23) Sulfur NO_2: 0.96 (0.92-0.99) CO: 0.97 (0.94-1.01) SO_2: 0.97 (0.93-1.00) O_3: 0.95 (0.91-1.00) Biomass Burning NO_2: 0.79 (0.65-0.98) CO: 0.80 (0.66-0.98) SO_2: 0.79 (0.64-0.98) O_3: 0.74 (0.57-0.97) Oil NO_2: 1.02 (0.87-1.21) CO: 1.02 (0.86-1.20) SO_2: 1.01 (0.86-1.19) O_3: 0.92 (0.62-1.39) Sea Salt NO_2: 0.96 (0.85-1.07) CO: 0.96 (0.86-1.08) SO_2: 0.95 (0.85-1.07) O_3: 1.01 (0.72-1.40) Inhaler Use Motor Vehicle NO_2: 1.02 (0.99-1.04) CO: 1.02 (0.99-1.05) SO_2: 1.02 (0.99-1.04) O_3: 1.02 (0.98-1.07) Road Dust NO_2: 1.06 (1.02-1.10) CO: 1.06 (1.02-1.11) SO_2: 1.06 (1.02-1.11) O_3: 1.06 (1.00-1.13) Sulfur NO_2: 0.98 (0.96-1.00) CO: 0.98 (0.96-1.00) SO_2: 0.98 (0.96-1.00)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			O_3: 0.97 (0.95-1.00) Biomass Burning NO_2: 1.00 (0.96-1.03) CO: 0.99 (0.96-1.03) SO_2: 0.99 (0.96-1.03) O_3: 0.99 (0.95-1.03) Oil NO_2: 0.98 (0.91-1.05) CO: 0.97 (0.91-1.04) SO_2: 0.97 (0.91-1.04) O_3: 1.03 (0.88-1.22) Sea Salt NO_2: 0.99 (0.94-1.04) CO: 0.99 (0.94-1.04) SO_2: 0.99 (0.94-1.04) O_3: 1.01 (0.88-1.15)
Reference: Girardot et al. (2006, 088271) **Period of Study:** Aug 2002-Oct 2002 Jun 2003-Aug 2003 **Location:** Charlies Bunion Trail (portion of Appalachia Trail)	**Outcome:** Pulmonary function/spirometry-FVC, FEV_1, PEF, FVC/FEV_1, FEF25-75 **Age Groups**: 18-82 yr **Study Design:** Cohort **N:** 354 hikers **Statistical Analyses:** Multiple linear regression **Covariates:** Age, h hiked, mean temperature, sex, smoking status, history of asthma or wheeze symptoms, carriage of backpack, whether reaching summit or not **Season:** Fall 2002, Summer 2003 **Dose-response Investigated?** No **Statistical Package**: SAS	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean:** Trail: 13.9 ± 8.2 Estimated personal: 15.0 ± 7.4 **Range (Min, Max):** Trail: 1.6 , 38.4 Estimated personal: 0.21, 41.9 **Copollutant (correlation):** O_3 (r=0.67, for estimated personal exposure)	**PM Increment:** 1 µg/m^3 % Change ± CI p value Univariate: FVC: 0.023 ± 0.035 0.51 FEV_1: 0.015 ± 0.029 0.607 PEF: 0.185 ± 0.091 0.043 FVC/FEV_1: 0.003 ± 0.023 0.905 FEF25-75%: 0.052 ± 0.093 0.578 Adjusted: FVC: 0.007 +/ 0.040 0.966 FEV_1: 0.003 ± 0.033 0.937 PEF: 0.258 ± 0.103 0.013 FVC/FEV_1: - 0.011 ± 0.027 0.676 FEF25-75%: - 0.041 ± 0.109 0.707 Spirometry result for each quintile ± CI **Quintile 1 (6.0** µg/m^3**):** FVC (L): Prehike: 4.32 ± 0.13 Posthike: 4.33 ± 0.12 FEV_1 (L): Prehike: 3.39 ± 0.10 Posthike: 3.40 ± 0.10 FEV_1/FVC (%): Prehike: 78.66 ± 0.86 Posthike: 78.63 ± 0.81 FEF25-75% (L/sec): Prehike: 3.27 ± 0.14 Posthike: 3.26 ± 0.14 PEF (L/sec): Prehike: 7.91 +/ 0.22 Posthike: 7.58 ± 0.22 **Quintile 2 (10.4** µg/m^3**):** FVC (L): Prehike: 4.30 ± 0.11 Posthike: 4.30 ± 0.11 FEV_1 (L): Prehike: 3.42 ± 0.09 Posthike: 3.43 ± 0.09 FEV_1/FVC (%): Prehike: 79.37 ± 0.71 Posthike: 79.55 ± 0.69 FEF25-75% (L/sec): Prehike: 3.39 ± 0.14 Posthike: 3.38 ± 0.14 PEF (L/sec): Prehike: 8.37 +/ 0.23 Posthike: 8.26 ± 0.25 **Quintile 3 (14.8** µg/m^3**):** FVC (L): Prehike: 4.34 ± 0.12 Posthike: 4.33 ± 0.12 FEV_1 (L): Prehike: 3.42 ± 0.10 Posthike: 3.40 ± 0.09 FEV_1/FVC (%): Prehike: 79.20 ± 0.81 Posthike: 78.83 ± 0.80 FEF25-75% (L/sec): Prehike: 3.19 ± 0.13 Posthike: 3.21 ± 0.13 PEF (L/sec): Prehike: 8.12 +/ 0.25 Posthike: 7.89 ± 0.25 **Quintile 4 (17.9** µg/m^3**):**

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			FVC (L): Prehike: 4.23 ± 0.11 Posthike: 4.23 ± 0.11 FEV_1 (L): Prehike: 3.36 ± 0.10 Posthike: 3.36 ± 0.10 FEV_1/FVC (%): Prehike: 79.18 ± 0.81 Posthike: 79.26 ± 0.79 FEF25-75% (L/sec): Prehike: 3.34 ± 0.15 Posthike: 3.30 ± 0.15 PEF (L/sec): Prehike: 7.75 +/ 0.25 Posthike: 7.73 ± 0.26 **Quintile 5 (25.6 µg/m^3):** FVC (L): Prehike: 4.15 ± 0.11 Posthike: 4.18 ± 0.12 FEV_1 (L): Prehike: 3.31 ± 0.09 Posthike: 3.33 ± 0.10 FEV_1/FVC (%): Prehike: 79.73 ± 0.66 Posthike: 79.55 ± 0.64 FEF25-75% (L/sec): Prehike: 3.22 ± 0.14 Posthike: 3.24 ± 0.14 PEF (L/sec): Prehike: 7.72 +/ 0.22 Posthike: 7.77 ± 0.23 **Overall (15.0 µg/m^3):** FVC (L): Prehike: 4.27 ± 0.05 Posthike: 4.27 ± 0.05 FEV_1 (L): Prehike: 3.38 ± 0.04 Posthike: 3.38 ± 0.04 FEV_1/FVC (%): Prehike: 79.2 ± 0.34 Posthike: 79.2 ± 0.33 FEF25-75% (L/sec): Prehike: 3.28 ± 0.06 Posthike: 3.28 ± 0.06 PEF (L/sec): Prehike: 7.97 +/ 0.11 Posthike: 7.97 ± 0.11
Reference: Hertz-Picciotta et al. (2007, 135917) **Period of Study:** 1994-2003 **Location:** Teplice and Prachatice, Czech Republic	**Outcome:** Lower respiratory illness-croup (J05, J04), acute bronchitis (J20), acute bronchiolitis (J21) **Age Groups**: Neonates followed for 2-4.5 yr **Study Design:** Cohort **N:** 1133 children **Statistical Analyses:** Generalized linear longitudinal models **Covariates:** District, mother's age, mother's education, mother or adult smoke, child's sex, season, day of the week, fuel for heating and/or cooking, breastfeeding category, number of other children, temperature **Season:** Winter, spring, summer and fall **Dose-response Investigated?** No **Statistical Package**: SUDAAN version 8 **Lags Considered:** 1-3, 1-7, 1-14, 1-30, 1-45	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** PAH: 22.3 (SD-16 for 3-day avg and 11 for 45-day avg)	**PM Increment:** 25 µg/m^3 **RR Estimate [Lower CI, Upper CI] lag:** Birth-23 mo: 1.30 [1.08, 1.58] lag 1-30 2-4.5 yr: 1.23 [0.94, 1.62] lag 1-30 **RR Estimate for categories of exposure [Lower CI, Upper CI] lag:** Crude RR: Birth-23 mo: > 50 µg/m^3: 2.26 [1.81, 2.82] lag 1-30 25-50 µg/m^3: 1.48 [1.32, 1.65] lag 1-30 < 25 µg/m^3: Referent 2-4.5 yr: > 50 µg/m^3: 3.66 [2.07, 6.48] lag 1-30 25-50 µg/m^3: 1.60 [1.41, 1.82] lag 1-30 < 25 µg/m^3: Referent

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
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Reference: Hogervorst, et al. (2006, 156559) **Period of Study:** 2002 **Location:** Maastricht, the Netherlands (six schools selected)	**Outcome**: Decreased lung function **Age Groups**: 8-13 yr **Study Design:** Multivariate linear regression (enter method) analysis **N:** 342 children **Statistical Analyses:** ANOVA, chi square **Covariates:** Independent variables: Age, height, gender, smoking at home by parents, pets, use of ventilation hoods during cooking, presence of unvented geysers, tapestry in the home, indoor/outdoor time, education level of parents. Dependent variables: lung function indices **Dose-response Investigated?** No	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily **Mean (SD):** 19.0 (3.2) **Monitoring Stations**: 6 **Copollutant:** PM_{10} Total Suspended Particles (TSP)	**PM Increment:** 10 µg/m^3 **RR Estimate [Lower CI, Upper CI]** **lag:** FEV: 3.62 [0.50,7.63] lag NR FVC: 1.80 [-2.10, 5.80] lag NR FEF: 5.93 [-2.34, 14.89] lag NR
Reference: Holguin et al, (2007, 099000) **Period of Study:** **Location:** Ciudad Juarez, Mexico	**Outcome:** FeNO, FEV_1 **Study Design:** Panel **Covariates:** sex, age, body mass index, day of week, season, yr of maternal and paternal education, passive smoking **Statistical Analysis:** linear and nonlinear mixed effects models **Age Groups:** 6-12 yr	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 48 h **Mean (SD) Unit:** 17.5 (8.9) µg/m^3 **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** NR **Relative Risk (Min CI, Max CI)** **Lag** Results not given in table form, but abstract states that no significant associations with $PM_{2.5}$ were observed.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Hong et al. (2007, 091347) **Period of Study:** Mar 23-May 2004 **Location:** School on the Dukjeok Island near Incheon City, Korea	**Outcome:** Peak expiratory flow rate (PEFR) **Age Groups**: 3rd-6th grade (mean age=9.6 yr) **Study Design: P**anel study **N:** 43 schoolchildren **Statistical Analyses:** Mixed linear regression **Covariates:** age, sex, height, weight, asthma history, and passive smoking exposure at home **Dose-response Investigated?** No **Lags Considered:** 0, 1, 2, 3, 4, 5	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** 20.27 (8.23) 50th(Median): 22.07 **Range (Min, Max):** 5.94-36.28 **Copollutant:** PM_{10} Components of PM_{10} (Fe, Mn, Pb, Zn, Al)	**Effect Estimate:** Regression coefficients of morning and daily mean PEFR on $PM_{2.5}$ Lag 1 ($PM_{2.5}$) Morning PEFR Crude: ß= -0.14, p=0.12 Adjusted: ß= -0.54, p,0.01 Mean PEFR Crude: ß= -0.15, p=0.02 Adjusted: ß= -0.54, p,0.01 Regression coefficients of morning and daily mean PEFR on $PM_{2.5}$ and GSTM1 and GSTT1 genotype using linear mixed-effects regression Lag 1 ($PM_{2.5}$) Morning PEFR: ß= -0.57, p < 0.01 Mean PEFR: ß= -0.56, p < 0.01 GSTM1 Morning PEFR: ß= 20.04, p=0.25 Mean PEFR: ß= 18.75, p=0.28 GSTT1 Morning PEFR: ß= 2.31, p=0.89 Mean PEFR: ß= 1.75, p=0.91
Reference: Jansen, et al. (2005, 082236) **Period of Study:** 1987-2000 **Location:** Seattle, WA	**Outcome:** FENO: fractional exhaled nitrogen oxide, Spirometry, Blood pressure, SaO_2: oxygen saturation, Pulse rate **Age Groups**: 60-86-yr-old **Study Design:** Short-term cross-sectional case series **N:** 16 subjects diagnosed with COPD, asthma, or both **Statistical Analyses:** Linear mixed effects model with random intercepts **Covariates:** Age, relative humidity, temperature, medication use **Season: W**inter 2002-2003 **Dose-response Investigated?** No **Statistical Package**: STATA	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** **Fixed-Site Monitor:** 14.0 All Subjects (N=16) Indoor, home: 7.29 Outdoor, home: 10.47 Asthmatic Subjects (N=7) Indoor, home: 7.25 Outdoor, home: 8.99 COPD Subjects (N=9) Indoor, home: 7.33 Outdoor, home: 11.66 **Range (Min, Max):** **Fixed-Site Monitor:** 1.3, 44 IQR All Subjects Indoor, home: 4.05 Outdoor, home: 8.87 Asthmatic Subjects Indoor, home: 5.72 Outdoor, home: 7.55 COPD Subjects Indoor, home: (3.18 Outdoor, home: 6.71	**PM Increment:** $PM_{2.5}$: 10 $\mu g/m^3$ Slope [95% CI]: dependence of FENO concentration [ppb] on $PM_{2.5}$ **Asthmatic Subjects** Indoor, home: 3.69 [-0.74: 8.12] Outdoor, home: 4.23 [1.33: 7.13]* **Copd Subjects** Indoor, home: -0.35 [-7.45: 6.75] Outdoor, home: 3.83 [-1.84: 9.49] Results indicate that FENO may be a more sensitive biomarker of PM exposure than other traditional health endpoints.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Johnston, et al. (2006, 091386) **Period of Study:** 7 mo (Apr-Nov 2004) **Location:** Darwin, Australia	**Outcome:** Asthma symptoms **Age Groups**: All Ages **Study Design:** Time-series **N:** 251 people (130 adults, 121 children **Statistical Analyses:** Logistic regression model **Covariates:** Minimum air temperature, doctor visits for influenza and the prevalence of asthma symptoms and, the fungal spore count and both onset of asthma symptoms and commencement of reliever medication **Season:** "Dry season"- note Southern Hemisphere **Dose-response Investigated?** No **Statistical Package**: STATA8 **Lags Considered:** 0-5 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily **Mean (SD):** 11.1 (5.4) **Range (Min, Max):** 2.2, 36.5 **PM Component:** Vegetation fire smoke (95%) and motor vehicle emissions (5%) **Monitoring Stations**: 1	**PM Increment:** 5 µg/m^3 **RR Estimate [Lower CI, Upper CI] lag:** **Symptoms attributable to asthma** Overall: 1.000 (0.98,1.01) Adults: 1.000 (0.976,1.026) Children: 1.008 (0.980, 1.037) Using preventer: 1.013 (0.990, 1.037) **Became symptomatic** Overall: 1.150 (1.07,1.23) Adults: 1.165 (1.058,1.284) Children: 1.148 (1.042,1.264) Using preventer: 1.181 (1.076,1.296) **Used Reliever** Overall: 1.000 (0.98,1.02) Adults: 1.007 (0.980, 1.035) Children: 1.002 (0.972,1.034) Using preventer: 1.020 (1.000,1.042) **Commenced Reliever** Overall: 1.120 (1.03,1.210) Adults: 1.141 (1.021, 1.275) Children: 1.112 (0.994,1.243) Using preventer: 1.129 (1.013,1.257) **Commenced Oral Steroids** Overall: 1.310 (1.03,1.66) Adults: 1.601 (1.192, 2.150) Children: 0.995 (0.625,1.459) Using preventer: 1.350 (1.040,1.752) **Asthma Attack** Overall: 0.980 (0.94,1.04) Adults: 1.026 (0.962, 1.095) Children: 0.832 (0.731, 0.946) Using preventer: 1.002 (0.934,1.075) **Exercise induced asthma** Overall: 0.990 (0.95,1.03) Adults: 0.998 (0.943, 1.056) Children: 0.982 (0.899,1.071) Using preventer: 1.002 (0.942,1.067) **Saw a health professional for asthma** Overall: 1.030 (0.91,1.16) Adults: 1.079 (0.899, 1.296) Children: 1.003 (0.841,1.195) Using preventer: 0.980 (0.847,1.133) **Missed school or work due to asthma** Overall: 1.025 (0.9284,1.131) Adults: 1.077 (0.923, 1.247) Children: 1.000 (0.873,1.458) Using preventer: 1.005 (0.897,1.124) **Mean daily number of asthma symptoms** Overall: 1.003 (0.99,1.01) Adults: 0.998 (0.984, 1.012) Children: 1.004 (0.985,1.023) Using preventer: 1.013 (0.999,1.028) **Mean Daily number of applications of reliever** Overall: 1.002 (0.993,1.010) Adults: 1.001 (0.986, 1.016) Children: 1.000 (0.980,1.021) Using preventer: 1.005 (0.994,1.017)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Koenig et al. (2003, 156653) **Period of Study:** Winter 2000-2001, Spring 2001 **Location:** Seattle, WA	**Outcome:** Exhaled NO (eNO) **Age Groups**: 6-13 yr old **Study Design:** Cohort **N:** 19 children **Statistical Analyses:** Linear mixed-effects regression **Covariates:** Medication use, ambient NO reading for specific individual on specific day of session, mean ambient NO for subject during session, mean ambient NO for subject during all sessions **Season:** Winter, Spring **Dose-response Investigated?** No **Statistical Package**: STATA	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 10 consecutive days **Mean (SD):** Outdoor: 13.3 (1.4) Indoor: 11.1 (4.9) Personal: 13.4 (3.2) Central-site: 10.1 (5.7) **Range (Min, Max):** Outdoor: Max: 40.4 Indoor: Max: 36.3 Personal: Max: 49.4 Central-site: NR **Monitoring Stations**: Outdoor: NR Indoor: NR Personal: NR Central-site: 3 **Copollutant (correlation):** Outdoor PM-central-site NO: 0.50 For NO values < 100 ppb, outdoor PM-central-site NO: 0.04	**PM Increment:** 10 µg/m^3 Results presented as change in eNO (95% CI) Among ICS* nonuser Personal monitor 4.48 (1.02, 7.93) Outdoor monitor 4.28 (1.38, 7.17) Indoor monitor 4.21 (1.02, 7.41) Central site 3.82 (1.22, 6.43) Among ICS* user Personal monitor -0.09 (-2.39, 2.21) Outdoor monitor 0.74 (-2.28, 3.76) Indoor monitor -1.11 (-5.08, 2.87) Central site 1.28 (-1.23, 3.79) * ICS: Inhaled corticosteroid
Reference: Koenig et al. (2003, 156653) **Period of Study:** Winter 2000-2001, Spring 2001 **Location:** Seattle, WA	**Outcome**: Increased exhaled nitric oxide (eNO) **Age Groups**: 6-13 yr of age **Study Design:** Combined recursive and predictive model **N:** 19 children with asthma **Statistical Analyses:** Linear mixed effects model **Covariates:** Residence type, air cleaner, avg outdoor temperature, avg daily rainfall **Season:** Winter, Spring **Dose-response Investigated?** No **Statistical Package**: STATA 7.0 for health analyses, SAS 8.0	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily **Mean:** Home indoor 9.5 Home outdoor 11.1 Recursive model Eag: 7.0 Recursive model Eig: 2.1 Predictive model Eag: 6.0 Predictive model Eig: 4.0 Combined model Eag: 6.4 Combined model Eig: 3.2 **25th:** Home indoor 5.7 Home outdoor 6.3 Recursive model Eag: 4.2 Recursive model Eig: 0.0 Predictive model Eag: 3.4 Predictive model Eig: 0.9 Combined model Eag: 3.7 Combined model Eig: 0.5 **50th(Median):** Home indoor 7.6 Home outdoor 9.5 Recursive model Eag: 5.9 Recursive model Eig: 1.2 Predictive model Eag: 5.0 Predictive model Eig: 2.2 Combined model Eag: 5.5 Combined model Eig: 1.7 **75th**: Home indoor 10.8 Home outdoor 14.6 Recursive model Eag: 9.2 Recursive model Eig: 2.3 Predictive model Eag: 7.5 Predictive model Eig: 4.9 Combined model Eag: 7.8 Combined model Eig: 4.2 **Range (Min, Max):** Home indoor 2.3, 36.3 Home outdoor 2.8, 40.4 Recursive Eag: 1.8,22.6 Recursive Eig: 0.0,17.2 Predictive Eag: 1.3,22.6 Predictive Eig: 0.0,33.0 Combined Eag: 1.3,22.6 Combined Eig: 0.0,33.0 **Monitoring Stations**: 19 personal environmental monitors	**PM Increment:** 10-µg/m^3 RR Estimate [Lower CI, Upper CI] lag: Eag= ambient-generated personal exposure Eig= indoor-generated personal exposure eNO= exhaled nitric oxide Recursive model with 8 children, Eag was marginally associated with increases in eNO [5.6 ppb [-0.6,11.9]. Eig was not associated with eNO (-0.19 ppb). For those combined estimates, only Eag was significantly associated with an increase in eNO: Eag: 5.0 ppb [0.3, 9.7] Eig: 3.3 ppb [1.1, 7.7] **Notes:** Effects were seen only in children who were not using corticosteroid therapy

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Kongtip et al. (2006, 096920) **Period of Study:** Sep-Oct 2004 **Location:** Dindang district, Bangkok metropolitan, Thailand	**Outcome:** respiratory and other Outcomes reported **Age Groups**: Age range 15-55 yr **Study Design:** Panel study **N:** 77 street vendors **Statistical Analyses:** Binary logistic regression **Covariates:** Gender, age, type of fuel used, working duration (months) **Dose-response Investigated?** No	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** 70.94 **Percentiles:** 50th(Median): 72.05 **Range (Min, Max):** 23.20-120.00 **Monitoring Stations**: 1 **Copollutant (correlation):** SO_2 NO_2 O_3 VOCs CO	**PM Increment:** 1 µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** **Model 1** Headache: 1.011 (0.999-1.022) Nose congestion: 1.006 (0.997-1.015) Sore throat: 1.000 (0.991-1.008) Cold: 1.006 (0.995-1.017) Cough: 0.989 (0.980-0.998) Phlegm: 0.998 (0.992-1.003) Chest tightness: 0.995 (0.955-1.036) Fever: 1.008 (0.993-1.024) Eye irritation: 1.022 (1.011-1.033) Dizziness: 1.027 (1.013-1.041) Weakness: 0.996 (0.983-1.008) Upper respiratory symptom: 1.001 (0.994-1.008) Lower respiratory symptom: 0.997 (0.992-1.002) **Model 2** Headache: 1.004 (0.996-1.013) Nose congestion: 1.003 (0.996-1.010) Sore throat: 0.995 (0.989-1.001) Cold: 0.996 (0.988-1.004) Cough: 0.990 (0.983-0.996) Phlegm: 0.995 (0.991-0.999) Chest tightness: 0.997 (0.970-1.025) Fever: 1.010 (0.998-1.022) Eye irritation: 1.019 (1.010-1.028) Dizziness: 1.020 (1.009-1.032) Weakness: 1.003 (0.994-1.012) Upper respiratory symptom: 0.995 (0.990-1.000) Lower respiratory symptom: 0.995 (0.991-0.999)
Reference: Lagorio et al. (2006, 089800) **Period of Study:** May-Jun1999 and Nov-Dec 1999 **Location:** Rome, Italy	**Outcome:** Lung function (FVC and FEV_1) of subjects with COPD, Asthma **Age Groups**: COPD 50-80 yr Asthma 18-64 yr **Study Design:** Time series **N:** COPD = 11 Asthma = 11 **Statistical Analyses:** Non-parametric Spearman correlation GEE **Covariates:** COPD and IHD: daily mean temperature, season variable (spring or winter), relative humidity, day of week Asthma: season variable, temperature, humidity, and β-2-agonist use **Season**: Spring and Winter **Dose-response Investigated?** Yes **Statistical Package**: STATA **Lags Considered:** 1-3 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** Overall: 27.2 (19.4) Spring: 18.2 (5.0) Winter: 36.7 (24.1) **Range (Min, Max):** 4.5, 100 **PM Component:** Cd: 0.46±0.40 ng/m^3 Cr: 1.9±1.7 ng/m^3 Fe: 283±167 ng/m^3 Ni: 4.8±6.5 ng/m^3 Pb: 30.6±19.0 ng/m^3 Pt: 5.0±8.6 pg/m^3 V: 1.8±1.4 ng/m^3 Zn: 45.8±33.1 ng/m^3 **Monitoring Stations**: 2 fixed sites: (Villa Ada and Istituto superior di Sanita) **Copollutant (correlation):** NO_2 r = 0.43 O_3 r = -0.51 CO r = 0.67 SO_2 r = 0.34 $PM_{10-2.5}$ r = 0.34 PM_{10} r = 0.93	**PM Increment:** 1 µg/m^3 They observed negative association between ambient $PM_{2.5}$ and respiratory function (FVC and FEV_1) in the COPD panel. The effect on FVC was seen at lag 24 h, 48 h, and 72 h. The effect on FEV_1 was evident at lag 72 h. There was no statistically significant effect of $PM_{2.5}$ on FVC and FEV_1 in the asthmatic and IHD panels. β **Coefficient (SE)** **COPD** FVC(%) 24 h -0.80 (0.36) 48-h -0.89 (0.41) 72-h -1.10 (0.55) FEV_1(%) 24 h -0.47 (0.33) 48-h -0.69 (0.37) 72-h -1.06 (0.50) **Asthma** FVC(%) 24 h -0.14 (0.29) 48-h -0.07 (0.33) 72-h -0.06 (0.39) FEV_1(%) 24 h -0.30 (0.34) 48-h -0.36 (0.39) 72-h -0.40 (0.46)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Lee et al. (2007, 093042) **Period of Study:** 2000-2001 **Location:** South-Western Seoul Metropolitan area, Seoul, South Korea	**Outcome:** PEFR (peak expiratory flow rate), lower respiratory symptoms (cold, cough, wheeze) **Age Groups**: 61-89 yr of age (77.8 mean age) **Study Design:** longitudinal panel survey **N:** 61 adults **Statistical Analyses:** SAS MIXED, logistic regression model **Covariates:** Temperature (Celsius), relative humidity, age, **Dose-response Investigated?** No **Statistical Package**: SAS 8.0 **Lags Considered:** 0-4 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** 51.15 (19.94) **Percentiles:** 25th: 33.00 50th(Median): 53.20 75th: 87.54 **Range (Min, Max):** 17.94, 92.71 **Monitoring Stations**: 2	**PM Increment:** 10 µg/m^3 **Effect Estimate [Lower CI, Upper CI]** **lag:** PEFR (peak expiratory flow rate) -0.54 (-0.89,-0.19) 1 day relative odds of a lower respiratory symptom (cold, cough, wheeze) 0.976 (0.849,1.121) 1 day
Reference: Lewis et al. (2005, 081079) **Period of Study:** Winter 2001-Spring 2002 **Location:** Detroit, Michigan, USA	**Outcome:** Poorer lung function (increased diurnal variability and decreased forced expiratory volume) **Age Groups**: 7-11 yr old **Study Design:** Longitudinal cohort study **N:** 86 children **Statistical Analyses: D**escriptive statistics and bivariate analyses of exposures, multivariable regression multivariate analog of linear regression. **Covariates:** Sex, home location, annual family income, presence of one or more smokers in household, race, season (entered as dummy variables), and parameters to account for intervention group effect. **Season:** Winter 2001 (Feb 10-23), Spring 2001 (May 5-18), Summer 2001 (Jul 14-27), Fall 2001 (Sep 22-Oct 5), Winter 2002 (Jan 18-31), and Spring 2002 (May 18-31)]. **Dose-response Investigated?** No **Lags Considered:** 1-2 days, 3-5 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 2 wk **Mean (SD):** Eastside 15.7 (10.6) Southwest 17.5 (12.2) **Range (Min, Max):** 1.0, 56.1 **Monitoring Stations**: 2 **Copollutant (correlation):** PM_{10} 0.93 O_3 Daily mean 0.57 O_3 8-h peak 0.53	**PM Increment:** 12.5 µg/m^3 **RR Estimate [Lower CI, Upper CI]** **lag:** Lung function among children reporting use of maintenance CSs **Diurnal variability** FEV_1 Lag 1: 1.61 [-0.5,3.72] Lag 1: 0.99 [-5.64, 7.62] $PM_{2.5}$ + O_3 Lag 2: 2.96 [-1.74,7.66] Lag 2: 4.62 [-4.31, 13.54] $PM_{2.5}$ + O_3 Lag 3-5: 1.37 [-1.49,4.22] Lag 3-5: 2.70 [1.0, 4.40] $PM_{2.5}$ + O_3 **Lowest daily value** FEV_1 Lag 1: -2.23 [-6.99,2.53] Lag 1: 3.36 [-3.92, 10.63] $PM_{2.5}$ + O_3 Lag 2: -0.21 [-4.09,3.68] Lag 2: 0.88 [-8.69, 10.46] $PM_{2.5}$ + O_3 Lag 3-5: -0.76 [-5.00, 3.49] Lag 3-5: -2.78 [-4.87 to -0.70] $PM_{2.5}$ + O_3 Lung function among children reporting presence of URI on day of lung function assessment **Diurnal variability** FEV_1 Lag 1: 4.08 [-1.78, 9.94] Lag 1: 3.99 [-2.76, 10.74] $PM_{2.5}$ + O_3 Lag 2: 7.62 [-0.49, 15.73] Lag 2: 4.10 [-1.41, 9.60] $PM_{2.5}$ + O_3 Lag 3-5: 1.47 [-7.73, 10.67] Lag 3-5: 3.81 [-1.83, 9.45] $PM_{2.5}$ + O_3 **Lowest daily value** FEV_1 Lag 1: -1.21 [5.62,3.21] Lag 1: -0.74 [-4.14, 2.65] $PM_{2.5}$ + O_3 Lag 2: -0.10 [4.36,4.16] Lag 2: -1.67 [-5.09, 1.75] $PM_{2.5}$ + O_3 Lag 3-5: -2.88 [-5.46 to -0.30] Lag 3-5: -2.78 [-4.79 to -0.77] $PM_{2.5}$ + O_3

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Liu et al. (2009, 192003) **Period of Study:** 4 wk in 2005 **Location:** Windsor, Ontario, Canada	**Outcome:** Decreased lung function **Study Design:** Panel **Statistical Analysis:** mixed-effects regression models **Statistical Package:** S-PLUS **Age Groups:** Asthmatic children, 9-14 yr	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 1, 2 & 3 days **Mean (SD) Unit (1d):** 6.5 µg/m^3 **Range (Min, Max):** 2.0-19.0 **Copollutant (correlation):** SO_2: 0.56 NO_2: 0.71 O_3: -0.41	**Increment:** 5.4 µg/m^3 **Percent Change (Min CI, Max CI)** **Lag** FEV_1 Same Day: -0.5 (-1.3-0.3) Lag 1 Day: -0.5 (-1.1-0.5) 2-Day Avg: -0.6 (-1.5-0.4) 3-Day Avg: -1.1 (-3.1-0.9) FEF 25%-75% Same Day: -1.9 (-3.5--0.3) Lag 1 Day: -1.2 (-2.8-0.3) 2-Day Avg: -2.0 (-3.8--0.2) 3-Day Avg: -3.3 (-7.2-0.8) FeNO Same Day: 5.3 (-3.6-15) Lag 1 Day: 1.7 (-6.3-15) 2-Day Avg: 4.3 (-5.4-15.1) 3-Day Avg: -17.3 (-33.5-2.9) TBARS Same Day: 16.9 (2.2-33.6) Lag 1 Day: 14.6 (0.8-30.4) 2-Day Avg: 22.0 (4.8-42.1) 3-Day Avg: 69.1 (20.1-138.2) 8-Isoprostane Same Day: 5.1 (-3.6-14.5) Lag 1 Day: -3.8 (-12.1-5.3) 2-Day Avg: 0.1 (-9.8-11.1) 3-Day Avg: 5.8 (-15.8-33.0)/

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Mar et al. (2004, 057309) **Period of Study:** 1997-1999 **Location:** Spokane, Washington	**Outcome:** Respiratory Symptoms **Age Groups**: Adults: Ages 20-51 yr Children: Ages 7-12 yr **N:** 25 people **Statistical Analyses:** Logistic regression **Covariates:** Temperature, relative humidity, day of-the-wk **Statistical Package**: STATA 6 **Lags Considered:** 0-2 days	**Pollutant:** $PM_{2.5}$ **Mean (SD):** 1997: 11.0 (5.9) 1998: 10.3 (5.4) 1999: 8.1 (3.8) Unit (i.e. $\mu g/m^3$): **Monitoring Stations**: 1 station **Copollutant (correlation):** $PM_{2.5}$ PM_1 r = 0.92 PM_{10} r = 0.61 $PM_{10-2.5}$ r = 0.28	**PM Increment:** 10 $\mu g/m^3$ **OR Estimate [Lower CI, Upper CI] lag:** **Adult Respiratory symptoms:** **Wheeze:** 1.04[0.86, 1.26] lag 0 1.00[0.83, 1.19] lag 1 0.99[0.84, 1.17] lag 2 **Breath:** 0.97[0.87, 1.08] lag 0 0.98[0.87, 1.10] lag 1 0.95[0.80, 1.13] lag 2 **Cough**: 0.86[0.62, 1.21] lag 0 0.87[0.63, 1.20] lag 1 0.89[0.66, 1.20] lag 2 **Sputum**: 0.94[0.63, 1.41] lag 0 0.90[0.62, 1.31] lag 1 0.92[0.66, 1.27] lag 2 **Runny Nose:** 0.98[0.83, 1.15] lag 0 0.95[0.82, 1.10] lag 1 0.93[0.80, 1.08] lag 2 **Eye Irritation:** 0.91[0.70, 1.20] lag 0 0.89[0.70, 1.13] lag 1 0.86[0.68, 1.08] lag 2 **Lower Symptoms:** 0.91[0.73, 1.13] lag 0 0.89[0.72, 1.10] lag 1 0.89[0.72, 1.10] lag 2 **Any Symptoms:** 0.92[0.80, 1.07] lag 0 0.89[0.76, 1.04] lag 1 0.89[0.75, 1.05] lag 2 **Children Respiratory symptoms:** **Wheeze:** 0.55[0.26, 1.19] lag 0 0.53[0.18, 1.58] lag 1 0.55[0.19, 1.64] lag 2 **Breath:** 1.13[0.86, 1.48] lag 0 1.12[0.86, 1.44] lag 1 1.10[0.82, 1.48] lag 2 **Cough:** 1.17[0.98, 1.40] lag 0 1.21[1.00, 1.47] lag 1 1.18[0.99, 1.42] lag 2 **Sputum:** 1.06[0.92, 1.22] lag 0 1.10[0.91, 1.34] lag 1 1.09[0.92, 1.30] lag 2 **Runny Nose**: 1.09[0.85, 1.39] lag 0 1.12[0.89, 1.41] lag 1 1.16[0.94, 1.42] lag 2 **Eye Irritation:** 0.93[0.53, 1.64] lag 0 0.75[0.45, 1.27] lag 1 0.77[0.65, 0.91] lag 2 **Lower Symptoms:** 1.18[1.00, 1.38] lag 0 1.21[1.00, 1.46] lag 1 1.17[0.96, 1.43] lag 2 **Any Symptoms:** 1.17[1.03, 1.34] lag 0 1.22[1.04, 1.43] lag 1 1.23[1.07, 1.42] lag 2

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Mar et al. (2005, 087566) **Period of Study:** 1999-2001 **Location:** Seattle, Washington	**Outcome:** Pulmonary function (arterial oxygen saturation) and cardiac function (heart rate and blood pressure) **Study Design:** Time series **Statistical Analyses:** Linear logistic regression **Age Groups**: > 57	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) Lag** **Personal:** Systolic: 0.37 (-0.93, 1.67) 0 Diastolic: -0.20 (-0.85, 0.46) 0 **Indoor:** Systolic: 0.92 (-2.04, 3.87) 0 Diastolic: 0.38 (-1.43, 2.20) 0 **Outdoor:** Systolic: -0.81 (-2.34, 0.73) 0 Diastolic: -0.46 (-1.49, 0.57) 0 % Increase between heart rate and $PM_{2.5}$ exposure for people > 57 $PM_{2.5}$**:** Personal: 0.44 (0.04, 0.84) 0 Indoor: 0.22 (-0.71, 1.16) 0 Outdoor: -0.75 (-1.42 to -0.07) 0
Reference: Mar et al. (2005, 088759) **Period of Study:** 1999-2002 **Location:** Seattle, Washington	**Outcome**: Respiratory Symptoms **Age Groups**: 6-13 yr **Study Design:** Time-Series **N:** 19 children **Statistical Analyses:** Polynomial distributed lag model, Poisson regression **Covariates:** Age, ambient NO levels, temperature, relative humidity, modification of use of inhaled corticosteroids **Season:** Winter, Spring **Dose-response Investigated?** No **Statistical Package**: STATA **Lags Considered:** 0-8 h	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** Results presented in Fig 1. **Monitoring Stations**: 3 Stations	**PM Increment:** 10 µg/m^3 **Change in FE(NO) (exhaled NO concentration) with air pollution** **[Lower CI, Upper CI] lag:** Medication use: No meds: 6.99[3.43, 10.55] lag 1-h Meds: -0.18[-3.33, 2.97] lag 1-h No meds: 6.30[2.64, 9.97] lag 4-h Meds: -0.77[-4.58, 3.04] lag 4-h No meds: 0.46[-1.18, 2.11] lag 8-h Meds: 0.40[-1.94, 2.74] lag 8-h
Reference: McCreanor et al. (2007, 092841) **Period of Study:** 2003-2005 **Location:** London, England	**Outcome**: Decreased Lung Function **Age Groups**: Adults **Study Design:** Crossover study **N:** 60 adults **Statistical Analyses:** Linear regression **Covariates:** Temperature, relative humidity, age, sex, bod-mass index, and race or ethnic group	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 1 h **Mean (SD):** NR 50th(Median): Oxford St: 28.3 Hyde Park: 11.9 **Range (Min, Max):** Oxford St: (13.9, 76.1) Hyde Park: (3, 55.9)	% changes in FEV and FVC are presented in Fig 1-3. Results are not presented quantitatively in text or tables. The authors did not find any significant differences in respiratory symptoms between the two locations. Also, there were no significant differences in sputum eosinophil counts or eosinophil cationic protein levels.
Reference: Moshammer and Neuberger (2003, 041956) **Period of Study:** 2000-2001 **Location:** Linz, Austria	**Outcome:** Lung Function: FVC, FEV_1, MEF_{25}, MEF_{50}, MEF_{75}, PEF, LQ Signal, PAS Signal **Age Groups**: Ages 7-10 **Study Design:** Case-crossover **N:** 161 children 1898-2120 "half-h means" **Statistical Analyses:** Correlations Regression Analysis **Covariates:** Morning, evening, night **Season:** Spring, Summer, Winter, Fall **Dose-response Investigated?** No	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 8 h means & daily means **Mean (SD):** 14.61 (10.83) **Range (Min, Max):** (NR, 119.92) **Monitoring Stations**: 1 **Copollutant (correlation):** LQ = 0.751 PAS = 0.354	**Notes:** "Acute effects of 'active particle surface' as measured by diffusion charging were found on pulmonary function (FVC, FEV_1, MEF_{50}) of elementary school children and on asthma-like symptoms of children who had been classified as sensitive."

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Moshammer et al. (2006, 090771) **Period of Study:** 2000-2001 **Location:** Linz, Austria	**Outcome**: Respiratory symptoms and decreased lung function **Age Groups**: Children ages 7-10 **Study Design:** Time-series **N:** 163 children **Statistical Analyses:** Generalized estimating equations model **Covariates:** Sex, age, height, weight **Dose-response Investigated?** NR **Statistical Package**: NR **Lags Considered:** 1	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 8 h **Mean (SD):** Maximum 24 h: 76.39 Annual avg: 19.06 **Percentiles:** 8-h mean 25th: 8.64 8-h mean 50th(Median): 15.70 8-h mean 75th: 25.82 **Monitoring Stations**: 1 station **Copollutant (correlation):** PM_1 r = 0.95 PM_{10} r = 0.93 NO_2 r = 0.54	**PM Increment:** 10 µg/m^3 **% change in Lung Function per 10 µg/m3** FEV: 0.23 FVC: 0.08 $FEV_{0.5}$: 0.33 MEF_{75}%: -0.49 MEF_{50}%: -0.58 MEF_{25}%: -0.83 PEF: 0.41 **% change in Lung Function per IQR** FEV: -0.59 FVC: -0.2 $FEV_{0.5}$: 0.85 MEF_{75}%: -1.25 MEF_{50}%: -1.48 MEF_{25}%: -2.14 PEF: -1.06 **Multiple pollutant model** FEV: 0.10 FVC: 0.21 $FEV_{0.5}$: 0.06 MEF_{75}%: -0.15 MEF_{50}%: 0.04 MEF_{25}%: -0.21 PEF: -0.18 **% change in Lung Function per IQR** FEV: 0.27 FVC: 0.54 $FEV_{0.5}$: 0.15 MEF_{75}%: -0.39 MEF_{50}%: 0.11 MEF_{25}%: 0.54 PEF: 0.015: -0.47
Reference: Murata et al. (2007, 189159) **Period of Study:** Nov 2004 **Location:** Tokyo, Japan	**Outcome:** Exhaled nitric oxide levels, (eNO), a marker of airway inflammation **Age Groups**: 5-10 yr **Study Design:** Cohort/Panel study **N:** 19 schoolchildren* **Statistical Analyses:** Linear regression **Covariates:** None **Season:** Nov (fall) **Dose-response Investigated?** No **Statistical Package**: SAS **Lags Considered:** Lag h 1-24, 8-h ma, 7-h ma, 6-h ma, 24-h ma	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Hourly, 24 h **Mean (SD):** 39.0 (16.9) µg/m^3 (daily mean) **Range (Min, Max):** 10, 120 (range of hourly values) **Monitoring Stations**: 1, on the street where the children lived	**PM Increment:** IQR 110 µg/m^3 **Mean [Lower CI, Upper CI] lag:** 0.145 [0.62, 0.228] ppb eNO 8-h ma **Notes:** Associations for lag h 1-24 presented in figures. Authors state "Individual hourly lag models showed a consistent association between the eNO value and $PM_{2.5}$ for exposure in the previous 24 h" "The trend on the graphs strongly suggest that fluctuations in eNO were affected by changes in air pollutants over at least the previous 8-h period" $PM_{2.5}$, black carbon, and NO_X were all highly correlated (shown in figures), so effects are difficult to separate Pollutant concentrations peaked in the morning and evening h during traffic peaks

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Neuberger et al. (2004, 093249) **Period of Study:** Jun 1999-Jun 2000 **Location:** Austria (Vienna and a rural area near Linz)	**Outcome:** Questionnaire derived asthma score, and a 1-5 point respiratory health rating by parent **Age Groups**: 7-10 yr **Study Design:** Cross-sectional survey **N:** about 2000 children **Statistical Analyses:** mixed models linear regression-used factor analysis to develop the "asthma score" **Covariates:** Pre-existing respiratory conditions, temperature, rainy days, # smokers in household, heavy traffic on residential street, gas stove or heating, molds, sex, age of child, allergies of child, asthma in other family members **Dose-response Investigated?** No **Statistical Package**: NR **Lags Considered:** 4-wk avg (preceding interview)	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Copollutant (correlation):** PM_{10} (r=0.94) in Vienna	**PM Increment:** 10 µg/m^3 **Change in mean associated unit increase in PM** **(p-value)** **lag** Respiratory Health score Vienna: 0.016 (p>0.05) lag 4 week avg Rural area: 0.022 (p < 0.05) lag 4 week avg Asthma score Vienna: 0.006 (p>0.05) lag 4 week avg Rural area: 0.004 (p>0.05) lag 4 week avg
Reference: Neuberger et al. (2004, 093249) **Period of Study:** Sep 1999-Mar 2000 **Location:** Vienna, Austria	**Outcome:** Ratio measure: Time to peak tidal expiratory flow divided by total expiration time (i.e., tidal lung function, a surrogate for bronchial obstruction) **Age Groups**: 3.0-5.9 yr (preschool children) **Study Design:** Longitudinal prospective cohort **N:** 56 children **Statistical Analyses:** mixed models linear regression, with autoregressive correlation structure **Covariates:** Age, sex, respiratory rate, phase angle, temperature, kindergarten, parental education, observer (also in sensitivity analyses: height, weight, cold/sneeze on same day, heating with fossil fuels, hair cotinine, number of tidal slopes used to measure tidal lung function) **Dose-response Investigated?** No **Statistical Package**: SAS 8.0 **Lags Considered:** Lag 0	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **PM Component:** Total carbon EC OC **Copollutant (correlation):** PM_{10} (r=0.94) in Vienna	**PM Increment:** Interquartile range (NR) **Change in mean associated with an IQR increase in PM (p-value)** **lag** $PM_{2.5}$ mass: -0.987 (0.091) lag 0 Total carbon: -0.815 (0.041) lag 0 EC: -0.657 (0.126) lag 0 OC: -0.942 (0.025) lag 0
Reference: Neuberger et al. (2004, 093249) **Period of Study:** Oct. 2000-May 2001 **Location:** Linz, Austria	**Outcome**: Forced oscillatory resistance (at zero Hz), FVC, FEV_1, MEF_{25}, MEF_{50}, MEF_{75}, PEF **Age Groups**: 7-10 yr **Study Design:** Longitudinal prospective cohort **N:** 164 children **Statistical Analyses: M**ixed models linear regression with autoregressive correlation structure **Covariates:** Sex, time and individual **Season:** Oct-May **Dose-response Investigated?** No **Statistical Package**: NR **Lags Considered:** Lag 0-7	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Monitoring Stations**: 1	**PM Increment:** 1 µg/m^3 **Notes:** Authors report increased oscillatory resistance significantly associated with $PM_{2.5}$ (lag 0)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: O'Connor et al. (2008, 156818) **Period of Study:** Aug 1998-Jul 2001 **Location:** Boston, the Bronx, Chicago, Dallas, New York, Seattle, Tucson	**Outcome:** Pulmonary function and respiratory symptoms **Age Groups**: 5-12 yr **Study Design:** Inner-City Asthma Study (ICAS)-Panel/cohort study **N:** 861 children **Statistical Analyses:** Mixed effects models **Lags Considered:** Lag 0-6, 0-4	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** 14 **Range (Min, Max):** 5-35 (estimated from Fig) **Copollutant (correlation):** NO_2 (r=0.59) SO_2 (r=0.37) CO (r=0.44) O_3 (r=-0.02)	**PM Increment:** 13.2 µg/m^3 90th-10th percentile **Change in pulmonary function lag** FEV_1: -1.47 (-2.00 to -0.94) lag 0-4 PEFR: -1.10 (-1.65 to -0.56) lag 0-4 $PM_{2.5}$+O_3+NO_2 FEV_1: -0.73 (-1.33 to -0.12) lag 0-4 PEFR: -0.25 (-0.88, 0.38) lag 0-4 **Risk of Respiratory Symptoms lag** Wheeze: 0.98 (0.88, 1.09) lag 0-4 Nighttime asthma: 1.11 (0.94, 1.30) lag 0-4 Slow play: 1.01 (0.89, 1.15) lag 0-4 Missed school: 1.33 (1.06, 1.66) lag 0-4 $PM_{2.5}$+O_3+NO_2 Wheeze: 0.92 (0.81, 1.05) lag 0-4 Nighttime asthma: 1.03 (0.86, 1.23) lag 0-4 Slow play: 0.92 (0.79, 1.06) lag 0-4 Missed school: 1.13 (0.87, 1.45) lag 0-4
Reference: Peacock et al. (2003, 042026) **Period of Study:** Nov 1996-Feb 1997 **Location:** northern Kent, UK	**Outcome:** Reduced peak expiratory flow rate (PEFR) **Age Groups**: 7-13 yr of age **Study Design:** Time Series **N:** 179 **Statistical Analyses:** generalized estimating equations **Covariates:** Day of the week, 24-h mean outside temperature. **Season:** Winter **Dose-response Investigated?** No **Statistical Package**: STATA **Lags Considered:** Same day, lag 1, lag 2, 5-day ma	**Pollutant:** Sulfate (SO_4^{2-}) **Averaging Time:** Daily avg **Mean (SD):** Urban 2 24 h avg: 1.3 (1.1) **Percentiles:** 10th: Urban 2 0.5 90th: Urban 2 2.4 **Range (Min, Max):** Urban 2 0.3, 6.7 **Monitoring Stations**: 3	Sulfate (SO_4^{2-}) Increment: 1.3 µg/m^3 **Odds ratio [Lower CI, Upper CI]** **lag:** 1.090 [0.898, 1.322] 5 days
Reference: Peled, et al. (2005, 156015) **Period of Study:** 5-6 wk between Mar-Jun 1999 and Sep-Dec 1999. **Location:** Ashdod, Ashkelon and Sderot, Israel	**Outcome:** Reduced peak expiratory flow (PEF) **Age Groups**: 7-10 yr **Study Design:** Nested cohort study **N:** 285 **Statistical Analyses:** Time series analysis Generalized linear model, generalized estimating equations, one-way ANOVA, generalized linear model **Covariates:** Seasonal changes, meteorological conditions and personal physiological, clinical and socioeconomic measurements **Season:** Spring, Fall **Dose-response Investigated?** No **Statistical Package**: STATA	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily **Mean:** Ashkelon: 24.0 Sderot: 29.2 Ashdod: 23.9 **PM Component:** Local industrial emissions, desert dust, vehicle emissions and emissions from two electric power plants **Monitoring Stations**: 6 **Copollutant:** PM_{10}	**PM Increment:** 1 µg/m^3 β coefficient (SE) [95% CI] Ashkelon: $PM_{2.5}$ MAX: -0.144 (0.12) [-0.38-0.09] Ashdod: $PM_{2.5}$ MAX: -2.74 (0.61) [-3.95-1.53] $PM_{2.5}$ MAX TMAX: 0.11 (0.02) [0.06-0.16] In Ashdod, $PM_{2.5}$ and an interaction between $PM_{2.5}$ and temperature were significantly associated.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Penttinen et al. (2006, 087988) **Period of Study:** Nov 1996-Apr 1997 **Location:** Helsinki, Finland	**Outcome:** Decreased lung function and respiratory symptoms **Age Groups**: Adults, mean age 53 yr **Study Design:** Time Series **N:** 78 people **Statistical Analyses:** Generalized least squares autoregressive model **Covariates:** Temperature, relative humidity, day of study, day of study squared, binary dummy variable for weekends **Season:** Winter, Spring **Dose-response Investigated?** NR **Statistical Package**: SAS version 6 **Lags Considered:** 0-3	**Pollutant:** $PM_{2.5}$ **PM Component:** Soil, heavy fuel oil, sea salt **Averaging Time:** 24 h **Percentiles: 25th:** Long range transport: 2.44 Local combustion: 1.75 Soil: 0.14 Heavy fuel oil: -0.13 Sea Salt: 0.22 Unidentifiable: -1.41 All sources: 6.47 **50th(Median):** Long range transport: 4.15 Local combustion: 2.41 Soil: 0.64 Heavy fuel oil: 0.10 Sea Salt: 0.27 Unidentifiable: 0.02 All sources: 8.37 **75th:** Long range transport: 7.33 Local combustion: 3.05 Soil: 1.46 Heavy fuel oil: 0.52 Sea Salt: 0.42 Unidentifiable: 0.74 All sources: 11.15 **Range (Min, Max):** Long range transport: (-0.89, 28.31) Local combustion: (0.83, 6.51) Soil: (-1.13, 6.43) Heavy fuel oil: (-0.67, 4.74) Sea Salt: (0.09, 0.98) Unidentifiable: (-4.40, 4.77) All sources: (4.11, 33.53) **Monitoring Stations**: 1 site	**PM Increment:** 1.3 µg/m^3 **$PM_{2.5}$, long range:** **PEF Morning:** 0.37[-0.59, 1.34] lag 0 -1.04[-1.88 to -0.19] lag 1 -0.82[-1.81, 0.16] lag 2 0.22[-0.64, 1.08] lag 3 -0.24[-1.12, 0.64] 5 day mean. **PEF Afternoon:** 0.20[-0.67, 1.06] lag 0 -0.20[-1.24, 0.83] lag 1 -0.30[-1.14, 0.53] lag 2 0.45[-0.57, 1.47] lag 3 0.03[-0.79, 0.85] 5 day mean. **PEF Evening:** -0.33[-1.30, 0.64] lag 0 -0.29[-1.13, 0.55] lag 1 -0.41[-1.46, 0.64] lag 2 0.39[-0.47, 1.24] lag 3 0.07[-0.81, 0.95] 5 day mean **$PM_{2.5}$, local combustion:** **PEF Morning:** -0.73[-1.69, 0.23] lag 0 -0.46[-1.24, 0.32] lag 1 -0.43[-1.49, 0.63] lag 2 0.34[-0.47, 1.15] lag 3 -0.25[-1.03, 0.53] 5 day mean. **PEF Afternoon:** -0.21[-1.07, 0.65] lag 0 -0.81 [-1.77, 0.16] lag 1 -0.83[-1.74, 0.09] lag 2 0.20[-0.80, 1.20] lag 3 -0.87[-1.63 to -0.12] 5 day mean. **PEF Evening:** -0.51[-1.48, 0.45] lag 0 -1.16[-1.93 to -0.39] lag 1 0.23[-1.35, 0.90] lag 2 0.56[-0.21, 1.32] lag 3 -1.14[-1.95 to -0.33] 5 day mean **$PM_{2.5}$, soil:** **PEF Morning:** 0.81[0.05, 1.57] lag 0 0.03 [-0.65, 0.71] lag 1 0.50[-0.34, 1.35] lag 2 -0.07[-0.74, 0.61] lag 3 0.39[-0.46, 1.23] 5 day mean. **PEF Afternoon:** 1.05[0.38, 1.72] lag 0 0.40[-0.38, 1.19] lag 1 0.66 [0.03, 1.30] lag 2 -0.36[-1.12, 0.41] lag 3 0.55 [-0.21, 1.32] 5 day mean. **PEF Evening:** 1.08[0.33, 1.84] lag 0 1.00[0.31, 1.68] lag 1 0.33[-0.56, 1.22] lag 2 -0.84 [-1.53 to -0.15]lag 3 0.90[0.08, 1.73] 5 day mean **$PM_{2.5}$, oil:** **PEF Morning:** -0.22[-1.00, 0.56] lag 0 -0.20[-1.24, 0.84] lag 1 0.66[-0.68, 2.00] lag 2 0.57 [-0.18, 1.32] lag 3 0.10[-0.61, 0.81] 5 day mean. **PEF Afternoon:** -0.04[-0.75, 0.67] lag 0

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			0.29[-0.98, 1.55] lag 1 0.08 [-1.13, 1.28] lag 2 0.62[-0.31, 1.54] lag 3 0.07 [-0.64, 0.78] 5 day mean. **PEF Evening:** 0.57[-0.23, 1.37] lag 0 0.12[-0.92, 1.15] lag 1 -0.97[-2.39, 0.45] lag 2 0.40[-0.31, 1.12] lag 3 0.43[-0.33, 1.19] 5 day mean **$PM_{2.5}$, salt:** **PEF Morning:** 0.76[-0.13, 1.65] lag 0 0.43 [-0.30, 1.16] lag 1 0.13[-0.75, 1.02] lag 2 0.38[-0.47, 1.23] lag 3 0.95[-0.18, 2.09] 5 day mean. **PEF Afternoon:** 0.62[-0.18, 1.41] lag 0 0.80[-0.08, 1.69] lag 1 0.14[-0.62, 0.90] lag 2 0.16[-0.83, 1.15] lag 3 0.88 [-0.18, 1.94] 5 day mean. **PEF Evening:** 1.09[0.19, 1.98] lag 0 0.63[-0.10, 1.35] lag 1 0.32[-0.62, 1.26] lag 2 -0.31[-1.16, 0.54] lag 3 0.88[-0.27, 2.02] 5 day mean **$PM_{2.5}$, unidentified:** **PEF Morning:** 0.38[-0.67, 1.43] lag 0 0.09[-0.83, 1.00] lag 1 0.22[-0.82, 1.26] lag 2 0.78 [-0.10, 1.66] lag 3 0.78[-0.14, 1.69] 5 day mean. **PEF Afternoon:** 0.02[-0.92, 0.96] lag 0 0.65[-0.48, 1.77] lag 1 0.17[-0.71, 1.05] lag 2 0.69[-0.36, 1.75] lag 3 0.17 [-0.72, 1.06] 5 day mean. **PEF Evening:** -0.11[-1.17, 0.95] lag 0 0.19[-0.72, 1.10] lag 1 0.86[-0.25, 1.96] lag 2 0.15[-0.70, 1.01] lag 3 -0.19[-1.15, 0.77] 5 day mean **$PM_{2.5}$, local combustion**: **PEF morning:** Cu: -0.25 [-1.25, 0.75] Zn: -0.45[-1.19, 0.29] Mn: 0.13[-0.83, 1.08] Fe: 0.08[-0.70, 0.85]. **PEF afternoon:** Cu: -0.37[-1.29, 0.55] Zn: -0.19[-0.87, 0.50] Mn: -0.48[-1.37, 0.42] Fe: 0.29[-0.45, 1.04]. **PEF evening:** Cu: -0.48[-1.47, 0.52] Zn: -0.17[-0.92, 0.57] Mn: 0.51[-0.44, 1.47] Fe: 0.34[-0.46, 1.14] **$PM_{2.5}$, long range:** **PEF morning:** S: 0.11[-0.886, 1.07] K: -0.10[-1.00, 0.80] Pb: -0.62[-1.37, 0.13]

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			Br: -0.40 [-1.40, 0.60]. **PEF afternoon:** S: -0.05[-0.92, 0.81] K: 0.26[-0.56, 1.07] Pb: -0.12[-0.84, 0.60] Br: 0.15[-0.81, 1.12]. **PEF evening:** S: 0.08[-0.86, 1.02] K: 0.18[-0.70, 1.07]; Pb: -0.20[-0.97, 0.58] Br: 0.35[-0.71, 1.40] **$PM_{2.5}$, soil:** **PEF morning:** Si: 0.27[-0.43, 0.97] Al: 0.17 [-0.72, 1.05] Ca: 0.13[-1.08, 1.35]. **PEF afternoon:** Si: 0.39[-0.24, 1.01] Al: 0.49[-0.29, 1.27] Ca: 0.15[-0.92, 1.22] **PEF evening:** Si: 0.60[-0.06, 1.26] Al: 0.76[-0.08, 1.60] Ca: 0.90[-0.22, 2.03] **$PM_{2.5}$, Oil combustion:** **PEF morning:** V: -0.01[-0.87, 0.86] Ni: -0.09[-1.08, 0.90]. **PEF afternoon:** V: -0.48[-1.32, 0.35] Ni: 0.26[-0.72, 1.23]. **PEF evening:** V: 0.02[-00.88, 0.92] Ni: 0.50[-0.55, 1.55] **$PM_{2.5}$, Sea salt:** **PEF morning:** Na: 0.92[-0.34, 2.17] Cl: 0.93[0.08, 1.79] **PEF afternoon:** Na: 0.96[-0.24, 2.16] Cl: 0.57[-0.22, 1.36] **PEF evening** Na: 0.87[-0.40, 2.15] Cl: 0.65[-0.19, 1.49]

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Pino et al. (2004, 050220) **Period of Study:** Apr 1995-Oct 1996 **Location:** Santiago, Chile	**Outcome:** Respiratory Symptoms, Wheezing bronchitis **Study Design:** Time-series **Statistical Analyses:** Bayesian hierarchical analysis, cubic spline **Age Groups**: 4 mo-2 yr old	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD) unit:** 52.0 (31.6) **Range (5th, 95th):** 17.0, 114.0 **Copollutants (correlation):** SO_2: r= 0.73 NO_2: r= 0.85	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** % increase in wheezing bronchitis and $PM_{2.5}$ exposure for infants 4 mo-2 yr old 4.75 (1.25, 8.25) 1 3.85 (0.45, 7.75) 2 2.25 (-1.00, 6.00) 3 1.75 (-2.20, 5.75) 4 4.00 (0.25, 8.00) 5 5.00 (1.00, 8.50) 6 7.00 (3.50, 11.00) 7 8.10 (4.00, 11.25) 8 9.00 (6.00, 12.00) 9 8.75 (5.75, 12.00) 10 1.50 (-3.50, 4.75) 11 0.25 (-3.75, 4.25) 12 0.00 (-4.00, 4.00) 13 1.00 (-3.50, 4.50) 14 1.50 (-3.50, 4.50) 15 OR for wheezing bronchitis and $PM_{2.5}$ exposure in infants 4 mo to 2 yr old according to family history of asthma Yes to family history of asthma 1.09 (1.00, 1.19) 1 1.10 (1.02, 1.20) 2 1.11 (1.02, 1.22) 3 No to family history of asthma 1.04 (1.00, 1.08) 1 1.02 (0.98, 1.06) 2 1.01 (0.96, 1.05) 3
Reference: Rabinovitch et al., (2006, 088031) **Period of Study:** 2001-2003 (two winters 2001-2002 and 2002-2003) **Location:** Denver, CO	**Outcome**: Bronchodilator doser activations (daily) and urinary leukotriene E4 (daily) **Age Groups**: Children 6-13 yr old **Study Design: S**chool-based cohort study **N:** 73 children **Statistical Analyses:** Doser activation: Poisson regression with GEE with AR1 working covariance Urinary leukotriene E4: linear mixed model with spatial exponential covariance **Covariates:** Temperature, pressure, humidity, time trend, Friday indicator, upper respiratory infection (URI), height (leukotriene E4 only). **Season:** Winter **Dose-response Investigated?** NR **Statistical Package**: SAS **Lags Considered:** 0-2 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Morning (midnight to 11: 00 AM) mean Morning (midnight to 11: 00 AM) maximum 24-h mean **Mean (SD):** 24-h mean, TEOM **Year 1, N: 55 days:** 6.5 (3.2) **Year 2, N: 128 days:** 8.2 (3.7) 24-h mean, FRM **Year 1, N: 55 days:** 11.8 (7.2) **Year 2, N: 122 days:** 11.2 (5.5) Morning mean, TEOM **Year 1, N: 71 days:** 7.4 (4.7) **Year 2, N: 127 days:** 9.1 (5.0) Morning maximum, TEOM **Year 1, N: 71 days:** 15.5 (9.5) **Year 2, N: 127 days:** 18.4 (9.6) **Percentiles**: 24-h mean, TEOM **Year 1** 25th: 4.4 50th(Median): 6.2 75th: 7.9 **Year 2** 25th: 55 50th(Median): 7.3 75th: 9.9 24-h mean, FRM **Year 1** 25th: 7.8 50th(Median): 10.1 75th: 14.1 **Year 2** 25th: 7.5 50th(Median): 9.3 75th: 13.3 Morning mean, TEOM **Year 1** 25th: 4.0	**PM Increment:** IQR (over current and previous day) **Doser Activation** **Morning avg $PM_{2.5}$ TEOM** Year 1: Pct Increase: 3.0 [-0.5: 6.6] p = 0.10 Year 2: Pct Increase: 2.7 [1.1: 4.4] p = 0.006 Aggregated yr: 2.2 [0.7: 3.6] p = 0.005 **Morning max $PM_{2.5}$ TEOM** Year 1 Pct Increase: 4.0 [0.5: 7.6] p = 0.02 Year 2 Pct Increase: 2.3 [0.7: 4.0] p = 0.009 Aggregated yr 2.6 [0.9: 4.2] p= 0.002 **24-h $PM_{2.5}$** **TEOM** Lag 0: 0.4 [-0.7: 1.6] p-value = 0.45 Lag 1: 0.9 [-0.7: 2.4] p-value = 0.27 Lag 2: -0.4 [-1.7: 0.9] p-value = 0.59 Lag 0-2 Avg: 0.6 [-1.0: 2.2] p-value = 0.43 **FRM** Lag 0: 0.2 [-1.2: 1.6] p-value = 0.81 Lag 1: 0.9 [-0.9: 2.6] p-value = 0.31 Lag 2: -0.2 [-2.2: 1.8] p-value = 0.88 Lag 0-2 Avg: 1.2 [-0.6: 2.9] p-value = 0.20 **Morning avg $PM_{2.5}$ TEOM** URI not adjusted Mild/Moderate Asthmatics: 1.5 [-0.5: 3.4] p = 0.14 Severe Asthmatics: 3.7 [1.6: 5.8] p- = 0.0006 Difference between severity groups, p = 0.12 Aggregated severity group: 2.2 [0.7: 3.6] p= 0.005 URI adjusted Mild/Moderate Asthmatics: 1.0 [-1.9: 3.9]p= 0.50 Severe Asthmatics: 6.0 [1.8: 10.1] p = 0.006 Difference between severity groups,

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
		50th(Median): 5.9 75th: 9.6 **Year 2** 25th: 5.2 50th (Median): 8.5 75th: 11.6 Morning maximum, TEOM **Year 1** 25th: 8 50th (Median): 13 75th: 20 **Year 2** 25th: 11 50th (Median): 16 75th: 23 **Range (Min, Max):** 24-h mean, TEOM Year 1 (2.1, 23.7) Year 2 (1.7, 20.5) 24-h mean, FRM Year 1 (4.3, 53.5) Year 2 (3.4, 26.3) Morning mean, TEOM Year 1 (1.4, 22.7) Year 2 (1.6, 30.2) Morning maximum, TEOM Year 1 (4, 42) Year 2 (4, 46) **Monitoring Stations**: 2 (1 TEOM and 1 Federal Reference Monitor [FRM])	p = 0.08 Aggregated severity groups: 2.7 [-0.1: 5.4] p= 0.06 **Morning maximum $PM_{2.5}$ TEOM** URI not adjusted Mild/Moderate Asthmatics: 1.9 [-0.2: 4.1] p= 0.07 Severe Asthmatics: 3.9 [1.1: 6.8] p = 0.006 Difference between severity groups, p = 0.29 Aggregated severity groups: 2.6 [0.9: 4.2] p= 0.002 URI adjusted Mild/Moderate Asthmatics: 1.6 [-2.2: 5.4] p = 0.41 Severe Asthmatics: 8.1 [2.9: 13.4] p = 0.003 Difference between severity groups, p = 0.03 Aggregated severity groups: 3.8 [0.2: 7.4] p = 0.04 **Leukotriene E4** **24-h $PM_{2.5}$** **TEOM** Lag 0: 3.3 [-0.7: 7.2] p = 0.09 Lag 1: -1.6[-5.7: 2.5] p = 0.40 Lag 2: 1.1 [-2.8: 5.1] p= 0.64 Lag 0-2 Avg: 2.3 [-4.0: 8.6] p = 0.45 **FRM** Lag 0: 2.7 [1.1: 6.5] p = 0.12 Lag 1: -0.8 [-4.9: 3.3] p = 0.65 Lag 2: -0.8 [-4.9: 3.3] p = 0.71 Lag 0-2 Avg: 2.6 [-2.3: 7.5] p = 0.27 **Leukotriene E4** **Morning avg $PM_{2.5}$ TEOM** Height 25percentile: 8.9 [3.0: 14.7] p= 0.004 Height 50percentile: 5.9 [1.4: 10.4] p = 0.01 Height 75percentile: 1.9 [-3.4: 7.3] p = 0.47 Model w/o Height × **Pollutant:** 5.6 [1.0: 10.2] p = 0.02 **Morning maximum $PM_{2.5}$ TEOM** Height 25percentile: 8.3 [3.4: 13.2] p = 0.001 Height 50percentile: 6.1 [2.1: 10.2] p= 0.004 Height 75 percentile: 3.2 [-2.0: 8.4] p= 0.23 Model w/o Height × **Pollutant:** 6.2 [1.9: 10.5] p = 0.006
Reference: Rabinovitch et al. (2004, 096753) **Periods of Study:** Nov 1999-Mar 2000 Nov 2000-Mar 2001 Nov 2001-Mar 2002 **Location:** Denver, Colorado	**Outcome:** Respiratory symptoms, Asthma symptoms (cough and wheeze), Upper respiratory symptoms **Study Design:** Time-series **Statistical Analyses:** Logistic linear regression, PROC Mixed, PROC Genmod **Age Groups**: 6-12	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** 10.8 (7.1) **Range (Min, Max):** (1.8, 53.5) **Copollutant (correlation):** CO NO_2 SO_2 O_3	**PM Increment:** 1 $\mu g/m^3$ β (SE) AM: -0.003 (0.009) PM: 0.004 (0.011) **Odds Ratio (Lower CI, Upper CI)** Lag 0.971 (0.843, 1.118) 0-3 avg.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ranzi et al. (2004, 089500) **Period of Study:** Feb-May 1999 **Location:** Emilia-Romagmna, Italy (urban-industrial and rural area)	**Outcome:** respiratory symptoms, PEF measurements, drug consumption and daily activity **Age Groups**: Children, mean age=(7.2-7.9 yr) **Study Design:** Panel study **N:** 120 children **Statistical Analyses:** Ecological analysis and Panel analysis **Covariates:** Temperature, humidity, gender, medicinal use, symptomatic status of previous day **Dose-response Investigated?** No **Statistical Package**: NR **Lags Considered:** 0, 1, 2, 3, 0-3 ma	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** Urban= 53.07 Rural= 29.11 **Monitoring Stations**: 3 **Copollutant (correlation):** TSP: r=0.613 Daily air pollution concentrations: r= 0.658	**PM Increment:** 10 µg/m^3 Effect Estimate: Urban-industrial panel Cough and Phlegm: RR=1.0044 (1.0011-1.0077)
Reference: Rodriguez et al. (2007, 092842) **Period of Study:** 1996-2003 **Location:** Perth, Australia	**Outcome:** Body temperature, cough, runny/ blocked nose, wheeze/ rattle chest (daily) **Age Groups**: Children 0-5 yr old **Study Design:** hospital-based cohort study **N:** 198-263 children **Statistical Analyses:** Logistic regression with GEE and AR (order not specified) working covariance **Covariates:** temperature, humidity **Dose-response Investigated?** No **Statistical Package**: SAS **Lags Considered:** 0-5 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 1 h and 24 h **Mean (SD):** 1-h averaging, 20.767 24-h averaging, 8.534 **Range (Min, Max):** 1-h averaging (0.012: 93.433) 24-h averaging (0.004: 39.404) **Monitoring Stations**: 10 total, usually 3-5 sites for each pollutant **Copollutant (correlation):** O_3 NO^+ CO	**PM Increment:** NR **[Lower CI, Upper CI]** **lag: NR** LAG: 0 day **$PM_{2.5}$, 1-h** Body temperature: 1.004 [0.998: 1.011] Cough: 1.006 [1.000: 1.012] Wheeze/rattle chest: 1.004 [0.998: 1.010] Runny/blocked nose: 0.997 [0.983: 1.010] **$PM_{2.5}$, 24-h** Body temperature: 1.005 [0.986: 1.024] Cough: 1.019 [0.999: 1.040] Wheeze/rattle chest: 0.990 [0.969: 1.012] Runny/blocked nose: 0.968 [0.926: 1.013] LAG: 5 days **$PM_{2.5}$, 1-h** Body temperature: 1.005 [0.999: 1.040] Cough: 1.003 [0.995: 1.010] Wheeze/rattle chest: 1.005 [0.998: 10.12] Runny/blocked nose: 1.015 [1.000: 1.030] **$PM_{2.5}$, 24-h** Body temperature: 1.020 [0.998: 1.011] Cough: 1.006 [0.984: 1.011] Wheeze/rattle chest: 1.018 [0.997: 1.040] Runny/blocked nose: 1.039 [0.990: 1.089] LAG: 0-5 days **$PM_{2.5}$, 1-h** Body temperature: 1.000 [0.998: 1.002] Cough: 1.001 [0.999: 1.003] Wheeze/rattle chest: 1.002 [1.000: 1.004] Runny/blocked nose: 1.01 [0.997: 1.006] 1.02 **$PM_{2.5}$, 24-h** Body temperature: 1.000 [0.994: 1.005] Cough: 1.004 [0.997: 1.011] Wheeze/rattle chest: 1.001 [0.995: 1.007] Runny/blocked nose: 0.998 [0.985: 1.011]

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Sakai et al. (2004, 087435) **Period of Study:** Nov 1999-Mar 2001 **Location:** Diesel-powered ship from Tokyo, Japan to Showa Station on Ongul Island, Antarctica for 366 days (from Feb 1, 2000) and then heading back to Japan on Feb 1, 2001	**Outcome:** circulating leukocyte counts and serum inflammatory cytokine levels **Age Groups**: 24-57 yr, mean=36.1 ± 4.7 yr **Study Design:** Cohort **N:** 39 members of 41st Japanese Antarctic Research Expedition (JARE-41) **Statistical Analyses:** ANOVA **Covariates:** Smoking history, occupational pollutant exposure **Dose-response Investigated?** No **Statistical Package**: SPSS 11.5J	**Pollutant:** $PM_{5.0-2.0}$ **Averaging Time:** 24 h **Unit (i.e. µg/m3):** particles/L PM Component: organic and inorganic substances, including microorganisms **Copollutant (correlation):** $PM_{2.0-0.3}$ $PM_{10-5.0}$	**Effect Estimate:** Multiple regression analysis between inhaled factors in Antarctica Total leukocyte Cigarette smoking= 0.211, p < 0.001 Support staff= 0.139, p=0.024 Total PM= 0.168, p=0.004 Segmented PMN Cigarette smoking= 0.015, p=0.805 Support staff= 0.097, p=0.119 Total PM= 0.272, p < 0.001 Band-formed PMN Cigarette smoking= 0.035, p=0.543 Support staff= 0.010, p=0.864 Total PM= 0.470, p < 0.001 Monocyte Cigarette smoking= 0.081, p=0.187 Support staff= -0.019, p=0.759 Total PM= 0.328, p < 0.001 G-CSF Cigarette smoking= 0.131, p < 0.038 Support staff= 0.176, p=0.005 Total PM= 0.078, p=0.186 IL-6 Cigarette smoking= 0.182, p=0.004 Support staff= 0.076, p=0.228 Total PM= 0.158, p=0.008
Reference: Sakai et al. (2004, 087435) **Period of Study:** Nov 1999-Mar 28, 2001 **Location:** Diesel-powered ship from Tokyo, Japan to Showa Station on Ongul Island, Antarctica for 366 days (from Feb 1, 2000) and then heading back to Japan on Feb 1, 2001	**Outcome:** circulating leukocyte counts and serum inflammatory cytokine levels **Age Groups**: 24-57 yr, mean=36.1 ± 4.7 yr **Study Design:** cohort **N:** 39 members of 41st Japanese Antarctic Research Expedition (JARE-41) **Statistical Analyses:** ANOVA **Covariates:** Smoking history, occupational pollutant exposure **Dose-response Investigated?** No **Statistical Package**: SPSS 11.5J	**Pollutant:** $PM_{10-5.0}$ **Averaging Time:** 24 h **Unit (i.e. µg/m3):** particles/L **Monitoring Stations**: NR **Copollutant (correlation):** $PM_{2.0-0.3}$ $PM_{10-5.0}$	**Effect Estimate**: Multiple regression analysis between inhaled factors in Antarctica Total leukocyte Cigarette smoking= 0.211, p < 0.001 Support staff= 0.139, p=0.024 Total PM= 0.168, p=0.004 Segmented PMN Cigarette smoking= 0.015, p=0.805 Support staff= 0.097, p=0.119 Total PM= 0.272, p < 0.001 Band-formed PMN Cigarette smoking= 0.035, p=0.543 Support staff= 0.010, p=0.864 Total PM= 0.470, p < 0.001 Monocyte Cigarette smoking= 0.081, p=0.187 Support staff= -0.019, p=0.759 Total PM= 0.328, p < 0.001 G-CSF Cigarette smoking= 0.131, p < 0.038 Support staff= 0.176, p=0.005 Total PM= 0.078, p=0.186 IL-6 Cigarette smoking= 0.182, p=0.004 Support staff= 0.076, p=0.228 Total PM= 0.158, p=0.008

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Silkoff et al. (2005, 087471) **Period of Study:** Winter 1999-2000, Winter 2000-2001 **Location:** Denver, CO	**Outcome:** Lung function: FEV_1, PEF **Age Groups**: Adults (>40 yr-old) with COPD, as well as >10 pack-yr tobacco use, FEV_1 < 70%, FEV_1/FVC < 60%, and no other lung disease **Study Design:** COPD patient panel study (2 independent panels One for each winter) **N:** 34 subjects (16 1st winter, 18 second winter) **Statistical Analyses:** Mixed effects models with first-order, autoregressive, ma variance-covariance Binary outcomes (rescue medication use, total symptom score) assessed using Poisson regression with GEE and first-order, auto-regressive variance-covariance **Covariates:** Temperature, relative humidity, barometric pressure analysis run separately for each winter **Season:** Winter **Dose-response Investigated?** No **Statistical Package**: SAS **Lags Considered:** 0-2 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** Winter 1999-2000: 9.0 (5.2) Winter 2000-2001: 14.3 (9.6) **Percentiles:** Winter 1999-2000 25th 5.4 50th(Median): 7.7 75th: 11.3 Winter 2000-2001 25th 7.6 50th(Median): 11.7 75th: 17.2 **Range (Min, Max):** Winter 1999-2000 (1.8, 36.6) Winter 2000-2001 (3.4, 59.6) **Monitoring Stations**: multiple sites **Copollutant (correlation):** CO NO_2 PM_{10}	**PM Increment:** SD Winter 1999-2000: 5.2 Winter 2000-2001: 9.6 Model results reported graphically only. No quantitative results reported. Direction of slope (±) and statistical significance (SIG: yes; NS: no) inferred from graphs. Among subjects with severe COPD observed in Winter 1999-2000, statistically significant, but marginal, improvements in PEF associated with morning lag 0 $PM_{2.5}$. There were no statistically significant associations between rescue medication use and symptom score with PM.
Reference: Sivacoumar et al. (2006, 111115) **Period of Study:** Apr 1998-May 1998; Sep 1998-Oct 1998 **Location:** Pammal, India	**Outcome:** Respiratory symptoms, Decreased pulmonary function **Study Design:** Case-control **Statistical Analyses:** Poisson **Age Groups**: >18	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg	The study does not present quantitative results of association.
Reference: Slaughter et al. (2003, 086294) **Period of Study:** 1994 **Location:** Seattle, WA	**Outcome:** Asthma attacks, asthma severity, medication use **Age Groups**: 5.1-13.1 yr old **Study Design:** Cross-sectional study **N:** 133 children **Statistical Analyses:** Ordinal Logistic Regression Poisson Modeling **Covariates:** Temperature, Day of the Week, Seasonality **Dose-response Investigated?** No **Statistical Package**: STATA **Lags Considered:** 1-, 2-, 3-day lag	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily Avg 25th: 5.0 50th(Median): 7.3 3 75th: 11.3 **Monitoring Stations**: 3 **Copollutant (correlation):** PM_{10} = 0.75 CO = 0.82	**PM Increment:** 10 µg/m^3 increase **RR Estimate [Lower CI, Upper CI] lag:** Inhaler use: 1-day lag: 1.04 (0.98, 1.10) OR Estimate [Lower CI, Upper CI] lag: Asthma Attack: 1-day lag: 1.20 (1.05, 1.37) Previous day: 1.13 (1.03, 1.23) Medication Use Nontransition model: Previous Day: 1.08 (1.01, 1.15) **Notes**: Figures of estimated odds ratios for having a more serious asthma attack for short-term, within-subject increases in $PM_{2.5}$, PM_{10}, and CO. Transition models additionally control for the previous day's severity. Figures of estimated relative risks for having inhaler use for short-term, within-subject increases in $PM_{2.5}$, PM_{10}, and CO. Transition models additionally control for the previous day's severity.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Strand et al. (2006, 089203) **Period of Study:** 2002-2004 **Location:** Denver, Colorado, United States	**Outcome:** Reduced forced expiratory volume (FEV_1) **Age Groups**: 6-12 yr old **Study Design:** Mixed model analysis (using the default restricted maximum likelihood (REML) estimators) **N:** 50 children **Statistical Analyses:** least squares regression, SAS "Output Delivery System" (ODS) **Season:** Fall and Winter **Dose-response Investigated?** Yes **Statistical Package**: SAS	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily **Mean (SD):** Outdoor: 12.699 (6.426) Indoor: 8.148 (4.348) Sulfate/$PM_{2.5}$/outdoor: 0.079 (0.067) Sulfate/$PM_{2.5}$/indoor: 0.074 (0.060) **Range (Min, Max):** Mean Personal: (0, 3.035) Outdoor: (0, 6.303) Indoor: (0, 2.759) PM Component: EC, sulfate, nitrate and ETS. **Monitoring Stations**: 2 fixed monitors and up to 10 personal monitors on a given day. **Copollutant (correlation):** Sulfate (0.63)	**PM Increment:** 10 µg/m^3 Effects Estimate: Using the estimated slope for the validation study model [Lower CI, Upper CI] lag: 2.2 percent decrease in FEV_1 per 10 µg/m^3 increase in ambient $PM_{2.5}$ [0.0, 4.3 decrease] 1 day
Reference: Tang et al. (2007, 091269) **Period of Study:** Dec 2003-Feb 2005 **Location:** Sin-Chung City, Taipei County, Taiwan	**Outcome:** Peak expiratory flow rate (PEFR) of asthmatic children **Age Groups**: 6-12 yr **Study Design:** Panel study **N:** 30 children **Statistical Analyses:** Linear mixed-effect models were used to estimate the effect of PM exposure on PEFR **Covariates:** Gender, age, BMI, history of respiratory or atopic disease in family, SHS, acute asthmatic exacerbation in past 12 mo, ambient temp and relative humidity, presence of indoor pollutants, and presence of outdoor pollutants, **Dose-response Investigated?** yes **Statistical Package**: S-Plus 2000 **Lags Considered:** 0-2	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 1 h **Mean (SD):** Personal: 27.8 (25.3) **Range (Min, Max):** Personal: 1.4-263.4 **Monitoring Stations**: 1	**PM Increment:** 24.5 µg/m^3 **RR Estimate [Lower CI, Upper CI] lag:** Change in morning PEFR: -6.00 (-29.85, 17.85) lag 0 -12.52 (-77.93, 52.9) lag 1 -24.87 (-71.49, 21.74) lag 2 -45.67 (-117.09, 25.74) 2-day mean -5.69 (-105.96, 94.59) 3-day mean Change in evening PEFR: 0.50 (-18.82, 19.82) lag 0 16.66 (-7.59, 40.9) lag 1 11.60 (-11.1, 34.31) lag 2 39.97 (7.1, 72.85) 2-day mean -3.32 (-66.14, 59.5) 3-day mean
Reference: Timonen et al. (2004, 087915) **Period of Study:** Oct 1998-Apr 1999 **Location:** Amsterdam, Netherlands Erfurt, Germany Helsinki, Finland	**Outcome:** Urinary concentration of Clara cell protein CC16 of subjects with coronary heart disease **Age Groups**: 50+ **Study Design:** Longitudinal cohort study (panel) **N:** 37 (Amsterdam) 47 (Erfurt) 47 (Helsinki) **Statistical Analyses:** The response of interest was log transformed, creatinine adjusted CC16. Mixed-effect model was used to investigate the association between CC16 and air pollutants. **Covariates:** Subjects, long term time trend, temperature (lags 0-3), relative humidity (lags 0-3), barometric pressure (lags 0-3), and weekday of visit. **Dose-response Investigated?** yes **Statistical Package**: S-Plus and SAS **Lags Considered:** 0-3	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** Amsterdam: 20.0 µg/m^3 Erfurt: 23.1 µg/m^3 Helsinki: 12.7 µg/m^3 **Range (Min, Max):** Amsterdam: 3.8-82.2 Erfurt: 4.5-118.1 Helsinki: 3.1-39.8 **Monitoring Stations**: 3 **Copollutant (correlation):** Spearman Correlation: NC 0.01-0.1: Amsterdam -0.15 Erfurt 0.62 Helsinki 0.14 NC0.1-1.0: Amsterdam 0.80 Erfurt 0.84 Helsinki 0.80 NO_2: Amsterdam 0.49 Erfurt 0.82 Helsinki 0.35 CO: Amsterdam 0.58 Erfurt 0.77 Helsinki 0.40	**PM Increment:** 10 µg/m^3 **RR Estimate [Lower CI, Upper CI] lag:** Pooled estimate; 2.8 (-1.1-6.7) lag 0 2.9 (-0.6-6.5) lag 1 5.0 (-2.4-12.4) lag 2 1.6 (-4.7-7.9) lag 3 9.7 (-6.0-25.4) 5-day mean CC16 was not associated to $PM_{2.5}$ in the pooled analysis but CC16 was significantly associated to $PM_{2.5}$ in Helsinki: 23.3 (6.3-40.3) lag 0 6.4 (-8.2-21.1) lag 1 20.2 (6.9-33.5) lag 2 17.6 (4.3-30.9) lag 3 38.8 (15.8-61.8) 5-day mean

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Trenga et al. (2006, 155209) **Period of Study:** 1999-2002 **Location:** Seattle, WA	**Outcome:** Lung function: FEV_1, PEF, MMEF (maximal midexpiratory flow assessed only for children) **Age Groups**: Adults (56-89-yr-old) healthy & with COPD Asthmatic children 6-13-yr-old **Study Design:** Adult and pediatric panel study over 3 yr with 1 monitoring period ("session") per yr **N:** 57 adults (33 healthy, 24 with COPD) = 692 subject-days = 207 study-days 17 asthmatic children = 319 subject-days = 98 study-days **Statistical Analyses:** Mixed effects, longitudinal regression models, with the effects of pollutant decomposed into each subject's a) overall mean b) Difference between their session-specific mean and overall mean c) Difference between their daily values and session-specific mean **Covariates: G**ender, age, ventral site temperature and relative humidity, CO, NO_2 **Dose-response Investigated?** No **Statistical Package**: SAS **Lags Considered:** 0-1 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Percentiles:** **Children** Personal 25th: 8.1 50th(Median): 11.3 75th: 16.3 Indoor 25th: 5.7 50th(Median): 7.5 75th: 10.2 Local outdoor 25th: 6.4 50th(Median): 9.6 75th: 14. **Adults** Personal 25th: 5.9 50th(Median): 8.5 75th: 12.4 Indoor 25th: 5.1 50th(Median): 7.6 75th: 10.8 Local outdoor 25th: 6 50th(Median): 8.6 75th: 13.1 **Range (Min, Max):** Children, Personal 1.0, 49.4 Indoor (2.2, 36.3) Local outdoor (2.8, 40.4) Adults, Personal 1.3, 66.6 Indoor(1.6, 65.3) Local outdoor (0.0, 41.5) **Monitoring Stations**: 2 also subject-specific local outdoors (i.e., at each home), indoor, and personal **Copollutant (correlation):** CO NO_2 $PM_{2.5}$ $PM_{10-2.5}$ (coarse)	**PM Increment:** 10 µg/m^3 **ADULT** **Personal** $PM_{2.5}$ **-** FEV_1 Overall: Lag 0 -6.0 [-29.1: 17.2] Lag 1 12.0 [-12.9: 36.9] No-COPD: Lag 0 -4.6 [-31.0: 21.9] Lag 1 19.3 [-8.2: 46.7] COPD: Lag 0 -10.2 [-55.8: 35.4] Lag 1 -19.0 [-74.1: 36.2] PEF: Lag 0 1.5 [-2.2: 5.2] Lag 1 2.1 [-1.9: 6.1] No-COPD: Lag 0 3.4 [-0.9: 7.6] Lag 1 1.9 [-2.5: 6.3] COPD: Lag 0 -4.3 [-11.5: 3.0] Lag 1 2.6 [-6.3: 11.5] **Indoor** $PM_{2.5}$ **-** FEV_1 Overall: Lag 0 -12.8 [-44.5: 19.0] Lag 1 19.4 [-11.3: 50.1] No-COPD: Lag 0 -15.8 [-50.0: 18.4] Lag 1 28.4 [-4.6: 61.3] COPD: Lag 0 2.6 [-71.7: 76.8] Lag 1 -29.7 [-102.9: 43.5] **PEF** Overall: Lag 0 -0.5 [-5.6: 4.6] Lag 1 2.3 [-3.3: 7.8] No-COPD: Lag 0 0.1 [-5.4: 5.6] Lag 1 2.5 [-3.5: 8.4] COPD: Lag 0 -3.2 [-15.1: 8.7] Lag 1 1.1 [-12.0: 14.3] **Outdoor Home** $PM_{2.5}$ **-** FEV_1 Overall: Lag 0 -1.4 [-35.6: 32.7] Lag 1 -2.4 [-37.6: 32.7]. No-COPD: Lag 0 1.5 [-36.1: 39.2] Lag 1 10.7 [-26.9: 48.4] COPD: Lag 0 -8.9 [-62.2: 44.4] Lag 1 -45.2 [-102.6: 12.1] **PEF** Overall: Lag 0 2.3 [-3.3: 7.9] Lag 1 0.4 [-5.6: 6.4] No-COPD: Lag 0 4.0 [-2.2: 10.1] Lag 1 2.0 [-4.4: 8.4] COPD: Lag 0 -1.8 [-10.6: 6.9] Lag 1 -4.8 [-14.6: 4.9] **Central Sites** $PM_{2.5}$ **-** FEV_1 Overall: Lag 0 -35.5 [-70.0: -1.0] Lag 1 -40.4 [-71.1: -9.6]. No-COPD: Lag 0 -32.6 [-69.5: 4.3] Lag 1 -29.0 [-62.5: 4.5] COPD: Lag 0 -43.6 [-95.0: 7.8] Lag 1 -70.8 [-118.4: 23.1] **PEF** Overall: Lag 0 1.5 [-4.2: 7.1] Lag 1 -2.3 [-7.4: 2.9] No-COPD: Lag 0 2.5 [-3.5: 8.6] Lag 1 -0.5 [-6.1: 5.0] COPD: Lag 0 -1.5 [-9.9: 6.9] Lag 1 -7.1 [-15.0: 0.9] **PEDIATRIC** FEV_1 **Personal** $PM_{2.5}$ Overall: Lag 0 -13.08 [-38.26: 12.10] Lag 1 -16.12 [-42.61: 10.37]. No anti-inflammatory medication: Lag 0 -41.73 [-94.31: 10.84] Lag 1 -30.99 [-82.17: 20.19]. Anti-inflammatory medication: Lag 0 -4.61 [-34.49: 25.28] Lag 1 -10.87 [-45.01: 23.27] **Indoor** $PM_{2.5}$ Overall: Lag 0 -45.90 [-89.92: 1.88] Lag 1 -64.78 [-111.27: 18.28] No anti-inflammatory medication: Lag 0 -75.92 [-145.16: 6.67] Lag 1 -65.08 [-136.98: 6.82]. Anti-inflammatory medication: Lag 0 -28.50 [-94.72: 37.71]

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Lag 1 -64.60 -147.23: 18.04] **Outdoor Home** $PM_{2.5}$ Overall: Lag 0 -13.11 [-57.41: 31.19] Lag 1 -9.37 [-54.73: 36.00]. No anti-inflammatory medication: Lag 0 -24.42 [-81.22: 32.38] Lag 1 16.52 [-45.76: 78.80]. Anti-inflammatory medication: Lag 0 -3.59 [-75.88: 68.70] Lag 1-26.76 [-89.53: 36.01] **Central Sites** $PM_{2.5}$. Overall: Lag 0 -12.32 [-53.21: 28.56] Lag 1 5.75 [-33.27: 44.76]. No anti-inflammatory medication: Lag 0 -33.59 [-89.99: 22.82] Lag 1 31.30 [-29.91: 92.51] Anti-inflammatory medication: Lag 0 -2.13 [-71.99: 67.73] Lag 1 -3.53 [-67.32: 60.27] **PEF:** **Personal** $PM_{2.5}$ Overall: Lag 0 0.31 [-4.02: 4.64] Lag 1 -2.19 [-6.49: 2.12] No anti-inflammatory medication: Lag 0 0.22 [-8.85: 9.29] Lag 1 -10.48 [-18.68: 2.28] Anti-inflammatory medication: Lag 0 0.34 [-4.67: 5.35] Lag 1 0.74 [-4.21: 5.69] **Indoor** $PM_{2.5}$ Overall: Lag 0 -8.68 [-16.64: -0.72] Lag 1 -9.22 [-17.51: -0.93] No anti-inflammatory medication: Lag 0 -13.34 [-25.90: -0.79] Lag 1 -17.13 [-29.86: 4.41]. Anti-inflammatory medication: Lag 0 -5.98 [-15.85: 3.89] Lag 1 -4.19 [-14.59: 6.20] **Outdoor Home** $PM_{2.5}$ Overall: Lag 0 -6.27 [-14.07: 1.53] Lag 1 -5.64 [-13.73: 2.44]. No anti-inflammatory medication: Lag 0 -7.52 [-17.56: 2.51] Lag 1 -6.92 [-18.03: 4.19]. Anti-inflammatory medication: Lag 0 -5.22 [-14.77: 4.34] Lag 1 -4.78 [-14.42: 4.86] **Central Sites** $PM_{2.5}$ Overall: Lag 0 -5.62 [-12.86: 1.62] Lag 1 -2.45 [-9.34: 4.43]. No anti-inflammatory medication: Lag 0 -6.32 [-16.31: 3.68] Lag 1 -0.83 [-11.60: 9.95] Anti-inflammatory medication: Lag 0 -5.29 [-13.42: 2.85] Lag 1 -3.04 [-10.76: 4.67] **MMEF** **Personal** $PM_{2.5}$ Overall: Lag 0 -0.99 [-3.96: 1.98] Lag 1 -1.08 [-4.05: 1.88]. No anti-inflammatory medication: Lag 0 -3.32 [-9.52: 2.88] Lag 1 -2.49 [-8.23: 3.25]. Anti-inflammatory medication: Lag 0 -0.31 [-3.77: 3.16] Lag 1 -0.59 [-4.06: 2.89] **Indoor** $PM_{2.5}$ Overall**:** Lag 0 -3.29 [-8.52: 1.94] Lag 1 -11.08 [-16.26: 5.90]**.** Anti-inflammatory medication: Lag 0-12.65 [-20.74: -4.56]' Lag 1 -

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			13.84 [-21.82: 5.85] Anti-inflammatory medication: Lag 0 2.14 [-4.17: 8.45] Lag 1 -9.33 [-15.89: -2.78] **Outdoor Home** $PM_{2.5}$ Overall**:** Lag 0 -4.13 [-9.28: 1.01] Lag 1 -0.73 [-6.02: 4.56] No anti-inflammatory medication: Lag 0 -8.23 [-14.77: 1.69] Lag 1 -1.19 [-8.45: 6.07] Anti-inflammatory medication: Lag 0 -0.68 [-6.87: 5.50] Lag 1 -0.42 [-6.72: 5.87] **Central Sites** $PM_{2.5}$**.** Overall**:** Lag 0 -2.10 [-6.99: 2.79] Lag 1 -0.12 [-4.67: 4.42] No anti-inflammatory medication: Lag 0 -8.21 [-14.79: 1.62] Lag 1 -0.22 [-7.34: 6.90] Anti-inflammatory medication: Lag 0 0.82 [-4.48: 6.12]. Lag 1 -0.09 [-5.19: 5.01]
Reference: Tang et al. (2007, 091269) **Period of Study:** Dec 2003-Feb 2005 **Location:** Sin-Chung City, Taipei County, Taiwan	**Outcome:** Peak expiratory flow rate (PEFR) of asthmatic children **Age Groups**: 6-12 yr **Study Design:** Panel study **N:** 30 children **Statistical Analyses:** Linear mixed-effect models were used to estimate the effect of PM exposure on PEFR **Covariates:** Gender, age, BMI, history of respiratory or atopic disease in family, SHS, acute asthmatic exacerbation in past 12 mo, ambient temp and relative humidity, presence of indoor pollutants, and presence of outdoor pollutants, **Dose-response Investigated?** Yes **Statistical Package**: S-Plus 2000 **Lags Considered:** 0-2	**Pollutant:** $PM_{2.5-1}$ **Averaging Time:** 1 h **Mean (SD):** Personal: 6.2 (4.8) **Range (Min, Max):** Personal: 0.3-86.8 **Monitoring Stations**: 1	No quantitative effects reported.
Reference: Tang et al. (2007, 091269) **Period of Study:** Dec 2003-Feb 2005 **Location:** Sin-Chung City, Taipei County, Taiwan	**Outcome:** Peak expiratory flow rate (PEFR) of asthmatic children **Age Groups**: 6-12 yr **Study Design:** Panel study **N:** 30 children **Statistical Analyses:** Linear mixed-effect models were used to estimate the effect of PM exposure on PEFR **Covariates:** Gender, age, BMI, history of respiratory or atopic disease in family, SHS, acute asthmatic exacerbation in past 12 mo, ambient temp and relative humidity, presence of indoor pollutants, and presence of outdoor pollutants, **Dose-response Investigated?** yes **Statistical Package**: S-Plus 2000 **Lags Considered:** 0-2	**Pollutant:** PM1 **Averaging Time:** 1 h **Mean (SD):** Personal: 34.0 (28.9) Ambient: 31.4 (18.8) **Range (Min, Max):** Personal: 1.8-284.6 Ambient: 0.1-128.4 **Monitoring Stations**: 1	**PM Increment:** 27.6 µg/m^3 **RR Estimate [Lower CI, Upper CI] lag:** Change in morning PEFR: -6.44 (-30.18, 17.29) lag 0 -12.26 (-77.6 , 53.09) lag 1 -4.38 (-54.79, 46.03) lag 2 -44.06 (-113.79, 25.67) 2-day mean -6.01 (-101.48, 89.46) 3-day mean Change in evening PEFR: 1.17 (-17.79, 20.13) lag 0 -4.98 (-27.77, 17.81) lag 1 11.30 (-11.55, 34.16) lag 2 41.74 (11.36, 72.13) 2-day mean 28.21 (-19.08, 75.5) 3-day mean

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Timonen et al. (2004, 087915) **Period of Study:** Oct 1998-Apr 1999 **Location:** Amsterdam, The Netherlands Erfurt, Germany Helsinki, Finland	**Outcome:** Urinary concentration of Clara cell protein CC16 of subjects with coronary heart disease **Age Groups**: 50+ **Study Design:** Longitudinal cohort study (panel) **N:** N=37 (Amsterdam) N=47 (Erfurt) N=47 (Helsinki) **Statistical Analyses:** The response of interest was log transformed, creatinine adjusted CC16. Mixed-effect model was used to investigate the association between CC16 and air pollutants. **Covariates:** Subjects, long term time trend, temperature (lags 0-3), relative humidity (lags 0-3), barometric pressure (lags 0-3), and weekday of visit. **Dose-response Investigated?** yes **Statistical Package**: S-Plus and SAS **Lags Considered:** 0-3	**Pollutant:** NC 0.01-0.1 **Averaging Time:** 24 h **Mean (SD):** Amsterdam: 17338 /cm^3 Erfurt: 21124 /cm^3 Helsinki: 17041 /cm^3 **Range (Min, Max):** Amsterdam: 5699-37195 Erfurt: 3867-96678 Helsinki: 2305-50306 Unit (i.e. µg/m^3): 1/cm^3 **Monitoring Stations**: 3 $PM_{2.5}$: Amsterdam -0.15 Erfurt 0.62 Helsinki 0.14 NO_2: Amsterdam 0.49 Erfurt 0.82 Helsinki 0.72 CO: Amsterdam 0.22 Erfurt 0.72 Helsinki 0.35	**PM Increment:** 10,000 /cm^3 **RR Estimate [Lower CI, Upper CI] lag:** Pooled estimate; 1.7 (-4.4-7.8) lag 0 -1.8 (-8.3-4.6) lag 1 1.5 (-5.6-8.6) lag 2 2.3 (-4.8-9.3) lag 3 1.8 (-9.4-13.0) 5-day mean There was no association between NC 0.01-0.1 and CC16 in the pooled analysis.
Reference: Timonen et al. (2004, 087915) **Period of Study:** Oct 1998-Apr 1999 **Location:** Amsterdam, The Netherlands Erfurt, Germany Helsinki, Finland	**Outcome:** Urinary concentration of Clara cell protein CC16 of subjects with coronary heart disease **Age Groups**: 50+ **Study Design:** Longitudinal cohort study (panel) **N:** N=37 (Amsterdam) N=47 (Erfurt) N=47 (Helsinki) **Statistical Analyses:** The response of interest was log transformed, creatinine adjusted CC16. Mixed-effect model was used to investigate the association between CC16 and air pollutants. **Covariates:** Subjects, long term time trend, temperature (lags 0-3), relative humidity (lags 0-3), barometric pressure (lags 0-3), and weekday of visit. **Dose-response Investigated?** Yes **Statistical Package**: S-Plus and SAS **Lags Considered:** 0-3	**Pollutant:** NC10-0.1 **Averaging Time:** 24 h **Mean (SD):** Amsterdam: 2131 /cm^3 Erfurt: 1829 /cm^3 Helsinki: 1390 /cm^3 **Range (Min, Max):** Amsterdam: 413-6413 Erfurt: 303-6848 Helsinki: 344-3782 Unit (i.e. µg/m^3): 1/cm^3 **Monitoring Stations**: 3 **Copollutant (correlation):** Spearman Correlation: NC 0.1-0.01: Amsterdam 0.16 Erfurt 0.67 Helsinki 0.53 $PM_{2.5}$: Amsterdam 0.80 Erfurt 0.84 Helsinki 0.80 NO_2: Amsterdam 0.67 Erfurt 0.82 Helsinki 0.72 CO: Amsterdam 0.60 Erfurt 0.78 Helsinki 0.51	**PM Increment:** 1000 /cm^3 RR Estimate [Lower CI, Upper CI] lag: Pooled estimate; 4.3 (-1.4-10.0) lag 0 5.1 (-0.6-10.7) lag 1 4.5 (-0.5-9.6) lag 2 1.6 (-3.5-6.7) lag 3 13.1 (-4.3-30.5) 5-day mean CC16 was not associated to NC 0.1-1.0 in the pooled analysis but CC16 was significantly associated to NC 0.1-1.0 in Helsinki: 15.5 (0.001-30.9) lag 0 10.8 (-4.2-25.8) lag 1 10.5 9-4.1-25.1) lag 2 17.4 (3.4-31.4) lag 3 43.2 (17.4-69.0) 5-day mean

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: von Klot et al. (2002, 034706) **Period of Study:** Sep 1996-Mar 1997 (winter) **Location:** Erfurt, Germany	**Outcome:** Asthma symptoms (wheezing, shortness of breath at rest, waking up with breathing problems, or coughing without having a cold) and Asthma medication (inhaled short-acting ß2- agonists, inhaled long-acting ß2-agonists, inhaled corticosteroids, cromolyn sodium, theophylline, oral corticosteroids, and N-acetylcysteine) **Age Groups**: Adults, mean=59.0 yr and range =37-77 yr **Study Design:** Panel study **N:** 53 adult asthmatics **Statistical Analyses:** Logistic regression models **Covariates:** Seasonal variation in medication use or symptom prevalence, meteorological factors (relative humidity, temperature), weekend, Christmas holidays **Season: W**inter **Dose-response Investigated?** No **Statistical Package**: NR **Lags Considered:** 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, ma calculated from same day and preceding days	**Pollutant:** MC0.5-0.1 **Averaging Time:** 10-min intervals **Mean (SD):** 24.8 Percentiles: 25th: 11.4 50th(Median): 19.6 75th: 33.1 **Range (Min, Max):** (2.4-108.3) **Copollutant (correlation):** $PM_{10-2.5}$: r= 0.51 NC0.1-0.01: r= 0.45 NC0.5-0.1: r= 0.95 NC2.5-0.5: r= 0.92 MC2.5-0.01: r= 1.00 PM_{10}: r= 0.91 NO_2: r= 0.69 CO: r= 0.66 SO_2: r= 0.60	**NC Increment:** 1 IQR **Effect Estimate [Lower CI, Upper CI]:** Association between the prevalence of inhaled ß2- agonist use and MC0.1-0.5 Same day, IQR= 21, OR= 0.98 (0.92-1.04) 5-day mean, IQR= 21 OR= 1.11 (1.02-1.20) 14-day mean IQR= 17, OR= 1.01 (0.93-1.10) Association between the prevalence of inhaled corticosteroid use and MC0.1-0.5 Same day, IQR= 2, OR= 1.09 (1.02-1.17) 5-day mean IQR= 21, OR= 1.28 (1.18-1.39) 14-day mean, IQR= 17, OR= 1.49 (1.38-1.61) Association between the prevalence of wheezing and MC0.1-0.5 Same day, IQR= 21, OR= 1.01 (0.94-1.08) 5-day mean, IQR= 21, OR= 1.08 (0.99-1.17) 14-day mean, IQR= 17, OR= 1.05 (0.96-1.15)
Reference: von Klot et al. (2002, 034706) **Period of Study:** Sep 1996-Mar 1997 (winter) **Location:** Erfurt, Germany	**Outcome:** Asthma symptoms (wheezing, shortness of breath at rest, waking up with breathing problems, or coughing without having a cold) and Asthma medication (inhaled short-acting ß2- agonists, inhaled long-acting ß2-agonists, inhaled corticosteroids, cromolyn sodium, theophylline, oral corticosteroids, and N-acetylcysteine) **Age Groups**: Adults, mean=59.0 yr and range =37-77 yr **Study Design:** Panel study **N:** 53 adult asthmatics **Statistical Analyses:** Logistic regression models **Covariates:** Seasonal variation in medication use or symptom prevalence, meteorological factors (relative humidity, temperature), weekend, Christmas holidays **Season:** Winter **Dose-response Investigated?** No **Statistical Package**: NR **Lags Considered:** 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, ma calculated from same day and preceding days	**Pollutant:** MC2.5-0.01 **Averaging Time:** 10-min intervals **Mean (SD):** 30.3 Percentiles: 25th: 13.5 50th(Median): 24.6 75th: 41.3 **Range (Min, Max):** (3.6-133.8) **Copollutant (correlation):** $PM_{10-2.5}$: r= 0.52 $NC_{0.5-0.1}$: r= 0.45 $NC_{2.5-0.5}$: r= 0.94 $MC_{0.5-0.1}$: r= 1.00 $NC_{0.1-0.01}$: r= 0.45 PM_{10}: r= 0.94 NO_2: r= 0.68 CO: r= 0.65 SO_2: r= 0.62	**NC Increment:** 1 IQR **Effect Estimate [Lower CI, Upper CI]:** Association between the prevalence of inhaled ß2- agonist use and MC0.01-2.5 Same day, IQR= 28, OR= 0.96 (0.90-1.04) 5-day mean, IQR= 26 , OR= 1.10 (1.01-1.20) 14-day mean, IQR= 20, OR= 1.03 (0.95-1.12)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: von Klot et al. (2002, 034706) **Period of Study:** Sep 1996-Mar 1997 (winter) **Location:** Erfurt, Germany	**Outcome:** Asthma symptoms (wheezing, shortness of breath at rest, waking up with breathing problems, or coughing without having a cold) and Asthma medication (inhaled short-acting ß2- agonists, inhaled long-acting ß2-agonists, inhaled corticosteroids, cromolyn sodium, theophylline, oral corticosteroids, and N-acetylcysteine) **Age Groups**: Adults, mean=59.0 yr and range =37-77 yr **Study Design:** Panel study **N:** 53 adult asthmatics **Statistical Analyses:** Logistic regression models **Covariates:** Seasonal variation in medication use or symptom prevalence, meteorological factors (relative humidity, temperature), weekend, Christmas holidays **Season:** Winter **Dose-response Investigated?** No **Statistical Package**: NR **Lags Considered:** 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, ma calculated from same day and preceding days	**Pollutant:** NC0.1-0.01 **Averaging Time:** 10-min intervals **Mean (SD):** 17,300 /cm^3 Percentiles: 25th: 9286 50th(Median): 16940 75th: 24484 **Range (Min, Max):** (3272-46195) Unit (i.e. µg/m^3): 1/cm^3 **Copollutant (correlation):** $PM_{10-2.5}$: r= 0.41 $NC_{0.5-0.1}$: r= 0.55 $NC_{2.5-0.5}$: r= 0.34 $MC_{0.5-0.1}$: r= 0.45 $MC_{2.5-0.01}$: r= 0.45 PM_{10}: r= 0.51 NO_2: r= 0.66 CO: r= 0.66 SO_2: r= 0.36	**NC Increment:** 1 IQR **Effect Estimate [Lower CI, Upper CI]:** Association between the prevalence of inhaled ß2- agonist use and NC0.01-0.1 Same day, IQR= 15000, OR= 0.97 (0.90-1.04) 5-day mean, IQR= 10000, OR= 1.11 (1.01-1.21) 14-day mean, IQR= 7700, OR= 1.08 (0.96-1.21) Association between two pollutants, jointly in one model, and the Outcomes Inhaled short-acting ß2- agonist use NC0.1-0.01 OR= 1.07 (0.97-1.18) MC0.5-0.1: OR= 1.07 (0.98-1.18) Inhaled corticosteroid use NC0.1-0.01 OR= 1.01 (0.87-1.18) MC0.5-0.1: OR= 1.53 (1.39-1.69) Wheezing NC0.1-0.01 OR= 1.12 (1.01-1.24) MC0.5-0.1: OR= 1.02 (0.92-1.12) Association between the prevalence of inhaled corticosteroid use and NC0.01-0.1 Same day, IQR= 15000, OR= 1.07 (1.00-1.15) 5-day mean, IQR= 10000, OR= 1.22 (1.12-1.33) 14-day mean, IQR= 7700, OR= 1.45 (1.29-1.63) Association between the prevalence of wheezing and NC0.1-0.01 Same day, IQR= 15000, OR= 0.94 (0.86-1.01) 5-day mean, IQR= 10000, OR= 1.13 (1.03-1.24) 14-day mean, IQR= 7700, OR= 1.27 (1.13-1.43) Association between the prevalence of respiratory symptoms and NC0.1-0.01 Attack of shortness of breath and wheezing Same day, IQR= 15000, OR= 1.01 (0.91-1.12) 5-day mean, IQR= 10000, OR= 1.08 (0.96-1.21) 14-day mean, IQR= 7700, OR= 1.26 (1.08-1.48) Walking up with breathing problems Same day, IQR= 15000, OR= 1.04 (0.96-1.13) 5-day mean, IQR= 10000, OR= 1.09 (0.99-1.19) 14-day mean, IQR= 7700, OR= 1.26 (1.13-1.41) Shortness of breath Same day, IQR= 15000, OR= 0.98 (0.90-1.06) 5-day mean, IQR= 10000, OR= 1.09 (0.99-1.19) 14-day mean, IQR= 7700, OR= 1.24 (1.11-1.40) Phlegm Same day, IQR= 15000, OR= 1.01 (0.94-1.09)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			5-day mean, IQR= 10000, OR= 1.11 (1.02-1.21) 14-day mean, IQR= 7700, OR= 1.11 (0.99-1.25) Cough Same day, IQR= 15000, OR= 1.07 (0.98-1.16) 5-day mean, IQR= 10000, OR= 1.17 (1.07-1.28) 14-day mean, IQR= 7700, OR= 1.20 (1.06-1.35)
Reference: von Klot et al. (2002, 034706) **Period of Study:** Sep 1996-Mar 1997 (winter) **Location:** Erfurt, Germany	**Outcome:** Asthma symptoms (wheezing, shortness of breath at rest, waking up with breathing problems, or coughing without having a cold) and Asthma medication (inhaled short-acting ß2- agonists, inhaled long-acting ß2-agonists, inhaled corticosteroids, cromolyn sodium, theophylline, oral corticosteroids, and N-acetylcysteine) **Age Groups**: Adults, mean=59.0 yr and range =37-77 yr **Study Design:** Panel study **N:** 53 adult asthmatics **Statistical Analyses:** Logistic regression models **Covariates:** Seasonal variation in medication use or symptom prevalence, meteorological factors (relative humidity, temperature), weekend, Christmas holidays **Season:** Winter **Dose-response Investigated?** No **Statistical Package**: NR **Lags Considered:** 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, ma calculated from same day and preceding days	**Pollutant:** NC0.5-0.1 **Averaging Time:** 10-min intervals **Mean (SD):** 2005 /cm^3 Percentiles: 25th: 958 50th(Median): 1610 75th: 2767 **Range (Min, Max):** (291-6700) Unit (i.e. µg/m^3): 1/cm^3 **Copollutant (correlation):** $PM_{10-2.5}$: r= 0.50 $NC_{0.1-0.01}$: r= 0.55 $NC_{2.5-0.5}$: r= 0.76 $MC_{0.5-0.1}$: r= 0.95 $MC_{2.5-0.01}$: r= 0.93 PM_{10}: r= 0.85 NO_2: r= 0.75 CO: r= 0.79 SO_2: r= 0.51	**NC Increment:** 1 IQR **Effect Estimate [Lower CI, Upper CI]:** Association between the prevalence of inhaled ß2- agonist use and NC0.5-0.1 Same day, IQR= 1800, OR= 0.99 (0.92-1.05) 5-day mean, IQR= 1500, OR= 1.10 (1.03-1.19) 14-day mean, IQR= 1450, OR= 0.95 (0.86-1.05) Association between the prevalence of inhaled corticosteroid use and NC0.5-0.1 Same day, IQR= 1800, OR= 1.06 (0.99-1.14) 5-day mean, IQR= 1500, OR= 1.23 (1.14-1.32) 14-day mean, IQR= 1450, OR= 1.51 (1.37-1.67) Association between the prevalence of wheezing and NC0.5-0.1 Same day, IQR= 1800, OR= 1.00 (0.93-1.07) 5-day mean, IQR= 1500, OR= 1.08 (1.00-1.17) 14-day mean, IQR= 1450, OR= 1.11 (1.00-1.24)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: von Klot et al. (2002, 034706) **Period of Study:** Sep 1996-Mar 1997 (winter) **Location:** Erfurt, Germany	**Outcome:** Asthma symptoms (wheezing, shortness of breath at rest, waking up with breathing problems, or coughing without having a cold) and Asthma medication (inhaled short-acting ß2- agonists, inhaled long-acting ß2-agonists, inhaled corticosteroids, cromolyn sodium, theophylline, oral corticosteroids, and N-acetylcysteine) **Age Groups**: Adults, mean=59.0 yr and range =37-77 yr **Study Design:** Panel study **N:** 53 adult asthmatics **Statistical Analyses:** Logistic regression models **Covariates:** Seasonal variation in medication use or symptom prevalence, meteorological factors (relative humidity, temperature), weekend, Christmas holidays **Season:** Winter **Dose-response Investigated?** No **Statistical Package**: NR **Lags Considered:** 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, ma calculated from same day and preceding days	**Pollutant:** NC2.5-0.5 **Averaging Time:** 10-min intervals **Mean (SD):** 21.4 /cm^3 Percentiles: 25th: 5.6 50th(Median): 13.0 75th: 31.6 **Range (Min, Max):** (0.9-127.6) Unit (i.e. µg/m^3): 1/cm^3 **Copollutant (correlation):** $PM_{10-2.5}$: r= 0.48 $NC_{0.1-0.01}$: r= 0.34 $NC_{0.5-0.1}$: r= 0.76 $MC_{0.5-0.1}$: r= 0.92 $MC_{2.5-0.01}$: r= 0.94 PM_{10}: r= 0.88 NO_2: r= 0.54 CO: r= 0.46 SO_2: r= 0.66	**NC Increment:** 1 IQR **Effect Estimate [Lower CI, Upper CI]:** Association between the prevalence of inhaled ß2- agonist use and NC2.5-0.5 Same day, IQR= 26, OR= 0.99 (0.93-1.05) 5-day mean, IQR= 22, OR= 1.09 (1.01-1.17) 14-day mean, IQR= 17, OR= 1.08 (1.02-1.15) Association between the prevalence of inhaled corticosteroid use and NC2.5-0.5 Same day, IQR= 26, OR= 1.13 (1.06-1.21) 5-day mean, IQR= 22, OR= 1.28 (1.19-1.37) 14-day mean, IQR= 17, OR= 1.44 (1.36-1.53) Association between the prevalence of wheezing and NC2.5-0.5 Same day, IQR= 26, OR= 1.03 (0.95-1.10) 5-day mean, IQR= 22, OR= 1.05 (0.97-1.13) 14-day mean, IQR= 17, OR= 1.03 (0.96-1.10)
Reference: von Klot et al. (2002, 034706) **Period of Study:** Sep 1996-Mar 1997 (winter) **Location:** Erfurt, Germany	**Outcome:** Asthma symptoms (wheezing, shortness of breath at rest, waking up with breathing problems, or coughing without having a cold) and Asthma medication (inhaled short-acting ß2- agonists, inhaled long-acting ß2-agonists, inhaled corticosteroids, cromolyn sodium, theophylline, oral corticosteroids, and N-acetylcysteine) **Age Groups**: Adults, mean=59.0 yr and range =37-77 yr **Study Design:** Panel study **N:** 53 adult asthmatics **Statistical Analyses:** Logistic regression models **Covariates:** Seasonal variation in medication use or symptom prevalence, meteorological factors (relative humidity, temperature), weekend, Christmas holidays **Season**: Winter **Dose-response Investigated?** No **Statistical Package**: NR **Lags Considered:** 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, ma calculated from same day and preceding days	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 24 h **Mean (SD):** 10.3 Percentiles: 25th: 2.9 50th(Median): 6.9 75th: 14.6 **Range (Min, Max):** (-8.7-64.3) **Copollutant (correlation):** $NC_{0.1-0.01}$: r= 0.41 $NC_{0.5-0.1}$: r= 0.50 $NC_{2.5-0.5}$: r= 0.48 $MC_{0.5-0.1}$: r= 0.51 $MC_{2.5-0.01}$: r= 0.52 PM_{10}: r= 0.67 NO_2: r= 0.45 CO: r= 0.42 SO_2: r= 0.28	**PM Increment:** 1 IQR Effect Estimate [Lower CI, Upper CI]: Association between the prevalence of inhaled ß2- agonist use and $PM_{10-2.5}$ Same day, IQR= 12, OR= 1.01 (0.95-1.06) 5-day mean, IQR= 11, OR= 1.01 (0.94-1.09) 14-day mean, IQR= 6.7, OR= 0.92 (0.86-1.00) Association between the prevalence of inhaled corticosteroid use and $PM_{10-2.5}$ Same day, IQR= 12, OR= 1.03 (0.98-1.08) 5-day mean, IQR= 11, OR= 1.12 (1.04-1.20) 14-day mean, IQR= 6.7, OR= 1.27 (1.18-1.37) Association between the prevalence of wheezing and $PM_{10-2.5}$ Same day, IQR= 12, OR= 0.97 (0.91-1.02) 5-day mean, IQR= 11, OR= 1.06 (0.98-1.15) 14-day mean, IQR= 6.7, OR= 1.05 (0.96-1.15)
Reference: Ward et al. (2002, 025839) **Period of Study:** 1997 (two 8-wk periods) **Location:** Birmingham and Sandwell, UK	**Outcome:** Change in PEF (peak expiratory flow), self reported respiratory symptoms (same day cough, illness, short of breath, waking up at night with cough or wheeze, wheeze) **Age Groups**: 9 yr olds **Study Design:**	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** Winter: 12.7 µg/m^3 Summer: 12.3 µg/m^3 **Range (Min, Max):**	**PM Increment:** Winter: 12.3 µg/m^3 Summer: 6.3 µg/m^3 Mean (PEF l/min) [Lower CI, Upper CI] lag: **Winter morning:** 0.80 [-1.97, 3.67] lag 0 0.62 [-2.22, 3.54] lag 1

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
	Time-series Panel study **N:** 162 children from 5 schools **Statistical Analyses:** Linear regression (PEF), Logistic regression (respiratory symptoms) **Covariates:** Trend, temperature, schooldays (yes/no) **Season:** Winter (Jan 13-Mar 10) Summer (May 19- Jul 14) **Dose-response Investigated?** No **Statistical Package**: Nr **Lags Considered:** Lag 0, lag 1, lag 2, lag 3, 7-day ma	Winter: 4, 37 Summer: 5, 28 PM Component: Total mass **Monitoring Stations**: 5 stations near the 5 schools **Copollutant (correlation):** Winter: PM_{10}(r=0.93) NO_2 (r=0.88) O_3 (r=-0.83) Summer: HNO_3 (r=0.81)	-0.86 [-4.32, 2.47] lag 2 -2.47 [-5.30, 0.36] lag 3 -4.07 [-10.60, 2.42] 7-day mean **Winter afternoon:** 0.95 [-2.22, 4.23] lag 0 -0.99 [-4.69, 2.72] lag 1 -1.60 [-5.18, 2.01] lag 2 -3.45 [-6.53 to -0.25] lag 3 1.00 [-11.47, 13.56] 7-day mean **Summer morning:** -1.49 [-3.65, 0.67] lag 0 0.21 [-2.12, 2.55] lag 1 2.50 [0.28, 4.72] lag 2 3.41 [1.40, 5.44] lag 3 3.90 [-2.53, 10.33] 7-day mean **Summer afternoon:** -0.49 [-2.43, 1.45] lag 0 -0.78 [-2.72, 1.16] lag 1 0.57 [-1.35, 2.49] lag 2 0.16 [-1.85, 2.17] lag 3 -0.08 [-5.43, 5.27] 7-day mean **Winter morning in atopy/recent wheezing subgroup:** -0.072 [-0.527, 0.383] lag 0 -0.271 [-0.701, 0.159] lag 1 0.127 [-0.354, 0.608] lag 2 0.055 [-0.391, 0.501] lag 3 **Winter morning in no atopy or recent wheezing subgroup:** 0.126 [-0.413 , 0.666] lag 0 0.193 [-0.340 , 0.728] lag 1 -0.170 [-0.788 , 0.447] lag 2 -0.314 [-0.846 , 0.216] lag 3 **Winter morning in subgroup with parental atopy/recent wheezing:** 0.187 [-0.008 , 0.382] lag 0 -0.006 [-0.207 , 0.195] lag 1 -0.011 [-0.226 , 0.204] lag 2 -0.037 [-0.228 , 0.154] lag 3 **Winter morning in subgroup without parental atopy/recent wheezing:** 0.026 [-0.341 , 0.395] lag 0 0.068 [-0.307 , 0.444] lag 1 -0.099 [-0.535 , 0.335] lag 2 -0.252 [-0.615 , 0.110] lag 3 **RR Estimate [Lower CI, Upper CI] lag:** **Cough:** **Winter:** 0.98 [0.80, 1.18] lag 0 0.95 [0.77, 1.17] lag 1 1.02 [0.83, 1.24] lag 2 1.01 [0.83, 1.23] lag 3 1.31 [0.82, 2.09] 7-day mean **Summer:** 1.13 [1.04, 1.22] lag 0 1.04 [0.94, 1.13] lag 1 0.94 [0.87, 1.02] lag 2 0.89 [0.82, 0.96] lag 3 0.81 [0.62, 1.06] 7 day mean **Illness:** **Winter:** 1.17 [1.05, 1.32] lag 0 1.07 [0.95, 1.23] lag 1 1.16 [1.01, 1.35] lag 2 1.01 [0.90, 1.16] lag 3 1.57 [1.15, 2.13] 7-day mean **Summer:** 1.02 [0.91, 1.13] lag 0 1.00 [0.89, 1.13] lag 1 0.96 [0.85, 1.07] lag 2 0.97 [0.86, 1.09] lag 3 0.68 [0.41, 1.13] 7-day mean

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Shortness of breath: **Winter:** 1.07 [0.94, 1.24] lag 0 0.98 [0.84, 1.13] lag 1 0.96 [0.82, 1.13] lag2 0.91 [0.79, 1.07] lag 3 0.82 [0.58, 1.18] 7-day mean **Summer:** 1.04 [0.90, 1.20] lag 0 1.08 [0.93, 1.25] lag 1 0.97 [0.84, 1.13] lag 2 0.93 [0.81, 1.08] lag 3 1.16 [0.76, 1.77] 7-day mean **Wake at night with cough/wheeze:** **Winter:** 1.10 [0.96, 1.26] lag 0 1.05 [0.90, 1.22] lag 1 0.98 [0.83, 1.13]; lag 2 0.94 [0.81, 1.09]; lag 3 0.93 [0.66, 1.32] 7-day mean **Summer:** 0.93 [0.78, 1.10] lag 0 0.81 [0.67, 0.98] lag 1 0.91 [0.77, 1.09] lag 2 0.97 [0.83, 1.13] lag 3 1.04 [0.57, 1.90] 7-day mean **Wheeze:** **Winter:** 0.98 [0.83, 1.16] lag 0 0.90 [0.75, 1.05] lag 1 1.00 [0.83, 1.20] lag 2 1.13 [0.95, 1.35] lag 3 1.02 [0.68, 1.57]; 7-day mean **Summer:** 1.02 [0.88, 1.19] lag 0 0.98 [0.84, 1.16] lag 1 0.87 [0.74, 1.02] lag 2 0.85 [0.72, 0.99] lag 3 0.96 [0.51, 1.81] 7-day mean
Reference: Ward et al. (2002, 025839) **Period of Study:** 1997 (two 8-wk periods) **Location:** Birmingham and Sandwell, UK	**Outcome:** Change in PEF (peak expiratory flow), self reported respiratory symptoms (same day cough, illness, short of breath, waking up at night with cough or wheeze, wheeze) **Age Groups**: 9 yr olds **Study Design:** Time-series panel study **N:** 162 children from 5 schools **Statistical Analyses:** Linear regression (PEF), Logistic regression (respiratory symptoms) **Covariates:** Trend, temperature, schooldays (yes/no) **Season:** Winter (Jan 13-Mar 10) Summer (May 19- Jul 14) **Dose-response Investigated?** No **Statistical Package**: Nr **Lags Considered:** Lag 0, lag 1, lag 2, lag 3, 7-day ma	**Pollutant:** Sulfate **Averaging Time:** 24 h **Mean (SD):** Winter: 2.4 µg/m^3 Summer: 3.8 µg/m^3 **Range (Min, Max):** Winter: 0.8, 14.9 Summer: 1.1, 7.8 PM Component: SO_4 **Monitoring Stations**: 2 stations	**PM Increment:** Winter: 4.8 µg/m^3 Summer: 3.1 µg/m^3 Mean (PEF l/min) [Lower CI, Upper CI] lag **Winter morning:** -1.75 [-4.00, 0.50] lag 0 -0.91 [-3.44, 1.62] lag 1 -0.62 [-3.16, 1.91] lag 2 -1.82 [-4.27, 0.64] lag 3 -3.22 [-8.03, 1.58] 7-day mean **Winter afternoon:** 0.99 [-1.58, 3.55] lag 0 0.79 [-2.42, 4.00] lag 1 -1.89 [-4.99, 1.21] lag 2 -1.73 [-4.69, 1.23] lag 3 -1.96 [-13.35, 9.42] 7-day mean **Summer morning:** -0.72 [-3.27, 1.82] lag 0 -1.69 [-4.28, 0.90] lag 1 1.35 [-1.27, 3.97] lag 2 3.38 [1.03, 5.72] lag 3 2.98 [-4.17, 10.13] 7-day mean **Summer afternoon:** -0.32 [-2.81, 2.17] lag 0 0.84 [-1.63, 3.30] lag 1 -0.08 [-2.61, 2.44] lag 2 -0.25 [-2.69, 2.19]lag 3 -2.20 [-9.51, 5.12] 7-day mean **Winter morning in atopy/recent wheezing subgroup:** 0.200 [-0.755, 1.156] lag 0 -0.219 [-1.318, 0.881] lag 1 -0.431 [-1.526, 0.664]; lag 2 1.200 [0.095, 2.305] lag 3

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Winter morning in no atopy or recent wheezing subgroup: -0.613 [-1.714, 0.488] lag 0 -0.174 [-1.423, 1.075] lag 1 0.006 [-1.243, 1.253] lag 2 -1.080 [-2.308, 0.148] lag 3 **Winter morning in subgroup with parental atopy/recent wheezing:** 0.457 [0.003 , 0.910] lag 0 0.078 [-0.503, 0.660] lag 1 -0.102 [-0.656, 0.452] lag 2 0.002 [-0.609, 0.613] lag 3 **Winter morning in subgroup without parental atopy/recent wheezing:** -0.622 [-1.379, 0.136] lag 0 -0.272 [-1.147, 0.602] lag 1 -0.138 [-1.005, 0.728] lag 2 -0.496 [-1.359, 0.367] lag 3 **RR Estimate [Lower CI, Upper CI] lag:** **Cough:** **Winter:** 1.01 [0.84, 1.20] lag 0 1.02 [0.85, 1.24] lag 1 0.99 [0.82, 1.20] lag 2 0.86 [0.71, 1.05] lag 3 0.78 [0.53, 1.14] 7-day mean **Summer:** 1.08 [0.98, 1.20] lag 0 1.03 [0.93, 1.15] lag 1 0.97 [0.88, 1.07] lag 2 0.90 [0.82, 0.99] lag 3 0.73 [0.54, 0.97] 7 day mean **Illness:** **Winter:** 1.06 [0.96, 1.17] lag 0 1.15 [1.03, 1.28] lag 1 1.14 [1.00, 1.28] lag 2 1.04 [0.92, 1.18] lag 3 1.30 [1.00, 1.66] 7-day mean **Summer:** 0.98 [0.86, 1.11] lag 0 0.97 [0.84, 1.12] lag 1 1.01 [0.88, 1.16] lag 2 0.95 [0.84, 1.09] lag 3 0.72 [0.46, 1.12] 7-day mean **Shortness of breath:** **Winter:** 0.96 [0.85, 1.07] lag 0 0.98 [0.86, 1.12] lag 1 0.94 [0.82, 1.07] lag2 0.93 [0.81, 1.08] lag 3 0.80 [0.59, 1.07] 7-day mean **Summer:** 0.95 [0.80, 1.14] lag 0 1.07 [0.89, 1.28] lag 1 1.04 [0.87, 1.24] lag 2 0.94 [0.80, 1.12] lag 3 |0.58 [0.33, 1.04] 7-day mean **Wake at night with cough/wheeze:** **Winter:** 0.97 [0.87, 1.08] lag 0 1.01 [0.89, 1.15] lag 1 1.00 [0.88, 1.14]; lag 2 0.93 [0.82, 1.07]; lag 3 0.79 [0.59, 1.05] 7-day mean **Summer:** 0.95 [0.78, 1.16] lag 0 0.81 [0.67, 0.99] lag 1 0.93 [0.76, 1.13] lag 2 0.87 [0.72, 1.05] lag 3 0.77 [0.41, 1.48] 7-day mean **Wheeze:** **Winter:** 1.00 [0.87, 1.15] lag 0 0.96 [0.82, 1.13] lag 1 0.88 [0.75, 1.04] lag 2 1.12 [0.95, 1.32] lag 3

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			0.83 [0.58, 1.20]; 7-day mean **Summer:** 0.97 [0.80, 1.17] lag 0 .09 [0.89, 1.32] lag 1 1.00 [0.82, 1.22] lag 2 0.81 [0.69, 0.97] lag 3 1.30 [0.68, 2.50] 7-day mean
Reference: Ward et al. (2002, 025839) **Period of Study:** 1997 (two 8-week periods) **Location:** Birmingham and Sandwell, UK	**Outcome:** Change in PEF (peak expiratory flow), self reported respiratory symptoms (same day cough, illness, short of breath, waking up at night with cough or wheeze, wheeze) **Age Groups**: 9 yr olds **Study Design:** Time-series panel study **N:** 162 children from 5 schools **Statistical Analyses:** Linear regression (PEF), Logistic regression (respiratory symptoms) **Covariates:** Trend, temperature, schooldays (yes/no) **Season:** Winter (Jan 13-Mar 10) Summer (May 19- Jul 14) **Dose-response Investigated?** No **Statistical Package**: Nr **Lags Considered:** Lag 0, lag 1, lag 2, lag 3, 7-day ma	**Pollutant:** NO_3 **Averaging Time:** 24 h **Mean (SD):** Winter: 3.6 µg/m^3 Summer: 3.5 µg/m^3 **Range (Min, Max):** Winter: 0.1, 29.9 Summer: 0.7, 13.2 **Monitoring Stations**: 2 stations	**PM Increment:** Winter: 6.7 µg/m^3 Summer: 3.7 µg/m^3 Mean (PEF l/min) [Lower CI, Upper CI] lag: **Winter morning:** -2.08 [-4.02 to -0.15] lag0 -0.64 [-2.87, 1.59] lag 1 0.71 [-1.69, 3.11] lag 2 -1.38 [-3.61, 0.84] lag 3 -0.92 [-5.32, 3.47] 7-day mean **Winter afternoon:** 0.24 [-1.89, 2.38] lag0 -0.72 [-3.87, 2.43] lag 1 -1.37 [-5.11, 2.38] lag 2 -2.54 [-5.74, 0.66] lag 3 0.21 [-7.67, 8.11] 7-day mean **Summer morning:** -0.80 [-2.74, 1.15] lag 0 0.68 [-1.31, 2.67] lag1 1.42 [-0.73, 3.58] lag2 2.54 [0.48, 4.59] lag3 1.74 [-2.66, 6.13] 7-day mean **Summer afternoon:** -0.72 [-2.47, 1.03] lag 0 -0.59 [-2.36, 1.18] lag 1 -0.33 [-2.11, 1.45] lag 2 0.66 [-1.26, 2.58] lag 3 0.47 [-3.36, 4.29] 7-day mean **Winter morning in atopy/recent wheezing subgroup:** -0.036 [-0.627 , 0.555] lag 0 0.142 [-0.573 , 0.857] lag 1 0.000 [-0.760, 0.759] lag 2 0.689 [-0.061, 1.439] lag 3 **Winter morning in no atopy or recent wheezing subgroup**: -0.434 [-1.116, 0.248] lag 0 -0.201 [-1.002 , 0.600] lag 1 0.154 [-0.703 , 1.010] lag 2 -0.605 [-1.422 , 0.210] lag 3 **Winter morning in subgroup with parental atopy/recent wheezing**: 0.228 [-0.054, 0.511] lag 0 0.476 [0.060, 0.892] lag 1 0.196 [-0.202, 0.594] lag 2 0.083 [-0.321, 0.487] lag 3 **Winter morning in subgroup without parental atopy/recent wheezing:** -0.482 [-0.952, -0.012] lag 0 -0.276 [-0.846, 0.294] lag 1 0.078 [-0.520, 0.675] lag 2 -0.298 [-0.864, 0.268] lag 3 **RR Estimate [Lower CI, Upper CI] lag:** **Cough: Winter:** 0.92 [0.80, 1.07] lag 0 0.91 [0.77, 1.07] lag 1 0.99 [0.83, 1.17] lag 2 0.87 [0.73, 1.03] lag 3 0.71 [0.52, 0.97] 7-day mean **Summer:** 1.05 [0.97, 1.13] lag 0

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			1.01 [0.93, 1.10] lag 1 0.95 [0.88, 1.03] lag 2 0.89 [0.83, 0.96] lag 3 0.81 [0.68, 0.97] 7 day mean **Illness: Winter:** 1.05 [0.97, 1.14] lag 0 1.11 [1.01, 1.22] lag 1 1.13 [1.01, 1.26] lag 2 1.13 [1.04, 1.26] lag 3 1.13 [0.92, 1.38] 7-day mean **Summer:** 0.97 [0.87, 1.09] lag 0 0.98 [0.87, 1.10] lag 1 0.95 [0.85, 1.06] lag 2 0.94 [0.85, 1.05] lag 3 0.74 [0.54, 1.03] 7-day mean **Shortness of breath: Winter:** 0.99 [0.90, 1.10] lag 0 1.01 [0.90, 1.13] lag 1 0.93 [0.82, 1.05] lag2 0.98 [0.86, 1.13] lag 3 0.85 [0.67, 1.08] 7-day mean **Summer:** 1.04 [0.90, 1.18] lag 0 1.12 [0.98, 1.28] lag 1 1.04 [0.90, 1.20] lag 2 0.90 [0.79, 1.03] lag 3 1.06 [0.78, 1.43] 7-day mean **Wake at night with cough/wheeze: Winter:** 0.98 [0.89, 1.08] lag 0 1.05 [0.94, 1.16] lag 1 0.99 [0.88, 1.12]; lag 2 0.99 [0.87, 1.12]; lag 3 0.84 [0.67, 1.05] 7-day mean **Summer:** 0.94 [0.80, 1.09] lag 0 0.86 [0.72, 1.01] lag 1 0.94 [0.79, 1.11] lag 2 0.92 [0.79, 1.07] lag 3 0.95 [0.62, 1.47] 7-day mean **Wheeze: Winter:** 0.98 [0.87, 1.10] lag 0 1.00 [0.87, 1.14] lag 1 0.89 [0.77, 1.03] lag 2 1.11 [0.95, 1.30] lag 3 0.80 [0.61, 1.07] 7-day mean **Summer:** 1.01 [0.87, 1.17] lag 0 0.96 [0.83, 1.11] lag 1 0.95 [0.82, 1.10] lag 2 0.87 [0.75, 1.01] lag 3 1.04 [0.67, 1.60] 7-day mean

[1]All units expressed in $\mu g/m^3$ unless otherwise specified.

E.2.2. Respiratory Emergency Department Visits and Hospital Admissions

Table E-12. Short-term exposure-respiratory-ED/HA-PM_{10}.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Andersen et al. (2008, 189651) 1st page: 458 **Period of Study:** May 2001- Dec 2004 **Location:** Copenhagen, Denmark	**Hospital Admissions/ED visits** **Outcome (ICD-10):** **RD**, including chronic bronchitis (J41-42), emphysema (J43), other chronic obstructive pulmonary disease (J44), asthma (J45), and status asthmaticus (J46). **Pediatric hospital admissions for asthma** (J45) and status asthmaticus (J46). **Age Groups Analyzed:** >65 yr (RD combined), 5-18 yr (asthma) **Study Design:** Time series **N:** NR **Statistical Analyses:** Poisson GAM **Covariates:** temperature, dew-point temperature, long-term trend, seasonality, influenza, day of the week, public holidays, school holidays (only for 5-18 yr olds), pollen (only for pediatric asthma outcome) **Season:** NR **Dose-response Investigated:** No **Statistical package:** R statistical software (gam procedure, mgcv package) **Lags Considered:** Lag 0 -5 days, 5-day avg (lag 0-4) for RD, and a 6-day avg (lag 0-5) for asthma.	**Pollutant:** PM_{10} ($\mu g/m^3$) **Averaging Time:** 24 h **Mean (SD):** 24(14) **Median:** 21 **IQR:** 16-29 **99th percentile:** 72 **Monitoring Stations:** 1 **Copollutant (correlation):** NCtot: r = 0.39 NC100: r = 0.28 NCa12: r = 0.02 Nca23: r = -0.12 NCa57: r = 0.45 Nca212: r = 0.63 $PM_{2.5}$: r = 0.80 CO: r = 0.37 NO_2: r = 0.35 : r = 0.32 curbside: r = 0.18 O_3: r = -0.21 **Other variables:** Temperature: r = 0.12 Relative humidity: r = 0.05	**PM Increment:** 13 $\mu g/m^3$ 3 (IQR) **Relative risk (RR) Estimate [CI]:** **RD hospital admissions (5 day avg, lag 0 -4), age 65+:** One-pollutant model: 1.06 [1.02-1.09] Adj for NCtot: 1.05 [1.01-1.10] Adj for NCa212: 1.04 [0.98-1.11] **Asthma hospital admissions (6-day avg lag 0-5), age 5 - 18:** One-pollutant model: 1.02 [0.93-1.12] Adj for NCtot: 1.01 [0.91-1.12] Adj for NCa212: 0.94 [0.81-1.09] Estimates for individual day lags reported only in Fig form (see notes): **Notes:** Fig 2: Relative risks and 95% confidence intervals per IQR in single day concentration (0-5 day lag). Summary of Fig 2: RD: Positive, statistically or marginally significant associations at Lag 2-5. Asthma: Wide confidence intervals make interpretation difficult. Positive associations at Lag 1, 2, 3, and 5.
Reference: Cheng et al. (2007, 093034) **Period of Study:** 1996-2004 **Location:** Kaohsiung, Taiwan	**Outcome (ICD-9: 480-486):** Pneumonia **Age Groups:** NR **Study Design:** Case-crossover **N:** 82,587 pneumonia hospital admissions **Statistical Analyses:** Conditional logistic regression **Covariates:** Temperature and humidity on the same day **Season:** NR **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** Cumulative lag period up to 2 previous days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (min-max):** 77.01 (16.7-232) Percentiles: 25%: 42.12 50%: 75.27 75%: 104.65 **Monitoring Stations:** 6 **Copollutant:** NR	**PM Increment:** 62.53 $\mu g/m^3$ (IQR) **OR Estimate [CI]:** Single Pollutant Model: Temp>25ºC: 1.21 [1.15,1.28] Temp < 25ºC: 1.57 [1.50,1.65] Two-Pollutant Model: Temp>25ºC Adj. for SO_2: 1.21 [1.14,1.28] Adj. for NO_2: 1.15 [1.07,1.24] Adj. for CO: 1.10 [1.03,1.17] Adj. for O_3: 0.96 [0.89,1.03] Temp < 25ºC Adj. for SO_2: 1.56 [1.48,1.65] Adj. for NO_2: 1.09 [1.02,1.16] Adj. for CO: 1.30 [1.22,1.39] Adj. for O_3: 1.56 [1.48,1.65]

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Chimonas and Gessner (2007, 093261) **Period of Study:** Jan 1999-Jun 2003 **Location:** Anchorage, Alaska	**Outcome (ICD-9):** Asthma (493.0-493.9); Lower respiratory illness-LRI (466.1, 466.0, 480-487, 490, 510-511); Inhaled quick-relief medication; Steroid medication **Age Groups:** <20 yr old **Study Design:** Time series **N:** 42,667 admissions **Statistical Analyses:** GEE for multivariable modeling **Covariates:** Season, serial correlation, yr, weekend, temperature, precipitation, and wind speed **Season:** NR **Dose-response Investigated?** No **Statistical Package:** SPSS (dataset), SAS (analysis) **Lags Considered:** 1 day and 1 week	**Pollutant:** PM_{10} **Averaging Time:** 24 h and 1 wk **Mean (min-max):** Daily: 27.6 (2-421) Weekly: 25.3 (5.0-116.0) **Monitoring Stations:** NR **Copollutant:** Daily $PM_{2.5}$ ρ = 0.25 (p < 0.01) Weekly $PM_{2.5}$ ρ = 0.08 (p = 0.21)	**PM Increment:** 10 μg/m^3 **RR Estimate [CI]:** Same Day Outpatient Asthma: 1.006 [1.001,1.013] Outpatient LRI: 1.001 [0.987,1.015] Inpatient Asthma: 1.003 [0.922,1.091] Inpatient LRI: 1.015 [0.978,1.053] Inhaled Steroid Prescriptions: 1.006 [0.996,1.011] Quick-relief Medication: 1.018 [1.006,1.030] Weekly (median increase) Outpatient Asthma: 1.021 [1.004,1.038] Outpatient LRI: 1.013 [0.978,1.049] Inpatient Asthma: 1.023 [0.948,1.104] Inpatient LRI: 1.025 [0.981,1.072] Inhaled Steroid Prescriptions: 0.989 [0.969,1.010] Quick-relief Medication: 1.057 [1.037,1.077]
Reference: Chiu et al. (2008, 191989) **Period of Study:** 1996-2001 **Location:** Taipei, Taiwan	**Outcome:** Hospital admissions for COPD **Study Design:** Time-series **Covariates:** Temperature, humidity, PM_{10} and O_3 **Statistical Analysis:** Poisson regression **Statistical Package:** SAS **Age Groups:** All	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD) Unit:** Index Days: 111.68 ± 38.32 μg/m^3 Comparison Days: 55.43 ± 24.66 μg/m^3 **Range (Min, Max):** NR **Copollutant (correlation):** NR	All results refer to "dust storm days" and can be found in Table 3
Reference: Chiu et al. (2009, 190249) **Period of Study:** 1996-2004 **Location:** Taipei, Taiwan	**Outcome:** Hospital admissions for pneumonia (ICD-9 480-486) **Study Design:** Time-series **Covariates:** Weather variables, day of the week, seasonality, long-term time trends **Statistical Analysis:** Conditional logistic regression **Statistical Package:** SAS **Age Groups:** All	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean Unit:** 49.47 μg/m^3 **Range (Min, Max):** 14.42, 234.91 **Copollutant (correlation):** SO_2: 0.50 NO_2: 0.58 CO: 0.34 O_3: 0.31	**Increment:** IQR **Odds Ratio (95% CI)** Temperature ≥ 23º C: 1.11 (1.08-1.14) Temperature < 23º C: 1.09 (1.07-1.11) Adjusted for SO_2 Temperature ≥ 23º C: 1.10 (1.08-1.13) Temperature < 23º C: 1.19 (1.17-1.22) Adjusted for NO_2 Temperature ≥ 23º C: 0.90 (0.88-0.93) Temperature < 23º C: 1.09 (1.07-1.12) Adjusted for CO Temperature ≥ 23º C: 1.03 (1.00-1.05) Temperature < 23º C: 1.07 (1.05-1.10) Adjusted for O_3 Temperature ≥ 23º C: 1.05 (1.03-1.08) Temperature < 23º C: 1.09 (1.07-1.11)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Erbas et al. (2005, 073849) **Period of Study:** Jan 2000-Dec 2001 **Location:** Melbourne, Australia	Hospital Admissions **Outcome (ICD-10):** Asthma (J45, J46) **Age Groups:** 1-15 yr **Study Design:** Time series **N:** 8955 asthma cases **Statistical Analyses:** GAM, GEE (if autocorrelation was present in residuals) **Covariates:** Temp and humidity **Season:** NR **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 0, 1, 2 days	**Pollutant:** PM_{10} **Averaging Time:** 1 h **Mean (SD):** Western: 2.99 (2.11) 10th percentile: 13.67 90th percentile: 48.00 Inner Melbourne: 4.54 (2.65) 10th percentile: 15.63 90th percentile: 59.73 South/Southeastern: 1.13 (1.18) 10th percentile: 12.00 90th percentile: 36.05 Eastern: 3.61 (2.39) 10th percentile: 16.00 90th percentile: 51.05 Combined: 30.07 (10.55-112.33) SD = 15.27 10th percentile: 16.00 90th percentile: 50.51 **Monitoring Stations:** Data obtained from an air quality simulation model (TAPM) by CSIRO Atmospheric Research **Copollutant:** NR	**PM Increment:** Increase from 10th to 90th percentile **RR Estimate [CI]:** Same day lag Western: NR Inner Melbourne: 1.17 [1.05,1.31] South/Southeastern: 1.14 [0.95,1.33] Eastern: 1.09 [1.01,1.18] **Notes:** All other lags NR
Reference: Farhat et al. (2005, 089461) **Period of Study:** Aug 1996-Aug 1997 **Location:** São Paulo, Brazil	Hospital Admissions and Emergency Room Visits **Outcome (ICD-9):** Lower respiratory tract diseases (466, 480-519) including pneumonia or bronchopneumonia (480-486), asthma (493), bronchiolitis (466) **Age Groups:** <13 yr **Study Design:** Time series **N:** 43,635 **Statistical Analyses:** GAM, Poisson regression, Pearson correlation **Covariates:** Time, temperature, humidity, weekday **Season:** NR **Dose-response Investigated?** No **Statistical Package:** S-Plus **Lags Considered:** 0-7 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (min-max):** 62.6 (25.5-186.3) SD = 26.6 IQr = 30 N = 396 **Monitoring Stations:** 13 **Copollutant (correlation):** SO_2: r = 0.69 NO_2: r = 0.83 O_3: r = 0.35 CO: r = 0.72 (all $p < 0.05$) **Additional correlations:** Rel humidity: r = -0.55 Min temp: r = -0.44 (both $p < 0.05$)	**PM Increment:** 30 $\mu g/m^3$ (IQR) **RR Estimate [CI]:** Lower respiratory tract disease 5-day ma Copollutant model: NO_2: 2.1 [-7.1,11.3] SO_2: 16.5 [10.5,22.6] O_3: 10.1 [5.0,15.2] CO: 14.1 [8.1,20.2] Multipollutant model: 5.2 [-4.6,15.1] Pneumonia or bronchopneumonia 6-day ma Copollutant model: NO_2: 14.8 [-3.8,33.4] SO_2: 14.8 [-0.3,30.0]; O_3: 16.2 [1.0,31.3] CO: 17.6 [0.4,34.8] Multipollutant model: 5.23 [-16.2,26.6] Asthma or bronchiolitis 2-day ma Copollutant model: NO_2: -11.04 [-50.0,28.0] SO_2: 15.8 [-7.8,39.3] O_3: 11.7 [-10.4, 33.9] CO: 12.4 [-14.8,39.7] Multipollutant model: -15.5 [-61.2,30.2]

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Fung et al. (2006, 089789) **Period of Study:** June 1995-Mar 99 **Location:** Vancouver, Canada	Hospital Admission/ED **Outcome:** Respiratory diseases (460-519) **Age Groups:** Age >65 **Study Design:** Time series **N:** 26,275 individuals admitted **Statistical Analyses:** Poisson regression (spline 12 knots), case-crossover (controls +/7 days from case date), Dewanji and Moolgavkar (DM) method **Covariates:** Long-term trends, day-of-the-week effect, weather **Season:** All yr **Dose-response Investigated?** No **Statistical Package:** SPlus, R **Lags Considered:** 0-7 days	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 13.31(6.13) µg/m^3 **Range (Min, Max):** (3.77, 52.17) **Monitoring Stations:** NR **Copollutant (correlation):** PM_{10}: $PM_{2.5}$ r = 0.80 $PM_{10-2.5}$ r = -0.11 CO r = 0.46 Coh r = 0.61 O_3 r = -0.08 NO_2 r = 0.54 SO_2 r = 0.61	**PM Increment: :** 7.9 µg/m^3 Rr Estimate (65+ Yr) Dm Method: 1.014[0.998,1.029] Lag 0 1.016[0.998,1.034] 3-day avg 0.988[0.970, 1.006] 5-day avg 0.983[0.963, 1.004] 7-day avg Time Series: 1.016[0.999, 1.033] Lag 0 1.015[0.996, 1.035] 3-day avg 1.009[0.987, 1.032] 5-day avg 1.009[0.983, 1.036] 7-day avg Case-Crossover: 1.017[0.998, 1.036] Lag 0 1.015[0.993, 1.037] 3-day avg 1.008[0.984, 1.033] 5-day avg 1.003[0.976, 1.031] 7-day avg
Reference: Fung al. (2005, 093262) **Period of Study:** Nov 1995-Dec 2000 **Location:** London, Ontario	Hospital Admissions **Outcome (ICD-9):** Asthma (493) and all other respiratory diseases (460-519) **Age Groups:** <65 yr 65+ yr **Study Design:** Time series **N:** 5574 respiratory admissions **Statistical Analyses:** GAM with locally weighted regression smoothers (LOESS) **Covariates:** Maximum and minimum temp, humidity, day of the week, seasonal cycles, secular trends **Season:** NR **Dose-response Investigated?** No **Statistical Package:** S-Plus **Lags Considered:** Current to 3-day mean	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (min-max):** 38.0 (5-248) SD = 23.5 **Monitoring Stations:** 4 **Copollutant (correlation):** NO_2: r = 0.30 SO_2: r = 0.24 CO: r = 0.21 O_3: r = 0.53 COH: r = 0.29	**PM Increment:** 26 µg/m^3 **% Change in Daily Admission [CI]:** Age <65 Current day mean: -0.9 [-6.8,5.4] 2-day mean: -1.3 [-8.5,6.6] 3-day mean: 1.9 [-6.5,11] Age 65+ Current day mean: 3.3 [-1.7,8.6] 2-day mean: 5 [-1.5,11.9] 3-day mean: 1.2 [-6.1,9.1]

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Galán et al. (2003, 087408) **Period of Study:** 1995-1998 **Location:** Madrid, Spain	Hospital Admissions **Outcome (ICD):** Asthma (493) **Age Groups:** All ages **Study Design:** Time series **N:** 555,153 at-risk **Statistical Analyses:** GAM, autoregressive Poisson regression **Covariates:** Temperature, relative humidity, pollen, yr, day of the week, public holiday **Season:** NR **Dose-response Investigated?** No **Statistical Package:** S-Plus **Lags Considered:** 0, 1, 2, 3, and 4 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (min-max):** 32.1 (11.2-108.6) SD = 12.1 **Monitoring Stations:** 13 **Copollutant (correlation):** SO_2: r = 0.581 NO_2: r = 0.717 O_3: r = -0.188 **Other variables:** O.europaea: r = -0.066 Plantago sp.: r = -0.202 Poaceae: r = -0.132 Urticaceae: r = -0.104 Temp: r = -0.122 Humidity: r = 0.119	**PM Increment:** 10 µg/m^3 **RR Estimate [CI]:** Single-pollutant Current-day lag: 1.011 (0.980-1.042) 1-day lag: 1.006 (0.976-1.037) 2-day lag: 1.008 (0.978-1.038) 3-day lag: 1.039 (1.010-1.068) 4-day lag: 1.027 (0.999-1.056) Adjustment for pollen (PM_{10} 3-day lag) O. europaea: 1.041 (1.011-1.071) Plantago sp.: 1.046 (1.017-1.076) Poaceae: 1.043 (1.015-1.073) Urticaceae: 1.038 (1.009-1.068) All four: 1.045 (1.016-1.074)
Reference: Hajat et al. (2002, 030358) **Period of Study:** Jan 1992-Dec 1994 **Location:** London, England	Family Practice consultations **Outcome:** Upper Resp Disease (excluding allergic rhinitis) (460-3), (465), (470-5), (478) **Age Groups:** 0-14, 15-64, >65 yr **Study Design:** Time series **N:** 268,718-295,740 registered patients **Statistical Analyses:** Poisson regression, GAM, LOESS smoothers, default convergence criteria **Covariates:** Long term trends, pollen counts, flu, meteorological variables **Season:** All yr **Dose-response Investigated?** No **Statistical Package:** SPLUS **Lags Considered:** 2-3	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 28.5 (13.7) µg/m^3 Percentiles: 10th: 15.8 90th: 46.5 **Monitoring Stations:** 1 **Copollutant:** NR	**PM Increment:** All Year: 18 Warm Season: 15 Cold Season: 20 **% Change, Single Pollutant Models:** All Year: Ages 0-14: 2.0[-0.2, 4.2] Lag 3 Ages 15-64: 5.7[2.9, 8.6] Lag 2 Ages >65: 10.2[5.3, 15.3] Lag 2 Warm Season: Ages 0-14: 1.1[-2.4, 4.8] Lag 3 Ages 15-64: 6.0[2.7, 9.4] Lag 2 Ages >65: 0.1[-7.7, 8.5] Lag 2 Cold Season: Ages 0-14: 2.7[-0.1, 5.5] Lag 3 Ages 15-64: 3.6[1.0, 6.4] Lag 2 Ages >65: 18.9[11.7, 26.7] Lag 2 **% Change, 2 Pollutant Models:** 0-14 Yr PM_{10} w/ NO_2: 3.8[1.6, 6.1] PM_{10} w/ O_3: 1.8[-0.4, 3.9] PM_{10} w/ SO_2: 2.0[-0.6, 4.6] 15-65 Yr PM_{10} w/ NO_2: 2.8[0.7, 4.9] PM_{10} w/ O_3: 4.8[2.6, 7.0] PM_{10} w/ SO_2: 4.8[2.2, 7.5] >65 Yr PM_{10} w/ NO_2: 4.6[0.5, 8.8] PM_{10} w/ O_3: 10.7[5.7, 16.0] PM_{10} w/ SO_2: 10.6[4.5, 17.1]

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Hanigan et al. (2008, 156518) **Period of Study:** 1996-2005 (Apr-Nov of each yr) **Location:** Darwin, Australia	**Outcome:** Cardiorespiratory Disease HA (ICD 9: 390-519 ICD 10: I00-99 & J00-99) **Age Groups:** NR **Study Design:** Time series **N:** 8279 events **Statistical Analyses:** Poisson regression **Covariates:** Indigenous status, **Dose-response Investigated?** No **Statistical Package:** R **Lags Considered:** Lags 0-3	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 21.2 (8.2) **Range:** 55.2 **Monitoring Stations:** 2 (monitored & modeled) **Copollutant:** NR **Co-pollutant Correlation** N/A	**PM Increment:** 10 $\mu g/m^3$ **Percent Change (Lower CI, Upper CI), lag:** Total Respiratory: 4.81 (-1.04, 11.01), lag 0 Total Resp., Indigenous: 9.40 (1.04, 18.46), lag 0 Total Resp., Non-Indigenous: 3.14 (-2.99, 9.66), lag Resp. Infection, Indigenous: 15.02 (3.73, 27.54), lag 3 Resp. Infection, Non-Indigenous: 0.67 (-7.55, 9.61), lag 3 Asthma Indigenous: 16.27 (3.55, 40.17), lag 1 Asthma Non-Indigenous: 8.54 (-5.60, 24.80), lag 1 *Fig 3. percent change in hospital admissions per 10 $\mu g/m^3$ increase in PM_{10}
Reference: Hanigan et al. (2008, 156518) **Period of Study:** 1996-2005 (Apr-Nov of each yr) **Location:** Darwin, Australia	Hospital Admissions/ED visits **Outcome (ICD-9 or ICD-10):** Daily emergency hospital admissions for total respiratory (ICD-9: 460-519 ICD-10: J00-J99), asthma (ICD-9: 493 ICD-10: J45-J47), COPD (ICD-9: 490-492, 494-496 ICD-10: J40-J44, J47, J67), and respiratory infections (ICD-9: 461-466, 480-487, 514 ICD-10: J00-J22). **Age Groups Analyzed:** All **Study Design:** Time series **N:** 8,279 hospital admissions **Statistical Analyses:** Poisson generalized linear models **Covariates:** Indigenous status, time in days, temperature, relative humidity, day of the week, influenza epidemics, change between ICD editions, holidays, yrly population **Season:** Apr-Nov (corresponding to the dry season) **Dose-response Investigated?** No **Statistical package:** R version 2.3.1 **Lags Considered:** Lag 0 -3	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD range)**: 21.2 (8.2- 55.2) **Monitoring Stations:** N/A (see notes) **Copollutant (correlation):** NR	**PM Increment:** 10 $\mu g/m^3$ **Percent change [95% CI]:** Overall respiratory disease: Lag 0: 4.81 [-1.04, 11.01] Lag 0 (indigenous people): 9.40 [1.04, 18.46] Lag 0 (non-indigenous people): 3.14 [-2.99, 9.66] In unstratified analyses, the subgroups of respiratory infections, asthma, and COPD all had positive associations with PM_{10} Lag 0. Asthma: Lag 1 (indigenous people): 16.27 [-3.55, 40.17] Lag 1 (non-indigenous people): 8.54 [-5.60, 24.80] Respiratory infections: Lag 3 (indigenous people): 15.02 [3.73, 27.54] Lag 3 (non-indigenous people): 0.67 [-7.55, 9.61] **Notes:** **Fig 3:** Associations between hospitalizations for non-indigenous and indigenous people with estimated ambient PM_{10}. **Summary of Fig 3:** Confidence intervals were wide, but indigenous people generally had stronger associations with PM_{10} than non-indigenous people. Daily PM_{10} exposure levels were estimated for the population of the city from visibility data using a previously validated models.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Hapcioglu et al. (2006, 093263) **Period of Study:** Jan 1997-Dec 2001 **Location:** Istanbul, Turkey	Hospital Admissions **Outcome (ICD-9):** COPD (ICD: NR) **Age Groups:** NR **Study Design:** Time series **N:** 1586 patients **Statistical Analyses:** Multiple stepwise regression, Pearson correlation **Covariates:** Humidity, temperature, and pressure **Season:** Summer, fall, winter, spring **Dose-response Investigated?** No **Statistical Package:** SPSS **Lags Considered:** NR	**Pollutant:** PM_{10} **Averaging Time:** 1 mo **Mean (SD):** NR **Monitoring Stations:** 1 **Copollutant:** NR **Correlation with COPD:** r = 0.28 p = 0.03 Adj for temp: r = 0.16 p = 0.23	**PM Increment:** NR **Notes:** RRs only provided for season, not PM
Reference: Hwang and Chan (2002, 023222) **Period of Study:** 1998 **Location:** Taiwan	Clinic visits **Outcome:** LRI 466, 480-486 (acute bronchitis, acute bronchiolitis, pneumonia) **Age Groups:** 0-14 yr, 15-64, 65+ yr **Study Design:** Cluster analysis of small study areas **N:** 50 communities **Statistical Analyses:** GLM to model temporal patterns, hierarchical model to obtain estimates across 50 communities **Covariates:** Day of week, temperature, dew point, summer/Winter **Season:** All **Dose-response Investigated?** Yes **Statistical Package:** NR **Lags Considered:** 0-2	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 58.9 µg/m^3 (14.0) **Range (Min, Max):** 33.3, 83.1 µg/m^3 **PM Component:** **Monitoring Stations:** 59 **Notes:** Number Of stations estimated from fig. **Copollutant:** NR	**PM Increment:** 10% Increase In PM_{10} (5.9 µg/m^3) Percent Change: 0-14 0.5% (-0.1, 0.8] Lag0 [-0.3, 0.3] Lag1 0.3 [0.0, 0.6] Lag2 15-64 0.6 [0.2, 0.9] Lag0 0.2 [-0.1, 0.5] Lag1 0.3 [0.0, 0.6] Lag2 65+ 0.8 [0.4, 1.1] Lag0 0.3 [-0.1, 0.6] Lag1 0.5 [0.1, 0.8] Lag2 All Ages 0.5 [0.2, N0.8] Lag0 [-0.3, 0.3] Lag1 0.3 [0.0, 0.6] Lag2
Reference: Jaffe et al. (2003, 041957) **Period of Study:** July 1991-June 1996 **Location:** Cincinnati, Cleveland, Columbus, Ohio	ED visits **Outcome (ICD10):** Asthma (493) **Age Groups:** Age 5-34 yr **Study Design:** Time-series **N:** 4,416 recipients **Statistical Analyses:** Poisson regression, GAM **Covariates:** City, day of week, wk, yr, minimum temperature, dispersion parameter **Season:** Jun-Aug only **Dose-response Investigated?** Yes **Statistical Package:** NR **Lags Considered:** 0-3 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** Cincinnati: 43.0(16.4) Cleveland: 60.8(28.4) Columbus: 37.4(16.3) **Range (Min, Max):** Cincinnati: (16,90) Cleveland: (12,183) Columbus: (7,87) **Monitoring Stations:** 3 **Copollutant (correlation):** Cincinnati: PM_{10} O_3 r = 0.42 NO_2 r = 0.36 SO_2 r = 0.31 Cleveland: PM_{10} O_3 r = 0.42 NO_2 r = 0.34 SO_2 r = 0.29 Columbus: PM_{10} O_3 r = 0.51 NO_2 r = Na SO_2 r = 0.42	**PM Increment:** 50 µg/m^3 **% Change** Asthma Cincinnati: -22%[-49,-19] Lag 3 Cleveland: 12%[0,27] Lag 2 Columbus: 32%[-6,-85] Lag 3 **Ar Estimate [Lower Ci, Upper Ci]** **Lag:** Asthma Cincinnati: PM_{10}: Nr Cleveland: PM_{10}: 1.32 Columbus: PM_{10}: 3.62 **Notes:** Dose response was investigated by assessing the relationship between odds of ed visit by quintile of PM_{10}. Results are displayed in Fig. "no consistent effects for all three cities were observed for PM_{10}." Rate ratios were also reported for each city.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Jalaludin et al. (2004, 056595) **Period of Study:** Feb-Dec 1994 **Location:** Sydney, Australia	Doctor Visits **Outcome (ICD- NR):** Respiratory symptoms (wheeze, dry cough, and wet cough), asthma medication use, and doctor visits for asthma **Age Groups:** Primary school children **Study Design:** Longitudinal cohort study **N:** 125 children **Statistical Analyses:** GEE logistic regression models **Covariates:** Temperature, humidity, daily pollen count, daily alternaria count, number of h spend outdoors, season **Season:** Fall (Feb-Apr), winter (May-Aug), spring/summer (Sep-Dec) **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 0-2 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 22.8 (13.8) **Monitoring Stations:** 4 **Copollutant (correlation):** O_3: r = 0.13 NO_2: r = 0.26 Other variables: Temp: r = 0.04 Humidity: r = -0.29 Total pollen: r = 0.04 Alternaria: r = 0.04	**PM Increment:** IQR (µg/m^3) Same day: 12.0 1-day lag: 12.02 2-day lag: 12.25 2-day avg: 11.15 5-day avg: 10.23 **OR Estimate [CI]:** Doctor Visits for Asthma Same day: 1.11 [1.04,1.19] 1-day lag: 1.10 [1.02,1.19] 2-day lag: 1.15 [1.06,1.24] 2-day avg: 1.11 [1.03,1.20] 5-day avg: 1.14 [0.98,1.31] **Prevalence of Doctor Visits for Asthma:** Quartile 1: 0.50 (mean PM = 12.4) Quartile 2: 0.38 (mean PM = 17.2) Quartile 3: 0.65 (mean PM = 23.0) Quartile 4: 0.63 (mean PM = 38.3) **Notes:** ORs and prevalence are also provided for wheeze, dry cough, wet cough, inhaled β2-agonist use, and inhaled corticosteroid use. None were statistically significant.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Johnston et al. (2007, 155882) **Period of Study:** 2000, 2004, 2005 (Apr-Nov of each yr) **Location:** Darwin, Australia	Hospital Admissions/ED visits **Outcome (ICD-10):** All respiratory conditions (J00-J99), including asthma (J45-46), COPD (J40-J44), and respiratory infections (J00-J22). **Age Groups Analyzed:** All **Study Design:** Case-crossover **N:** 2466 emergency admissions **Statistical Analyses:** Conditional logistic regression **Covariates:** Weekly influenza rates, temperature, humidity, days with rainfall >5mm, public holidays, school holiday periods (for respiratory conditions only) **Season:** Apr-Nov (dry season) **Dose-response Investigated?** No **Statistical package:** NR **Lags Considered:** 0-3 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Median:** 17.4 **IQR:** 13.6-22.3 **10-90th Percentile:** 10.3-27.7 **Range:** 1.1-70.0 **Monitoring Stations:** 1 **Copollutant (correlation):** NR	**PM Increment:** 10 $\mu g/m^3$ **OR Estimate [95% CI]: All respiratory conditions:** Lag 0: 1.08 [0.98-1.18] Lag 0 (indigenous): 1.17 [0.98-1.40] **COPD:** Lag 0: 1.21 [1.0-1.47] Lag 0 (indigenous): 1.98 [1.10-3.59] **Asthma:** Lag 0: 1.14 [0.90-1.44] **Asthma + COPD:** Lag 0: 1.19 [1.03-1.38] **Notes: Fig 1:** Adjusted OR and 95% CI for hospital admissions for all respiratory conditions per 10 $\mu g/m^3$ rise in PM_{10} for the same day and lags up to 3 days, overall and stratified by indigenous status. **Summary of Fig 1 results:** Marginally significant positive association at Lag 0 in overall study population. Larger marginally significant positive association among indigenous people. **Fig 2**: OR and 95% CI for hospital admissions for COPD. **Summary of Fig 2 results:** Marginally significant positive associations at Lag 0 and Lag 1 in overall study population and among non-indigenous people. Large, statistically significant positive association at Lag 0 for indigenous people, with smaller, non-significant positive associations at Lag 1 and Lag2. **Fig 3:** OR and 95% CI for hospital admissions for asthma. **Summary of Fig 3 results:** Positive, non-significant (sometime marginally significant) associations at Lag 0, Lag 2, and Lag 3 for overall population and indigenous status strata. **Fig 4:** OR and 95% CI for hospital admissions for respiratory infections. **Summary of Fig 4 results:** Negative associations at Lag 2 and Lag 3 in all population strata.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Kim et al. (2007, 092837) **Period of Study:** 2002 **Location:** Seoul, Korea	Ed Visits **Outcome (ICD10):** Asthma (J45), (J46) **Age Groups:** All Ages **Study Design:** Cass-Crossover **N:** 92,535 Visits **Statistical Analyses:** Conditional Logistic Regression, Relative Effect Modification (Rem) **Covariates:** Time Trend, Season, Daily Mean Temperature, Relative Humidity, Air Pressure. Sep As Modifier Of Air Pollution Asthma Visit Association. **Season:** All Year **Dose-response Investigated?** No **Statistical Package:** Nr **Lags Considered:** 0-2 days	**Pollutant:** PM_{10} **Averaging Time:** 8 h **Mean (SD):** Daily Concentration: 67.6 (39.0) µg/m^3 Relevant Exposure Term (Difference Between Concentration On Event Day And Mean Of Concentrations On Control Days): 26.0 (19.7) **Percentiles:** 50th(Median): Daily Concentration: 61.9 Relevant Exposure Term: 21.6 **Range (Min, Max):** Daily Concentration: (4.9, 302.0) Relevant Exposure Term: (0.0, 143.1) **Monitoring Stations:** 3 **Copollutant:** Nr	**PM Increment:** 47.4 µg/m^3 **Rr Estimate For Asthma (Stratified By Sep):** Individual Level Sep: Quintile 1-1.06[1.02, 1.09] Quintile 2-1.07[1.04, 1.10] Quintile 3-1.06[1.03, 1.10] Quintile 4-1.03[0.99, 1.07] Quintile 5-1.10[1.05, 1.14] Regional Level Sep: Quintile 1-1.04[0.99, 1.10] Quintile 2-1.03[1.00, 1.07] Quintile 3-1.05[1.03, 1.08] Quintile 4-1.06[1.02, 1.10] Quintile 5-1.09[1.06, 1.13] Total-1.06[1.04, 1.08], 3 D Ma **Notes:** Relative Effect Modification (Rem) Estimates Presented In Paper.
Reference: Ko et al. (2007, 091639) **Period of Study: Jan** 2000-Dec 2004 **Location:** Hong Kong, China	Ed Visits **Outcome (ICD-9):** COPD: chronic bronchitis (491), emphysema (492), chronic airway obstruction (496) **Age Groups:** All Ages **Study Design:** Time Series **N:** 15 hospitals, 119,225 admissions **Statistical Analyses:** Poisson regression, gam with stringent convergence criteria, aphea2 protocol. **Covariates:** Time trend, season, temperature, humidity, other cyclical factors, day, day of wk, holidays **Season:** All yr, interactions with season tested **Dose-response Investigated?** No **Statistical Package:** Splus 4.0 **Lags Considered:** 0-5 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 50.1(23.9) µg/m^3 **Percentiles**: 25th: 31.9 50th(Median): 44.5 75th: 64.1 **Range (Min, Max):** (13.6, 172.2) **Monitoring Stations:** 14 Stations **Copollutant (correlation):** PM_{10}: SO_2 r = 0.436 NO_2 r = 0.229 O_3 r = 0.421 $PM_{2.5}$ r = 0.952	**PM Increment:** 10 µg/m^3 **Rr Estimate** COPD: 1.003[1.000, 1.005] Lag 0 1.005[1.002, 1.007] Lag 1 1.010[1.007, 1.012] Lag 2 1.011[1.008, 1.013] Lag 3 1.008[1.006, 1.011] Lag 4 1.007[1.004, 1.009] Lag 5 1.005[1.002, 1.008] Lag 0-1 1.011[1.008, 1.014] Lag 0-2 1.016[1.013, 1.019] Lag 0-3 1.020[1.017, 1.024] Lag 0-4 1.024[1.021, 1.028] Lag 0-5

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ko et al. (2007, 091639) **Period of Study:** Jan 2000–Dec 2004 **Location:** Hong Kong, China	Hospital Admission **Outcome (ICD-9):** Asthma (493) **Age Groups:** All, 0-14, 15-56, 65+ **Study Design:** Time series **N:** 69,716 admissions, 15 hospitals **Statistical Analyses:** Poisson regression, with GAM with stringent convergence criteria. **Covariates:** Time trend, season, temperature, humidity, other cyclical factors **Season:** All yr, evaluated effect of season in analysis **Dose-response Investigated?** No **Statistical Package:** SPLUS 4.0 **Lags Considered:** 0-5 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 52.5(27.1) µg/m^3 **Percentiles: 25th:** 30.9 **50th(Median):** 47.1 **75th:** 68.8 **Range (Min, Max):** (13.4, 198.9) **Monitoring Stations:** 14 stations **Copollutant (correlation):** PM_{10}: SO_2 r = 0.436 NO_2 r = 0.761 O_3 r = 0.600 $PM_{2.5}$ r = 0.956	**PM Increment:** 10.0 µg/m^3 **RR Estimate:** Asthma (Single-pollutant model): 1.006[1.003, 1.010] lag 0 1.005[1.002, 1.009] lag 1 1.005[1.002, 1.009] lag 2 1.008[1.005, 1.012] lag 3 1.006[1.002, 1.009] lag 4 1.006[0.999, 1.006] lag 5 1.008[1.004, 1.012]; lag 0-1 1.012[1.008, 1.016] lag 0-2 1.015[1.011, 1.019] lag 0-3 1.018[1.013, 1.022] lag 0-4 1.019[1.015, 1.024] lag 0-5 Asthma by age group 0-14: 1.023[1.015, 1.031] lag 0-5 14-65: 1.014[1.006, 1.022] lag 0-5 >65: 1.015[1.009, 1.022] lag 0-4 Asthma-Effect of season: 1.148[1.051, 1.245] lag 0-5
Reference: Kuo et al. (2002, 036310) **Period of Study:** 1 yr **Location:** central Taiwan	Hospital Admissions **Outcome (ICD-NR):** Asthma **Age Groups:** 13-16 yr **Study Design:** Cohort **N:** 12,926 **Statistical Analyses:** Multiple logistic regression, Pearson correlation **Covariates:** Sex, age, residential area, level of parents' education, number of cigarettes smoked by smokers in the family, incense burning, frequency of physical activity **Season:** NR **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** NR	**Pollutant:** PM_{10} **Averaging Time:** 1 h **Mean (min-max):** NR Range: (54.1-84.3) **Monitoring Stations:** 8 **Copollutant:** Values NR **Notes:** Author states that a positive correlation was found between NO_2 and PM_{10}	**PM Increment:** NR **OR Estimate:** PM_{10} <65.9 µg/m^3-referent PM_{10} >65.9 µg/m^3 Crude OR: 0.837 Adj OR: 0.947 95% CI: (0.640,1.401)
Reference: Langley-Turnbaugh et al. (2005, 093269) **Period of Study:** 2000-2001 **Location:** Portland, Bridgeton, and Presque Isle, Maine	Hospital Admissions **Outcome (ICD-9):** Asthma (493xx) **Age Groups:** 0-18 yr, 19+ yr **Study Design:** Time series **N:** NR **Statistical Analyses:** NR **Covariates:** NR **Season:** Winter, spring, summer, fall **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** NR **Notes:** Hospital admissions were used to determine seasonality of asthma admissions so that PM components from those time periods could be analyzed	**Pollutant:** PM_{10} **Averaging Time:** NR **Mean (min-max):** NR **Monitoring Stations:** NR **Copollutant:** NR	**PM Increment:** NR **RR Estimate [CI]:** NR **Notes:** Portland filters contained more PM in the winter (Jan) and Bridgeton filters contained more PM in the spring (May) study analyzed metal components of PM_{10} (Mn, Cu, Pb, As, V, Ni, Al) Clinical data shows a strong peak in fall and weaker peaks in Jan and May for asthma admissions

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Lee et al. (2002, 034826) **Period of Study:** Dec 1997-Dec 1999 **Location:** Seoul, Korea	Hospital Admissions **Outcome (ICD10):** Asthma, J45, J46, **Age Groups:** Children <15 yr **Study Design:** Time-Series **N:** 822 days, 6,436 admissions **Statistical Analyses:** Poisson regression, GAM, LOESS smoothers. **Covariates:** Days of the week, temperature, humidity **Season:** All **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 0-5, 0-1 ma for 1-2, 2-3, and 3-4 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 64.0 (31.8) µg/m^3 **Percentiles: 25th:** 40.5 µg/m^3 **50th(Median):** 59.1 µg/m^3 **75th:** 80.9 µg/m^3 **Range (Min, Max):** NR **Monitoring Stations:** 27 **Notes: Copollutant (correlation):** PM_{10}-SO_2: 0.585 PM_{10}-NO_2: 0.738 PM_{10}-O_3: 0.106 PM_{10}-CO: 0.598	**PM Increment:** IQR: 40.4 µg/m^3 **RR Estimate:** Single Pollutant: 1.07 (1.04, 1.11) lag 1 Two pollutant models: +SO_2: 1.05 (1.01, 1.09) lag 1 +NO_2: 1.03 (0.99, 1.07) lag 1 +O_3: 1.06 (1.03, 1.10) lag 1 +CO: 1.04 (1.00, 1.08) lag 1 Three pollutant models: +O_3 + CO: 1.02 (0.98, 1.06), lag 1 Four pollutant models: +O_3 + CO +SO_2: 1.02 (0.98, 1.06), lag 1 Five pollutant model: 1.016 (0.975, 1.059) lag 1 **Notes:** Investigated the association between outdoor air pollution and asthma attacks in children <15 yr.
Reference: Lee et al. (2006, 090176) **Period of Study:** Jan 1997-Dec 2002 **Location:** Hong Kong, China	**Hospital Admission** **Outcome:** Asthma (493) **Age Groups:** <18 yr **Study Design**: Time series **N:** 26,663 asthma admissions for asthma and 5821 admissions for influenza **Statistical Analyses:** Poisson regression, GAM **Covariates:** Temperature, atmospheric pressure, relative humidity **Season:** All **Dose-response Investigated?** No **Statistical Package:** SAS 8.02 **Lags Considered:** 0-5 **Notes:** Controls were admissions for influenza ICD9 487	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 56.1 (24.2) **Percentiles: 25th:** 37.3 50th(Median): 51.1 75th: 70.7 **Monitoring Stations:** 10 **Notes: Copollutant (correlation):** PM_{10}-$PM_{2.5}$: 0.90 PM_{10}-SO_2: 0.39 PM_{10}-NO_2: 0.80 PM_{10}-O_3: 0.60	**PM Increment:** IQr = 33.4 **Percent Increase:** Single pollutant model: 4.97 [2.96, 7.03], lag 0 5.71 [3.78, 7.68], lag 1 6.40 [4.51, 8.32], lag 2 7.25 [5.38, 9.16], lag 3 7.45 [5.58, 9.35], lag 4 5.96 [4.11, 7.85], lag 5 Multipollutant model (SO_2, CO, NO_2, O_3) 3.67 [1.52,5.86] lag4
Reference: Lin et al. (2005, 087828) **Period of Study:** 1998-2001 **Location:** Toronto, North York, East York, Etobicoke, Scarborough, and York (Canada)	Hospital Admissions **Outcome (ICD-9):** Respiratory infections including laryngitis, tracheitis, bronchitis, bronchiolitis, pneumonia, and influenza (464, 466, 480-487) **Age Groups:** 0-14 yr **Study Design:** Bidirectional case-crossover **N:** 6782 respiratory infection hospitalizations **Statistical Analyses:** Conditional logistic regression (Cox proportional hazards model) **Covariates:** Daily mean temp and dew point temp **Season:** NR **Dose-response Investigated?** No **Statistical Package:** SAS 8.2 PHREG procedure **Lags Considered:** 1-7 day avg	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (min-max):** 20.41 (4.00-73.00) SD = 10.14 **Monitoring Stations:** 4 **Copollutant (correlation):** $PM_{2.5}$: r = 0.87 $PM_{10-2.5}$: r = 0.76 CO: r = 0.10 SO_2: r = 0.48 NO_2: r = 0.54 O_3: r = 0.54	**PM Increment:** 12.5 µg/m^3 **OR Estimate [CI]:** Adjusted for weather 4-day avg: 1.22 [1.10,1.34] 6-day avg: 1.25 [1.11,1.40] Adj for weather and other gaseous pollutants 4-day avg: 1.14 [0.99,1.32] 6-day avg: 1.20 [1.01,1.42] **Notes:** OR's were also categorized into "Boys" and "Girls," yielding similar results

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Lin et al, (2008, 126812) **Period of Study:** 1991-2001 **Location:** New York State, U.S.	**Outcome:** Respiratory hospital admissions (ICD-9 466, 490-493, 496 **Study Design:** Time-series **Covariates:** Demographic characteristics, PM_{10}, meteorological conditions, day of the week, seasonality, long term trends and different lag periods **Statistical Analysis:** GAM and case-crossover design at the regional level and Bayesian hierarchical model at the state level **Age Groups:** Children 0-17 yr	**Pollutant:** O_3 (PM_{10} is secondary) **Averaging Time:** 24 h **Mean (SD) Unit:** 19.56 (10.92) µg/m^3 **Range (Min, Max):** 1.0, 90.00 **Copollutant (correlation):** Given in Fig 3	All PM_{10} results are given in Fig 3
Reference: Lin et al. (2002, 026067) **Period of Study:** Jan 1981-Dec 1993 **Location:** Toronto	Hospital Admissions **Outcome (ICD-9):** Asthma (493) **Age Groups:** 6-12 yr **Study Design:** Uni- and bi-directional case-crossover (UCC, BCC) and time-series (TS) **N:** 7,319 asthma admissions **Statistical Analyses:** Conditional logistic regression, GAM **Covariates:** Maximum and minimum temp, avg relative humidity **Season:** Apr-Sep, Oct-Mar **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 1-7 day avg	**Pollutant:** PM_{10} **Averaging Time:** 6 days (predicted daily values) **Mean (min-max):** 30.16 (3.03-116.20) SD = 13.61 **Monitoring Stations:** 1 **Copollutant (correlation):** $PM_{2.5}$: r = 0.87 $PM_{10-2.5}$: r = 0.83 CO: r = 0.38 SO_2: r = 0.44 NO_2: r = 0.52 O_3: r = 0.44	**PM Increment:** 14.8 µg/m^3 **RR Estimate [CI]:** Adj for weather and gaseous pollutants BCC 5-day avg: 0.99 [0.90,1.09] BCC 6-day avg: 1.01 [0.90,1.12] TS 5-day avg: 1.03 [0.95,1.11] TS 6-day avg: 1.02 [0.94,1.11] Boys-adj for weather UCC 1-day avg: 1.10 [1.04,1.17] UCC 2-day avg: 1.10 [1.02,1.17] BCC 1-day avg: 1.04 [0.98,1.09] BCC 2-day avg: 1.01 [0.95,1.08] TS 1-day avg: 1.03 [0.99,1.07] TS 2-day avg: 1.01 [0.96,1.05] Girls-adj for weather UCC 1-day avg: 1.07 [0.99,1.16] UCC 2-day avg: 1.15 [1.04,1.26] BCC 1-day avg: 0.99 [0.92,1.06] BCC 2-day avg: 1.03 [0.95,1.12] TS 1-day avg: 0.99 [0.94,1.04] TS 2-day avg: 1.02 [0.96,1.08] **Notes:** The author also provides RR using UCC, BCC, and TS analysis for female and male groups for days 3-7, yielding similar results
Reference: Linares et al. (2006, 092846) **Period of Study:** Jan 1995-Dec 2000 **Location:** Madrid, Spain	**Outcome:** Respiratory system diseases 460-519, bronchitis 460-496, pneumonia 480-487 **Age Groups:** <10 yr **Study Design:** Time series **N:** ~15,000 admissions, 2192 days **Statistical Analyses:** Poisson regression, dummy variables to adjust for season and weather **Covariates:** Temperature, difference in barometric pressure, relative humidity, pollen counts, influenza epidemics **Season:** All **Dose-response Investigated?** Yes **Statistical Package:** S-Plus 2000 **Lags Considered:** 0-13	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 33.4 µg/m^3, (13.7) **Range (Min, Max):** 6, 109 µg/m^3 **Monitoring Stations:** 24 **Notes: Copollutant (correlation):** PM_{10}-SO_2: 0.532 PM_{10}-O_3: -0.289 PM_{10}-: 0.721 PM_{10}-NO_2: 0.711	**PM Increment:** 10 µg/m^3 **RR Estimate** Bronchitis 1.09 [1.01, 1.16] lag 2 **AR% Estimate** Bronchitis 7.9 [CI NR] lag2 **Notes:** Only statistically significant relative and attributable risks were presented by the authors. The authors conducted multivariate modeling using a linear term to represent PM_{10}. They also report an apparent estimated PM_{10} effect threshold of 60 µg/m^3, based on examination of a scatter plot of respiratory emergency hospital admissions and PM_{10} levels.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Luginaah, et al. (2005, 057327) **Period of Study:** Apr 1995-Dec 2000 **Location:** Windsor, Ontario, Canada	**Hospital Admission/ED:** admission **Outcome:** All respiratory: 460-519 **Age Groups: A**ll, 0-14, 15-64, and >65 **Study Design:** Times-series, bi-directional case-crossover **N:** 4214 admissions **Statistical Analyses:** Poisson regression, GAM w/ stringent convergence criteria or natural splines, conditional logistic regression **Covariates:** Age, sex Maximum & minimum temperature, change in barometric pressure from previous day **Season:** All **Dose-response Investigated?** No **Statistical Package:** S-Plus **Lags Considered:** 1-3	**Pollutant:** PM_{10} **Averaging Time:** 24-h max **Mean (SD):** 50.6 ,(35.5) **Range (Min, Max):** 9, 349 **Monitoring Stations:** 4 **Notes: Copollutant (correlation):** PM_{10}-NO_2: 0.33 PM_{10}-SO_2: 0.22 PM_{10}-CO: 0.21 PM_{10}-O_3: 0.33	**PM Increment:** Interquartile range (75th-25th) 31 µg/m^3 **RR Estimates (Time Series)** **All Age Groups Females** 0.996 [0.950, 1.044], lag 1 1.015 [0.963, 1.069], lag 2 1.022 [0.968, 1.078], lag 3 **All Age Groups Males** 1.008 [0.965, 1.054], lag 1 1.036 [0.986, 1.089], lag 2 1.027 [0.974, 1.083], lag 3 **RR Estimates (Case Crossover)** **All Age Groups Females** 1.034 [0.974, 1.098], lag 1 1.045 [0.972, 1.124], lag 2 1.054 [0.970, 1.145], lag 3 **All Age Groups Males** 0.997 [0.942, 1.056], lag 1 1.022 [0.953, 1.097], lag 2 1.008 [0.930, 1.092], lag 3 **Notes:** Results, stratified by age group available in manuscript.
Reference: Martins et al. (2002, 035059) **Period of Study:** May 1996-Sep 1998 **Location:** Sao Paulo, Brazil	Hospital Admission/ED: ER visits **Outcome (ICD10):** Chronic lower respiratory disease (CLRD) (40-47) Includes chronic bronchitis, emphysema, other COPDs, asthma, bronchiectasia **Age Groups:** >64 yr **Study Design:** Time series **N:** 712 for CLRD 1 hospital **Statistical Analyses:** Poisson regression GAM, LOESS smoothers, no mention of stringent criteria **Covariates:** Day of week, time minimum temperature, relative humidity **Season:** All **Statistical Package:** S-Plus **Lags Considered:** 2-7 3 day ma	**Pollutant:** PM_{10} **Averaging Time:** Daily **Mean (SD):** 60.0 µg/m^3, (26.3) **Range (Min, Max):** 22.8. 186.5 µg/m^3 **PM Component:** None **Monitoring Stations:** 12 **Notes: Copollutant (correlation):** PM_{10}-CO: 0.73 PM_{10}- NO_2: 0.83 PM_{10}-SO_2: 0.72 PM_{10}-O_3: 0.35	**PM Increment:** 1 µg/m^3 Regression Coefficients (SE): 0.0024 (0.0023), 6 day ma **Notes:** % Increase (SD) for ER visits per 2435 µg/m^3 (IQR) PM_{10} (lag 6 day ma) presented graphically in text.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Masjedi et al. (2003, 052100) **Period of Study:** Sep 1997-Feb 1998 **Location:** Tehran, Iran	Hospital Admissions **Outcome (ICD-9):** Acute asthma and COPD exacerbations (ICD: NR) **Age Groups:** NR **Study Design:** Time series **N:** 355 patients **Statistical Analyses:** Multiple stepwise regression, autoregression method (time series), Pearson correlation **Covariates:** NR **Season:** NR **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 3-, 7-, and 10-day mean	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (min-max):** 108.41 (14.5-506.60) SD = 59.55 **Monitoring Stations:** 3 **Copollutant:** NR	**PM Increment:** NR **Results:** Time-series analysis Asthma: β = 0.002 p = 0.32 COPD: β = 0.004 p = 0.02 Total Acute Resp Conditions: β = 0.006 p = 0.27 Correlation of 3-day mean Asthma: r = -0.21 β = -0.16 p = 0.08 Correlation of weekly mean Asthma: r = -0.27 β = -0.008 p = 0.12 Correlation of 10-day mean Asthma: r = -0.38 β = -0.066 p = 0.089
Reference: McGowan et al. (2002, 030325) **Period of Study:** Jun 1988-Dec 1998 **Location:** Christchurch, New Zealand	Hospital Admissions **Outcome (ICD-9):** Pneumonia (480-487), acute respiratory infections (460-466), chronic lung diseases (491-492, 494-496), asthma (493) **Age Groups:** <15 yr, 15-64, 65+ **Study Design:** Time series **N:** 20,938 admissions **Statistical Analyses:** GAM with log link, Linear Regression Model **Covariates:** Wind speed, relative humidity, temperature **Season:** NR **Dose-response Investigated?** No **Statistical Package:** S-PLUS **Lags Considered:** 0-6 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (min-max):** 25.17 (0-283) SD = 25.49 **Monitoring Stations:** 1 **Copollutant:** NR	**PM Increment:** 14.8 µg/m^3 (IQR) **% Increase [CI]:** Respiratory Admissions (2-day lag) 0-14 yr: 3.62 [2.34,4.90] 15-64 yr: 3.39 [1.85,4.93] 65+ yr: 2.86 [1.23,4.49] All ages: 3.37 [2.34,4.40] Overall Acute respiratory infections: 4.53 [2.82,6.24] Pneumonia/influenza: 5.32 [3.46,7.18] Chronic lung diseases: 3.95 [2.15,5.75] Asthma: 1.86 [0.48,.3.24] Total Respiratory Admissions Same day lag: 2.52 [1.49,3.55] 1-day lag: 2.56 [1.53,3.59] 2-day lag: 3.37 [2.34,4.40] 3-day lag: 3.09 [2.06,4.12] 4-day lag: 3.13 [2.10,4.16] 5-day lag: 3.21 [2.18,4.24]; 6-day lag: 3.09 [2.06,4.12]

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Medina-Ramon et al. (2006, 087721) **Period of Study:** 1986-99 **Location:** 36 U.S. Cities	**Outcome:** 490-496, except 493 (COPD), 480-487 (Pneumonia) **Age Groups:** 65 + (U.S. Medicare beneficiaries) **Study Design:** Case crossover **N:** 578,006 COPD admissions 1,384,813 Pneumonia admissions **Statistical Analyses:** Conditional logistic regression, Meta-analysis using REML random effects models **Covariates:** Mean and variance of daily summer apparent temperature index, % 65+ living in poverty,% households with central air-conditioning mortality rate for emphysema among 65+(surrogate for smoking history), % PM_{10} from traffic **Season:** Warm(May -Sepnd Cold(Oct-Apr) **Dose-response Investigated?** No **Statistical Package:** SAS STATA **Lags Considered:** 0-1 days	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 30.4 µg/m^3 (5.1) **Monitoring Stations:** at least one per city **Notes:** PM_{10} measurements made every 2, 3 or 6 days depending on the city. **Copollutant:** NR	**PM Increment:** 10 µg/m^3 **% change [Lower CI, Upper CI]** **lag:** COPD warm season 0.81(0.22,1.41) at lag 0 1.47(0.93,2.01) at lag 1 COPD cold season 0.06(-0.40,0.51) at lag 0 0.10(-0.30,0.49) at lag 1 Pneumonia warm season 0.84 (0.50,1.19) at lag 0 0.79 (0.45,1.13) at lag 1 Pneumonia cold season 0.30 (0.07,0.53) at lag 0 0.14 (-0.17,0.45) at lag 1
Reference: Meng et al., (2007, 093275) **Period of Study:** Nov 2000-Sep 2001 **Location:** Los Angeles and San Diego counties, California	**Outcome (ICD-NR):** Poorly controlled asthma defined as (1) daily or weekly asthma symptoms or (2) at least 1 ED visit or hospitalization due to asthma over the past 12 mo **Age Groups: >**18 yr **Study Design:** Time series **N:** 1609 asthma patients **Statistical Analyses:** Logistic regression **Covariates:** Age, sex, race/ethnicity, poverty level, insurance status, smoking behavior, employment, asthma medication use, and county **Season:** NR **Dose-response Investigated:** No **Statistical Package:** NR **Lags Considered:** NR	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (25-75th percentile):** NR **Monitoring Stations:** NR **Copollutant (correlation):** $PM_{2.5}$: r = 0.84 O_3: r = -0.72 NO_2: r = 0.83 CO: r = 0.42 Other variables: Traffic: r = 0.14	**PM Increment:** 10 µg/m^3 **OR Estimate [CI]:** All Adults: 1.08 [0.82,1.43] 18-64 yr: 1.14 [0.84,1.55] 65+: 0.84 [0.41,1.73] Men: 0.72 [0.42,1.21] Women: 1.38 [0.99,1.94] Exposure above 44.01 µg/m^3 (annual concentration) All Adults: 1.56 [0.96,2.52] 18-64 yr: 1.40 [0.81,2.41] 65+: 2.23 [0.60,8.27] Men: 0.80 [0.27,2.41] Women: 2.06 [1.17,3.61] **Notes:** This study focused more on the relation between poorly controlled asthma and traffic density.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Middleton et al. (2008, 156760) **Period of Study:** 1995-1998, 2000-2004 **Location:** Nicosia, Cyprus	Hospital Admissions/ED visits **Outcome (ICD-NR):** Hospital admissions for all respiratory disease (ICD-10: J00-J99). **Age Groups Analyzed:** All, also stratified by age (<15 vs.. >15 yr) **Study Design:** Time series **N: Statistical Analyses:** Generalized additive Poisson models **Covariates:** Seasonality, day of the week, long- and short-term trend, temperature, relative humidity **Season:** NR **Dose-response Investigated:** No **Statistical package:** STATA SE 9.0, and the MGCV package in the R software (R 2.2.0) **Lags Considered:** lag 0 -2 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD** **median** **5% - 95%** **range):** **Cold:** 57.6 (52.5 50.8 20.0-103.0 5.0-1370.6) **Warm:** 53.4 (50.5 30.7 32.0-77.6 18.4-933.5) **Monitoring Stations:** 2 **Copollutant (correlation):** NR Other variables:	**PM Increment:** 10 µg/m^3 , and across quartiles of increasing levels of PM_{10} **Percentage increase estimate [CI]:** **All age/sex groups (Lag 0):** All admissions: 0.85 (0.55, 1.15) Respiratory (all): 0.10 (-0.91, 1.11) Respiratory (cold months): -0.33 (-1.47, 0.82) Respiratory (warm months): 1.42 (-0.42, 3.31) CVD + RD: 0.56 (-0.21, 1.34) **Nicosia residents (Lag 0):** Respiratory (all): 0.25 (-0.84, 1.36) Respiratory (cold months): -0.22 (-1.45, 1.02) Respiratory (warm months): 1.80 (-0.22, 3.85) CVD + RD: 0.38 (-0.47, 1.23) **Males (Lag 0):** All admissions: 0.96 (0.54, 1.39) Respiratory (all): -0.06 (-1.37, 1.26) Respiratory (cold months): -0.16 (-1.76, 1.46) Respiratory (warm months): 1.10 (-1.47, 3.74) CVD + RD: 0.63 (-0.34, 1.62) **Females (Lag 0):** All admissions: 0.74 (0.31, 1.18) Respiratory (all): 0.39 (-1.21, 2.02) Respiratory (cold months): -0.26 (-2.18, 1.70) Respiratory (warm months): 3.27 (-0.00, 6.65) CVD + RD: 0.59 (-0.68, 1.87) **Aged <15 yr (Lag 0):** All admissions: 0.47 (-0.13, 1.08) Respiratory (all): -0.35 (-1.77, 1.08) Respiratory (cold months): -0.31 (-2.02, 1.42) Respiratory (warm months): -0.59 (-3.53, 2.45) **Aged >15 yr (Lag 0):** All admissions: 0.98 (0.63, 1.33) Respiratory (all): 0.59 (-0.87, 2.07) Respiratory (cold months): 0.02 (-1.76, 1.83) Respiratory (warm months): 3.89 (1.05, 6.80)
Reference: Moore et al. (2008, 196685) **Period of Study:** 1983-2000 **Location:** California's South Coast Air Basin	**Outcome:** Hospital admissions for asthma (ICD-9 493) **Study Design:** Time-series **Covariates:** Income, demographic and residential variables **Statistical Analysis:** HRMSM **Age Groups:** Children ages 0-19 yr	**Pollutant:** O_3 (PM_{10} secondary) **Averaging Time:** Quarterly **Mean (SD) Unit:** NR **Range (Min, Max):** NR **Copollutant (correlation):** 1hr O_3: 0.52 8hr O_3: 0.46 24 h NO_2: 0.53 24 h CO: 0.36 24 h SO_2: 0.13	Results given are for O_3

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Nascimento et al. (2006, 093247) **Period of Study:** May 2000-Dec 2001 **Location:** São Jose dos Campos, Brazil	Hospital Admissions **Outcome (ICD-10):** Pneumonia (J12-J18) **Age Groups:** 0-10 yr **Study Design:** Time series **N:** 1265 admissions **Statistical Analyses:** GAM, Poisson regression **Covariates:** Temperature, humidity **Season:** NR **Dose-response Investigated?** Yes **Statistical Package:** S-Plus, SPSS **Lags Considered:** 0-7 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (min-max):** 40.2 (3.4-196.6) SD = 26.9 **Monitoring Stations:** 2 **Copollutant (correlation):** SO_2: r = 0.30 O_3: r = 0.09 Other variables: Admissions: r = 0.21 Temp: r = -0.14 **Notes:** All p < 0.05	**PM Increment:** 24.7 µg/m^3 **Regression coefficients (SE):** Same day: -0.00053 (0.00125) 1-day lag: 0.00029 (0.00057) 2-day lag: 0.00089 (0.00069) 3-day lag: 0.00122 (0.00053)* 4-day lag: 0.00126 (0.00055)* 5-day lag: 0.00098 (0.00071) 6-day lag: 0.00035 (0.00056) 7-day lag: -0.00067 (0.00123) *p < 0.05 **Notes:** Percent increase over all lag days is displayed in Fig 2
Reference: Neuberger et al. (2004, 093249) **Period of Study:** 1999-2000 (1 yr period) **Location:** Vienna and Lower Austria	Hospital Admissions **Outcome (ICD-9):** Bronchitis, emphysema, asthma, bronchiectasis, extrinsic allergic alveolitis, and chronic airway obstruction (490-496) **Age Groups:** 3.0-5.9 yr 7-10 yr 65+ **Study Design:** Time series **N:** 366 days (admissions NR) **Statistical Analyses:** GAM **Covariates:** SO_2, NO, NO_2, O_3, temperature, humidity, and day of the week **Season:** NR **Dose-response Investigated?** Yes **Statistical Package:** S-Plus 2000 **Lags Considered:** 0-14 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Maximum daily mean:** Vienna: 105 Rural area: NR **Monitoring Stations:** NR **Copollutant:** NR	**PM Increment:** 10 µg/m^3 **Log Relative Rate Estimate (p-value):** Vienna Male: 2 day lag = 4.217 (0.030) Association with tidal lung function: β = -1.067 (p-value = 0.241) **Notes:** Effect parameters with significant coefficients for respiratory health included: male sex, allergy, asthma in family, and traffic for Vienna and age, allergy, asthma in family, and passive smoking for the rural area. Effect parameters with significant coefficients for log asthma score were allergy, asthma in family, and rain for Vienna and allergy, asthma in family, and passive smoking for the rural area.
Reference: Oftedal et al. (2003, 055623) **Period of Study:** 1995-2000 **Location:** Drammen, Norway	**Hospital** Admissions **Outcome:** All Respiratory (460-517) **Age Groups:** All **Study Design:** Time-series **N:** ~4,458 admissions **Statistical Analyses:** Poisson regression, GAM w/ stringent convergence criteria **Covariates:** Temperature, humidity, influenza epidemics, summer and Christmas vacation **Season:** All **Dose-response Investigated?** Yes **Statistical Package:** S-Plus **Lags Considered:** 2-3	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 16.8 µg/m^3, (10.2) 1994-1997 16.5 µg/m^3, (10.3) 1998-2000 16.6 , µg/m^3 (10.2) total period **PM Component:** Benzene, formaldehyde, toluene **Monitoring Stations:** NR **Notes: Copollutant (correlation):** Correlation between pollutants ranged from -0.47-0.78 with the exception of the VOCs studied **Notes:** Benzene, formaldehyde and toluene also evaluated	**PM Increment:** IQr = 11.04 **RR Estimate** 1.035 [0.990, 1.083] 1994-1997 0.992 [0.948, 1.037] 1998-2000 1.021 [0.990, 1.053] 1994-2000 2 Pollutant Model PM_{10} w/ benzene: 1.01 (0.978, 1.043)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Peel et al. (2005, 056305) **Period of Study:** Jan 1993-Aug 2000 **Location:** Atlanta, Georgia	ED visits **Outcome:** Asthma (493, 786.09) COPD (491, 492, 496) URI (460-466, 477) Pneumonia (480-486) **Age Groups:** All ages. Secondary analyses conducted by age group: 0-1, 2-18, >18 **Study Design:** Time series **N:** 31 hospitals **Statistical Analyses:** Poisson GEE for URI, asthma and all RD Poisson GLM for pneumonia and COPD) **Covariates:** Avg temperature and dew point, pollen counts **Season:** All (secondary analyses of warm season) **Dose-response Investigated?** Yes **Statistical Package:** SAS 8.3, S-Plus 2000 **Lags Considered:** 0-7 day , 3 day ma, 0-13 days unconstrained distributed lag	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 27.9 (12.3) µg/m^3 **Percentiles: 10th:** 13.2 **90th:** 44.7 **Monitoring Stations:** "Several" **Copollutant (correlation):** 8 h O_3: r = 0.59 1 h NO_2: r = 0.49 1 h CO: r = 0.47 1 h SO_2: r = 0.20 24-h $PM_{2.5}$: 0.84 24 h $PM_{10-2.5}$: r = 0.59 24 h UF: r = -0.13 Components: r ranged from 0.42-0.74	**PM Increment:** PM_{10}: 10 µg/m^3 RR Estimate [Lower CI, Upper CI] All Respiratory Outcomes: 1.013 (1.004-1.021), 3 day ma URI: 1.014 (1.004-1.025) , 3 day ma 1.073 (1.048-1.099) , 14-day dist. lag Asthma: 1.009 (0.996-1.022), 3 day ma 1.099 (1.065-1.135), 14-day dist. lag: Pediatric Asthma 2-18yrs): 1.016 (0.998 -1.034) Pneumonia: 1.011 (0.996-1.027) , 3 day ma 1.087 (1.044-1.132), 14-day dist. lag COPD: 1.018 (0.994-1.043), 3 day ma 1.092 (1.023-1.165), 14-day dist. lag **Notes:** RRs obtained using AQS 1993-2000, AQS 1998-2000 and ARIES data compared. Infant (0-1 y) and pediatric (2-18 y) asthma was associated more strongly with PM_{10}, $PM_{2.5}$ and OC than adult asthma.
Reference: Ren et al. (2006, 092824) **Period of Study:** Jan 1996-Dec 2001 **Location:** Brisbane, Australia	Hospital Admissions **Outcome (ICD-9):** Respiratory diseases (460-519) excluding influenza (487.0-487.8) **Age Groups:** NR **Study Design:** Time series **N:** NR **Statistical Analyses:** GAM **Covariates:** Day of week, relative humidity, influenza outbreaks **Season:** NR **Dose-response Investigated?** Yes **Statistical Package:** S-Plus **Lags Considered:** 0, 1, and 2 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (min-max):** 15.84 (2.5-60) **Monitoring Stations:** 1 **Copollutant:** NR	**PM Increment:** NR **Coefficient Estimates:** Respiratory Hospital Admissions Same day: -0.004296 1-day lag: -0.002474 2-day lag: -0.004229 *all statistically significant Respiratory Emergency Visits Same day: -0.000887 1-day lag: -0.004209 2-day lag: -0.003440 **Notes:** Relative risks were provided in graphical form (Fig 3)
Reference: Sauerzapf et al. (2009, 180082) **Period of Study:** Mar 2006-Mar 2007 **Location:** Norfolk, UK	**Outcome:** COPD **Study Design:** Case-Crossover **Covariates:** Environmental factors and Influenza **Statistical Analysis:** Logistic regression **Statistical Package:** SPSS 14 **Age Groups:** >18 yr **N:** 1050 adult COPD admissions	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD) Unit:** Control: 19.87 (8.51) µg/m^3 Case: 20.47 (9.27) µg/m^3 **Range (Min, Max):** Control: 9.77-34.27 Case: 10.04-35.03 **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **Odds Ratio (95% CI)** Lag 0-7, unadjusted: 1.079 (0.980-1.188) Lag 0-8, adjusted: 1.101 (0.988-1.226) Lag 1-8, unadjusted: 1.056 (0.961-1.161) Lag 1-8, adjusted: 1.054 (0.949-1.170)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Sinclair and Tolsma (2004, 088696) **Period of Study:** 25 Months **Location:** Atlanta, Georgia	**Outpatient Visits** **Outcome:** Asthma (493) URI (460, 461, 462, 463, 464, 465, 466, 477) LRI (466.1, 480, 481, 482, 483, 484, 485, 486). **Age Groups:** < = 18 yr, 18+ yr (asthma) All ages (URI//LRI) **Study Design:** Times series **N:** 25 mo 260,000-275,000 health plan members (Aug 1998-Aug 2000) **Statistical Analyses:** Poisson GLM **Covariates:** Season, Day of week, Federal Holidays, Study Months **Season:** NR **Dose-response Investigated?:** No **Statistical Package:** SAS **Lags Considered:** Three 3-day ma (0-2, 2-5, 6-8)	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** PM_{10} mass-29.03 µg/m^3 (11.61) **Monitoring Stations:** 1 **Notes: Copollutant:** NR	**PM Increment:** 11.61 (1 SD) **RR Estimate [Lower CI, Upper CI]** **lag:** Child Asthma: 1.049 (S), lag 3-5 day LRI: 1.074 (S), 3-5 day lag **Notes:** Numerical findings for significant results only presented in manuscript. Results for all lags presented graphically for each outcome (asthma, URI, and LRI).
Reference: Slaughter et al. (2005, 073854) **Period of Study:** Jan 1995-Jun 2001 **Location:** Spokane, WA	Hospital Admissions and ED visits **Outcome:** All respiratory (460-519) Asthma (493) COPD (491,492, 494,496) Pneumonia (480-487) Acute URI not including colds and sinusitis (464, 466, 490) **Age Groups:** All, 15+ yr for COPD **Study Design:** Time series **N:** 2373 visit records **Statistical Analyses:** Poisson regression, GLM with natural splines. For comparison also used GAM with smoothing splines and default convergence criteria. **Covariates:** Season, temperature, relative humidity, day of week **Season:** All **Dose-response Investigated?:** No **Statistical Package:** SAS, SPLUS **Lags Considered:** 1 -3 day	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Range (90% of concentrations):** 7.9-41.9 µg/m^3 **Monitoring Stations:** 1 **Notes: Copollutant (correlation):** PM_{10} PM1 r = 0.50 $PM_{2.5}$ r = 0.62 $PM_{10-2.5}$ r = 0.94 CO r = 0.32 Temperature r = 0.11	**PM Increment:** 25 µg/m^3 **RR Estimate [Lower CI, Upper CI]** **lag:** **ER visits --** PM_{10} All Respiratory Lag 1: 1.01 [0.99, 1.04] Lag 2: 1.01 [0.98, 1.03] Lag 3: 1.02 [0.99, 1.04] Acute Asthma Lag 1: 1.03 [0.98, 1.07] Lag 2: 1.01 [0.96, 1.05] Lag 3: 1.00 [0.95, 1.04] COPD (adult) Lag 1: 1.00 [0.93, 1.07] Lag 2: 0.99 [0.92, 1.06] Lag 3: 1.02 [0.95, 1.08] **Hospital Admissions --** PM_{10} All Respiratory Lag 1: 0.99 [0.95, 1.02] Lag 2: 0.99 [0.96, 1.02] Lag 3: 1.00 [0.97, 1.03] Asthma Lag 1: 1.03 [0.95, 1.12] Lag 2: 1.01 [0.94, 1.10] Lag 3: 1.00 [0.92, 1.09] COPD (adult) Lag 1: 0.98 [0.90, 1.07] Lag 2: 1.03 [0.96, 1.11] Lag 3: 1.02 [0.94, 1.09]

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Sun et al. (2006, 090768) **Period of Study:** Jan 2004-Dec 2004 **Location:** Taichung, Taiwan (Central Taiwan)	ED visits **Outcome:** Asthma (493.xx) **Age Groups:** <55, <16, 16-55 yr **Study Design:** Cross-sectional **N:** NR All diagnoses for all patients at 4 medical centers **Statistical Analyses:** Pearson's correlations, multiple correlation coefficients from regression analyses. **Covariates:** Only copollutants considered **Dose-response Investigated?** No **Statistical Package:** SPSS **Lags Considered:** None	**Pollutant:** PM_{10} **Averaging Time:** Monthly avg for 2004 **Mean (SD):** ~ 60.3 µg/m^3 (NR) (estimated from Fig)* **Range (Min, Max):** (~35, 80) **Monitoring Stations:** 11 **Copollutant:** NR	Children ED Visits r = 0.626 P = 0.015 Adult ED Visits r = 0.384 P = 0.109
Reference: Szyszkowicz (2007, 092829) **Period of Study:** Jan 1992-Mar 2002 **Location:** Edmonton, Canada	**Outcome:** ED visits for asthma (ICD-(493) **Study Design:** Time-series **Covariates:** Temperature, relative humidity **Statistical Analysis:** Poisson regression **Age Groups:** All	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD) Unit:** 22.6 (13.1) µg/m^3 **Median, IQR:** 19.4, 15.0 **Copollutant (correlation):** NR	**Increment:** IQR **Percent Relative Risk (95% CI)** *Only statistically significant results are presented in the paper* No lag, ≥ 10 yr Apr-Sep, All: 3.7 (1.5-6.0) Apr-Sep, Female: 4.5 (1.8-7.3) Apr-Sep, Male: 3.3 (0.1-6.7) 2 day lag, < 10 yr Year round, All: 2.7 (0.1-5.4) Apr-Sep, All: 6.3 (2.6-10.2) Apr-Sep, Male: 7.4 (3.1-11.9) 2 day lag, ≥ 10 yr Apr-Sep, All: 2.4 (0.1-4.7) Apr-Sep, Female: 3.9 (1.1-6.7)
Reference: Tecer et al, (2008, 180030) **Period of Study:** Dec 2004-Oct 2005 **Location:** Zonguldak, Turkey	**Outcome:** ED visits for respiratory problems (ICD-9 470-478, 493) **Study Design:** Bidirectional Case-crossover **Covariates:** Daily meteorological parameters **Statistical Analysis:** Conditional logistic regression **Statistical Package:** Stata **Age Groups:** 0-14 yr	**Pollutant:** PM_{10} **Averaging Time:** NR **Mean, Unit:** 53.3 µg/m^3 **Range (Min, Max):** 12-237.5 **Copollutant (correlation):** $PM_{2.5}/PM_{10}$ Mean: 0.56 Range: 0.17-0.88	**Increment:** 10 µg/m^3 **Odds Ratio (95% CI)** Asthma Lag 0: 1.14 (1.03-1.26) Lag 1: 0.92 (0.83-1.02) Lag 2: 0.92 (0.81-1.03) Lag 3: 1.01 (0.92-1.11) Lag 4: 1.16 (1.06-1.26) Allergic Rhinitis with Asthma Lag 0: 1.07 (1.01-1.13) Lag 1: 0.96 (0.91-1.02) Lag 2: 0.93 (0.88-0.99) Lag 3: 0.96 (0.90-1.02) Lag 4: 1.08 (1.02-1.14) Allergic Rhinitis Lag 0: 1.06 (0.99-1.13) Lag 1: 1.08 (1.01-1.16) Lag 2: 0.92 (0.87-0.99) Lag 3: 0.97 (0.92-1.03) Lag 4: 1.09 (1.03-1.16) Upper Respiratory Disease Lag 0: 0.88 (0.68-1.14) Lag 1: 1.17 (0.91-1.51) Lag 2: 1.00 (0.76-1.31) Lag 3: 0.95 (0.76-1.19) Lag 4: 1.15 (0.97-1.35) Lower Respiratory Disease Lag 0: 1.01 (0.86-1.19) Lag 1: 1.04 (0.88-1.23) Lag 2: 1.04 (0.92-1.18) Lag 3: 1.23 (1.07-1.41) Lag 4: 0.99 (0.90-1.08)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Tolbert et al. (2007, 090316) **Period of Study:** 1993-2004 **Location:** Atlanta Metropolitan area, Georgia	Hospital Admissions/ED visits **Outcome (ICD-9):** **Combined RD group, including:** Asthma (493, 786.07, 786.09), COPD (491, 492, 496), URI (460-465, 460.0, 477), pneumonia (480-486), and bronchiolitis (466.1, 466.11, and 466.19)) **Age Groups Analyzed:** All **Study Design:** Time series **N:** 10,234,490 ER visits (283,360 and 1,072,429 visits included in the CVD and RD groups, respectively) **Statistical Analyses:** Poisson generalized linear models **Covariates:** Long-term temporal trends, season (for RD outcome), temperature, dew point, days of week, federal holidays, hospital entry and exit **Season:** All **Dose-response Investigated:** No **Statistical package:** SAS version 9.1 **Lags Considered:** 3-day ma(lag 0 -2)	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (median** **IQR, range, 10th-90th percentiles):** 26.6 (24.8 17.5-33.8 0.5-98.4 12.3-42.8) **Monitoring Stations:** NR **Copollutant (correlation):** O_3: r = 0.59 NO_2: r = 0.53 CO: r = 0.51 SO_2: r = 0.21 Coarse PM: r = 0.67 $PM_{2.5}$: r = 0.84 $PM_{2.5}$ SO_4: r = 0.69 $PM_{2.5}$ EC: r = 0.61 $PM_{2.5}$ OC: r = 0.65 $PM_{2.5}$ TC: r = 0.67 $PM_{2.5}$ water-sol metals: r = 0.73 OHC: r = 0.53	**PM Increment:** 16.30 µg/m^3 (IQR) **Risk ratio [95% CI]:** **Single pollutant models:** RD: 1.015 (1.006-1.024) **Notes:** Results of selected multi-pollutant models for respiratory disease are presented in Fig 2. **Fig 2:** PM_{10} adjusted for CO, O_3, NO_2, or NO_2/O_3 (nonwinter months only) **Summary of results:** PM_{10} remained predictive of RD in non-winter months after adjustment for pollutants.
Reference: Tsai et al. (2006, 089768) **Period of Study:** 1996-2003 **Location:** Kaohsiung City, Taiwan	**Outcome:** Asthma (493) **Age Groups:** All (universal health care covers >96% of the population) **Study Design:** Case crossover **N:** 17,682 admissions 63 hospitals **Statistical Analyses:** Conditional Logistic Regression **Covariates:** Temperature, humidity **Season:** Warm and cool seasons **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 0-2 day cumulative	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 76.62 µg/m^3 (NR) **Percentiles:** 25th: 41.73 50th(Median): 74.40 75th: 104.01 **Range (Min, Max):** (16.70, 232.00) **Monitoring Stations:** 6 **Copollutant:** NR	**PM Increment:** 62.28 µg/m^3 **OR Estimate [Lower CI, Upper CI]** **lag:** **Single-pollutant model, 0-2 day cumulative lag** ≥ 25oC: 1.302 [1.155, 1.467] <25oC: 1.556 [1.398, 1.371] **Two-pollutant models, 0-2 day cumulative lag** PM_{10} w/ SO_2 ≥ 25oC: 1.305 [1.156, 1.473] <25oC: 1.540 [1.374, 1.727] PM_{10} w/ O_3 ≥ 25oC: 0.985 [0.842, 1.152] <25oC: 1.581 [1.402, 1.783] PM_{10} w/ NO_2 ≥ 25oC: 1.237 [1.052, 1.455] <25oC: 1.009 [0.875, 1.163] PM_{10} w/ CO ≥ 25oC: 1.156 [1.012, 1.320] <25oC: 1.300 [1.134, 1.490]

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ulirsch et al. (2007, 091332) **Period of Study:** Nov 1994-Mar 2000 **Location:** Pocatello, Idaho Chubbuck, Idaho	**Outcome:** Respiratory Disease (460-499, 509-519) Reactive Airway Disease (786.09) **Age Groups:** All age groups **Study Design:** Time series **N:** 39,347 visits (TS1) 29,513 visits (TS2) **Statistical Analyses:** Poisson regression, GLM. Sensitivity Analyses **Covariates:** Time, Temperature, Relative Humidity Influenza **Season:** Warm/Cool **Dose-response Investigated?** No **Statistical Package:** S-Plus **Lags Considered:** 0-4 day lags **Notes:** Time series (TS) 1 includes HA, ED and urgent care visits. TS 2 includes family practice data available after 1997	**Pollutant:** PM_{10} **Averaging Time:** NR **Mean (SD):** TS1: 24.2 µg/m^3 (NR) 10th: 10.5 90th: 40.7 TS2: 23.2 10th: 10.0 90th: 37.4 **Range (Min, Max):** TS1: (3.0, 183.0) TS2: (3.0, 183.0) **Monitoring Stations:** 4 **Notes: Copollutant (correlation):** PM_{10} w/ NO_2: r = 0.47. PM_{10} with other copollutants weakly correlated.	**PM Increment:** Single Pollutant Models, TS1: 24.4 µg/m^3 Single Pollutant Models: TS2: 23.2 µg/m^3 Multipollutant Models: TS1/TS2: 50 µg/m^3 **Mean Percentage Change, lag 0** TS 1: Single Pollutant All-age (all yr): 4.0 [1.4,6.7] 18-64: 3.4 [0.2, 6.7] 0-17: 4.3 [-0.1, 8.9] 65+: 5.6 [-1.4, 13.1] 0-17/65+: 5.5 [1.4, 9.6] All age (Cool season): 4.3 [1.3, 7.5] All age (Warm season): 6.7 [-0.8, 14.8] TS2: Single Pollutant All-age: 3.3 [0.3, 6.3] 18-64: 3.3 [-0.4, 7.0] 0-17: 5.0 [0.1, 10.1] 65+: 6.9 [-0.4, 14.7] Multipollutant (PM_{10} + SO_2) All-age (all yr): TS1 10.8 TS2 17.5 18-64: TS1 8.0 TS2 9.1 0-17: TS1 10.8 TS2 32.7 65+: TS1 8.7 TS2 31.3 0-17/65+: TS1 14.2 TS2 25.3 All age (Cool season) TS1 11.9 Multipollutant (PM_{10} + NO_2) All-age (all yr) TS1: TS2 16.3 18-64: TS1 9.3 TS2 17.3 0-17: TS1 4.6 TS2 18.7 65+: TS1 12.4 TS2 32.7 0-17/65+: TS1 9.5 32.7 All age (Cool season): TS1 11.1 TS2 16.8 **Notes:** Results from multipollutant model with PM_{10}, SO_2 and NO_2 also available.
Reference: Vegni and Ros (2004, 087448) **Period of Study:** Sep 2001-Sep 2002 **Location:** Milan area, Italy	Hospital Admissions **Outcome (ICD-9):** Respiratory, non-infectious admissions (ICD: NR) **Age Groups:** NR **Study Design:** Time series **N:** 9881 admissions **Statistical Analyses:** Poisson regression **Covariates:** Temperature, wind velocity, relative humidity, week day, holidays **Season:** Spring, summer, fall, winter **Dose-response Investigated?** No **Statistical Package:** STATA v. 5 **Lags Considered:** 0, 1, and 2 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (5th-95th percentile):** Overall: 41.5 (13-98) SD = 28.2 Spring: 29.0 (10-51) SD = 12.6 Summer: 24.8 (10-40) SD = 9.9 Fall: 51.8 (21-114) SD = 27.1 Winter: 64.1 (20-135) SD = 35.7 **Monitoring Stations:** 1 **Copollutant:** NR	**PM Increment:** Increase from 5th-95th percentile Spring: 85 µg/m^3 summer: 30 µg/m^3 Fall: 93 µg/m^3 Winter: 115 µg/m^3 **RR Estimate [CI]:** Overall: 1.10 [0.83,1.46] Adjusted: 0.97 [0.67,1.41] **Notes:** 1-day and 2-day lags show similar results, with no association between PM_{10} and daily hospital admissions

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Vigotti et al. (2007, 090711) **Period of Study: Jan** 2000-Dec 2000 **Location:** Pisa, Italy	**ED Visits** **Outcome:** Asthmatic attack (493), dry cough (468), acute bronchitis (466) **Age Groups:** <10 yr; 65+ yr **Study Design:** Time series **N:** 966 Emergency room visits **Statistical Analyses:** Poisson regression, GAM, LOESS smoothers, stringent criteria **Covariates:** Temperature, humidity, relative humidity, day of study, rainfall, influenza, day of-the-wk, holidays, time trend **Season:** All yr **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 0-5 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 35.4 (15.8) µg/m^3 **Percentiles:** 25th: NR 50th(Median): 31.6 75th: NR **Range (Min, Max):** (9.5, 100.1) **Monitoring Stations:** 2 **Copollutant (correlation):** PM_{10}: NO_2 r = 0.58 CO r = 0.70	**PM Increment:** 10 µg/m^3 **RR Estimate [Lower CI, Upper CI]** **lag:** <10 y: 10%[2.3, 18.2] lag 1 65+: 8.5% [1.5, 16.1] lag 2
Reference: Xirasagar et al. (2006, 093267) **Period of Study:** 1998-2001 **Location:** Taiwan	**Hospital Admission/ED:** **Outcome:** Asthma or Asthmatic Bronchitis (493) **Age Groups:** <2 yr old, 2~5 yr old, 6~14 yr old **Study Design:** **N:** 27, 275 pediatric hospitalizations **Statistical Analyses:** ARIMA Modeling Spearman's Correlations **Covariates:** Season, ambient temp., rel. humidity, atmospheric pressure, rainfall, h of sunshine **Season:** Spring: Feb-Apr Summer: May-Jul Fall: Aug-Oct Winter: Nov-Jan **Dose-response Investigated?** No **Statistical Package:** EViews 4 **Lags Considered:** NR	**Pollutant:** PM_{10} **Averaging Time:** Monthly means **Mean (SD):** 24.4 µg/m^3 (NR) **Percentiles:** NR **Range (Min, Max):** NR **PM Component:** NR **Monitoring Stations:** 44 air quality monitoring banks. 23 weather observatories **Notes: Copollutant (correlation):** <2 yr old: r = 0.315 2~5 yr old: r = 0.589 6~14 yr old: r = 0.493	**PM Increment:** NR **RR Estimate [Lower CI, Upper CI]** **lag:** NR **AR Estimate [Lower CI, Upper CI]** **lag:** NR **Notes:** Plot of monthly asthma admission rates per 100,000 population by age group Plot of mean monthly concentration trends of criteria air pollutants Mean monthly trends of climatic factors **Other Outcomes Assessed?** NR **Other Exposures Assessed?** Seasonality

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Wong et al., (2002, 023232) **Period of Study:** 1995-1997 (Hong Kong) and 1992-1994 (London) **Location:** Hong Kong and London	Hospital Admissions **Outcome (ICD- NR):** Asthma (493) for ages 15-64 and respiratory disease (460-519) for ages 65+ **Age Groups:** 15-64, 65+ **Study Design:** Time series **N:** NR **Statistical Analyses:** Poisson regression, GAM **Covariates:** Temperature, humidity, and influenza **Season:** Warm (Apr-Sep) and cool (Oct-Mar) **Dose-response Investigated?** Yes **Statistical Package:** S-Plus **Lags Considered:** 0-3 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (min-max):** Hong Kong: 51.8 (14.1-163.8) SD = 25.0 London: 28.5 (6.8-99.8) SD = 13.7 **Monitoring Stations:** NR **Copollutant (correlation):** Hong Kong NO_2: r = 0.82 SO_2: r = 0.30 O_3: r = 0.54 London NO_2: r = 0.68 SO_2: r = 0.64 O_3: r = 0.17 **Other variables:** Hong Kong Temp: r = -0.42 Humidity: r = -0.53 London Temp: r = 0.02 Humidity: r = -0.05	**PM Increment:** 10 µg/m^3 **ER Estimate [CI]:** Single-pollutant excess risk (mean lag 0-1 day) Asthma-Hong Kong: -1.1 [-2.4,0.1] Asthma-London: 1.4 [-0.1,3.0] Respiratory Disease-Hong Kong: 1.0 [0.5,1.5] Respiratory Disease-London: 0.4 [-0.3,1.2] Warm season Asthma-Hong Kong: -1.0 [-2.8, 0.8] Asthma-London: 0.6 [-1.9,3.1] Respiratory Disease-Hong Kong: 0.8 [0.1,1.4] Respiratory Disease-London: 1.8 [0.5,3.1] Cool season Asthma-Hong Kong: -1.2 [-2.8,0.4] Asthma-London: 1.6 [-0.3,3.6] Respiratory Disease-Hong Kong: 1.2 [0.6,1.9] Respiratory Disease-London: -0.5 [-1.5,0.5] **Notes:** RRs are shown graphically in Fig 1 and 2. Exposure response curves are provided in Fig 5 of the article
Reference: Wong et al. (2006, 093266) **Period of Study:** 2000-2002 **Location:** Hong Kong (8 districts)	General Practitioner Visits **Outcome (ICPC-2):** Respiratory diseases/symptoms: upper respiratory tract infections (URTI), lower respiratory infections, influenza, asthma, COPD, allergic rhinitis, cough, and other respiratory diseases **Age Groups:** All ages **Study Design:** Time series **N:** 269,579 visits **Statistical Analyses:** GAM, Poisson regression **Covariates:** Season, day of the week, climate **Season:** NR **Dose-response Investigated?** No **Statistical Package:** S-Plus **Lags Considered:** 0-3 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (min-max):** Ranged from 43.4-56.9 (dependent on location) **Monitoring Stations:** 1 per district **Copollutant (correlation):** $PM_{2.5}$: r = 0.94 O_3: r = 0.40 SO_2: r = 0.28	**PM Increment:** 10 µg/m^3 **RR Estimate [CI]:** Overall URTI 1.020 [1.016,1.025] Overall Non-UTRI 1.025 [1.018,1.032] **Notes:** RRs are also reported for each individual general practitioner yielding similar results

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Yang et al. (2007, 092847) **Period of Study:** 1996-2003 **Location:** Taipei, Taiwan	**Hospital Admission/ED:** **Outcome:** Asthma (493) **Age Groups:** All ages **Study Design:** Case-crossover **N:** 25,602 asthma hospital admissions **Statistical Analyses:** NR **Covariates:** Temperature, humidity, day of-the-wk, seasonality, long term trends **Season:** All yr **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 0-2	**Pollutant:** PM_{10} **Averaging Time:** NR **Mean (SD):** 48.99 µg/m^3 **Percentiles: 25th:** 32.64 **50th(Median):** 44.13 **75th:** 59.05 **Range (Min, Max):** (14.44, 234.91) **PM Component:** NR **Monitoring Stations:** 6 Stations **Notes: Copollutant:** NR	**PM Increment:** 26.41 µg/m^3 **OR Estimate [Lower CI, Upper CI] lag:** **Asthma** Single-Pollutant Model: Temperature >25° C: 1.046[0.971, 1.128] Temperature <25° C: 1.048[1.011, 1.251] Two-Pollutant Model: Adjusted for SO_2: >25° C-1.006[0.920, 1.099] <25° C-1.088[1.040, 1.138] Adjusted for NO_2: >25° C-0.800[0.717, 0.892] <25° C-0.982[0.937, 1.029] Adjusted for CO: >25° C-0.920[0.844, 1.002] <25° C-1.029[0.984, 1.076] Adjusted for O_3: >25° C-1.038[0.950, 1.134] <25° C-1.042[1.004, 1.081] **AR Estimate [Lower CI, Upper CI] lag:** NR **Notes: Other Outcomes Assessed?** NR **Other Exposures Assessed?** SO_2, NO_2, CO, O_3
Reference: Yang et al. (2007, 092847) **Period of Study:** 1996-2003 **Location:** Taipei, Taiwan	Hospital Admission **Outcome:** COPD (490-192), (494), (496) **Age Groups:** All ages **Study Design:** Case-crossover **N:** 46,491COPD admissions, 47 hospitals **Statistical Analyses:** Conditional logistic regression **Covariates:** Weather, day of-the-wk, seasonality, long term trends **Season: Warm/Cool** **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 0-2 cumulative	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 48.99 µg/m^3 **25th:** 32.64 **50th(Median):** 44.13 **75th:** 59.05 **Range (Min, Max):** (14.44, 48.99) **Monitoring Stations:** 6 Stations **Notes: Copollutant:** NR	**PM Increment:** 26.41 µg/m^3 **OR Estimate [Lower CI, Upper CI]** Single-Pollutant Model (0-2 day cum lag): Temperature >20° C: 1.133[1.098, 1.168] Temperature <20° C: 1.035[0.994, 1.077] Two-Pollutant Model: PM_{10} w/ SO_2: >20° C-1.180[1.139, 1.223] <20° C-1.004[0.954, 1.057] PM_{10} w/ NO_2: >20° C-1.013[0.973, 1.055] <20° C-1.074[1.022, 1.129] PM_{10} w/ CO: >20° C-1.061[1.023, 1.100] <20° C-1.067[1.016, 1.120] PM_{10} w/ O_3: >20° C-1.097[1.062, 1.133] <20° C-1.036[0.996, 1.079]

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Yang et al. (2004, 087488) **Period of Study:** Jun 1995-Mar 1999 **Location:** Vancouver area, British Columbia	Hospital Admissions **Outcome (ICD-9):** Respiratory diseases (460-519), pneumonia only (480-486), asthma only (493) **Age Groups:** 0-3 yr **Study Design:** Case control, bidirectional case-crossover (BCC), and time series (TS) **N:** 1610 cases **Statistical Analyses:** Chi-square test, Logistic regression, GAM (time-series), GLM with parametric natural cubic splines **Covariates:** Gender, socioeconomic status, weekday, season, study yr, influenza epidemic month **Season:** Spring, summer, fall, winter **Dose-response Investigated?** No **Statistical Package:** SAS (Case control and BCC), S-Plus (TS) **Lags Considered:** 0-7 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (min-max):** 13.3 (3.8-52.2) SD = 6.1 **Monitoring Stations:** NR (data obtained from Greater Vancouver Regional District Air Quality Dept) **Copollutant (correlation):** $PM_{2.5}$: r = 0.83 $PM_{10-2.5}$: r = 0.83 CO: r = 0.46 O_3: r = -0.08 NO_2: r = 0.54 SO_2: r = 0.61	**PM Increment:** 7.9 µg/m^3 (IQR) **OR Estimate [CI]:** Values NR **Notes:** Author states that ORs for PM_{10} increased with lag time up to 3 days for both single and multiple-pollutant models.

[1]All units expressed in µg/m^3 unless otherwise specified.

Table E-13. Short-term exposure-respiratory-ED/HA-$PM_{10-2.5}$.

Reference	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Chen et al. (2005, 087555) **Period of Study:** Jun 1995-Mar 1999 **Location:** Vancouver area, BC	Hospital Admissions **Outcome (ICD-9):** Acute respiratory infections (460-466), upper respiratory tract infections (470-478), pneumonia and influenza (480-487), COPD and allied conditions (490-496), other respiratory diseases (500-519) **Age Groups:** >65 yr **Study Design:** Time series **N:** 12,869 **Statistical Analyses:** GLM **Covariates:** Temp and relative humidity **Season:** NR **Dose-response Investigated?** No **Statistical Package:** S-Plus **Lags Considered:** 1, 2, 3, 4, 5, 6, and 7-day avg	**Pollutant:** $PM_{10-2.5}$ (µg/m^3) **Averaging Time:** 24 h **Mean (min-max):** 5.6 (0.1-24.6) SD = 3.6 **Monitoring Stations:** 13 **Copollutant (correlation):** $PM_{2.5}$: r = 0.38 PM_{10}: r = 0.83 COH: r = 0.63 CO: r = 0.53 O_3: r = -0.13 NO_2: r = 0.54 SO_2: r = 0.57 **Other variables:** Mean temp: r = 0.13 Rel humidity: r = -0.27	**PM Increment:** 4.2 µg/m^3 RR Estimate [CI]: Adj for weather conditions Overall admission 1-day avg: 1.03 [1.00,1.06] 2-day avg: 1.05 [1.02,1.08] 3-day avg: 1.06 [1.02,1.09] Adj for weather conditions and copollutants Overall admission 1-day avg: 1.02 [0.98,1.06] 2-day avg: 1.05 [1.01,1.10] 3-day avg: 1.06 [1.02,1.11] **Notes:** RR's were also provided for lags 4-7 in Table 3, yielding similar results

Reference	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Fung et al. (2006, 089789) **Period of Study:** Jun 1995-Mar 1999 **Location:** Vancouver, Canada	**Hospital Admission/ED:** Hospital Admission **Outcome:** Respiratory diseases (460-519) **Age Groups:** Age >65 **Study Design:** Time series **N:** 26,275 individuals admitted **Statistical Analyses:** Poisson regression (spline 12 knots), case-crossover (controls +/7 days from case date), Dewanji and Moolgavkar (DM) method **Covariates:** Long-term trends, day-of-the-week effect, weather **Season:** All yr **Dose-response Investigated?** No **Statistical Package:** SPlus, R **Lags Considered:** 0-7 days	**Pollutant:** $PM_{10-2.5}$ ($\mu g/m^3$) **Averaging Time:** 24-h avg **Mean (SD)** 5.6(3.88) $\mu g/m^3$ **Range (Min, Max):** (-2.9, 27.07) **Monitoring Stations:** NR **Notes: Copollutant (correlation):** $PM_{10-2.5}$ PM_{10} r = 0.83 $PM_{2.5}$ r = 0.34 CO r = 0.51 CoH r = 0.61 O_3 r = -0.11 NO_2 r = 0.52 SO_2 r = 0.57	**PM Increment: :** 4.3 $\mu g/m^3$ **RR Estimate** (65+ yr) DM method: 1.011[0.998,1.024] lag 0 1.016[1.0,1.032] 3-day avg 1.020[1.001,1.039] 5-day avg 1.020[0.998,1.042] 7-day avg Time series: 1.0168[1.003, 1.031] lag 0 1.020[1.003, 1.037] 3-day avg 1.019[0.999, 1.039] 5-day avg 1.018[0.994, 1.042] 7-day avg Case-crossover: 1.019[1.003, 1.034] lag 0 1.019[1.009, 1.038] 3-day avg 1.020[0.999, 1.042] 5-day avg 1.018[0.994, 1.043] 7-day avg
Reference: Halonen et al. (2009, 180379) **Period of Study:** 1998-2004 **Location:** Helsinki, Finland	**Outcome:** Hospital Admissions **Age Groups:** 65+ yr **Study Design:** Time series **N:** NR **Statistical Analyses:** Poisson, GAM **Covariates:** Temperature, humidity, influenza epidemics, high pollen episodes, holidays **Dose-response Investigated?** No **Statistical Package:** R **Lags Considered:** Lags 0-3 & 5-day (0-4) mean	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** Daily **Mean (SD):** NR **Min:** 0.0 **25th percentile:** 4.9 **50th percentile:** 7.5 **75th percentile:** 12.1 **Max:** 101.4 **Monitoring Stations:** NR **Copollutant:** PM<0.03, PM0.03-0.1, PM<0.1, PM<0.10.29, $PM_{2.5}$, CO, NO_2 **Co-pollutant Correlation** PM<0.03: 0.14 PM0.03-0.1: 0.28 PM<0.1: 0.24 PM<0.10.29: 0.20 $PM_{2.5}$: 0.25	**PM Increment:** Interquartile Range **Percent Change (Lower CI, Upper CI):** All Respiratory Mortality Lag 0: -0.66 (-4.16, 2.97) Lag 1: 2.90 (-0.48, 6.39) ‡ Lag 2: 0.35 (-3.03, 3.84) Lag 3: -0.38 (-3.67, 3.02) 5-day mean: 0.36 (-4.54, 5.51) Pneumonia HA Lag 0: 0.72 (-1.28, 2.77) Lag 1: 0.55 (-1.34, 2.49) Lag 2: 0.65 (-1.24, 2.58) Lag 3: 0.03 (-1.86, 1.96) 5-day mean: Asthma + COPD HA Lag 0: 2.49 (0.47, 4.56)* Lag 1: 1.37 (-0.66, 3.44) Lag 2: 0.7 (-1.36, 2.80) Lag 3: 1.97 (-0.02, 4.00)‡ 5-day mean: 2.67 (-0.17, 5.58)‡ Other HA Lag 0: 1.38 (-1.24, 4.06) Lag 1: -1.62 (-4.22, 1.05) Lag 2: -1.25 (-3.88, 1.45) Lag 3: 0.04 (-2.52, 2.67) 5-day mean: 0.24 (-3.62, 4.26) *p < 0.05, ‡p < 0.10

Reference	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Host et al. (2007, 155851) **Period of Study:** 2000-2003 **Location:** Six French cities: Le Havre, Lille, Marseille, Paris, Rouen, and Toulouse	**Outcome (ICD-10):** Daily hospitalizations for all respiratory diseases (J00-J99), respiratory infections (J10-J22). **Age Groups:** For all respiratory diseases: 0-14 yr, 15-64 yr, and ≥ 65 yr For respiratory infections: All ages **Study Design:** Time series **N:** NR (Total population of cities: approximately 10 million) **Statistical Analyses:** Poisson regression **Covariates:** Seasons, days of the week, holidays, influenza epidemics, pollen counts, temperature, and temporal trends **Dose-response Investigated:** No **Statistical Package:** MGCV package in R software (R 2.1.1) **Lags Considered:** Avg of 0-1 days	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 24 h **Mean µg/m3 (5th -95th percentile):** Le Havre: 7.3 (2.5-14.0) Lille: 7.9 (2.2-13.7) Marseille: 11.0 (4.5-21.0) Paris: 8.3 (3.2-15.9) Rouen: 7.0 (3.0-12.5) Toulouse: 7.7 (3.0-15.0) **Monitoring Stations:** 13 total: 1 in Toulouse 4 in Paris 2 each in other cities **Copollutant (correlation):** $PM_{2.5}$: Overall: r>0.6 Ranged between r = 0.28 and r = 0.73 across the six cities.	**PM Increment:** 10 µg/m^3 , and an 18.8 µg/m^3 increase (corresponding to an increase in pollutant levels between the lowest of the 5th percentiles and the highest of the 95th percentiles of the cities' distributions) ERR (excess relative risk) Estimate [CI]: For all respiratory diseases (10 µg/m^3 increase): 0-14 yr: 6.2% [0.4, 12.3] 15-64 yr: 2.6% [-0.5, 5.8] ≥ 65 yr: 1.9% [-1.9, 5.9] For all respiratory diseases (18.8 µg/m^3 increase): 0-14 yr: 12.0 [0.8, 24.3] 15-64 yr: 5.0 [-0.9, 11.1] ≥ 65 yr: 3.7 [-3.6, 11.4] For respiratory infections (10 µg/m^3): All ages: 4.4% [0.9, 8.0] For respiratory infections (18 µg/m^3): All ages: 8.4% [1.7, 15.5]
Reference: Lin et al. (2005, 087828) **Period of Study:** 1998-2001 **Location:** Toronto, North York, East York, Etobicoke, Scarborough, and York (Canada)	Hospital Admissions **Outcome (ICD-9):** Respiratory infections including laryngitis, tracheitis, bronchitis, bronchiolitis, pneumonia, and influenza (464, 466, 480-487) **Age Groups:** 0-14 yr **Study Design:** Bidirectional case-crossover **N:** 6782 respiratory infection hospitalizations **Statistical Analyses:** Conditional logistic regression (Cox proportional hazards model) **Covariates:** Daily mean temp and dew point temp **Season:** NR **Dose-response Investigated?** No **Statistical Package:** SAS 8.2 PHREG procedure **Lags Considered:** 1- to 7-day avg	**Pollutant:** $PM_{10-2.5}$ (µg/m^3) **Averaging Time:** 24 h **Mean (min-max):** 10.86 (0-45.00) SD = 5.37 **Monitoring Stations:** 4 **Copollutant (correlation):** $PM_{2.5}$: r = 0.33 PM_{10}: r = 0.76 CO: r = 0.06 SO_2: r = 0.29 NO_2: r = 0.40 O_3: r = 0.30	**PM Increment:** 6.5 µg/m^3 OR Estimate [CI]: Adjusted for weather 4-day avg: 1.16 [1.07,1.26] 6-day avg: 1.21 [1.10,1.32] Adj for weather and other gaseous pollutants 4-day avg: 1.13 [1.03,1.23] 6-day avg: 1.17 [1.06,1.29] **Notes:** OR's were also categorized into "Boys" and "Girls," yielding similar results

Reference	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Lin et al. (2002, 026067) **Period of Study:** Jan 1981-Dec 1993 **Location:** Toronto	Hospital Admissions **Outcome (ICD-9)**: Asthma (493) **Age Groups:** 6-12 yr **Study Design:** Uni- and bi-directional case-crossover (UCC, BCC) and time-series (TS) **N:** 7,319 asthma admissions **Statistical Analyses:** Conditional logistic regression, GAM **Covariates:** Maximum and minimum temp, avg relative humidity **Season:** Apr-Sep, Oct-Mar **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 1- to 7-day avg	**Pollutant:** $PM_{10-2.5}$ ($\mu g/m^3$) **Averaging Time:** 6 days (predicted daily values) **Mean (min-max):** 12.17 (0-68.00) SD = 7.55 **Monitoring Stations:** 1 **Copollutant (correlation):** $PM_{2.5}$: r = 0.44 PM_{10}: r = 0.83 CO: r = 0.17 SO_2: r = 0.28 NO_2: r = 0.38 O_3: r = 0.56	**PM Increment:** 8.4 $\mu g/m^3$ **RR Estimate [CI]:** Adj for weather and gaseous pollutants BCC 5-day avg: 1.14 [1.01,1.28] BCC 6-day avg: 1.17 [1.03,1.33] TS 5-day avg: 1.14 [1.05,1.23] TS 6-day avg: 1.15 [1.06,1.25] Boys-adj for weather UCC 1-day avg: 1.08 [1.01,1.16] UCC 2-day avg: 1.08 [0.99,1.17] BCC 1-day avg: 1.06 [1.00,1.14] BCC 2-day avg: 1.06 [0.98,1.14] TS 1-day avg: 1.08 [1.03,1.12] TS 2-day avg: 1.07 [1.01,1.13] Girls-adj for weather UCC 1-day avg: 1.07 [0.97,1.18] UCC 2-day avg: 1.16 [1.03,1.31] BCC 1-day avg: 0.98 [0.90,1.07] BCC 2-day avg: 1.05 [0.94,1.16] TS 1-day avg: 1.00 [0.94,1.06] TS 2-day avg: 1.05 [0.98,1.13] **Notes:** The author also provides RR using UCC, BCC, and TS analysis for female and male groups for day 3-7, yielding similar results
Reference: Peel et al. (2005, 056305) **Period of Study:** Jan 1993-Aug 2000 **Location:** Atlanta, Georgia	ED visits **Outcome:** Asthma (493, 786.09) COPD (491, 492, 496) URI (460-466, 477) Pneumonia (480-486) **Age Groups:** All ages. Secondary analyses conducted by age group: 0-1, 2-18, >18 **Study Design:** Time series **N:** 31 hospitals **Statistical Analyses:** Poisson GEE for URI, asthma and all RD Poisson GLM for pneumonia and COPD) **Covariates:** Avg temperature and dew point, pollen counts **Season:** All (secondary analyses of warm season) **Dose-response Investigated?** Yes **Statistical Package:** SAS 8.3 S-Plus 2000 **Lags Considered:** 0-7 days, 3-day ma, 0-13 days unconstrained distributed lag	**Pollutant:** $PM_{10-2.5}$ ($\mu g/m^3$) **Averaging Time:** 24 h avg **Mean (SD):** 9.7 (4.7) Percentiles: 10th: 4.4 90th: 16.2 **Monitoring Stations:** "Several" **Copollutant (correlation):** 24 h PM_{10}: r = 0.59 8 h O_3: r = 0.35 1 h NO_2: r = 0.46 1 h CO: r = 0.32 1 h SO_2: r = 0.21 24 h $PM_{2.5}$: r = 0.43 Components: r ranged from 0.23-0.51	**PM Increment:** 5 RR Estimate [Lower CI, Upper CI] All Respiratory Outcomes: 1.003 [0.982, 1.025] URI: 1.013 [0.987, 1.039] Asthma: 0.998 [0.987, 1.039] Pneumonia: 0.975 [0.940, 1.011] COPD: 0.948 [0.897, 1.003]

Reference	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Peng et al. (2008, 156850) **Period of Study:** Jan 1999-Dec 2005 **Location:** 108 U.S. counties in the following states: Alabama, Arizona, California, Colorado, Connecticut, District of Columbia, Florida, Georgia, Idaho, Illinois, Indiana, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Missouri, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, Tennessee, Texas, Utah, Virginia, Washington, West Virginia, Wisconsin	**Outcome (ICD-9):** Emergency hospitalizations for respiratory disease, including COPD (490-492) and respiratory tract infections (464-466, 480 - 487) **Age Groups:** 65 + yr, 65-74, ,75 + **Study Design:** Time series **N:** Approximately 12 million Medicare enrollees (1.4 million RD admissions) **Statistical Analyses:** Two-stage Bayesian hierarchical models: Over dispersed Poisson models for county-specific data. Bayesian hierarchical models to obtain national avg estimate **Covariates:** Day of the week, age-specific intercept, temperature, dew point temperature, calendar time, indicator for age of 75 yr or older. Some models were adjusted for $PM_{2.5}$. **Dose-response Investigated:** No **Statistical Package:** R version 2.6.2 **Lags Considered:** 0-2 days	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 24 h Mean (IQR): All counties assessed: 9.8 (6.9-15.0) Counties in Eastern U.S.: 9.1 (6.6-13.1) Counties in Western U.S.: 15.4 (10.3-21.8) **Monitoring Stations:** At least 1 pair of co-located monitors (physically located in the same place) for PM_{10} and $PM_{2.5}$ per county **Copollutant (correlation):** $PM_{2.5}$: r = 0.12 PM_{10}: r = 0.75 Other variables: Median within-county correlations between monitors: r = 0.60	**PM Increment:** 10 µg/m^3 Percentage change [95% CI]: Respiratory disease (RD): Lag 0 (unadjusted for $PM_{2.5}$): 0.33 [-0.21, 0.86] Lag 0 (adjusted for $PM_{2.5}$): 0.26 [-0.32, 0.84] Most values NR (see note) Notes: Fig 3: Percentage change in emergency hospital admissions for RD per 10 µg/m^3 increase in PM (single pollutant model and model adjusted for $PM_{2.5}$ concentration) Fig 4: Percentage change in emergency hospital admissions rate for CVD and RD per a 10 µg/m^3 increase in $PM_{10-2.5}$ (0-2 day lags, Eastern vs.. Western USA)
Reference: Slaughter et al. (2005, 073854) **Period of Study:** Jan 1995-Jun 2001 **Location:** Spokane, WA	Hospital Admissions and ED visits **Outcome:** All respiratory (460-519) Asthma (493) COPD (491,492, 494,496) Pneumonia (480-487) Acute URI not including colds and sinusitis (464, 466, 490) **Age Groups:** All, 15+ yr for COPD **Study Design:** Time series **N:** 2373 visit records **Statistical Analyses:** Poisson regression, GLM with natural splines. For comparison also used GAM with smoothing splines and default convergence criteria. **Covariates:** Season, temperature, relative humidity, day of week **Season:** All **Dose-response Investigated?**: No **Statistical Package:** SAS, SPLUS **Lags Considered:** 1 -3 days	**Pollutant:** $PM_{10-2.5}$ (µg/m^3) **Averaging Time:** 24 h avg **Range (90% of Concentrations):** Reported for $PM_{2.5}$ and PM_{10} only **Monitoring Stations:** 1 **Copollutant (correlation):** $PM_{10-2.5}$ PM1 r = 0.19 $PM_{2.5}$ r = 0.31 PM_{10} r = 0.94 CO r = 0.32 Temperature r = 0.11	**PM Increment:** 25 µg/m^3 **RR Estimate [Lower CI, Upper CI] lag:** ER visits: $PM_{10-2.5}$ All Respiratory Lag 1: 1.01 [0.98, 1.04] Lag 2: 1.01 [0.98, 1.04] Lag 3: 1.02 [0.99, 1.05] Acute Asthma Lag 1: 1.03 [0.98, 1.08] Lag 2: 1.01 [0.96, 1.07] Lag 3: 0.99 [0.94, 1.05] COPD (adult) Lag 1: 1.01 [0.93, 1.09] Lag 2: 0.98 [0.90, 1.06] Lag 3: 1.02 [0.95, 1.10]

Reference	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Tecer et al. (2008, 180030) **Period of Study:** Dec 2004-Oct 2005 **Location:** Zonguldak, Turkey	**Outcome:** ED visits for respiratory problems (ICD-9 470-478, 493) **Study Design:** Bidirectional Case-crossover **Covariates:** Daily meteorological parameters **Statistical Analysis:** Conditional logistic regression **Statistical Package:** Stata **Age Groups:** 0-14 yr	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** NR **Mean, Unit:** 24.3 µg/m^3 **Range (Min, Max):** 4, 195.8 **Copollutant (correlation):** $PM_{2.5}/PM_{10-2.5}$ Mean: 1.49 Range: 0.21, 7.53	**Increment:** 10 µg/m^3 **Odds Ratio (95% CI)** Asthma Lag 0: 1.18 (1.01-1.39) Lag 1: 0.92 (0.78-1.08) Lag 2: 0.98 (0.84-1.15) Lag 3: 1.11 (0.97-1.27) Lag 4: 1.17 (1.05-1.31) Allergic Rhinitis with Asthma Lag 0: 0.96 (0.88-1.04) Lag 1: 1.08 (0.99-1.18) Lag 2: 0.93 (0.86-1.02) Lag 3: 0.94 (0.86-1.03) Lag 4: 1.10 (1.03-1.18) Allergic Rhinitis Lag 0: 1.06 (0.95-1.19) Lag 1: 1.17 (1.04-1.31) Lag 2: 0.92 (0.84-1.02) Lag 3: 0.99 (0.91-1.08) Lag 4: 1.15 (1.06-1.25) Upper Respiratory Disease Lag 0: 0.80 (0.54-1.19) Lag 1: 1.22 (0.92-1.61) Lag 2: 0.97 (0.70-1.33) Lag 3: 0.94 (0.66-1.33) Lag 4: 1.08 (0.88-1.32) Lower Respiratory Disease Lag 0: 0.90 (0.71-1.16) Lag 1: 1.20 (0.97-1.50) Lag 2: 1.00 (0.84-1.19) Lag 3: 1.26 (1.08-1.47) Lag 4: 1.02 (0.93-1.13)
Reference: Yang et al., (2004, 087488) **Period of Study:** Jun 1995-Mar 1999 **Location:** Vancouver area, British Columbia	Hospital Admissions **Outcome (ICD-9):** Respiratory diseases (460-519), pneumonia only (480-486), asthma only (493) **Age Groups:** 0-3 yr **Study Design:** Case control, bidirectional case-crossover (BCC), and time series (TS) **N:** 1610 cases **Statistical Analyses:** Chi-square test, Logistic regression, GAM (time-series), GLM with parametric natural cubic splines **Covariates:** Gender, socioeconomic status, weekday, season, study yr, influenza epidemic month **Season:** Spring, summer, fall, winter **Dose-response Investigated?** No **Statistical Package:** SAS (Case control and BCC), S-Plus (TS) **Lags Considered:** 0-7 days	**Pollutant:** $PM_{10-2.5}$ (µg/m^3) **Averaging Time:** 24 h **Mean (min-max):** 5.6 (0-24.6) SD = 3.6 **Monitoring Stations:** NR (data obtained from Greater Vancouver Regional District Air Quality Dept) **Copollutant (correlation):** $PM_{2.5}$: r = 0.39 PM_{10}: r = 0.83 CO: r = 0.33 O_3: r = -0.16 NO_2: r = 0.37 SO_2: r = 0.54	**PM Increment:** 4.2 µg/m^3 (IQR) OR Estimate [CI]: 3-day lag 1.12 [0.98,1.28] Adj for gaseous pollutants: 1.22 [1.02,1.48] Notes: Author states that ORs for $PM_{10-2.5}$ increased with lag time up to 3 days for both single and multiple-pollutant models. More adjusted ORs and RRs are provided in Fig 1.

[1]All units expressed in µg/m^3 unless otherwise specified.

Table E-14. Short-term exposure-respiratory-ED/HA-$PM_{2.5}$ (including PM components/sources).

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Andersen et al. (2008, 189651) **Period of Study:** May 2001-Dec 2004 **Location:** Copenhagen, Denmark	**Outcome (ICD-10):** RD, including chronic bronchitis (J41-42), emphysema (J43), other chronic obstructive pulmonary disease (J44), asthma (J45), and status asthmaticus (J46). Pediatric hospital admissions for asthma (J45) and status asthmaticus (J46). **Age Groups:** > 5-18 yr (asthma) **Study Design:** Time series **N:** NR **Statistical Analyses:** Poisson GAM **Covariates:** Temperature, dew-point temperature, long-term trend, seasonality, influenza, day of the week, public holidays, school holidays (only for 5-18 yr olds), pollen (only for pediatric asthma outcome) **Season:** NR **Dose-response Investigated:** No **Statistical Package:** R statistical software (gam procedure, mgcv package) **Lags Considered:** Lag 0-5 days, 4-day pollutant avg (lag 0-3) for CVD, 5-day avg (lag 0-4) for RD, and a 6-day avg (lag 0-5) for asthma.	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean µg/m3 (SD):** 10(5) **Median:** 9 **IQR:** 7-12 **99th percentile:** 28 **Monitoring Stations:** 1 **Copollutant (correlation):** NCtot: r = 0.40 NC100: r = 0.29 NCa12: r = 0.07 Nca23: r = -0.25 NCa57: r = 0.51 NCa212: r = 0.82 PM_{10}: r = 0.80 CO: r = 0.46 NO_2: r = 0.42 : r = 0.40 NO_X curbside: r = 0.28 O_3: r = -0.20 **Other variables:** Temperature: r = -0.01 Relative humidity: r = 0.21	**PM Increment:** 5 µg/m^3 (IQR) Relative risk (RR) Estimate [CI]: RD hospital admissions (5-day avg, lag 0-4), age 65+: One-pollutant model: 1.00 [0.95-1.00] Adj for NCtot: 1.00 [0.95-1.06] Asthma hospital admissions (6-day avg lag 0-5), age 5-18: One-pollutant model: 1.15 [1.00-1.32] Adj for NCtot: 1.13 [0.98-1.32] Estimates for individual day lags reported only in Fig form (see notes): Notes: RD: No statistically or marginally significant associations. Positive associatons at Lag 4-5.Asthma: Wide confidence intervals make interpretation dificult. Positive associations at Lag 1, 2, 3.
Reference: Babin et al. (2007, 093250) **Period of Study:** Oct 2001-Sep 2004 **Location:** Washington, DC	ED Visit/Admissions **Outcome:** Asthma-493 **Age Groups:** 1-17 yr,1-4, 5-12, 13-17 **Study Design:** Time-series **N:** NR **Statistical Analyses:** Poisson regression, spline w/ 12 knots to adjust for long term trend **Covariates:** Temperature, mold, pollen, seasonal trends, **Season:** All **Dose-response Investigated?**No **Statistical Package:** STATA **Lags Considered:** 0-4	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean:** "low, never reached code red" **Percentiles:** NR **Range (Min, Max):** NR **Monitoring Stations:** 3 **Copollutant (correlation):** NR	**PM Increment:** 1 µg/m^3 %Change ED Visits Ages 5-12: -0.2 (-0.6,0.2), lag 0 % Change ED Admissions: Ages 5-12: -0.4 (-1.6,0.8), lag 0 Ages 1-17: 0.2 (-0.6,1.1), lag 0 AR Estimate [Lower CI, Upper CI] lag: NR **Notes:** No significant interactions between PM and O_3 or other covariates were observed.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Barnett et al. (2005, 087394) **Period of Study:** 1998-2001 **Location:** 5 Australian cities (Brisbane, Canberra, Melbourne, Perth, and Sydney) and 2 New Zealand cities (Auckland, Christchurch)	**Outcome (ICD: NR):** All respiratory admissions (including asthma, pneumonia, and acute bronchitis) **Age Groups:** Children aged <1 yr, 1-4 yr, and 5-14 yr **Study Design:** Matched case-crossover **N:** ~2.4 million children <15 yr old **Statistical Analyses:** Random effects meta-analysis **Covariates:** Temperature, current minus previous day's temperature, relative humidity, pressure, extremes of hot and cold, day of the week, public holiday, and day after public holiday **Season:** Warm (Nov-Apr) and Cool (May-Oct) **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** NR	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (min-max):** Auckland (A): 11.0 (2.1-37.6) Brisbane (B): 9.7 (3.2-122.8) Canberra (Ca): NR Christchurch (Ch): NR Melbourne (M): 8.9 (2.8-43.3) Perth (P): 8.1 (1.7-29.3) Sydney (S): 9.4 (2.4-82.1) **Monitoring Stations:** 1-3 per city **Copollutant:** NR	**PM Increment:** 3.8 µg/m^3 (IQR) **Percent Increase Estimate [CI]:** Pneumonia & Acute Bronchitis: Single Pollutant Model <1 yr (B,M,P,S): 1.7 [0.0,3.4] 1-4 yr (B,M,P,S): 2.4 [0.1,4.7] Matched Multipollutant Model 1-4 yr with 1-h SO_2 (B,S): 1.9 [-1.7,5.6] 1-4 yr with temp (B,M,P,S): 2.3 [-0.4,5.1] Respiratory Admissions: Single Pollutant Model <1 yr (B,M,P,S): 2.4 [1.0,3.8] 1-4 yr (B,M,P,S): 1.7 [0.7,2.7] Matched Pollutant Model <1 yr with 1-h SO_2 (B,S): 3.1 [0.5,5.7] <1 yr with temp (B,M,P,S): 1.8 [0.2,3.4] 1-4 yr with PM_{10} (B,M,P,S): 2.9 [0.2,5.6] 1-4 yr with 1-h SO_2 (B,S): 1.3 [-1.8,4.4] 1-4 yr with 1-h NO_2 (B,M,P,S): -1.5 [-3.2,0.2] 1-4 yr with temp (B,M,P,S,): 1.5 [-0.2,3.1]
Reference: Bell et al. (2008, 091268) **Period of Study:** 1995-2002 **Location:** Taipei, Taiwan	**Outcome (ICD-9):** Hospital admissions for asthma (493), and pneumonia (486). **Age Groups:** All **Study Design:** Time series **N:** 19,966 hospital admissions for pneumonia, and 10,231 for asthma **Statistical Analyses:** Poisson regression **Covariates:** Day of the week, time, apparent temperature, long-term trends, seasonality **Season:** All **Dose-response Investigated:** No **Statistical Package:** NR **Lags Considered:** lags 0-3 days, mean of lags 0-3	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h Mean (range IQR): 31.6 (0.50-355.0 20.2) **Monitoring Stations:** 2 **Copollutant (correlation):** NR	**PM Increment:** 20 µg/m^3 (near IQR) Percentage increase estimate [95% CI]: Asthma: L0: 0.46 (-2.41, 3.42) L1: -1.36 (-4.33, 1.71) L2: -0.83 (-3.67, 2.10) L3: -0.78 (-3.63, 2.16) L03: -1.75 (-6.21, 2.92) Pneumonia: L0: 0.06 (-2.74, 2.94) L1: 0.34 (-2.446, 3.20) L2: -0.59 (-3.38, 2.29) L3: -0.44 (-3.22, 2.41) L03: -0.61 (-4.87, 3.85)
Reference: Bell et al. (2008, 091268) **Period of Study:** 1999-2005 **Location:** 202 U.S. counties	**Outcome (ICD-9):** COPD (490-492), respiratory tract infections (464-466, 480-487) **Age Groups:** 65+ **Study Design:** Time series **N:** NR **Statistical Analyses:** Two-stage Bayesian hierarchical model to find national avg First stage: Poisson regression (county-specific) **Covariates:** Day of the week, temperature, dew point temperature, temporal trends, indicator for persons 75+ yr, population size **Season:** All, Jun-Aug (Summer), Sep-Nov (Fall), Dec-Feb (Winter), Mar-May (Spring) **Dose-response Investigated:** No	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (µg/m3):** Descriptive information presented in Fig S2 (boxplots): IQR: 8.7 µg/m^3 **Monitoring Stations:** NR **Copollutant (correlation):** NR	**PM Increment:** 10 µg/m^3 Percent increase [95% PI]: **Respiratory admissions:** Lag 0 (all seasons): 0.22 [-0.12-0.56] Lag 0 (winter, national): 1.05 [0.29-1.82] Lag 0 (winter, northeast): 1.76 [0.60-2.93] Lag 0 (winter, southeast): 0.59 [-1.35-2.58] Lag 0 (winter, northwest): -0.07 [-6.74-7.08] Lag 0 (winter, southwest): 0.03 [-1.25-1.34] Lag 0 (spring, national): 0.31 [-0.47-1.11] Lag 0 (spring, northeast): 0.34 [-0.66-1.34] Lag 0 (spring, southeast): -0.06 [-1.77-1.68] Lag 0 (spring, northwest): -8.52 [-25.62-12.51] Lag 0 (spring, southwest): 1.87 [-2.00-5.90] Lag 0 (summer, national): -0.62 [-1.33-0.09]

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
	Statistical Package: NR **Lags Considered:** 0-2 day lags		Lag 0 (summer, northeast): -0.8 [-1.65-0.07] Lag 0 (summer, southeast): -0.15 [-1.88-1.61] Lag 0 (summer, northwest): 0.25 [-21.46-27.96] Lag 0 (summer, southwest): 0.64 [-5.38-7.04] Lag 0 (fall, national): 0.02 [-0.63-0.67] Lag 0 (fall, northeast): -0.01 [-0.87-0.85] Lag 0 (fall, southeast): -0.58 [-2.06-0.91] Lag 0 (fall, northwest): -1.38 [-11.84-10.32] Lag 0 (fall, southwest): 1.77 [-0.73-4.33] Lag 1 (all seasons): 0.05 [-0.29-0.39] Lag 1 (winter): 0.50 [-0.27-1.27] Lag 1 (spring): -0.24 [-1.01-0.53] Lag 1 (summer): 0.28 [-0.39-0.95] Lag 1 (fall): 0.15 [-0.49-0.79] Lag 2 (all seasons): 0.41 [0.09-0.74] Lag 2 (winter, national): 0.72 [0.01-1.43] Lag 2 (winter, northeast): 0.79 [-0.21-1.80] Lag 2 (winter, southeast): 0.4 [-1.45, 2.27] Lag 2 (winter, northwest): -0.06 [-6.52-6.85] Lag 2 (winter, southwest): 1.2 [-0.10-2.52] Lag 2 (spring, national): 0.35 [-0.29-0.99] Lag 2 (spring, northeast): 0.04 [-0.88-0.97] Lag 2 (spring, southeast): 0.75 [-0.82-2.34] Lag 2 (spring, northwest): 2.29 [-14.26-22.03] Lag 2 (spring, southwest): 1.05 [-2.18-4.39] Lag 2 (summer, national): 0.57 [-0.07-1.23] Lag 2 (summer, northeast): 0.77 [-0.01-1.56] |Lag 2 (summer, southeast): -0.52 [-2.07-1.06] Lag 2 (summer, northwest): 0.74 [-18.73-24.86] Lag 2 (summer, southwest): 2.41 [-2.61-7.69] Lag 2 (fall, national): 0.39 [-0.22-1.01] Lag 2 (fall, northeast): 0.12 [-0.82-1.07] Lag 2 (fall, southeast): 0.14 [-1.29-1.59] Lag 2 (fall, northwest): -0.74 [-10.08-9.58] Lag 2 (fall, southwest): 0.97[-1.36-3.36]
Reference: Bell et al. (2009, 191007) **Period of Study:** 1999-2005 **Location:** 168 U.S. Counties	**Outcome:** Respiratory hospital admissions **Study Design:** Retrospective Cohort **Covariates:** Socio-economic conditions, long term temperature **Statistical Analysis:** Bayesian hierarchical model **Age Groups:** ≥65	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD) Unit:** NR **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** 20% of the population acquiring air conditioning **Percent Change (95% CI) in community-specific PM health effect estimates for respiratory hospital admissions** Any AC, including window units Yearly health effect: 44.5 (-87.5-176) Summer health effect: -74.8 (-417-267) Winter health effect: -32.5 (-245-180) Central AC Yearly health effect: 27.6 (-46.7-102) Summer health effect: -38.6 (-160-82.6) Winter health effect: 43.8 (-125-213)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Bell et al. (2009, 191007) **Period of Study:** 1999-2005 **Location:** 168 U.S. Counties	**Outcome:** Respiratory HA **Age Groups:** 65+ **Study Design:** Time series **N:** NR **Statistical Analyses:** Bayesian Hierarchical Regression **Covariates:** Time trend, day of week, seasonality, dew point, temperature **Statistical Package:** NR **Lags Considered:** 0-2	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily **Mean:** EC: 0.715 Ni: 0.002 V: 0.003 **Min:** EC: 0.309 Ni: 0.003 V: 0.001 **Max:** EC: 1.73 Ni: 0.021 V: 0.010 **Interquartile Range:** EC: 0.245 Ni: 0.001 V: 0.001 **Interquartile Range of Percents:** EC: 1.7 Ni: 0.01 V: 0.01 **Monitoring Stations:** NR **Copollutant:** Al, NH4+, As, Ca, Cl, Cu, EC, OMC, Fe, Pb, Mg. Ni, NO_3-, K, Si, Na+, SO_4=, Ti, V, Zn **Co-pollutant Correlation:** Ni, V: 0.48 V, EC: 0.33 Ni, EC: 0.30 **Note:** Pollutant concentrations available for all fractions of $PM_{2.5}$	**PM Increment:** Interquartile Range in the fraction of $PM_{2.5}$ **Percent Increase (Lower CI, Upper CI):** EC: 511 (80.7, 941), lag 0 EC + Ni: 399 (-45.1, 843), lag 0 EC + V: 386 (-74.8, 846), lag 0 EC + Ni, V: 362 (-98.0, 823), lag 0 Ni: 223 (36.9, 410), lag 0 Ni + EC: 176 (-18.7, 370), lag 0 Ni + V: 151 (-78.4, 381), lag 0 Ni + EC, V: 136 (-94.9, 368), lag 0 V: 392 (46.3, 738), lag 0 V + EC: 279 (-93.2, 651), lag 0 V+ Ni: 230 (-193.7, 653), lag 0 V + EC, Ni: 140 (-300, 579), lag 0 EC: -1.5 (80.7, 941), lag 1 EC: 17.5 (-22.3, 57.3), lag 2 Ni: -7.2 (-66.6. 52.1), lag 1 Ni: -4.9 (-22.3, 12.5), lag 2 V: -19.6 (-127, 88.3), lag 1 V: 10.5 (-21.5, 42.4), lag 2 HS education: -77.8 (-390, 234), lag 0 median income: 45.9 (-411, 503), lag0 Percent black: -53.1 (-557, 451), lag 0 Percent living in urban area: -41.9 (-774.7, 691), lag 0 Population: -22.9 (-121, 75.3), lag 0 **Notes:** Interquartile ranges in percent HS education, median income, percent black, percent living in urban area, and population are 5.2 %, $9,223, 17.3%, 11.0%, and 549,283 respectively.
Reference: Chardon et al. (2007, 091308) **Period of Study:** 2000-2003 **Location:** Greater Paris Area, France	Doctors house calls **Outcome (ICPC2):** Asthma (R96), Upper respiratory disease (URD R07, R21, R29, R75, R76, R02) , Lower respiratory disease (LRD, R05, R78) **Age Groups:** All **Study Design:** Time series **N:** 8027 for asthma 52928 for LRD 74845 for URD **Statistical Analyses:** Quasi-Poisson, GAM, parametric penalized spline smoothers. **Covariates:** Lagged and current temperature, humidity, long term trends, seasonality, pollen counts, influenza epidemic, days of the week, holidays, bank holidays **Season:** All **Dose-response Investigated?** No **Statistical Package:** R **Lags Considered:** 0-3 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Mean of the daily means **Mean (SD):** 14.7(7.34) µg/m^3 **Percentiles**: 25th: 9.5 50th(Median): 12.9 75th: 18.2 **Range (Min, Max):** (3, 69.6) **Monitoring Stations**: 1- 4 **Copollutant:** PM_{10}: r = 0.95 NO_2: r = 0.68	**PM Increment:** 10 µg/m^3 % Change, lag 0-3-day avg URD 6.0 (3.1, 9.1) LRD 5.8 (2.8, 8.9) Asthma 4.4 (-1.3, 10.4)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Chen et al. (2005, 087555) **Period of Study:** Jun 1995-Mar 1999 **Location:** Vancouver area, BC	Hospital Admissions **Outcome (ICD-9):** Acute respiratory infections (460-466), upper respiratory tract infections (470-478), pneumonia and influenza (480-487), COPD and allied conditions (490-496), other respiratory diseases (500-519) **Age Groups:** >65 yr **Study Design:** Time series **N:** 12,869 **Statistical Analyses:** GLM **Covariates:** Temp and relative humidity **Season:** NR **Dose-response Investigated?** No **Statistical Package:** S-Plus **Lags Considered:** 1-, 2-, 3-, 4-, 5-, 6-, and 7-day avg	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (min-max):** 7.7 (2.0-32.0) SD = 3.7 **Monitoring Stations:** 13 **Copollutant (correlation):** PM_{10}: r = 0.83 $PM_{10-2.5}$: r = 0.38 COH: r = 0.39 CO: r = 0.23 O_3: r = -0.01 NO_2: r = 0.36 SO_2: r = 0.42 **Other variables:** Mean temp: r = 0.41 Rel humidity: r = -0.23	**PM Increment:** 4.0 µg/m^3 (IQR) **RR Estimate [CI]:** Adj for weather conditions Overall admission 1-day avg: 1.02 [0.99,1.05] 2-day avg: 1.02 [0.99,1.06] 3-day avg: 1.02 [0.98,1.05] Adj for weather conditions and copollutants Overall admission 1-day avg: 1.01 [0.98,1.06] 2-day avg: 1.01 [0.98,1.05] 3-day avg: 1.00 [0.96,1.04] **Notes:** RR's were also provided for lags 4-7 in Table 3, yielding similar results
Reference: Chimonas and Gessner (2007, 093261) **Period of Study:** Jan 1999-Jun 2003 **Location:** Anchorage, Alaska	**Outcome (ICD-9):** Asthma (493.0-493.9) Lower respiratory illness-LRI (466.1, 466.0, 480-487, 490, 510-511) Inhaled quick-relief medication Steroid medication **Age Groups:** <20 yr old **Study Design:** Time series **N:** 42,667 admissions **Statistical Analyses:** GEE for multivariable modeling **Covariates:** Season, serial correlation, yr, weekend, temperature, precipitation, and wind speed **Season:** NR **Dose-response Investigated?** No **Statistical Package:** SPSS (dataset), SAS (analysis) **Lags Considered:** 1 day and 1 wk	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h and 1 wk **Mean (min-max):** Daily: 6.1 (0.5-69.8) Weekly: 5.8 (1.8-45.0) **Monitoring Stations:** NR **Copollutant:** N/A	**PM Increment:** 5 µg/m^3 RR Estimate [CI]: Same Day Outpatient Asthma: 0.992 [0.964,1.024] Outpatient LRI: 0.952 [0.907,1.001] Inpatient Asthma: 0.936 [0.798,1.098] Inpatient LRI: 0.919 [0.823,1.027] Inhaled Steroid Prescriptions: 0.988 [0.902,1.083] Quick-relief Medication: 0.962 [0.901,1.028] Weekly (median increase) Outpatient Asthma: 0.983 [0.935,1.038] Outpatient LRI: 0.969 [0.874,1.075] Inpatient Asthma: 0.754 [0.513.1.109] Inpatient LRI: 0.943 [0.715,1.245] Inhaled Steroid Prescriptions: 1.018 [0.883,1.175] Quick-relief Medication: 0.978 [0.882,1.087]
Reference: Delfino et al. (2009, 191994) **Period of Study:** Oct 2003-Nov 2003 **Location:** Southern California	**Outcome:** Respiratory hospital admissions **Study Design:** Time series **Statistical Analysis:** Poisson regression with GEE **Age Groups:** All	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Hourly **Mean (SD) Unit by county:** Los Angeles Before Fires: 27.2 (12.4) µg/m^3 During Fires: 54.1 (21.0) µg/m^3 After Fires: 15.9 (5.5) µg/m^3 Orange Before Fires: 23.2 (9.6) µg/m^3 During Fires: 64.3 (26.5) µg/m^3 After Fires: 15.5 (10.2) µg/m^3 Riverside Before Fires: 32.7 (14.7) µg/m^3 During Fires: 42.1 (25.5) µg/m^3 After Fires: 16.9 (10.2) µg/m^3 San Bernadino Before Fires: 35.7 (16.6) µg/m^3 During Fires: 45.3 (28.7) µg/m^3 After Fires: 18.5 (8.3) µg/m^3 San Diego Before Fires: 18.5 (6.7) µg/m^3 During Fires: 76.1 (66.6) µg/m^3 After Fires: 14.2 (7.2) µg/m^3 Ventura	**Increment:** 10 µg/m^3 **Relative Rate (Min CI, Max CI)** All Respiratory, All Ages: All Periods: 1.009 (0.999-1.018) Pre-Wildfire: 1.022 (1.004-1.040) Wildfire: 1.028 (1.014-1.041), p = 0.639 Post-Wildfire: 0.999 (0.968-1.031), p = 0.198 All Respiratory, Ages 0-4: All Periods: 0.994 (0.967-1.021) Pre-Wildfire: 0.982 (0.921-1.046) Wildfire: 1.045 (1.010-1.082), p = 0.103 Post-Wildfire: 0.894 (0.807-0.991), p = 0.126 All Respiratory, Ages 5-19: All Periods: 1.014 (0.983-1.046) Pre-Wildfire: 1.026 (0.946-1.113) Wildfire: 1.027 (0.984-1.076), p = 0.990 Post-Wildfire: 0.958 (0.852-1.077), p = 0.354 All Respiratory, Ages 20-64: All Periods:

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
		Before Fires: 18.4 (8.3) µg/m^3 During Fires: 50.1 (50.5) µg/m^3 After Fires: 12.9 (4.3) µg/m^3 **Copollutant (correlation):** NR	1.015 (1.002-1.029) Pre-Wildfire: 1.036 (1.007-1.066) Wildfire: 1.024 (1.005-1.044), p = 0.534 Post-Wildfire: 1.007 (0.960-1.056), p = 0.315 All Respiratory, Ages 65-99: All Periods: 1.009 (0.996-1.022) Pre-Wildfire: 1.022 (0.994-1.050) Wildfire: 1.030 (1.011-1.049), p = 0.649 Post-Wildfire: 1.024 (0.967-1.074), p = 0.932 Asthma, All Ages, Male and Female: All Periods: 1.022 (1.001-1.042) Pre-Wildfire: 0.998 (0.949-1.050) Wildfire: 1.048 (1.021-1.076), p = 0.097 Post-Wildfire: 0.986 (0.910-1.068), p = 0.792 Asthma, All Ages, Male: All Periods: 1.010 (0.980-1.040) Pre-Wildfire: 1.021 (0.944-1.106) Wildfire: 1.031 (0.990-1.073), p = 0.848 Post-Wildfire: 1.063 (0.948-1.192), p = 0.553 Asthma, All Ages, Female: All Periods: 1.029 (1.001-1.058) Pre-Wildfire: 0.979 (0.913-1.050) Wildfire: 1.059 (1.022-1.097), p = 0.056 Post-Wildfire: 0.928 (0.829-1.037), p = 0.412 Asthma, Ages 0-4, Males and Females: All Periods: 0.996 (0.947-1.048) Pre-Wildfire: 0.924 (0.824-1.035) Wildfire: 1.083 (1.021-1.149), p = 0.017 Post-Wildfire: 0.924 (0.767-1.113), p = 0.999 Asthma, Ages 0-4, Males: All Periods: 1.018 (0.963-1.076) Pre-Wildfire: 0.942 (0.815-1.089) Wildfire: 1.086 (1.016-1.162), p = 0.101 Post-Wildfire: 1.057 (0.839-1.332), p = 0.380 Asthma, Ages 0-4, Females: All Periods: 0.937 (0.845-1.040) Pre-Wildfire: 0.880 (0.706-1.099) Wildfire: 1.073 (0.965-1.194), p = 0.116 Post-Wildfire: 0.699 (0.515-0.949), p = 0.214 Asthma, Ages 5-19, Males and Females: All Periods: 1.006 (0.966-1.048) Pre-Wildfire: 1.045 (0.936-1.167) Wildfire: 0.999 (0.935-1.068), p = 0.492 Post-Wildfire: 0.918 (0.788-1.069), p = 0.198 Asthma, Ages 5-19, Males: All Periods: 0.991 (0.935-1.051) Pre-Wildfire: 1.034 (0.892-1.198) Wildfire: 0.969 (0.883-1.064), p = 0.462 Post-Wildfire: 0.979 (0.806-1.189), p = 0.671 Asthma, Ages 5-19, Females: All Periods: 1.026 (0.964-1.092) Pre-Wildfire: 1.065 (0.901-1.260) Wildfire: 1.033 (0.943-1.132), p = 0.768 Post-Wildfire: 0.831 (0.640-1.079), p = 0.136 Asthma, Ages 20-64, Males and Females: All Periods: 1.043 (1.012-

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			1.076) Pre-Wildfire: 1.037 (0.957-1.123) Wildfire: 1.041 (0.995-1.090), p = 0.931 Post-Wildfire: 1.000 (0.882-1.132), p = 0.624 Asthma, Ages 20-64, Males: All Periods: 1.013 (0.954-1.077) Pre-Wildfire: 1.159 (0.996-1.349) Wildfire: 0.939 (0.837-1.053), p = 0.026 Post-Wildfire: 1.275 (1.020-1.595), p = 0.486 Asthma, Ages 20-64, Females: All Periods: 1.052 (1.015-1.090) Pre-Wildfire: 0.995 (0.904-1.096) Wildfire: 1.064 (1.014-1.116), p = 0.247 Post-Wildfire: 0.908 (0.780-1.056), p = 0.310 Asthma, Ages 65-99, Males and Females: All Periods: 1.027 (0.974-1.082) Pre-Wildfire: 0.951 (0.849-1.064) Wildfire: 1.101 (1.030-1.178), p = 0.032 Post-Wildfire: 1.168 (0.967-1.412), p = 0.072 Asthma, Ages 65-99, Males: All Periods: 1.046 (0.957-1.142) Pre-Wildfire: 0.948 (0.804-1.116) Wildfire: 1.185 (1.077-1.305), p = 0.029 Post-Wildfire: 0.902 (0.629-1.294), p = 0.804 Asthma, Ages 65-99, Females: All Periods: 1.018 (0.958-1.081) Pre-Wildfire: 0.947 (0.813-1.102) Wildfire: 1.065 (0.977-1.162), p = 0.195 Post-Wildfire: 1.263 (1.024-1.557), p = 0.032 Acute Bronchitis and Bronchiolitis, All Ages: All Periods: 1.044 (0.990-1.102) Pre-Wildfire: 1.001 (0.890-1.126) Wildfire: 1.096 (1.018-1.179), p = 0.223 Post-Wildfire: 1.031 (0.870-1.222), p = 0.779 Acute Bronchitis and Bronchiolitis, Ages 0-4: All Periods: 1.017 (0.949-1.089) Pre-Wildfire: 0.987 (0.847-1.149) Wildfire: 1.092 (0.997-1.195), p = 0.276 Post-Wildfire: 0.910 (0.700-1.183), p = 0.588 Acute Bronchitis and Bronchiolitis, Ages 5-19: No Convergence Acute Bronchitis and Bronchiolitis, Ages 20-64: All Periods: 1.039 (0.912-1.183) Pre-Wildfire: 1.001 (0.792-1.266) Wildfire: 1.044 (0.872-1.252), p = 0.778 Post-Wildfire: 1.259 (0.921-1.722), p = 0.275 Acute Bronchitis and Bronchiolitis, Ages 65-99: All Periods: 1.134 (1039-1.238) Pre-Wildfire: 1.073 (0.764-1.505) Wildfire: 1.143 (1.032-1.265), p = 0.730 Post-Wildfire: 1.190 (0.865-1.638), p = 0.652 COPD, Ages 20-99: All Periods: 1.018 (0.994-1.042) Pre-Wildfire: 1.007 (0.958-1.058) Wildfire: 1.038 (1.004-1.075), p = 0.320 Post-Wildfire: 1.024 (0.943-1.112),

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			p = 0.728 COPD, Ages 20-64: All Periods: 1.022 (0.980-1.066) Pre-Wildfire: 0.995 (0.916-1.081) Wildfire: 1.068 (1.009-1.131), p = 0.161 Post-Wildfire: 1.015 (0.893-1.153), p = 0.728 COPD, Ages 65-99: All Periods: 1.019 (0.992-1.048) Pre-Wildfire: 1.014 (0.955-1.077) Wildfire: 1.031 (0.990-1.074), p = 0.660 Post-Wildfire: 1.023 (0.928-1.128), p = 0.878 Pneumonia, All Ages: All Periods: 1.009 (0.994-1.024) Pre-Wildfire: 1.045 (0.931-1.180) Wildfire: 1.028 (1.007-1.050), p = 0.420 Post-Wildfire: 0.980 (0.927-1.035), p = 0.045 Pneumonia, Ages 0-4: All Periods: 0.995 (0.944-1.049) Pre-Wildfire: 1.048 (0.931-1.180) Wildfire: 1.018 (0.948-1.092), p = 0.691 Post-Wildfire: 0.823 (0.649-1.044), p = 0.089 Pneumonia, Ages 5-19: All Periods: 1.031 (0.966-1.098) Pre-Wildfire: 1.017 (0.882-1.172) Wildfire: 1.064 (0.990-1.142), p = 0.586 Post-Wildfire: 1.017 (0.767-1.349), p = 0.998 Pneumonia, Ages 20-64: All Periods: 1.008 (0.982-1.035) Pre-Wildfire: 1.041 (0.982-1.104) Wildfire: 1.032 (0.994-1.072), p = 0.823 Post-Wildfire: 1.013 (0.913-1.124), p = 0.633 Pneumonia, Ages 65-99: All Periods: 1.011 (0.993-1.030) Pre-Wildfire: 1.050 (1.006-1.097) Wildfire: 1.029 (1.002-1.057), p = 0.445 Post-Wildfire: 0.985 (0.920-1.055), p = 0.127 **Relative Rate (Min CI, Max CI) in relation to pre-wildfire period (1)** All Respiratory, All Ages: Wildfire, unadjusted for $PM_{2.5}$: 0.961 (0.916-1.008) Wildfire, adjusted for $PM_{2.5}$: 0.903 (0.850-0.960) Post-wildfire, unadjusted for $PM_{2.5}$: 1.143 (1.072-1.219) Post-wildfire, adjusted for $PM_{2.5}$: 1.173 (1.097-1.253) All Respiratory, Ages 0-4: Wildfire, unadjusted for $PM_{2.5}$: 0.865 (0.757-0.989) Wildfire, adjusted for $PM_{2.5}$: 0.842 (0.717-0.988) Post-wildfire, unadjusted for $PM_{2.5}$: 1.152 (0.957-1.388) Post-wildfire, adjusted for $PM_{2.5}$: 1.162 (0.954-1.415) All Respiratory, Ages 5-19: Wildfire, unadjusted for $PM_{2.5}$: 1.098 (0.901-1.324) Wildfire, adjusted for $PM_{2.5}$: 1.087 (0.863-1.370)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Post-wildfire, unadjusted for $PM_{2.5}$: 1.373 (1.089-1.732) Post-wildfire, adjusted for $PM_{2.5}$: 1.467 (1.142-1.883) All Respiratory, Ages 20-64: Wildfire, unadjusted for $PM_{2.5}$: 0.991 (0.922-1.066) Wildfire, adjusted for $PM_{2.5}$: 0.923 (0.843-1.012) Post-wildfire, unadjusted for $PM_{2.5}$: 1.074 (0.971-1.188) Post-wildfire, adjusted for $PM_{2.5}$: 1.104 (0.992-1.228) All Respiratory, Ages 65-99: Wildfire, unadjusted for $PM_{2.5}$: 0.932 (0.867-1.003) Wildfire, adjusted for $PM_{2.5}$: 0.874 (0.795-0.959) Post-wildfire, unadjusted for $PM_{2.5}$: 1.147 (1.045-1.259) Post-wildfire, adjusted for $PM_{2.5}$: 1.193 (1.084-1.313) Asthma, All Ages: Wildfire, unadjusted for $PM_{2.5}$: 1.088 (0.965-1.227) Wildfire, adjusted for $PM_{2.5}$: 0.992 (0.856-1.149) Post-wildfire, unadjusted for $PM_{2.5}$: 1.264 (1.085-1.473) Post-wildfire, adjusted for $PM_{2.5}$: 1.336 (1.134-1.573) Asthma, Ages 0-4: Wildfire, unadjusted for $PM_{2.5}$: 0.806 (0.632-1.029) Wildfire, adjusted for $PM_{2.5}$: 1.282 (0.958-1.716) Post-wildfire, unadjusted for $PM_{2.5}$: 1.092 (1.759-1.572) Post-wildfire, adjusted for $PM_{2.5}$: 1.133 (0.777-1.654) Asthma, Ages 5-19: Wildfire, unadjusted for $PM_{2.5}$: 1.254 (0.999-1.575) Wildfire, adjusted for $PM_{2.5}$: 1.282 (0.958-1.716) Post-wildfire, unadjusted for $PM_{2.5}$: 1.564 (1.160-2.109) Post-wildfire, adjusted for $PM_{2.5}$: 1.629 (1.184-2.243) Asthma, Ages 20-64: Wildfire, unadjusted for $PM_{2.5}$: 1.273 (1.067-1.518) Wildfire, adjusted for $PM_{2.5}$: 1.221 (0.979-1.524) Post-wildfire, unadjusted for $PM_{2.5}$: 1.362 (1.043-1.779) Post-wildfire, adjusted for $PM_{2.5}$: 1.486 (1.111-1.987) Asthma, Ages 65-99: Wildfire, unadjusted for $PM_{2.5}$: 0.869 (0.657-1.151) Wildfire, adjusted for $PM_{2.5}$: 0.645 (0.450-0.925) Post-wildfire, unadjusted for $PM_{2.5}$: 0.924 (0.606-1.408) Post-wildfire, adjusted for $PM_{2.5}$: 1.005 (0.650-1.552) Acute Bronchitis and Bronchiolitis, All Ages: Wildfire, unadjusted for $PM_{2.5}$: 1.143 (0.878-1.490) Wildfire, adjusted for $PM_{2.5}$: 0.959 (0.696-1.321)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Post-wildfire, unadjusted for $PM_{2.5}$: 1.482 (1.042-2.109) Post-wildfire, adjusted for $PM_{2.5}$: 1.580 (1.089-2.291) Acute Bronchitis and Bronchiolitis, Ages 0-4: Wildfire, unadjusted for $PM_{2.5}$: 1.128 (0.819-1.555) Wildfire, adjusted for $PM_{2.5}$: 0.899 (0.607-1.333) Post-wildfire, unadjusted for $PM_{2.5}$: 1.520 (0.947-2.440) Post-wildfire, adjusted for $PM_{2.5}$: 1.547 (0.954-2.507) Acute Bronchitis and Bronchiolitis, Ages 5-19 No Correlation Acute Bronchitis and Bronchiolitis, Ages 20-64: Wildfire, unadjusted for $PM_{2.5}$: 1.350 (0.688-2.648) Wildfire, adjusted for $PM_{2.5}$: 1.320 (0.608-2.863) Post-wildfire, unadjusted for $PM_{2.5}$: 2.454 (1.068-5.640) Post-wildfire, adjusted for $PM_{2.5}$: 2.515 (1.055-5.998) Acute Bronchitis and Bronchiolitis, Ages 65-99: Wildfire, unadjusted for $PM_{2.5}$: 1.166 (0.643-2.115) Wildfire, adjusted for $PM_{2.5}$: 0.934 (0.422-20.66) Post-wildfire, unadjusted for $PM_{2.5}$: 0.911 (0.428-1.942) Post-wildfire, adjusted for $PM_{2.5}$: 0.997 (0.439-2.262) COPD, Ages 20-99: Wildfire, unadjusted for $PM_{2.5}$: 0.988 (0.875-1.115) Wildfire, adjusted for $PM_{2.5}$: 0.913 (0.779-1.069) Post-wildfire, unadjusted for $PM_{2.5}$: 1.043 (0.885-1.228) Post-wildfire, adjusted for $PM_{2.5}$: 1.064 (0.897-1.262) COPD, Ages 20-64: Wildfire, unadjusted for $PM_{2.5}$: 0.967 (0.779-1.201) Wildfire, adjusted for $PM_{2.5}$: 0.873 (0.660-1.156) Post-wildfire, unadjusted for $PM_{2.5}$: 1.175 (0.862-1.601) Post-wildfire, adjusted for $PM_{2.5}$: 1.311 (0.954-1.802) COPD, Ages 65-99: Wildfire, unadjusted for $PM_{2.5}$: 1.002 (0.869-1.156) Wildfire, adjusted for $PM_{2.5}$: 0.926 (0.767-1.117) Post-wildfire, unadjusted for $PM_{2.5}$: 0.985 (0.811-1.196) Post-wildfire, adjusted for $PM_{2.5}$: 0.981 (0.798-1.206) Pneumonia, All Ages: Wildfire, unadjusted for $PM_{2.5}$: 0.943 (0.868-1.025) Wildfire, adjusted for $PM_{2.5}$: 0.888 (0.799-0.986) Post-wildfire, unadjusted for $PM_{2.5}$: 1.294 (1.158-1.446) Post-wildfire, adjusted for $PM_{2.5}$: 1.318 (1.174-1.479)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Pneumonia, Ages 0-4: Wildfire, unadjusted for $PM_{2.5}$: 0.938 (0.705-1.247) Wildfire, adjusted for $PM_{2.5}$: 0.951 (0.678-1.333) Post-wildfire, unadjusted for $PM_{2.5}$: 1.458 (0.974-20182) Post-wildfire, adjusted for $PM_{2.5}$: 1.374 (0.885-2.133) Pneumonia, Ages 5-19: Wildfire, unadjusted for $PM_{2.5}$: 0.891 (0.604-1.312) Wildfire, adjusted for $PM_{2.5}$: 0.830 (0.541-1.272) Post-wildfire, unadjusted for $PM_{2.5}$: 0.960 (0.588-1.569) Post-wildfire, adjusted for $PM_{2.5}$: 0.969 (0.578-1.624) Pneumonia, Ages 20-64: Wildfire, unadjusted for $PM_{2.5}$: 0.927 (0.795-1.081) Wildfire, adjusted for $PM_{2.5}$: 0.837 (0.690-1.016) Post-wildfire, unadjusted for $PM_{2.5}$: 1.314 (1.064-1.622) Post-wildfire, adjusted for $PM_{2.5}$: 1.300 (1.047-1.615) Pneumonia, Ages 65-99: Wildfire, unadjusted for $PM_{2.5}$: 0.959 (0.861-1.068) Wildfire, adjusted for $PM_{2.5}$: 0.899 (1.782-1.033) Post-wildfire, unadjusted for $PM_{2.5}$: 1.277 (1.102-1.481) Post-wildfire, adjusted for $PM_{2.5}$: 1.331 (1.142-1.552)
Reference: Dominici et al. (2006, 088398) **Period of Study:** 1999-2002 **Location:** 204 U.S. counties, located in: Alabama, Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, District of Columbia, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, Tennessee, Texas, Utah, Virginia, Washington, West Virginia, Wisconsin	Outcome (ICD-9: Daily counts of hospital admissions for primary diagnosis of chronic obstructive pulmonary disease (490-492), and respiratory tract infections (464-466, 480-487). **Age Groups:** >65 yr **Study Design:** Time series **N:** 11.5 million Medicare enrollees **Statistical Analyses:** Bayesian 2-stage hierarchical models. First stage: Poisson regression (county-specific) Second stage: Bayesian hierarchical models, to produce a national avg estimate **Covariates:** Day of the week, seasonality, temperature, dew point temperature, long-term trends **Season:** NR **Dose-response Investigated:** No **Statistical Package:** R statistical software version 2.2.0 **Lags Considered:** 0-2 days, avg of days 0-2	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h Mean ($\mu g/m^3$) (IQR): 13.4 (11.3-15.2) **Monitoring Stations:** NR **Copollutant (correlation):** NR **Other variables:** Median of pairwise correlations among $PM_{2.5}$ monitors within the same county for 2000: r = 0.91 (IQR: 0.81-0.95)	**PM Increment:** 10 $\mu g/m^3$ (Results in figures see notes) Percent increase in risk [95% PI]: COPD (Lag 0): Age 65 +: 0.91 [0.18, 1.64] Age 65-74: 0.42 [-0.64, 1.48] Age 75+: 1.47 [0.54, 2.40] Respiratory tract infection: Age 65+: 0.92 [0.41, 1.43] Age 65-74: 0.93 [0.04, 1.82] Age 75+: 0.92 [0.32, 1.53] Annual reduction in admissions attributable to a 10 $\mu g/m^3$ reduction in daily $PM_{2.5}$ level (95% PI): Cerebrovascular disease: Annual number of admissions: 226,641 Annual reduction in admissions: 1836 [680, 2992] COPD: Annual number of admissions: 108,812 Annual reduction in admissions: 990 [196, 1785] Respiratory tract infections: Annual number of admissions: 226,620 Annual reduction in admissions: 2085 [929, 3241]

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Dominici et al. (2006, 088398) **Period of Study:** 1999-2002 **Location:** U.S. (mainland)	**Outcome (ICD-9):** Respiratory tract infections (464-466, 480-487) and Chronic Obstructive Pulmonary Disease (490-492) **Age Groups:** All >65 yr 65-74 yr >75 yr **Study Design:** Time series **N:** 11.5 million at-risk **Statistical Analyses:** Bayesian 2-stage hierarchical models (day-to-day variation), Poisson regression (county-specific RRs) **Covariates:** Calendar time (seasonality and yr), temperature, dew point **Season:** NR **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 0, 1, 2 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily or every 3 days (depending on county) **Mean:** 13.4 (IQR: 11.3-15.2) **Monitoring Stations:** NR (used data from Air Quality System database) **Copollutant:** NR	**PM Increment:** 10 µg/m^3 **Percentage Change in Hospital Admission Rates [PI]:** COPD-Same day All >65: 0.91 [0.18,1.64] 65-74 yr: 0.42 [-0.64,1.48] >75: 1.47 [0.54,2.40] Respiratory Tract Infections-2-day lag All >65: 0.92 [0.41,1.43] 65-74 yr: 0.93 [0.04,1.82] >75: 0.92 [0.32,1.53] **Notes:** Other lag data shown in Fig 2-4
Reference: Erbas et al. (2005, 073849) **Period of Study:** Jul 1989-Dec 1992 **Location:** Melbourne, Australia	**Outcome (ICD):** COPD (490-492, 494, 496) Asthma (493) **Age Groups:** NR **Study Design:** Time series **N:** NR **Statistical Analyses:** GLM, GAM, Parameter Driven Poisson Regression, Transitional Regression, Seasonal-Trend decomposition based on Loess smoothing for seasonal adjustment **Covariates:** Secular trends, seasonality, relative humidity, dry bulb temp, dew point temp **Season:** NR **Dose-response Investigated?** Yes **Statistical Package:** S-Plus, SAS **Lags Considered:** 0-5 days	**Pollutant:** PM0.1-1 (API) **Averaging Time:** 24 h **Mean (min-max):** NR **Monitoring Stations:** 9 **Copollutant (correlation):** NR	**PM Increment:** Increase from the 10^{th}-90th percentile (value NR) **RR Estimate [CI]:** COPD GAM: 0.95 [0.91,1.00] GLM, PDM, TRM: NR Asthma NR **Notes:** This study was used to demonstrate that conclusions are highly dependent on the type of model used

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Fung et al. (2006, 089789) **Period of Study:** Jun 1995-Mar 1999 **Location:** Vancouver, Canada	Hospital Admission/ED: Hospital Admission **Outcome:** Respiratory diseases (460-519) **Age Groups:** Age >65 **Study Design:** Time series, case crossover **N:** 26,275 individuals admitted **Statistical Analyses:** Poisson regression (spline 12 knots), case-crossover (controls +/7 days from case date), Dewanji and Moolgavkar (DM) method **Covariates:** Long-term trends, day-of-the-week effect, weather **Season:** All yr **Dose-response Investigated?** No **Statistical Package:** SPlus, R **Lags Considered:** 0-7 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** 7.72(3.61) **Range (Min, Max):** (2, 32) **Monitoring Stations:** NR **Copollutant (correlation):** $PM_{2.5}$: PM_{10} r = 0.80 $PM_{10-2.5}$ r = 0.34 CO r = 0.23 CoH r = 0.38 O_3 r = -0.03 NO_2 r = 0.36 SO_2 r = 0.42	**PM Increment: :** 4 µg/m^3 **RR Estimate (65+ yr)** DM method: 1.007[0.994, 1.020] Current 1.007[0.990,1.023] 3 day 0.995[0.979,1.012] 5 day 0.995[0.971,1.020] 7 day Time series: 1.003[0.989, 1.018] Current 1.000[0.982, 1.018] 3 day 0.993[0.972, 1.014] 5 day 0.995[0.971, 1.020] 7 day Case-crossover: 1.002[0.986, 1.019] Current 1.001[0.981, 1.021] 3 day 0.988[0.966, 1.011] 5 day 0.984[0.959, 1.010] 7 day
Reference: Hinwood et al. (2006, 088976) **Period of Study:** Jan 1992-Dec 1998 **Location:** Perth, Australia	Hospital Admission **Outcome (ICD-9):** COPD (490-496.99, except asthma), pneumonia /influenza (480-489.99), asthma **Age Groups:** All ages **Study Design:** Time stratified case-crossover **N:** NR **Statistical Analyses:** Conditional logistic regression **Covariates:** Time trend, season, temperature, humidity, day of wk, holidays **Season:** All yr **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 0-3 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** 9.2 (4.3) **Percentiles:** 10th: 5.0 90th: 14.5 **Monitoring Stations:** 13 **Notes: Copollutant:** NR	**Increment:** 1 µg/m^3 **Notes:** Odds ratio for $PM_{2.5}$ and all respiratory, COPD, pneumonia and asthma. Authors found an elevation in the odds ratio for lags 2 and 3 reaaching significance in all age groups for lag 3. For each increase of 1 µg/m^3, the number of hospitalizations increases 0.2% for respiratory disease, 0.5% for pneumonia and 0.3% for asthna. $PM_{2.5}$ concentrations were also significantly associated with asthma for those aged under 15 yr with an estimated 0.5% increase in hospitalizations.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Hirshon et al. (2008, 180375) **Period of Study:** Jun 2002-Nov 2002 **Location:** Baltimore, Maryland	**Outcome:** Hospital admissions for asthma **Study Design:** Time-series **Covariates:** Spatial distance from pollution monitor, demographic variation, long term, seasonal and daily trends, weather and other pollutants **Statistical Analysis:** Overdispersed Poisson regression **Age Groups:** 0-17 yr	**Pollutant:** $PM_{2.5}$ zinc **Averaging Time:** 24 h **Mean (SD) Unit:** 22.42 (25.14) µg/m^3 **Range (Min, Max):** NR **Copollutant (correlation):** Ni: 0.41 Cr: 0.17 Fe: 0.54 Sulfate: 0.01 CO: 0.40 $PM_{2.5}$: 0.39 O_3: 0.01 NO_2: 0.66 EC: 0.48	**Increment:** NR **Relative Risk (95% CI), Best fit Model** Medium = 8.63-20.76 ng/m^3 High = >20.76 ng/m^3 No Lag Medium: 1.12 (0.98-1.28) High: 1.09 (0.91-1.30) 1-day Lag Medium: 1.23 (1.07-1.41) High: 1.16 (0.97-1.39) 2-day Lag Medium: 1.11 (0.94-1.30) High: 1.15 (0.96-1.38) **Controlling for Time Trends** No Lag Medium: 1.08 (0.95-1.23) High: 0.98 (0.86-1.11) 1-day Lag Medium: 1.13 (1.003-1.28) High: 1.03 (0.91-1.16) 2-day Lag Medium: 1.13 () High: 0.98-1.31 **Controlling for Time Trends and Additional Copollutants** No Lag Medium: 1.12 (0.98-1.29) High: 1.09 (1.01-1.30) 1-day Lag Medium: 1.20 (1.04-1.38) High: 1.12 (0.93-1.35) 2-day Lag Medium: 1.12 (0.95-1.32) High: 1.19 (0.98-1.44)
Reference: Host et al. (2007, 155851) **Period of Study:** 2000-2003 **Location:** Six French cities: Le Havre, Lille, Marseille, Paris, Rouen, and Toulouse	**Outcome (ICD-10):** Daily hospitalizations for all respiratory diseases (J00-J99), respiratory infections (J10-J22). **Age Groups:** For all respiratory diseases: 0-14 yr, 15-64 yr, and ≥ 65 yr. For respiratory infections: All ages **Study Design:** Time series **N:** NR (Total population of cities: approximately 10 million) **Statistical Analyses:** Poisson regression **Covariates:** Seasons, days of the week, holidays, influenza epidemics, pollen counts, temperature, and temporal trends **Season:** NR **Dose-response Investigated:** No **Statistical Package:** MGCV package in R software (R 2.1.1) **Lags Considered:** Avg of 0-1 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (5th -95th percentile):** Le Havre: 13.8 (6.0-30.5) Lille: 15.9 (6.9-26.3) Marseille: 18.8 (8.0-33.0) Paris: 14.7 (6.5-28.8) Rouen: 14.4 (7.5-28.0) Toulouse: 13.8 (6.0-25.0) **Monitoring Stations:** 13 total: 1 in Toulouse 4 in Paris 2 each in other cities **Copollutant (correlation):** $PM_{10-2.5}$: Overall: r > 0.6 Ranged between r = 0.28 and r = 0.73 across the six cities.	**PM Increment:** 10 µg/m^3 increase, and a 27 µg/m^3 increase (corresponding to the difference between the lowest of the 5th percentiles and the highest of the 95th percentiles of the cities' distributions) ERR (excess relative risk) Estimate [CI]: For all respiratory diseases (27 µg/m^3 increase): 0-14 yr: 1.1% [-3.1, 5.5] 15-64 yr: 2.2% [-1.8, 6.4]; ≥ 65 yr: 1.3% [-5.3, 8.2] For respiratory infections (10 µg/m^3 increase): All ages: 2.5% [0.1, 4.8] For respiratory infections (27 µg/m^3 increase): All ages: 7.0% [0.7, 13.6]

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ko et al. (2007, 091639) **Period of Study:** Jan 2000-Dec 2004 **Location:** Hong Kong, China	ED Visits **Outcome (ICD-9):** COPD: Chronic bronchitis (491), Emphysema (492), Chronic airway obstruction (496) **Age Groups:** All ages **Study Design:** Time series **N:** 15 hospitals, 119,225 admissions **Statistical Analyses:** Poisson regression, GAM with stringent convergence criteria, APHEA2 protocol. **Covariates:** Time trend, season, temperature, humidity, other cyclical factors, day, day of wk, holidays **Season:** All yr, interactions with season tested **Dose-response Investigated?** No **Statistical Package:** SPLUS 4.0 **Lags Considered:** 0-5 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** 35.7 (20.6) **Percentiles:** 25th: 19.4 50th(Median): 31.7 75th: 46.7 **Range (Min, Max):** (6.0, 163.2) **Monitoring Stations:** 14 **Copollutant (correlation):** $PM_{2.5}$: PM_{10} r = 0.952 NO_2 r = 0.441 O_3 r = 0.394 SO_2 r = 0.282	**PM Increment:** PM_{10} **RR Estimate** COPD: 1.002[0.998, 1.001] lag 0 1.003[0.999, 1.007] lag 1 1.011[1.007, 1.014] lag 2 1.013[1.010, 1.017] lag 3 1.011[1.008, 1.015] lag 4 1.009[1.006, 1.013] lag 5 1.004[0.999, 1.008]lag 0-1 1.010[1.006, 1.015]lag 0-2 1.018[1.013, 1.022]lag 0-3 1.024[1.019, 1.029]lag 0-4 1.031[1.026, 1.036]lag 0-5 4-Pollutant model: 1.014[1.007, 1.022] lag 0-5 3-Pollutant model: 1.011[1.004, 1.017] lag 0-5
Reference: Ko et al. (2007, 092844) **Period of Study:** Jan 2000-Dec 2005 **Location:** Hong Kong, China	Hospital Admission **Outcome (ICD-9):** Asthma (493) **Age Groups:** All, 0-14, 15-56, 65+ **Study Design:** Time series **N:** 69,716 admissions, 15 hospitals **Statistical Analyses:** Poisson regression, with GAM with stringent convergence criteria. **Covariates:** Time trend, season, temperature, humidity, other cyclical factors **Season:** All yr, evaluated effect of season in analysis **Dose-response Investigated?** No **Statistical Package:** SPLUS 4.0 **Lags Considered:** 0-5 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** 36.4 (21.1) **Percentiles**: 25th: 20.0 50th(Median): 32.5 75th: 47.7 **Range (Min, Max):** (6, 163) **Monitoring Stations:** 14 **Copollutant (correlation):** $PM_{2.5}$: PM_{10} r = 0.956 NO_2 r = 0.774 O_3 r = 0.585 SO_2 r = 0.482	**PM Increment:** 10.0 µg/m^3 **RR Estimate** Asthma (Single-pollutant model): 1.008[1.004, 1.013] lag 0 1.004[1.000, 1.009] lag 1 1.004[1.000, 1.009] lag 2 1.009[1.005, 1.014] lag 3 1.006[1.001, 1.011] lag 4 1.002[0.998, 1.007] lag 5 1.009[1.004, 1.014] lag 0-1 1.012[1.007, 1.018] lag 0-2 1.017[1.011, 1.022] lag 0-3 1.020[1.014, 1.026] lag 0-4 1.021[1.015, 1.028] lag 0-5 Asthma in Age: 0-14: 1.024[1.013, 1.034] lag 0-5 14-65: 1.018[1.008, 1.029] lag 0-5 >65: 1.021[1.012, 1.030] lag 0-4 Asthma-Cold Season: 1.139[1.043, 1.244] lag 0-5
Reference: Lee et al. (2006, 090176) **Period of Study:** Jan 1997-Dec 2002 **Location:** Hong Kong, China	Hospital Admission **Outcome:** Asthma (493) **Age Groups:** <18 yr **Study Design:** Time series **N:** 26,663 asthma admissions for asthma and 5821 admissions for influenza **Statistical Analyses:** Poisson regression, GAM **Covariates:** Temperature, atmospheric pressure, relative humidity **Season:** All **Dose-response Investigated?** No **Statistical Package:** SAS 8.02 **Lags Considered:** 0-5 **Notes:** Controls were admissions for influenza ICD9 487	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** 45.3 µg/m^3, (16.2) **Percentiles:** 25th: 33.4 50th(Median): 43.0 75th: 54.0 **Range (Min, Max):** NR **Monitoring Stations:** 10 **Copollutant (correlation):** $PM_{2.5}$-PM_{10}: 0.89 $PM_{2.5}$-SO_2: 0.48 $PM_{2.5}$-NO_2: 0.74 $PM_{2.5}$-O_3: 0.47	**PM Increment:** IQr = 20.6 µg/m^3 Percent increase: Single pollutant model: 5.10 [2.95, 7.30], lag 0 5.00 [2.88, 7.16], lag 1 5.48 [2.75, 6.95], lag 2 4.83 [2.78, 6.93], lag 3 6.59 [4.51, 8.72], lag 4 5.24 [3.18, 7.34], lag 5 Multipollutant model (SO_2, NO_2, CO, O_3) 3.24 [0.93, 5.60], lag 4

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Letz and Quinn (2005, 088752) **Period of Study:** Oct 2001-Aug 2002 **Location:** San Antonio,Texas	Emergency Dept Visits **Outcome (ICD-9):** Asthma or reactive airway disease (493.0-493.9), wheezing (786.07), dyspnea (786.01-786.9), shortness of breath (786.05), bronchitis (490-496), or cough (786.2) **Age Groups:** NR (basic air force trainees) **Study Design:** Historic (retrospective) cohort **N:** 149 ED visits **Statistical Analyses:** Pearson correlation **Covariates:** NR **Season:** NR **Dose-response Investigated?** No **Statistical Package:** SPSS **Lags Considered:** NR	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h AQI **AQI Range (min-max):** (4-109) **Monitoring Stations:** Data obtained from the Texas Commission on Environmental Quality **Copollutant (correlation):** NR	**PM Increment:** NR Correlation with Outcomes: Same-day All visits: r = 0.082 Proven asthmatic events: r = -0.042 3-day All visits: r = 0.097 Proven asthmatic events: r = 0.011
Reference: Lin et al. (2005, 087828) **Period of Study:** 1998-2001 **Location:** Toronto, North York, East York, Etobicoke, Scarborough, and York (Canada)	Hospital Admissions **Outcome (ICD-9):** Respiratory infections including laryngitis, tracheitis, bronchitis, bronchiolitis, pneumonia, and influenza (464, 466, 480-487) **Age Groups:** 0-14 yr **Study Design**: Bidirectional case-crossover **N:** 6782 respiratory infection hospitalizations **Statistical Analyses:** Conditional logistic regression (Cox proportional hazards model) **Covariates:** Daily mean temp and dew point temp **Season:** NR **Dose-response Investigated?** No **Statistical Package:** SAS 8.2 PHREG procedure **Lags Considered:** 1- to 7-day avg	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (min-max):** 9.59 (0.25-50.50) SD = 7.06 **Monitoring Stations:** 4 **Copollutant (correlation):** $PM_{10-2.5}$: r = 0.33 PM_{10}: r = 0.87 CO: r = 0.10 SO_2: r = 0.47 NO_2: r = 0.48 O_3: r = 0.56	**PM Increment:** 7.8 µg/m^3 OR Estimate [CI]: Adjusted for weather 4-day avg: 1.11 [1.02,1.22] 6-day avg: 1.11 [1.00,1.24] Adj for weather and other gaseous pollutants 4-day avg: 0.94 [0.81,1.08] 6-day avg: 0.90 [0.76,1.07] **Notes:** OR's were also categorized into "Boys" and "Girls," yielding similar results

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Lin et al. (2002, 026067) **Period of Study:** Jan 1981-Dec 1993 **Location:** Toronto	Hospital Admissions **Outcome (ICD-9):** Asthma (493) **Age Groups:** 6-12 yr **Study Design:** Uni- and bi-directional case-crossover (UCC, BCC) and time-series (TS) **N:** 7,319 asthma admissions **Statistical Analyses:** Conditional logistic regression, GAM **Covariates:** Maximum and minimum temp, avg relative humidity **Season:** Apr-Sep, Oct-Mar **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 1- to 7-day avg	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 6 days (predicted daily values) **Mean (min-max):** 17.99 (1.22-89.59) SD = 8.49 **Monitoring Stations:** 1 **Copollutant (correlation):** PM_{10}: r = 0.87 $PM_{10-2.5}$: r = 0.44 CO: r = 0.45 SO_2: r = 0.46 NO_2: r = 0.50 O_3: r = 0.21	**PM Increment:** 9.3 µg/m^3 **RR Estimate [CI]:** Adj for weather and gaseous pollutants BCC 5-day avg: 0.94 [0.85,1.03] BCC 6-day avg: 0.92 [0.83,1.02] TS 5-day avg: 0.96 [0.90,1.02] TS 6-day avg: 0.94 [0.88,1.01] Boys-adj for weather UCC 1-day avg: 1.09 [1.04,1.15] UCC 2-day avg: 1.09 [1.02,1.16] BCC 1-day avg: 1.01 [0.97,1.06] BCC 2-day avg: 0.99 [0.93,1.05] TS 1-day avg: 1.00 [0.97,1.04] TS 2-day avg: 0.98 [0.94,1.02] Girls-adj for weather UCC 1-day avg: 1.06 [0.99,1.14] UCC 2-day avg: 1.11 [1.02,1.21] BCC 1-day avg: 0.99 [0.93,1.06] BCC 2-day avg: 1.02 [0.94,1.09] TS 1-day avg: 0.99 [0.95,1.04] TS 2-day avg: 1.00 [0.95,1.06] **Notes:** The author also provides RR using UCC, BCC, and TS analysis for female and male groups for days 3-7, yielding similar results
Reference: Magas et al. (2007, 090714) **Period of Study:** 2001-2003 **Location:** Oklahoma City Metro area, Oklahoma and Cleveland counties	Hospital Admission/ED: Admissions **Outcome:** Asthma 493.01-493.99 **Age Groups:** <15 yr **Study Design:** Time series **N:** 1,270 admissions **Statistical Analyses:** Negative binomial regression **Covariates:** Temperature, humidity, pollen count, mold **Season:** All **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 1	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR **Monitoring Stations:** 10 **Copollutant (correlation):** NR	**Notes:** Coefficient for $PM_{2.5}$ was not significant and thus not reported.
Reference: Mohr et al. (2008, 180215) **Period of Study:** Jun 2001-May 2003 **Location:** St. Louis, MO	**Outcome:** Asthma ER Visits **Age Groups:** 2-17 yr **Study Design:** Time series **Statistical Analyses:** GEE Poisson models **Covariates:** Season, weekend exposure, allergens **Dose-response Investigated:** No **Statistical Package:** SAS **Lags Considered:** 1 day	**Pollutant:** $PM_{2.5}$ EC **Averaging Time:** 24 h **Std Dev:** 0.1 **Monitoring Stations:** 1 **Copollutant:** NO_X, SO_2, O_3 **Co-pollutant Correlation** NO_X: 0.68* SO_2: 0.09 O_3: -0 06 *p≤0.05	**PM Increment:** 0.1 µg/m^3 **Relative Risk Effect (Lower CI, Upper CI):** Weekend Exposure Summer: 1.05 (1.00, 1.11) Fall: 0.99 (0.97, 1.01) Winter: 0.96 (0.92, 1.00) Spring: 0.96 (0.92, 1.00) Weekday Exposure Summer: 1.01 (0.98, 1.03) Fall: 1.00 (0.99, 1.01) Winter: 0.99 (0.96, 1.01) Spring: 0.98 (0.96, 1.01)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Neuberger et al. (2004, 093249) **Period of Study:** 1999-2000 (1-yr period) **Location:** Vienna and Lower Austria	Hospital Admissions **Outcome (ICD-9):** Bronchitis, emphysema, asthma, bronchiectasis, extrinsic allergic alveolitis, and chronic airway obstruction (490-496) **Age Groups:** 3.0-5.9 yr 7-10 yr 65+ yr **Study Design:** Time series **N:** 366 days (admissions NR) **Statistical Analyses:** GAM **Covariates:** SO_2, NO, NO_2, O_3, temperature, humidity, and day of the week **Season:** NR **Dose-response Investigated?** Yes **Statistical Package:** S-Plus 2000 **Lags Considered:** 0-14 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Maximum daily mean:** Vienna: 96.4 Rural area: 48.0 **Monitoring Stations:** NR **Copollutant (correlation):** NR	**PM Increment:** 10 µg/m^3 Log Relative Rate Estimate (p-value): Vienna Male: 2-day lag = 5.467 (0.019) Female: 3-day lag = 5.596 (0.009) Rural Male: 10-day lag = 9.893 (0.012) Female: 11-day lag = 10.529 (0.011) Association with tidal lung functioN: β = -0.987 (p-value = 0.091) **Notes:** Effect parameters with significant coefficients for respiratory health included: male sex, allergy, asthma in family, and traffic for Vienna and age, allergy, asthma in family, passive smoking, and PM fraction for the rural area. Effect parameters with significant coefficients for log asthma score were allergy, asthma in family, and rain for Vienna and allergy, asthma in family, and passive smoking for the rural area. Cross-correlation coefficients are provided in Fig 1.
Reference: Ostro et al. (2008, 097971) **Period of Study:** 2000-2003 **Location:** Six California Counties	**Outcome:** Respiratory disease (ICD-9 460-519) **Study Design:** Time-Series **Statistical Analysis:** Poisson Regression **Statistical Package:** R **Age Groups:** Children <19 yr	**Pollutant:** $PM_{2.5}$ and components **Averaging Time:** 24 h **Mean (SD) Unit:** 19.4 µg/m^3 **IQR:** 14.6 µg/m^3 **Copollutants:** EC, OC, NO_2, SO_4, Cu, Fe, K, Si, Zn	**Increment:** NR **Relative Risk (Min CI, Max CI)** **Lag** Full results are presented graphically in figures 1 and 2. Excess risks for all-yr respiratory hospital admissions in children <19yrs, 3-day lag $PM_{2.5}$: 4.1% (1.8-6.4) EC: 5.4% (0.8-10.3) Fe: 4.7% (2.2-7.2) OC: 3.4% (1.1-5.7) Nitrates: 3.3% (1.1-5.5) Sulfates: 3.0% (0.4-5.7) Excess risks for cool season (Oct-Mar) respiratory hospital admissions in children <19yrs, 3 day lag $PM_{2.5}$: 5.1% (1.6-8.9) EC: 6.8% (-0.2-14.2) Fe: 4.8% (1.7-8.0) K: 4.0% (0.3-7.7)

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Slaughter et al. (2005, 073854) **Period of Study:** Jan 1995-Jun 2001 **Location:** Spokane, WA	Hospital Admissions and ED visits **Outcome:** All respiratory (460-519) Asthma (493) COPD (491,492, 494,496) Pneumonia (480-487) Acute URI not including colds and sinusitis (464, 466, 490) **Age Groups:** All, 15+ yr for COPD **Study Design:** Time series **N:** 2373 visit records **Statistical Analyses:** Poisson regression, GLM with natural splines. For comparison also used GAM with smoothing splines and default convergence criteria. **Covariates:** Season, temperature, relative humidity, day of week **Season:** All **Dose-response Investigated?:** No **Statistical Package:** SAS, SPLUS **Lags Considered:** 1 -3 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Range (90% of Concentrations):** 4.2-20.2 µg/m^3 **Monitoring Stations:** One **Notes: Copollutant (correlation):** $PM_{2.5}$ PM1 r = 0.95 PM_{10} r = 0.62 $PM_{10-2.5}$ r = 0.31 CO r = 0.62 Temperature r = 0.21	**PM Increment:** 10 µg/m^3 **RR Estimate [Lower CI, Upper CI] lag:** **ER visits:** $PM_{2.5}$ All Respiratory Lag 1: 1.01 [0.98, 1.04] Lag 2: 1.02 [0.99, 1.04] Lag 3: 1.02 [0.99, 1.05] Acute Asthma Lag 1: 1.03 [0.98, 1.09] Lag 2: 1.00 [0.95, 1.05] Lag 3: 1.01 [0.96, 1.06] COPD (adult) Lag 1: 0.96 [0.89, 1.04] Lag 2: 1.01 [0.93, 1.09] Lag 3: 1.00 [0.93, 1.08] **Hospital Admissions:** $PM_{2.5}$ All Respiratory Lag 1: 0.98 [0.94, 1.01] Lag 2: 0.99 [0.96, 1.03] Lag 3: 1.01 [0.98, 1.05] Asthma Lag 1: 1.01 [0.91, 1.11] Lag 2: 1.03 [0.94, 1.13] Lag 3: 1.02 [0.93, 1.13] COPD (adult) Lag 1: 0.99 [0.91, 1.08] Lag 2: 1.06 [0.98, 1.16] Lag 3: 1.03 [0.94, 1.12]
Reference: Tecer et al. (2008, 180030) **Period of Study:** Dec 2004-Oct 2005 **Location:** Zonguldak, Turkey	**Outcome:** ED visits for respiratory problems (ICD-9 470-478, 493) **Study Design:** Bidirectional Case-crossover **Covariates:** Daily meteorological parameters **Statistical Analysis:** Conditional logistic regression **Statistical Package:** Stata **Age Groups:** 0-14 yr	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **Mean, Unit:** 29.1 µg/m^3 **Range (Min, Max):** 4.55, 95.65 **Copollutant (correlation):** $PM_{2.5}/PM_{10}$ Mean: 0.56 Range: 0.17-0.88 $PM_{2.5}/PM_{10-2.5}$ Mean: 1.49 Range: 0.21-7.53	**Increment:** 10 µg/m^3 **Odds Ratio (95% CI)** Asthma Lag 0: 1.15 (0.99-1.34) Lag 1: 0.85 (0.70-1.03) Lag 2: 0.87 (0.73-1.04) Lag 3: 0.93 (0.79-1.10) Lag 4: 1.25 (1.05-1.50) Allergic Rhinitis with Asthma Lag 0: 1.21 (1.10-1.33) Lag 1: 0.84 (0.75-0.93) Lag 2: 0.89 (0.81-0.98) Lag 3: 0.99 (0.90-1.09) Lag 4: 1.06 (0.95-1.19) Allergic Rhinitis Lag 0: 1.08 (0.98-1.20) Lag 1: 1.03 (0.93-1.13) Lag 2: 0.89 (0.80-0.99) Lag 3: 0.98 (0.89-1.09) Lag 4: 1.18 (1.00-1.24) Upper Respiratory Disease Lag 0: 0.99 (0.49-2.00) Lag 1: 0.52 (0.22-1.20) Lag 2: 1.29 (0.75-2.22) Lag 3: 1.29 (0.69-2.43) Lag 4: 1.47 (0.87-2.50) Lower Respiratory Disease Lag 0: 1.06 (0.78-1.44) Lag 1: 0.85 (0.59-1.22) Lag 2: 1.08 (0.72-1.61) Lag 3: 1.18 (0.92-1.52) Lag 4: 0.72 (0.54-0.96)h
Reference: Tolbert et al. (2007, 090316) **Period of Study:** Aug 1998-Dec 2004 **Location:** Atlanta Metropolitan area, Georgia	**Outcome (ICD-9):** Combined RD group, including: Asthma (493, 786.07, 786.09), COPD (491, 492, 496), URI (460-465, 460.0, 477), pneumonia (480-486), and bronchiolitis (466.1, 466.11, and 466.19)) **Age Groups:** All	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (median IQR, range, 10th-90th percentiles):** $PM_{2.5}$: 17.1 (15.6 11.0-21.9 0.8-65.8 7.9-28.8) $PM_{2.5}$ sulfate: 4.9 (3.9 2.4-6.2	**PM Increment:** $PM_{2.5}$: 10.96 µg/m^3 (IQR) $PM_{2.5}$ sulfate: 3.82 µg/m^3 (IQR) $PM_{2.5}$ total carbon: 3.63 µg/m^3 (IQR) $PM_{2.5}$ OC: 2.61 µg/m^3 (IQR) $PM_{2.5}$ EC: 1.15 µg/m^3 (IQR) $PM_{2.5}$ water-soluble metals: 0.03 µg/m^3

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
	Study Design: Time series **N:** NR for 1998-2004. For 1993-2004: 10,234,490 ER visits (283,360 and 1,072,429 visits included in the CVD and RD groups, respectively) **Statistical Analyses:** Poisson generalized linear models **Covariates:** Long-term temporal trends, season (for RD outcome), temperature, dew point, days of week, federal holidays, hospital entry and exit **Season:** All **Dose-response Investigated:** No **Statistical Package:** SAS version 9.1 **Lags Considered:** 3-day ma(lag 0 -2)	0.5-21.9 1.7-9.5) $PM_{2.5}$ OC: 4.4 (3.8 2.7-5.3 0.4-25.9 2.1-7.2) $PM_{2.5}$ EC: 1.6 (1.3 0.9-2.0 0.1-11.9 0.6-3.0) $PM_{2.5}$ water-soluble metals: 0.030 (0.023 0.014-0.039 0.003-0.202 0.009-0.059) **Monitoring Stations:** 1 **Copollutant (correlation):** Between $PM_{2.5}$ and: PM_{10}: r = 0.84 O_3: r = 0.62 NO_2: r = 0.47 CO: r = 0.47 SO_2: r = 0.17 $PM_{10-2.5}$: r = 0.47; $PM_{2.5}$ SO_4: r = 0.76; $PM_{2.5}$ EC: r = 0.65; $PM_{2.5}$ OC: r = 0.70; $PM_{2.5}$ TC: r = 0.71; $PM_{2.5}$ water-sol metals: r = 0.69 OHC: r = 0.50 Between $PM_{2.5}$ SO_4 and: PM_{10}: r = 0.69 O_3: r = 0.56 NO_2: r = 0.14 CO: r = 0.14 SO_2: r = 0.09 $PM_{10-2.5}$: r = 0.32; $PM_{2.5}$: r = 0.76; $PM_{2.5}$ EC: r = 0.32; $PM_{2.5}$ OC: r = 0.33; $PM_{2.5}$ TC: r = 0.34; $PM_{2.5}$ water-sol metals: r = 0.65 OHC: r = 0.47 Between $PM_{2.5}$ EC and: PM_{10}: r = 0.61 O_3: r = 0.40 NO_2: r = 0.64 CO: r = 0.66 SO_2: r = 0.22 $PM_{10-2.5}$: r = 0.49 $PM_{2.5}$: r = 0.65 $PM_{2.5}$ SO_4: r = 0.32 $PM_{2.5}$ OC: r = 0.82 $PM_{2.5}$ TC: r = 0.91 $PM_{2.5}$ water soluble metals: r = 0.52 OHC: r = 0.35 Between $PM_{2.5}$ OC and: PM_{10}: r = 0.65 O_3: r = 0.54 NO_2: r = 0.62 CO: r = 0.59 SO_2: r = 0.17 $PM_{10-2.5}$: r = 0.49 $PM_{2.5}$: r = 0.70 $PM_{2.5}$ SO_4: r = 0.33 $PM_{2.5}$ EC: r = 0.82 $PM_{2.5}$ TC: r = 0.98 $PM_{2.5}$ water-sol metals: r = 0.49 OHC: r = 0.37 Between $PM_{2.5}$ total carbon and: PM_{10}: r = 0.67 O_3: r = 0.52 NO_2: r = 0.65 CO: r = 0.63 SO_2: r = 0.19 $PM_{10-2.5}$: r = 0.51 $PM_{2.5}$: r = 0.71	(IQR) Risk ratio [95% CI] (single pollutant models): $PM_{2.5}$: RD: 1.005 [0.995-1.015] $PM_{2.5}$ sulfate: RD: 1.007 [0.996-1.018] $PM_{2.5}$ total carbon: RD: 1.001 [0.993-1.008] $PM_{2.5}$ OC: RD: 1.003 [0.995-1.011] $PM_{2.5}$ EC: RD: 0.996 [0.989-1.004] $PM_{2.5}$ water-soluble metals: RD: 1.005 [0.995-1.015]

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
		$PM_{2.5}$ SO_4: r = 0.34 $PM_{2.5}$ EC: r = 0.91 $PM_{2.5}$ OC: r = 0.98 $PM_{2.5}$ water-sol metals: r = 0.52 OHC: r = 0.38 Between $PM_{2.5}$ water-soluble metals and: PM_{10}: r = 0.73 O_3: r = 0.43 NO_2: r = 0.32 CO: r = 0.35 SO_2: r = 0.06 $PM_{10-2.5}$: r = 0.50 $PM_{2.5}$: r = 0.69 $PM_{2.5}$ SO_4: r = 0.65 $PM_{2.5}$ EC: r = 0.52 $PM_{2.5}$ OC: r = 0.49 $PM_{2.5}$ TC: r = 0.52	
Reference: Wong et al. (2006, 093266) **Period of Study:** 2000-2002 **Location:** Hong Kong (8 districts)	General Practitioner Visits **Outcome (ICPC-2):** Respiratory diseases/symptoms: upper respiratory tract infections (URTI), lower respiratory infections, influenza, asthma, COPD, allergic rhinitis, cough, and other respiratory diseases **Age Groups:** All ages **Study Design:** Time series **N:** 269,579 visits **Statistical Analyses:** GAM, Poisson regression **Covariates:** Season, day of the week, climate **Season:** NR **Dose-response Investigated?** No **Statistical Package:** S-Plus **Lags Considered:** 0-3 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (min-max):** 35.7 (9-120) SD = 16.7 **Monitoring Stations:** 1 per district **Copollutant (correlation):** PM_{10}: r = 0.94	**PM Increment:** 10 µg/m^3 RR Estimate [CI]: Overall URTI 1.021 [1.010,1.032] **Notes:** RRs are also reported for each individual general practitioner yielding similar results
Reference: Yang Q et al. (2004, 087488) **Period of Study:** Jun 1995-Mar 1999 **Location:** Vancouver area, British Columbia	Hospital Admissions **Outcome (ICD-9):** Respiratory diseases (460-519), pneumonia only (480-486), asthma only (493) **Age Groups:** 0-3 yr **Study Design:** Case control, bidirectional case-crossover (BCC), and time series (TS) **N:** 1610 cases **Statistical Analyses:** Chi-square test, Logistic regression, GAM (time-series), GLM with parametric natural cubic splines **Covariates:** Gender, socioeconomic status, weekday, season, study yr, influenza epidemic month **Season:** Spring, summer, fall, winter **Dose-response Investigated?** No **Statistical Package:** SAS (Case control and BCC), S-Plus (TS) **Lags Considered:** 0-7 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (min-max):** 7.7 (2.0-32.0) SD = 3.7 **Monitoring Stations:** NR (data obtained from Greater Vancouver Regional District Air Quality Dept) **Copollutant (correlation):** PM_{10}: r = 0.83 $PM_{10-2.5}$: r = 0.39 CO: r = 0.24 O_3: r = -0.03 NO_2: r = 0.37 SO_2: r = 0.43	**PM Increment:** 4.0 µg/m^3 (IQR) OR Estimate [CI]: Values NR **Notes:** Author states that no significant association was found between $PM_{2.5}$ and respiratory disease hospitalizations.

Reference	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Zanobetti and Schwartz (2006, 090195) **Period of Study:** 1995-1999 **Location:** Boston, MA	Hospital Admission/ED: **Outcome:** Pneumonia (480-487) **Age Groups:** >65 y **Study Design:** Case-crossover, time stratified **N:** 24,857 for Pneumonia **Statistical Analyses:** Condition logistic regression **Covariates:** Season, long term trend, day of-the-wk, mean temperature, relative humidity, barometric pressure, extinction coefficient **Season:** All yr **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 0-1 **Notes:** Also looked at MI cohort	**Pollutant:** PM non-traffic **Averaging Time:** 24 h **Percentiles (pneumonia cohort):** 5th: -7.3 25th: -3.28 µg/m^3 50th(Median): -0.88 75th: 1.92 95th: 12.11 **PM Component:** BC **Monitoring Stations:** 4-5 monitors **Copollutant (correlation):** PM non-traffic: $PM_{2.5}$ r = 0.74 CO r = -0.01 NO_2 r = 0.14 O_3 r = -0.47 BC r = -0.01	**PM Increment:** PM non-traffic lag 0: 13.44 µg/m^3 PM non-traffic lag 0-1 avg: 10.28 µg/m^3 % change in Pneumonia: PM non-traffic -0.57 [-7.51, 6.36] lag 0 PM non-traffic -0.94 [-7.20, 5.32] mean lag 1
Reference: Zhong et al. (2006, 093264) **Period of Study:** Apr-Oct 2002 **Location:** Cincinnati, Ohio	Hospital Admissions **Outcome (ICD-9):** Asthma (493-493.91) **Age Groups:** 1-18 yr **Study Design:** Time series **N:** 1254 admissions **Statistical Analyses:** Poisson multiple regression, GAM **Covariates:** Season, temperature, humidity, O_3, day of the week **Season:** NR **Dose-response Investigated?** Yes **Statistical Package:** NR **Lags Considered:** 1-5 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** Apr: 12.4 (3.8) May: 13.6 (5.8) Jun: 21.6 (9.9) Jul: 25.8 (11.9) Aug: 20.3 (8.7) Sep: 19.5 (11.1) Oct: 12.8 (6.4) **Monitoring Stations:** NR (data obtained from the National Virtual Data System) **Copollutant (correlation):** NR **Notes:** Author states all pairwise correlations were insignificant	**PM Increment:** NR RR Estimate [CI]: NR **Notes:** This study focused primarily on aeroallergens and asthma visits
Reference: Zanobetti and Schwartz (2006, 090195) **Period of Study:** 1995-1999 **Location:** Boston, MA	**Outcome:** Pneumonia (480-487) **Age Groups:** >65 y **Study Design:** Case-crossover, time stratified **N:** 24,857 for Pneumonia **Statistical Analyses:** Condition logistic regression **Covariates:** Season, long term trend, day of-the-wk, mean temperature, relative humidity, barometric pressure, extinction coefficient **Season:** All yr **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 0-1 **Notes:** Also looked at MI cohort	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Percentiles** (pneumonia cohort)**:** 25th: 7.23 µg/m^3 50th(Median): 11.10 75th: 16.14 **PM Component:** Black Carbon (BC), PM non-traffic **Monitoring Stations:** 4-5 monitors **Copollutant (correlation):** $PM_{2.5}$: CO r = 0.52 NO_2 r = 0.55 O_3 r = 0.20 BC r = 0.66 PM non-traffic r = 0.74	**PM Increment:** $PM_{2.5}$ lag 0: 17.17 µg/m^3 $PM_{2.5}$ lag 0-1 avg: 16.32 µg/m^3 % change in Pneumonia: 6.48[1.13, 11.43] lag 0 5.56[-0.45, 11.27] mean lag 1

[1]All units expressed in µg/m^3 unless otherwise specified.

Table E-15. Short-term exposure-respiratory-ED/HA-Other Size Fractions.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Andersen et al. (2007, 093201) **Period of Study:** 2001-2004 **Location:** Copenhagen, Denmark	**Outcome (ICD10):** Respiratory disease (J41-46) Asthma (J45, 46) **Age Groups:** 5-18 and >65 **Study Design:** Time-series **N:** 1327 days ~1.5 million people at-risk **Statistical Analyses:** Poisson regression, GAM. **Covariates:** Influenza epidemics, pollen, temperature, dew point, day-of-week, holiday, season. **Season:** All **Dose-response Investigated?** No **Statistical Package:** R with gam and mgcv packages. **Lags Considered:** 0-5	**Pollutant:** Number concentration (NC) of ultrafine & accumulation mode particles **Averaging Time:** 24 h **Mean particles/cm3 (SD):** NCtot (total): 8116 (3502) 25th: 4959 50th: 6243 75th: 8218 99th: 16189 IQR: 3259 NC100 (<100 nm): 6847 (2864) 25th: 5738 50th (Median): 7358 75th: 9645 99th: 19895 IQR: 3907 Mean particles/cm^3 for 4 size modes (median diameter (nm) noted): NCa12: 493(315) NCa23: 2253 (1364) NCa57: 5104 (2687) NCa212: 6847 (2864) **Monitoring Stations:** 3 (Background, rural Background, urban Curbside, urban) **Notes:** NC exposure data available for n = 578 days. Information on distribution of 4 size modes provided in the paper. **Copollutant (correlation):** NCtot and PM_{10}: r = 0.39 NCtot and $PM_{2.5}$: r = 0.40 NCtot and NO_2: r = 0.68 PM_{10} and $PM_{2.5}$: r = 0.8 "Low or no" correlations between 4 size modes NCa212 and $PM_{2.5}$: r = 0.8 NCa212 and PM_{10}: r = 0.63 NCa57 and NO_2: r = 0.57 **Notes:** selected correlations reported in text, all correlations in annex to the manuscript	**PM Increment:** Based on the IQR, specific to metric (see below). **RR Estimate:** Single pollutant results, Asthma, (5-18 yr), lag 0-5: $PM_{2.5}$: 1.15 [1, 1.32], IQr = 5 NCtot: 1.07 [0.98, 1.17], IQr = 3907 NC100: 1.06 [0.97, 1.16], IQr = 3259 NCa12: 1.08 [0.99,1.18], IQr = 342 NCa212: 1.08 [1, 1.17], IQr = 495 NCa23: 1.09 [0.98,1.21], IQr = 1786 NCa57: 1.02 [0.94,1.12], IQr = 3026 2-pollutant results: NCa212 w/ PM_{10}: 1.1 [0.96, 1.13], IQr = 495 NCtot w/ PM_{10}: 1.03 [0.92, 1.15] NCtot w/ $PM_{2.5}$: 1.04 [0.85, 1.28] All RD, (>65 yr), lag 0-4, single pollutant results: $PM_{2.5}$: 1 [0.95, 1.05] NCtot: 1.04 [1, 1.07] IQr = 3907 NC100: 1.03 [0.99, 1.07], IQr = 3259 NC12: 1.01 [0.98, 1.05], IQr = 342 NC212: 1.04 [1.01, 1.08], IQr = 495 NCa23: 0.99 [0.94, 1.03], IQr = 1786 NCa57: 1.04 [1, 1.08], IQr = 3026 2-pollutant results: NCa212 w/ PM_{10}: 1.01 [0.96, 1.07], IQr = 495 NCtot w/ $PM_{2.5}$: 0.97 [0.89, 1.05] NCtot w/ PM_{10}: 1 [0.96, 1.05] **Notes:** Multipollutant model results also included for models with 4 size modes.
Reference: Agarwal et al. (2006, 099086) **Period of Study:** 2000-2003 **Location:** Safdarjung area of Delhi	**Outcome (ICD-NR):** COPD, asthma, emphysema **Age Groups:** NR **Study Design:** Time series **N:** NR **Statistical Analyses:** Kruskal-Wallis one-way analysis, Chi-square, Multivariate linear regression **Covariates:** Temp (min & max), relative humidity at 0830 and 1730 h, wind speed **Season:** I (Jan-Mar), II (Apr-Jun), III (Jul-Sep), IV (Oct-Dec) **Dose-response Investigated?** Yes **Statistical Package:** SPSS **Lags Considered:** NR	**Pollutant:** SPM (Suspended PM) **Averaging Time:** 8 h **Mean** µg/m^3 **(SD):** Qtr I: 297.5 (34.6) Qtr II: 398.0 (85.6) Qtr III: 220.0 (78.0) Qtr IV: 399.0 (54.6) **Monitoring Stations:** 2 **Copollutant (correlation):** RSPM: r = 0.771 **Other variables:** RH0830: r = -0.482 RH1730: r = -0.531 COPD: r = 0.474	**PM Increment:** NR **RR Estimate [CI]:** NR **Notes:** This study analyzed seasonal variation of pollutants and health outcomes and correlations among the variables

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Agarwal et al. (2006, 099086) **Period of Study:** 2000-2003 **Location:** Safdarjung area of Delhi	**Outcome (ICD-NR):** COPD, asthma, emphysema **Age Groups:** NR **Study Design:** Time series **N:** NR **Statistical Analyses:** Kruskal-Wallis one-way analysis, Chi-square, Multivariate linear regression **Covariates:** Temp (min & max), relative humidity at 0830 and 1730 h, wind speed **Season:** I (Jan-Mar), II (Apr-Jun), III (Jul-Sep), IV (Oct-Dec) **Dose-response Investigated?** Yes **Statistical Package:** SPSS **Lags Considered:** NR	**Pollutant:** RSPM (Respirable Suspended PM <10 µm) **Averaging Time:** 8 h **Mean µg/m^3 (SD):** Qtr I: 119.0 (19.8) Qtr II: 132.0 (28.4) Qtr III: 75.0 (23.4) Qtr IV: 168.0 (40.6) **Monitoring Stations:** 2 **Copollutant (correlation):** SPM: r = 0.771 **Other variables:** Temp (min): r = -0.420 COPD: r = 0.353	**PM Increment:** NR **RR Estimate [CI]:** NR **Notes:** This study analyzed seasonal variation of pollutants and health outcomes and correlations among the variables
Reference: Arbex et al. (2007, 091637) **Period of Study:** Mar 2003-Jul 2004 **Location:** Araraquara, Sao Paulo State, Brazil	Hospital Admission **Outcome (ICD10):** Asthma (J15, J45) **Age Groups:** All **Study Design:** Time-series **N:** 493 days, 1 hospital, 640 admissions **Statistical Analyses:** Generalized linear Poisson regression model with natural cubic spline, Mann-Whitney U Test **Covariates:** Temperature and humidity **Season:** All **Dose-response Investigated?** Yes, quintile analysis **Statistical Package:** SPSS V.11 & Splus 4.5 **Lags Considered:** 0-9	**Pollutant:** TSP **Averaging Time:** 24 h **Mean (SD):** 46.8 µg/m^3 (24.4) **Range (Min, Max):** 6.7-137.8 µg/m^3 **Monitoring Stations:** 1 **Notes:** TSP used as a proxy for fine & ultrafine particles since it is composed of 85-95% $PM_{2.5}$. **Copollutant (correlation):** NR	**PM Increment:** 10 µg/m^3 **% Increase** 6.96 [1.4-12.86] 2-day ma 9.090 [3.12-15.40] 3 day ma 10.28 [4.05-16.90] 4-day ma 11.63 [5.46-19.318] 5 day ma 12.61 [5.68-20.00] 6-day ma 12.56 [5.47-20.13] 7-day ma **% Increase by TSP quintile:** 9.25-28.45 µg/m^3: : 1.00 28.46-48.85 µg/m^3: : 1.55 [045-5.77] 48.86-69.06 µg/m^3: : 2.46 [1.08-5.60] 69.07-88.44 µg/m^3: : 2.77 [1.32-5.84] 88.45-108.9 µg/m^3: : 2.94 [1.48-5.85] **Notes:** No TSP threshold for asthma admissions noted. Analysis of lag structure indicated that the acute effect of TSP on admissions started 1 day after TSP concentration increase and remained unchanged for next 4 days. **Notes:** To evaluate the association between TSP generated from burning sugar cane and asthma hospital admissions.
Reference: Bartzokas et al. (2004, 093252) **Period of Study:** Jun 1992-May 2000 **Location:** Athens, Greece	**Outcome:** Respiratory and cardiovascular diseases (combined) **Age Groups:** NR **Study Design:** Time series **N:** 1554 patients **Statistical Analyses:** Simple linear regression and linear stepwise regression, Pearson correlation **Covariates:** Temperature, atmospheric pressure, relative humidity, wind speed **Season:** Warm (May-Sep) and cold (Nov-Mar) **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** NR	**Pollutant:** PM4.5 (black smoke) **Averaging Time:** 10-day ma **Mean µg/m^3 (SD):** NR **Monitoring Stations:** 1 **Copollutant (correlation):** N	**PM Increment:** NR **Correlation with Number of Admissions:** Entire yr Original: r = 0.18 Smoothed: r = 0.31 Warm period Original: r = 0.19 Smoothed: r = 0.30 Cold period Original: r = 0.18 Smoothed: r = 0.34 *All above values are statistically significant

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Erbas et al. (2005, 073849) **Period of Study:** Jul 1989-Dec 1992 **Location:** Melbourne, Australia	**Outcome (ICD):** COPD (490-492, 494, 496) Asthma (493) **Age Groups:** NR **Study Design:** Time series **N:** NR **Statistical Analyses:** GLM, GAM, Parameter Driven Poisson Regression, Transitional Regression, Seasonal-Trend decomposition based on Loess smoothing for seasonal adjustment **Covariates:** Secular trends, seasonality, relative humidity, dry bulb temp, dew point temp **Season:** NR **Dose-response Investigated?** Yes **Statistical Package:** S-Plus, SAS **Lags Considered:** 0-5 days	**Pollutant:** PM 0.1-1 (API) **Averaging Time:** 24 h **Mean (min-max):** NR **Monitoring Stations:** 9 **Copollutant (correlation):** NR	**PM Increment:** Increase from the 10th-90th percentile (value NR) **RR Estimate [CI]:** COPD GAM: 0.95 [0.91,1.00] GLM, PDM, TRM: NR Asthma NR **Notes:** This study was used to demonstrate that conclusions are highly dependent on the type of model used
Reference: Halonen et al. (2008, 189507) **Period of Study:** 1998-2004 **Location:** Helsinki, Finland	**Outcome:** Respiratory Hospitalizations & Mortality (ICD 10: J00-99) **Age Groups:** 65+ yr **Study Design:** Time series **N:** NR **Statistical Analyses:** Poisson, GAM **Covariates:** Temperature, humidity, influenza epidemics, high pollen episodes, holidays **Dose-response Investigated?** No **Statistical Package:** R **Lags Considered:** Lags 0-3 & 5-day (0-4) mean	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily **Mean (SD):** NR **Min:** 1.1 **25th percentile:** 5.5 **50th percentile:** 9.5 **75th percentile:** 11.7 **Max:** 69.5 **Monitoring Stations:** NR **Copollutant:** PM<0.03, PM0.03-0.1, PM<0.1, PM<0.10.29, $PM_{10-2.5}$, CO, NO_2 **Co-pollutant Correlation** PM<0.03: 0.14 PM0.03-0.1: 0.48 PM<0.1: 0.35 PM<0.10.29: 0.88 $PM_{10-2.5}$: 0.25	**PM Increment:** Interquartile **Percent Change (Lower CI, Upper CI):** All Respiratory Mortality Lag 0: 2.67 (-0.39, 5.82) ‡ Lag 1: 1.59 (-1.43, 4.70) Lag 2: 0.03 (-2.99, 3.16) Lag 3: -0.11 (-3.13, 3.01) 5-day mean: 1.39 (-2.83, 5.81) Pneumonia HA Lag 0: 0.93 (-0.85, 2.75) Lag 1: 2.41 (0.64, 4.21) Lag 2: 1.48 (-0.27, 3.26) Lag 3: 1.91 (0.14, 3.70) 5-day mean: 3.10 (0.60, 5.65) Asthma + COPD HA Lag 0: 2.48 (0.60, 4.39) Lag 1: 2.62 (0.78, 4.49) Lag 2: 1.22(-0.62, 3.10) Lag 3: 0.59 (-1.28, 2.49) 5-day mean: 2.49 (-0.08, 5.12) Other HA Lag 0: 0.05 (-2.38, 2.54) Lag 1: 0.2 (-2.17, 2.62) Lag 2: 2.03 (-0.29, 4.41) Lag 3: 1.72 (-0.63, 4.12) 5-day mean: 1.88 (-1.50, 5.36) *p < 0.05, ‡p < 0.10

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Llorca et al. (2005, 087825) **Period of Study:** Jan 1992-Dec 1995 **Location:** Torrelavega, Spain	**Outcome (ICD-9):** Respiratory (460-519) and cardiac (390-459) admissions (analyzed combined and individually) **Age Groups:** NR **Study Design:** Time series **N:** 18,137 admissions **Statistical Analyses:** Stepwise multiple linear regression, Poisson regression, Spearman correlation **Covariates:** Influenza, day of week, wind speed, northeast and southwest winds, minimum and maximum temperature **Season:** NR **Dose-response Investigated?** No **Statistical Package:** STATA Intercooled, Release 6 **Lags Considered:** NR	**Pollutant:** TSP (total suspended particles) **Averaging Time:** 24 h **Mean** µg/m^3 **(SD):** 48.8 (23.7) **Monitoring Stations:** 3 **Copollutant (correlation):** SO_2: r = -0.400 SH2: r = -0.392 NO: r = -0.109 NO_2: r = -0.120 **Other variables:** Rain: r = -0.339 Max temp: r = 0.071 Min temp: r = -0.003 Avg temp: r = 0.035 Wind speed: r = -0.357	**PM Increment:** NR **Rate Ratio Estimate [CI]:** Cardiorespiratory Admissions Single-pollutant model: 0.92 [0.86,0.98] Five-pollutant model: 1.05 [0.97,1.14] Respiratory Admissions Single-pollutant model: 0.98 [0.89,1.08] Five-pollutant model: 0.91 [0.80,1.02]
Reference: Michaud et al. (2004, 188530) **Period of Study:** Jan 1997-May 2001 **Location:** Hilo, Hawaii	ED visits **Outcome:** Asthma/COPD (490-496) Respiratory Irritation (506-508) **Age Groups:** All **Study Design:** Time-series **N:** 1,561 ER visits **Statistical Analyses:** Multiple linear regression **Covariates:** Hourly temperature, minimum daily temperature, minimum daily temperature, humidity, yr, month, day of the week **Season:** all **Dose-response Investigated?** No **Statistical Package:** STATA 6.0 SAS **Lags Considered:** Previous night, 1,2,3	**Pollutant:** PM1 **Averaging Time:** 24-h avg **Mean (SD):** 1.91 (2.95) µg/m^3 **Range (Min, Max):** 0.0, 56.6 µg/m^3 **Monitoring Stations:** 2 **Notes: Copollutant (correlation):** NR	**PM Increment:** 10 µg/m^3 **RR Estimate [Lower CI, Upper CI] lag:** Asthma, COPD (499-496): Adjusted for day, month & yr: 1.11 (0.92, 1.34), 00: 00-6: 00AM 1.14 (1.03, 1.26), lag 1 1.06 (0.83, 0.94), lag 2 0.91 (0.06, 1.05), lag 3 Asthma (493, 495): Adjusted for day, month & yr: 1.03 (0.90, 1.42), 00: 00-6: 00AM 1.02 (0.94, 1.21), lag 1 1.02 (0.99, 1.23), lag 2 0.97 (0.69, 1.15), lag 3 Bronchitis (490, 491): Adjusted for day, month & yr: 1.02 (0.82, 1.41), 00: 00-6: 00AM 1.07 (1.18, 1.49), lag 1 0.97 (0.60, 1.34), lag 2 0.93 (0.43, 1.18), lag 3 **Notes:** Crude and estimates adjusted for month and yr only also presented. **Notes:** Volcanic fog = vog

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Migliaretti et al. (2005, 088689) **Period of Study:** 1997-1999 **Location:** Turin, Italy	**Cases:** Asthma (493) **Controls:** Admissions for non-respiratory or cardiac conditions (460-487, 490-493, 494-496, 500-519, 390-405, 410-429) **Age Groups:** 0-14, 15-64, >64 **Study Design:** Case-control **N:** Cases: 1,401 **Controls:** 201,071 **Statistical Analyses:** Logistic regression **Covariates:** Gender, age, daily mean temperature, season, day of week, holidays, education level **Season:** All **Dose-response Investigated?** No **Lag:** 0- to 2-day avg	**Pollutant:** TSP **Averaging Time:** Means of daily total levels at stations **Mean (SD):** 105.3 µg/m^3 , (44.2) **Percentiles: 25th:** NR **50th(Median):** 96.0 µg/m^3 **75th** NR **Monitoring Stations:** 10 **Notes: Copollutant (correlation):** All seasons: NO_3^-TSP = 0.80 Winter: NO_3^-TSP = 0.77 Summer: NO_3^-TSP = 0.69	**PM Increment:** 10 µg/m^3 increase **% Increase, lag 0-2-day avg** **1 pollutant model:** <15: 1.90[0.40, 3.40] 15-64: 2.30 [-0.01, 5.20] >64: 2.30 [1.10, 3.60] Total: 2.30[1.10, 3.60] **% Increase, lag 0-2-day avg** **2 pollutant model:** <15: -0.12 [-0.03, 2.50] 15-64: 0.90 [-0.04, 5.61] >64: 1.2 [-0.01, 4.32] Total: 0.91 [-0.02, 3.11]
Reference: Migliaretti et al. (2004, 087425) **Period of Study:** 1997-1999 **Location:** Turin, Italy	**Outcome:** **Cases:** Asthma (493) **Controls:** Non-respiratory or cardiac admissions (460-487, 490-493, 494-496, 500-519, 390-405, 410-429) **Age Groups:** 0-15 **Study Design:** Case-control **N: Cases:** 1,060 **Controls:** 25,523 **Statistical Analyses:** Logistic regression µg/m^3 increase **Covariates:** Gender, age, daily mean temperature, season, day of week, holidays, solar radiation **Season:** All **Lags Considered:** 1- to 3-day avg	**Pollutant:** Total suspended particulate **Averaging Time:** Mean of admission day and 3 preceding days **Mean (SD):** 114.5 µg/m^3, (42.8) **Percentiles:** 25th: NR 50th(Median): 109.9 µg/m^3 75th: NR **Monitoring Stations:** 10 **Notes: Copollutant (correlation):** TSP-NO: 0.76	**PM Increment:** 10 µg/m^3 % Increase, lag 1-3-day avg <4 yr: 1.8% [0.00, 3.05] 4-15 yr: 3.0% [0.01, 5.08] all: 1.8% [0.03, 3.02] adjusted for all covariates **Notes:** Multipollutant models also used
Reference: Neuberger et al. (2004, 093249) **Period of Study:** 1999-2000 (1-yr period) **Location:** Vienna and Lower Austria	**Outcome (ICD-9):** Bronchitis, emphysema, asthma, bronchiectasis, extrinsic allergic alveolitis, and chronic airway obstruction (490-496) **Age Groups:** 3.0-5.9 yr 7-10 yr 65+ yr **Study Design:** Time series **N:** 366 days (admissions NR) **Statistical Analyses:** GAM **Covariates:** SO_2, NO, NO_2, O_3, temperature, humidity, and day of the week **Season:** NR **Dose-response Investigated?** Yes **Statistical Package:** S-Plus 2000 **Lags Considered:** 0-14 days	**Pollutant:** PM_1 **Averaging Time:** 24 h **Mean** µg/m^3 **(SD):** NR **Monitoring Stations:** NR **Copollutant (correlation):** NR	**PM Increment:** NR **Effect parameters (Vienna children):** Respiratory Health Male sex = 0.098 Allergy = 0.238 Asthma in family = 0.190 Traffic = 0.112 Log Asthma Score Allergy = 0.210 Asthma in family = 0.112 Rain = 0.257 *only significant coefficients are presented Association with tidal lung function: β = -1.059 (p-value = 0.060) **Notes:** No significant associations between PM and respiratory mortality were found for either sex. Data is also provided for children in the rural area where age, allergy, asthma in family, passive smoking, and PM fraction had significant coefficients.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Peel et al. (2005, 056305) **Period of Study:** Jan 1993-Aug 2000 **Location:** Atlanta, Georgia	**Hospital Admission/ED:** ED visits **Outcome:** Asthma 493, 786.09 COPD 491, 492, 496 URI 460-466, 477 Pneumonia 480-486 **Age Groups:** All ages. Secondary analyses conducted by age group: Infants 0-1 yr Pediatric asthma 2-18 yr Adults >18 yr **Study Design:** Case-control All respiratory disease vs. finger wounds **N:** 31 hospitals ED visits NR **Statistical Analyses:** Poisson generalized linear models General linear models **Covariates:** Avg temperature and dew point, pollen counts **Season:** All **Dose-response Investigated? Y**es **Statistical Package:** SAS 8.3 S-Plus 2000 **Lags Considered:** 0-7 days and 14-day distributed lag	**Pollutant:** UF (10-100nm) **Averaging Time:** 24-h avg **Mean (SD):** 3800 (40700) **Percentiles:** 10th: 11500 90th: 74600 **PM Component:** Oxygenated hydrocarbons (OH), sulfate, acidity, EC (EC), OC (OC), water-soluble transition metals **Monitoring Stations:** "Several" **Copollutant (correlation):** PM_{10}: r = -0.13 O_3: r = -0.13 NO_2: r = 0.26 CO: r = 0.10 SO_2: r = 0.24 $PM_{2.5}$: r = -0.16 $PM_{10-2.5}$: r = 0.13	**Increment:** 30,000 #/cm^3 All Respiratory Disease 0.984 [0.968-1.000] URI 0.986 [0.966, 1.006] Asthma 0.999 [0.977, 1.021] Pneumonia 0.997 [0.953, 1.002] COPD 0.982 [0.942, 1.022]
Reference: Simpson et al. (2005, 087438) **Period of Study:** 1996-1999 **Location:** Brisbane, Sydney, Melbourne, and Perth, Australia	**Outcome:** All Respiratory (460-519) Asthma (493) COPD (490-492) Pneumonia, acute bronchitis (466, 480-486) **Age Groups:** All ages, split into f15-64 and >64 yr **Study Design:** Time-series **N:** NR ~64,000 admissions **Statistical Analyses:** GAM w/ LOESS smoothers GLM w/ natural and penalized spline smoothers **Covariates:** Temperature, relative humidity, rain, day of the week, public and school holidays, influenza epidemics, and controlled burn events **Season:** All **Dose-response Investigated?** Yes **Statistical Package:** S-Plus R **Lags Considered:** 1-3 days, 0- to 1-day avg	**Pollutant:** BSP (indicator of particles <2 µm in diameter) (10 -4 m -1) **Averaging Time:** 24-h avg **Mean (SD): Means only** Brisbane 0.3 10 -4 m -1 Sydney 0.3 10 -4 m -1 Melbourne 0.3 10 -4 m -1 Perth 0.3 10 -4 m -1 **Range (Min, Max):** Brisbane 0.0, 2.5 10 -4 m -1 Sydney 0.0, 1.6 10 -4 m -1 Melbourne 0.0, 2.2 10 -4 m -1 Perth 0.1, 1.8 10 -4 m -1 **PM Component: Monitoring Stations:** "network of sites across each city" **Copollutant (correlation):** NR	**PM Increment:** "per unit increase" **RR Estimate [Lower CI, Upper CI]** **lag:** **Single pollutant model** Respiratory >64 yr 1.0401 [1.0045, 1.0770] lag1 1.0520 [1.0164, 1.0889] lag2; 1.0451 [1.0093, 1.0821] lag3 1.0552 [1.0082, 1.1045] lag 0-1 avg Asthma 15-64 yr 1.0641 [1.0006, 1.1315] lag2 1.0893 [1.0240, 1.1587] lag3 Asthma + COPD >64 yr 1.0713 [1.0179, 1.1276] lag3 1.0552 [1.0082, 1.1045] lag 0-1 avg Pneumonia & Acute Bronchitis >64 yr 1.0587 [1.0013, 1.1193] lag1 1.0636 [1.0056, 1.1249] lag 2 1.0769 [1.0046, 1.1544] lag 0-1 avg **Multipollutant model** Respiratory admissions >64 yr No other pollutants: 1.0552 [1.0082, 1.1045] lag 0-1 avg Max 1 h NO_2 1.0028 [0.9513, 1.0572] lag 0-1 avg Max 1 h O_3 1.0534 [1.0058-1.1033] lag 0-1 avg

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Sinclair and Tolsma (2004, 088696) **Period of Study:** 25 mo **Location:** Atlanta, Georgia	Outpatient Visits **Outcome:** Asthma (493) URI (460, 461, 462, 463, 464, 465, 466, 477) LRI (466.1, 480, 481, 482, 483, 484, 485, 486). **Age Groups:** < = 18 yr; 18+ yr (asthma); All ages (URI//LRI) **Study Design:** Times series **N:** 25 mo 260,000-275,000 health plan members (Aug 1998-Aug 2000) **Statistical Analyses:** Poisson GLM **Covariates:** Season, day of week, federal holidays, study months **Season:** NR **Dose-response Investigated?:** No **Statistical Package:** SAS **Lags Considered:** Three 3-day ma (0-2, 2-5, 6-8)	**Pollutant:** $PM_{2.5-10}$ ($\mu g/m^3$) **Averaging Time:** 24-h avg **Mean (SD):** PM coarse mass (2.5-10 µm)-9.67 $\mu g/m^3$ (4.74) **Monitoring Stations:** 1 **Copollutant (correlation):** NR	**PM Increment:** 4.74 (1 SD) **RR Estimate [Lower CI, Upper CI]** **lag:** Child Asthma: Coarse PM = 1.053 (S) 3-5 day lag URI: Course PM = 1.021 (S) 3-5 day lag LRI: Coarse PM = 1.07 (S) 3-5 day lag **Notes:** Numerical findings for significant results only presented in manuscript. Results for all lags presented graphically for each outcome (asthma, URI, and LRI).
Reference: Sinclair and Tolsma (2004, 088696) **Period of Study:** 25 mo **Location:** Atlanta, Georgia	**Outpatient Visits** **Outcome:** Asthma (493) URI (460, 461, 462, 463, 464, 465, 466, 477) LRI (466.1, 480, 481, 482, 483, 484, 485, 486). **Age Groups:** < = 18 yr, 18+ yr (asthma) All ages (URI//LRI) **Study Design:** Times series **N:** 25 mo 260,000-275,000 health plan members (Aug 1998-Aug 2000) **Statistical Analyses:** Poisson GLM **Covariates:** Season, day of week, federal holidays, study months **Season:** NR **Dose-response Investigated?:** No **Statistical Package:** SAS **Lags Considered:** Three 3-day ma (0-2, 2-5, 6-8)	**Pollutant:** UF (PM_{10}-100 nm) **Averaging Time:** 24 h avg **Mean (SD):** PM_{10}-100 nm area ($\mu m2/cm^3$)- 249.33 (244.09) **Monitoring Stations:** 1 **Copollutant (correlation):** NR	**PM Increment:** NR **RR Estimate [Lower CI, Upper CI]** **lag:** Adult Asthma: Ultrafine PM area = 1.223 (S) 3-5 days lag URI: Ultrafine PM: = 1.041 (S) 0-2 days lag LRI: Ultrafine PM area = 1.099 (S) 6-8 days lag **Notes:** Numerical findings for significant results only presented in manuscript. Results for all lags presented graphically for each outcome (asthma, URI, and LRI).

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Slaughter et al. (2005, 073854) **Period of Study:** Jan 1995-Jun 2001 **Location:** Spokane, WA	Hospital Admissions and ED visits **Outcome:** All respiratory (460-519) Asthma (493) COPD (491,492, 494,496) Pneumonia (480-487) Acute URI not including colds and sinusitis (464, 466, 490) **Age Groups:** All, 15+ yr for COPD **Study Design:** Time series **N:** 2373 visit records **Statistical Analyses:** Poisson regression, GLM with natural splines. For comparison also used GAM with smoothing splines and default convergence criteria. **Covariates:** Season, temperature, relative humidity, day of week **Season:** All **Dose-response Investigated?:** No **Statistical Package:** SAS, SPLUS **Lags Considered:** 1 -3 days	**Pollutant:** PM_1 **Averaging Time:** 24-h avg **Range (90% of concentrations):** 3.3-17.6 µg/m^3 **Monitoring Stations: 1** **Copollutant (correlation):** PM_1 $PM_{2.5}$ r = 0.95 PM_{10} r = 0.50 $PM_{10-2.5}$ r = 0.19 CO r = 0.63	**PM Increment:** 10 µg/m^3 **RR Estimate [Lower CI, Upper CI]** **lag:** ED visits: PM_1 All Respiratory Lag 1: 1.01 [0.98, 1.04] Lag 2: 1.02 [0.99, 1.06] Lag 3: 1.02 [0.99,1.06] Acute Asthma Lag 1: 1.03 [0.97, 1.09] Lag 2: 0.99 [0.93, 1.05] Lag 3: 1.02 [0.96, 1.08] COPD (adult) Lag 1: 0.96 [0.87, 1.05] Lag 2: 1.02 [0.93, 1.12] Lag 3: 0.99 [0.90, 1.09]
Reference: Slaughter et al. (2005, 073854) **Period of Study:** Jan 1995-Jun 2001 **Location:** Spokane, WA	Hospital Admissions and ED visits **Outcome:** All respiratory (460-519) Asthma (493) COPD (491,492, 494,496) Pneumonia (480-487) Acute URI not including colds and sinusitis (464, 466, 490) **Age Groups:** All, 15+ yr for COPD **Study Design:** Time series **N:** 2373 visit records **Statistical Analyses:** Poisson regression, GLM with natural splines. For comparison also used GAM with smoothing splines and default convergence criteria. **Covariates:** Season, temperature, relative humidity, day of week **Season:** All **Dose-response Investigated?:** No **Statistical Package:** SAS, SPLUS **Lags Considered:** 1 -3 days	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Range (90% of Concentrations):** 4.2-20.2 µg/m^3 **Monitoring Stations: 1** **Notes: Copollutant (correlation):** $PM_{2.5}$ PM1 r = 0.95 PM_{10} r = 0.62 $PM_{10-2.5}$ r = 0.31 CO r = 0.62 Temperature r = 0.21	**PM Increment:** 10 µg/m^3 **RR Estimate [Lower CI, Upper CI]** **lag:** **ER visits:** $PM_{2.5}$ All Respiratory Lag 1: 1.01 [0.98, 1.04] Lag 2: 1.02 [0.99, 1.04] Lag 3: 1.02 [0.99, 1.05] Acute Asthma Lag 1: 1.03 [0.98, 1.09] Lag 2: 1.00 [0.95, 1.05] Lag 3: 1.01 [0.96, 1.06] COPD (adult) Lag 1: 0.96 [0.89, 1.04] Lag 2: 1.01 [0.93, 1.09] Lag 3: 1.00 [0.93, 1.08] **Hospital Admissions:** $PM_{2.5}$ All Respiratory Lag 1: 0.98 [0.94, 1.01] Lag 2: 0.99 [0.96, 1.03] Lag 3: 1.01 [0.98, 1.05] Asthma Lag 1: 1.01 [0.91, 1.11] Lag 2: 1.03 [0.94, 1.13] Lag 3: 1.02 [0.93, 1.13] COPD (adult) Lag 1: 0.99 [0.91, 1.08] Lag 2: 1.06 [0.98, 1.16] Lag 3: 1.03 [0.94, 1.12]

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Zanobetti and Schwartz (2006, 090195) **Period of Study:** 1995-1999 **Location:** Boston, MA	**Outcome:** Pneumonia (480-487) **Age Groups:** >65 y **Study Design:** Case-crossover, time stratified **N:** 24,857 for Pneumonia **Statistical Analyses:** Condition logistic regression **Covariates:** Season, long term trend, day of-the-wk, mean temperature, relative humidity, barometric pressure, extinction coefficient **Season:** All yr **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 0-1 **Notes:** Also looked at MI cohort	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Percentiles** (pneumonia cohort)**:** 25th: 7.23 µg/m^3 50th(Median): 11.10 75th: 16.14 **PM Component:** Black Carbon (BC), PM non-traffic **Monitoring Stations:** 4-5 monitors **Copollutant (correlation):** $PM_{2.5}$: CO r = 0.52 NO_2 r = 0.55 O_3 r = 0.20 BC r = 0.66 PM non-traffic r = 0.74	**PM Increment:** $PM_{2.5}$ lag 0: 17.17 µg/m^3 $PM_{2.5}$ lag 0-1 avg: 16.32 µg/m^3 % change in Pneumonia: 6.48[1.13, 11.43] lag 0 5.56[-0.45, 11.27] mean lag 1
Reference: Zanobetti and Schwartz (2006, 090195) **Period of Study:** 1995-1999 **Location:** Boston, MA	**Outcome:** Pneumonia (480-487) **Age Groups:** >65 y **Study Design:** Case-crossover, time stratified **N:** 24,857 for Pneumonia **Statistical Analyses:** Condition logistic regression **Covariates:** Season, long term trend, day of-the-wk, mean temperature, relative humidity, barometric pressure, extinction coefficient **Season:** All yr **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** 0-1 **Notes:** Also looked at MI cohort	**Pollutant:** BC **Averaging Time:** 24 h **Percentiles** (pneumonia cohort)**:** 5th: 0.42 25th: 0.74 µg/m^3 50th(Median): 1.15 75th: 1.72 95th: 2.83 **PM Component:** PM non-traffic **Monitoring Stations:** 4-5 monitors **Copollutant (correlation):** BC: $PM_{2.5}$ r = 0.66 CO r = 0.82 NO_2 r = 0.70 O_3 r = -0.25 PM non-traffic r = -0.01	**PM Increment:** BC lag 0: 2.05 µg/m^3 BC lag 0-1 avg: 1.69 µg/m^3 % change in Pneumonia: BC-10.76[4.54, 15.89] lag 0 BC-11.71[4.79, 17.36] mean lag 1

[1]All units expressed in µg/m^3 unless otherwise specified.

E.3. Short-Term Exposure and Mortality

Table E-16. Short-term exposure-mortality - PM_{10}.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Aga et al. (2003, 054808) **Period of Study:** ~5 yr for most cities, during the 1990s **Location:** 28 European cities (APHEA2)	**Outcome:** Nonaccidental Mortality (<800) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups:** All ages >65	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** (15, 66) **Copollutant:** BS **Note:** PM_{10} only measured in 21 cities.	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** All ages Fixed effects: 0.71% (0.60,0.83) 0-1 Random effects: 0.67% (0.47,0.87) 0-1 >65 Fixed effects: 0.79% (0.66,0.92) 0-1 Random effects: 0.74% (0.52,0.95) 0-1 Models with effect modifiers (>65) 24-h NO_2: 25th Percentile: 0.30% (0.07,0.53) 75th Percentile: 0.97% (0.82,1.11) 24-h temperature: 25th Percentile: 0.44% (0.25,0.64) 75th Percentile: 0.91% (0.77,1.05) 24-h relative humidity: 25th Percentile: 0.98% (0.82,1.14) 75th Percentile: 0.52% (0.33,0.71) Age standardized annual mortality rate: 25th Percentile: 0.93% (0.77,1.09) 75th Percentile: 0.61% (0.43,0.79) Proportion individuals >65 25th Percentile: 0.67% (0.50,0.83) 75th Percentile: 0.85% (0.71,0.99) Northwest/Central East: 25th Percentile: 0.81% (0.63,0.98) 75th Percentile: 0.26% (-0.05,0.57) Northwest/South: 25th Percentile: 0.81% (0.63,0.98) 75th Percentile: 1.04% (0.81,1.27)
Reference: Analitis et al. (2006, 088177) **Period of Study:** NR **Location:** 29 European cities (APHEA2)	**Outcome:** Mortality: Cardiovascular diseases (390-459) Respiratory diseases (460-519) **Study Design:** Time-series **Statistical Analyses:** 2-stage hierarchical modeling **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Median (SD)** unit: Range: 9-64 µg/m^3 **Range (Min, Max):** NR **Copollutant:** BS **Note:** PM_{10} only measured in 21 cities.	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Cardiovascular: Fixed effects: 0.64% (0.47, 0.80) 0-1 Random effects: 0.76% (0.47, 1.05) 0-1 0.90% (0.57, 1.23) 0-5 Respiratory: Fixed effects: 0.58% (0.21, 0.95) 0-1 Random effects: 0.71% (0.22, 1.20) 0-1 1.24% (0.49, 1.99) 0-5
Reference: Ballester et al. (2002, 030371) **Period of Study:** 1990-1996 **Location:** 13 Spanish cities	**Outcome:** Mortality: Nonaccidental (<800) Cardiovascular diseases (390-459) Respiratory diseases (460-519) **Study Design:** Ecological time series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD): Huelva:** 42.5 (15) Madrid: 37.8 (17.7) Sevilla: 45.1 (14) **Range (Min, Max):** NR **Copollutant:** BS TSP SO_2 **Note:** PM_{10} only measured in 3 cities.	**Increment:** 10 µg/m^3 **Relative Risk (Lower CI, Upper CI) lag:** Nonaccidental: Random effects: 1.006 (0.998, 1.015) 0-1 Fixed Effects: 1.005 (1.001, 1.010) 0-1 PM_{10}+SO_2: 1.013 (1.006, 1.020) 0-1 Cardiovascular: 1.012 (1.005, 1.018) 0-1 PM_{10}+SO_2: Random effects: 1.024 (1.001, 1.048) 0-1 Fixed effects: 1.021 (1.007, 1.035) 0-1 Respiratory: 1.013 (1.001, 1.026) 0-1 PM_{10}+SO_2: 1.003 (0.983, 1.023) 0-1

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Bateson and Schwartz (2004, 086244) **Period of Study:** 1988-1991 **Location:** Cook County, Illinois	**Outcome:** Mortality: Heart Disease (390-429) Respiratory (460-519) **Study Design:** Bi-directional case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups:** ≥ 65 Study population: 65,180 elderly residents with history of hospitalization for heart or lung disease	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SE) unit:** 37.6 (15.5) µg/m^3 **Range (Min, Max):** (3.7, 128) **Copollutant:** NR	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** All-cause: 1.14% (0.44, 1.85) 0-1 Modification of Effect by Prior Diagnosis Myocardial Infarction: 1.98% (-0.25, 4.26) 0-1 Diabetes: 1.49% (-0.06, 3.07) 0-1 Congestive heart failure: 1.28% (-0.06, 2.64) 0-1 COPD: 0.58% (-0.82, 2.00) 0-1 Conduction Disorders: 0.64% (-0.61, 1.90) 0-1 All other heart or lung diseases: 0.74% (-0.29, 1.79) 0-1 All-cause Men 65: 2.0% (0.3, 3.8) 0-1 75: 1.5% (-0.2, 3.1) 0-1 85: 0.9% (-0.7, 2.5) 0-1 95: 0.3% (-1.3, 1.9) 0-1 All: 1.3% (0.4, 2.3) 0-1 Women 65: 0.1% (-1.6, 1.9) 0-1 75: 0.7% (-1.1, 2.4) 0-1 85: 1.2% (-0.5, 3.0) 0-1 95: 1.8% (0.03, 3.6) 0-1 All: 1.0% (0.1, 1.9) 0-1 Total 65: 1.1% (-0.12, 2.3) 0-1 75: 1.1% (-0.1, 2.3) 0-1 85: 1.2% (-0.0, 2.4) 0-1 95: 1.2% (0.0, 2.4) 0-1 All: 1.1% (0.4, 1.9) 0-1
Reference: Bell et al. (2009, 191007) **Period of Study:** 1987-2000 **Location:** 84 U.S. Counties	**Outcome:** Mortality **Study Design:** Time-series **Covariates:** Socio-economic conditions, long term temperature **Statistical Analysis:** Bayesian hierarchical model **Age Groups:** All	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD) Unit:** NR **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** 20% of the population acquiring air conditioning **Percent Change (95% CI) in community-specific PM health effect estimates for mortality** Any AC, including window units Yearly health effect: -30.4 (-80.4-19.6) Summer health effect: 29.9 (-84-144) Winter health effect: -573 (-9100-7955) Central AC Yearly health effect: -39 (-81.4-3.3) Summer health effect: 20. (-60.3-64.3) Winter health effect: -1777 (-5755-2201)
Reference: Bell et al. (2007, 093256) **Period of Study:** 1999-2005 **Location:** U.S.	**Outcome:** Mortality **Age Groups:** 65+ **Study Design:** Time series **N:** NR **Statistical Analyses:** Bayesian Hierarchical Regression **Covariates:** Time trend, day of week, seasonality, dew point, temperature **Statistical Package:** NR **Lags Considered:** 0-2	**Pollutant:** PM_{10} **Averaging Time:** Daily **Mean:** Ni: 0.002 **Min:** Ni: 0.003 **Max:** Ni: 0.021 **Interquartile Range:** Ni: 0.001 **Interquartile Range of Percents:** Ni: 0.01 **Monitoring Stations:** NR **Copollutant:** Al, NH4+, As, Ca, Cl, Cu, EC, OMC, Fe, Pb, Mg. Ni, NO_3-, K, Si, Na+, SO_4=, Ti, V, Zn **Co-pollutant Correlation** Ni, V: 0.48 Ni, EC: 0.30 **Note:** Pollutant concentrations available for all fractions of $PM_{2.5}$	**PM Increment:** Interquartile Range in the fraction of $PM_{2.5}$ **Percent Increase in PM_{10} Health Effect (Lower CI, Upper CI)** Ni: 14.8 (-8.1, 37.7), lag 0 Ni: 14.7 (4.0, 25.3), lag 1 Ni: 14.7 (1.8, 27.5), lag 2 HS education: -31.9 (-82.4, 18.6) median income: -12.3 (-62.3, 37.7) Percent black: 48.7 (-15.8, 113) Percent living in urban area: -20.1 (-102, 61.7) Population: 5.1 (-14.4, 24.5) **Notes:** Interquartile ranges in percent HS education, median income, percent black, percent living in urban area, and population are 5.2 %, $9,223, 17.3%, 11.0%, and 549,283 respectively.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Bellini et al. (2007, 097787) **Period of Study:** 1996-2002 **Location:** 15 Italian cities	**Outcome:** Mortality All-cause (nonaccidental) (<800) Cardiovascular (390-459) Respiratory (460-519) **Study Design:** Meta-analysis **Statistical Analyses:** Poisson GLM **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR **Copollutant:** SO_2 NO_2 CO O_3	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** All-cause: 0.31% (-0.19, 0.74) 0-1 Winter: 0.08% 0-1 Summer: 1.95% 0-1 $PM_{10}+O_3$: 0.30% 0-1 $PM_{10}+NO_2$: 0.08% 0-1 Respiratory: 0.54% (-0.91, 1.74) 0-1 Winter: 0.27% 0-1 Summer: 3.61% 0-1 $PM_{10}+O_3$: 0.55% 0-1 $PM_{10}+NO_2$: 0.19% 0-1 Cardiovascular: 0.54% (0.02, 1.02) 0-1 Winter: 0.20% 0-1 Summer: 2.79% 0-1 $PM_{10}+O_3$: 0.57% 0-1 $PM_{10}+NO_2$: 0.39% 0-1
Reference: Burnett et al. (2004, 086247) **Period of Study:** 1981-1999 **Location:** 12 Canadian cities	**Outcome:** Mortality: Nonaccidental (<800) **Study Design:** Time-series **Statistical Analyses:** 1. Poisson, natural splines 2. Random effects regression model **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** $PM_{2.5}$: 12.8 $PM_{10-2.5}$: 11.4 **Range (Min, Max):** NR **Copollutant (correlation):** NO_2 O_3 SO_2 CO **Note:** PM_{10} measurement calculated as the sum of $PM_{2.5}$ and $PM_{10-2.5}$ measurements.	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI)** **lag:** 1981-1999 PM_{10}: 0.57% (0.05, 0.89) 1 $PM_{10}+NO_2$: 0.07% (-0.44, 0.58) 1
Reference: Cakmak et al. (2007, 091170) **Period of Study:** Jan 1997-Dec 2003 **Location:** Chile-7 cities	**Outcome:** Mortality: Nonaccidental (<800) Cardiovascular diseases (390-459) Respiratory diseases (460-519) **Study Design:** Time-series **Statistical Analyses:** Poisson Random effects regression model **Age Groups:** All age ≤ 64 yr 65-74 yr 75-84 yr ≥ 85 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 84.9 **Range (Min, Max):** NR **Copollutant (correlation):** O_3: r = -0.16-0.13 SO_2: r = 0.37-0.77 CO: r = 0.49-0.82 **Note:** Correlations are between pollutants for seven monitoring stations.	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Nonaccidental: 0.97% (-1.09, 2.76) 0 1.31% (-1.56, 3.68) 0-5 $PM_{10}+O_3+SO_2+CO$: 0.80% (-0.87, 2.28) 0 ≤ 64: 0.52% (-0.55, 1.51) 0 0.49% (-0.51, 1.43) 0-5 65-75: 1.07% (-1.23, 3.03) 0 1.31% (-1.57, 3.69) 0-5 75-84: 1.41% (-1.71, 3.94) 0 1.93% (-2.57, 5.30) 0-5 ≥ 85: 1.56% (-1.94, 4.34) 0 2.14% (-2.97, 5.85) 0-5 Apr-Sep: 1.03% (-1.17, 2.93) 0 1.37% (-1.64, 3.82) 0-5 Oct-Mar: 0.07% (-0.07, 0.21) 0 0.15% (-0.15, 0.44) 0-5 Cardiovascular: 1.14% (-1.31, 3.21) 0 1.49% (-1.82, 4.14) 0-5 Respiratory: 2.03% (-2.75, 5.56) 0 3.11% (-5.25, 8.25) 0-5

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Chen et al. (2008, 190106) **Period of Study:** 2001-2004 **Location:** Shanghai, China	**Outcome** (ICD9: 2001; ICD10: 2002-2004): Mortality: Nonaccidental causes (ICD9 <800; ICD10 A00-R99) Cardiovascular (ICD9 390-459; I CD10 I00-I99) Respiratory (ICD9 460-519; ICD10 J00-J98) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 102.0 **Range (Min, Max):** (14.0-566.8) **Copollutant (correlation):** SO_2 r = 0.64 NO_2 r = 0.71	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Nonaccidental Single Pollutant: 0.26% (0.14, 0.37) PM_{10}+SO_2: 0.08% (-0.07, 0.22) PM_{10}+NO_2: 0.01% (-0.14, 0.17) PM_{10}+SO_2+NO_2: 0.00% (-0.16, 0.16) Cardiovascular mortality Single Pollutant: 0.27% (0.10, 0.44) PM_{10}+SO_2: 0.12% (-0.10, 0.34) PM_{10}+NO_2: 0.01% (-0.22, 0.25) PM_{10}+SO_2+NO_2: 0.01% (-0.23, 0.25) Respiratory mortality Single Pollutant: 0.27% (-0.01, 0.56) PM_{10}+SO_2: -0.04% (-0.41, 0.33) PM_{10}+NO_2: -0.05% (-0.45, 0.34) PM_{10}+SO_2+NO_2: -0.10% (-0.50, 0.30)
Reference: Daniels et al. (2004, 087343) **Period of Study:** 1987-1994 **Location:** 20 Largest U.S. cities	**Outcome:** Mortality: Total (Nonaccidental) mortality Cardiovascular-Respiratory (390-448) (480-486, 487, 490-496, 507) Other-cause mortality **Study Design:** Time-series **Statistical Analyses:** City-Specific Estimates: Poisson GLM, natural cubic splines Combined Estimates: 2-stage Bayesian hierarchical model **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** Los Angeles: 46.0 New York: 28.8 Chicago: 35.6 Dallas-Ft. Worth: 23.8 Houston: 30.0 San Diego: 33.6 Santa Ana-Anaheim: 37.4 Phoenix: 39.7 Detroit: 40.9 Miami: 25.7 Philadelphia: 35.4 Minneapolis: 26.9 Seattle: 25.3 San Jose: 30.4 Cleveland: 45.1 San Bernardino: 37.0 Pittsburgh: 31.6 Oakland: 26.3 Atlanta: 34.4 San Antonio: 23.8	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Total (nonaccidental): 0.17% (0.03, 0.30) 0 0.20% (0.07, 0.33) 1 0.28% (0.16, 0.41) 0-1 avg Cardiovascular-Respiratory: 0.17% (-0.01, 0.35) 0 0.27% (0.09, 0.44) 1 0.30% (0.18, 0.51) 0-1 avg Other-cause: 0.17% (-0.03, 0.37) 0 0.12% (-0.07, 0.31) 1 0.20% (0.01, 0.38) 0-1 avg Threshold Models: Total Mortality Threshold = 15 µg/m^3 0.30% (0.17, 0.42) 0-1 avg Threshold = 0 µg/m^3 0.28% (0.16, 0.41) 0-1 avg Threshold = 20 µg/m^3 0.30% (0.16, 0.43) 0-1 avg

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: De Leon et al. (2003, 055688) **Period of Study:** Jan 1985-Dec 1994 **Location:** New York, New York	**Outcome:** Mortality: Circulatory (390-459) Cancer (140-239) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM **Age Groups:** All ages <75 yr >75 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 33.27 µg/m^3 IQR (25th, 75th): (22.67, 40.83) **Copollutant (correlation):** O_3 CO SO_2 NO_2	**Increment:** 18.16 µg/m^3 **Relative Risk (Lower CI, Upper CI) lag:** All Ages Cancer: 1.014 (1.000, 1.029) 0-1 -w/out respiratory: 1.011 (0.996, 1.026) 0-1 -w/ respiratory: 1.051 (0.998, 1.107) 0-1 Circulatory: 1.025 (1.014, 1.035) 0-1 -w/out respiratory: 1.022 (1.012, 1.033) 0-1 -w/ respiratory: 1.054 (1.022, 1.086) 0-1 <75 yr Cancer: 1.003 (0.985, 1.021) 0-1 -w/out respiratory: 1.002 (0.983, 1.022) 0-1 -w/ respiratory: 1.009 (0.943, 1.078) 0-1 Circulatory: 1.027 (1.012, 1.043) 0-1 -w/out respiratory: 1.027 (1.011, 1.043) 0-1 -w/ respiratory: 1.033 (0.980, 1.089) 0-1 >75 yr Cancer: 1.033 (1.009, 1.058) 0-1 -w/out respiratory: 1.025 (1.000, 1.050) 0-1 -w/ respiratory: 1.129 (1.041, 1.225) 0-1 -w/out pneumonia: 1.026 (1.002, 1.050) 0-1 -w/ pneumonia: 1.183 (1.058, 1.323) 0-1 -w/out COPD: 1.032 (1.008, 1.057) 0-1 -w/ COPD: 1.008 (0.849, 1.197) 0-1 Circulatory: 1.025 (1.012, 1.038) 0-1 -w/out respiratory: 1.022 (1.008, 1.035) 0-1 -w/ respiratory: 1.066 (1.027, 1.106) 0-1 -w/out pneumonia: 1.023 (1.010, 1.036) 0-1 -w/ pneumonia: 1.078 (1.018, 1.141) 0-1 -w/out COPD: 1.025 (1.012, 1.038) 0-1 -w/ COPD: 1.058 (0.991, 1.130) 0-1
Reference: Dominici et al. (2003, 042804) **Period of Study:** 1987-1994 **Location:** 88 U.S. cities	**Outcome:** Mortality: All-cause (nonaccidental) (<800) Cardiac (390-448) Respiratory (490-496) Influenza (487) Pneumonia (480-486, 507) Other causes **Study Design:** Time-series **Statistical Analyses:** 2-stage Bayesian hierarchical model **Age Groups:** <65 yr; 65-74 yr; ≥ 75 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Cardio-respiratory 0.31% (0.15, 0.50) 1 All-cause 0.22% (0.10, 0.38) 1 Other causes 0.13% (-0.05, 0.29) 1
Reference: Dominici et al. (2004, 059158) **Period of Study:** 1987-1994 **Location:** 90 U.S. cities (NMMAPS)	**Outcome:** Mortality: Total (nonaccidental) **Study Design:** Time-series **Statistical Analyses:** Poisson. GAM, GLM **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** α = 3 0.2% (0.05, 0.35)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Dominici et al. (2004, 096951) **Period of Study:** 1986-1993 **Location:** 10 U.S. cities	**Outcome:** Mortality: Total (nonaccidental) **Study Design:** Time-series **Statistical Analyses:** 2-stage Bayesian hierarchical model **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** Birmingham 34.8 Canton 28.4 Colorado Springs 27.5 Minneapolis/St. Paul 28.1 Seattle 32.2 Spokane 42.9 Chicago 36.3 Detroit 36.7 New Haven 28.6 Pittsburgh 36.0 New York: 28.8	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Combined analysis: 0.26% (-0.37, 0.65) 0-1 Separate analysis: 0.28% (-0.12, 0.63) 0-1 **Notes:** A separate analysis assumes the mortality data does not provide any information on the log relative rates of mortality.
Reference: Dominici et al. (2007, 097361) **Period of Study:** PM_{10}: 1987-2000 $PM_{2.5}$: 1999-2000 **Location:** 100 U.S. counties (NMMAPS)	**Outcome:** Mortality: All-cause (nonaccidental) Cardiorespiratory Other-cause **Study Design:** Time-series **Statistical Analyses:** 2-stage Bayesian hierarchical model **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** PM_{10} All-cause: East: 1987-1994: 0.29% (0.12, 0.46) 1 1995-2000: 0.13% (-0.19, 0.44) 1 1987-2000: 0.25% (0.11, 0.39) 1 West: 1987-1994: 0.12% (-0.07, 0.30) 1 1995-2000: 0.18% (-0.07, 0.44) 1 1987-2000: 0.12% (-0.02, 0.26) 1 National: 1987-1994: 0.21% (0.10, 0.32) 1 1995-2000: 0.18% (0.00, 0.35) 1 1987-2000: 0.19% (0.10, 0.28) 1 Cardiorespiratory: East: 1987-1994: 0.39% (0.16, 0.63) 1 1995-2000: 0.30% (-0.13, 0.73) 1 1987-2000: 0.34% (0.15, 0.54) 1 West: 1987-1994: 0.17% (-0.07, 0.40) 1 1995-2000: 0.13% (-0.23, 0.50) 1 1987-2000: 0.14% (-0.05, 0.33) 1 National: 1987-1994: 0.28% (0.14, 0.43) 1 1995-2000: 0.21% (-0.03, 0.44) 1 1987-2000: 0.24% (0.13, 0.36) 1 Other-cause: East: 1987-1994: 0.21% (-0.03, 0.44) 1 1995-2000: 0.00% (-0.49, 0.50) 1 1987-2000: 0.15% (-0.09, 0.39) 1 West: 1987-1994: 0.09% (-0.21, 0.38) 1 1995-2000: 0.23% (-0.15, 0.62) 1 1987-2000: 0.17% (-0.07, 0.41) 1 National: 1987-1994: 0.15% (-0.02, 0.32) 1 1995-2000: 0.17% (-0.07, 0.41) 1 1987-2000: 0.15% (0.00, 0.29)1
Reference: Dominici et al. (2007, 099135) **Period of Study:** 2000-2005 **Location:** 72 U.S. counties representing 69 communities	**Outcome:** Total mortality **Study Design:** Time-series **Statistical Analyses:** 2-stage Bayesian hierarchical model **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR **Copollutant (correlation):** NR	The study does not provide results quantitatively. **Note:** The study investigated whether county-specific short-term effects of PM_{10} on mortality are modified by long-term county-specific nickel or vanadium $PM_{2.5}$ concentrations.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Fischer et al. (2003, 043739) **Period of Study:** 1986-1994 **Location:** The Netherlands	**Outcome:** Mortality: Nonaccidental (<800) Pneumonia (480-486) COPD (490-496) Cardiovascular (390-448) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups:** <45 yr 45-64 yr 65-74 yr ≥ 75 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Median (SD) unit:** 34 **Range (Min, Max):** (10, 278) **Copollutant:** BS O_3 NO_2 SO_2 CO	**Increment:** 80 µg/m^3 **Relative Risk (Lower CI, Upper CI) lag:** Cardiovascular <45: 0.906 (0.728, 1.128) 0-6 45-64: 1.023 (0.945, 1.106) 0-6 65-74: 1.002 (0.945, 1.062) 0-6 ≥ 75: 1.016 (0.981, 1.052) 0-6 COPD <45: 1.153 (0.587, 2.268) 0-6 45-64: 1.139 (0.841, 1.541) 0-6 65-74: 1.166 (0.991, 1.372) 0-6 ≥ 75: 1.066 (0.965, 1.178) 0-6 Pneumonia <45: 1.427 (0.806, 2.525) 0-6 45-64: 1.712 (1.042, 2.815) 0-6 65-74: 1.240 (0.879, 1.748) 0-6 ≥ 75: 1.123 (1.011, 1.247) 0-6
Reference: Fischer et al. (2004, 055605) **Period of Study:** Jun 2003-Aug 2003 **Location:** The Netherlands	**Outcome:** Total mortality **Study Design:** NR **Statistical Analyses:** NR **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** Weekly avg **Mean (SD):** 2000: 31 2002: 33 2003: 35 **IQR (25th, 75th):** NR **Copollutant:** O_3	The study does not present quantitative results. **Notes:** The study estimates the number of deaths attributable to PM_{10} during the summers of 2000, 2002, and 2003.
Reference: Forastiere et al. (2005, 086323) **Period of Study:** 1998-2000 **Location:** Rome, Italy	**Outcome:** Mortality: Ischemic heart disease (410-414) **Study Design:** Time-stratified case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups:** >35	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 52.1 (22.2) IQR (25th, 75th): (36.0, 65.7) **Copollutant (correlation):** PNC: r = 0.38 CO: r = 0.34 NO_2: r = 0.45 SO_2: r = 0.23 O_3: r = 0.13	**Increment:** 29.7 µg/m^3 **% Increase (Lower CI, Upper CI)** **lag:** 4.8% (0.1, 9.8) 0 4.9% (0.0, 10.1) 1 3.8% (-1.0, 8.9) 2 2.8% (-2.0, 7.7) 3 6.1% (0.6, 11.9) 0-1
Reference: Forastiere et al. (2007, 090720) **Period of Study:** 1998-2001 **Location:** Rome, Italy	**Outcome:** Mortality: Natural (<800) Malignant neoplasms (140-208) Diabetes mellitus (250) Hypertensive disease (401-405) Previous acute myocardial infarction (410, 412) Other ischemic heart diseases (411, 413-414) Conduction disorders (426) Dysrhythmia (427) Heart failure (428) Cerebrovascular disease (430-438) Peripherical artery disease (440-448) COPD (490-496) **Study Design:** Time-stratified case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups:** >35	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean Range (SD) unit:** 51.0 (21.0) µg/m^3 IQR (25th, 75th): (36.1, 63.0) **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI)** **lag:** Nonaccidental: 1.1% (0.7, 1.6) 0-1 Low income: 1.9% 0-1 Low SES: 1.4% 0-1 High income: 0.0% 0-1 High SES: 0.1% 0-1 Low PM Area: 0.9% (-0.4, 2.1) 0-1 High PM Area: 1.47% (0.4, 2.5) 0-1

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Forastiere et al. (2008, 186937) **Period of Study:** 1997-2004 **Location:** 9 Italian cities	**Outcome:** Mortality: Nonaccidental (<800) **Study Design:** Time-stratified case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups:** >35	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean Range (SD) unit:** 35.1-71.5 Range (5th, 95th): Lowest 5th: 14.3 Highest 95th: 147.0 **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Total: 0.60% (0.31, 0.89) 0-1 Age 35-64: -0.20% (-0.77, 0.37) 0-1 65-74: 0.51% (0.05, 0.98) 0-1 75-84: 0.59%(0.20, 0.97) 0-1 ≥ 85: 0.97% (0.53, 1.42) 0-1 ≥ 65: 0.75% (0.42, 1.09) Sex Men: 0.72% (0.37, 1.07) 0-1 Women: 0.83% (0.33, 1.33) 0-1 Median income (by census block) Low (<20th percentile): 0.80% (-0.02, 1.62) 0-1 Mid-low (20th-50th percentile): 0.68% (0.25, 1.12) 0-1 Mid-high (51st-80th percentile): 0.85% (0.40, 1.30) 0-1 High (>80th percentile): 0.30% (-0.25, 0.86) 0-1 Location of death Out-of-hospital: 0.71% (0.32, 1.11) 0-1 Discharged 2-28 days before death: 1.34% (0.49, 2.20) 0-1 In-hospital: 0.65% (0.33, 0.97) 0-1 Nursing home: -0.04% (-1.02, 0.95) 0-1
Reference: Goldberg et al. (2003, 035202) **Period of Study:** 1984-1993 **Location:** Montreal, Quebec, Canada	**Outcome:** Mortality: Congestive Heart Failure (428) **Study Design:** Time-series **Statistical Analyses:** Poisson, natural splines **Age Groups:** ≥ 65	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** PM_{10}: 32.2 (17.6) IQR (25th, 75th): PM_{10}: (19.7, 41.1) **Copollutant (correlation):** $PM_{2.5}$, TSP, Sulfate, CoH, SO_2, NO_2, CO, O_3	This study does not present results quantitatively for PM_{10}
Reference: Goldberg et al. (2003, 035202) **Period of Study:** 1984-1993 **Location:** Montreal, Quebec, Canada	**Outcome:** Mortality: Diabetes (250) **Study Design:** Time-series **Statistical Analyses:** Poisson, natural spline **Age Groups:** ≥ 65	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** PM_{10}: 32.2 (17.6) µg/m^3 IQR (25th, 75th): PM_{10}: (19.7, 41.1) **Copollutant (correlation):** $PM_{2.5}$, Sulfate, CoH, SO_2, NO_2, CO, O_3	This study does not present results quantitatively for PM_{10}
Reference: Kan and Chen (2003, 087372) **Period of Study:** Jan 2000-Dec 2001 **Location:** Shanghai, China	**Outcome:** Mortality: Nonaccidental (<800) Cardiovascular (390-459) COPD (490-496) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups:** All ages <65 yr 65-75 yr >75 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 91.14 (51.85) **Range (Min, Max):** (17.0, 385.0) **Copollutant (correlation):** SO_2: r = 0.71 NO_2: r = 0.73	**Increment:** 10 µg/m^3 **Relative Risk (Lower CI, Upper CI) lag:** Nonaccidental: All ages: 1.003 (1.001, 1.005) 0 <65: 1.001 (0.997, 1.005) 0 65-75: 1.005 (1.001, 1.008) 0 >75: 1.003 (1.001, 1.006) 0 Cardiovascular: All ages: 1.003 (1.000, 1.006) 0 <65: 1.002 (0.994, 1.010) 0 65-75: 1.003 (0.998, 1.008) 0 >75: 1.003 (1.000, 1.006) 0 COPD: All ages: 1.005 (0.999, 1.011) 0 <65: 1.004 (0.981, 1.027) 0 65-75: 0.996 (0.986, 1.007) 0 >75: 1.006 (1.000, 1.012) 0 Multipollutant models: SO_2: 1.001 (0.998, 1.003) 0 NO_2: 1.001 (0.998, 1.003) 0 SO_2+NO_2: 1.000 (0.997, 1.003) 0

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Kan and Chen (2003, 087372) **Period of Study:** Jan 2000-Dec 2001 **Location:** Shanghai, China	**Outcome:** Mortality: Nonaccidental (<800) Cardiovascular (390-459) COPD (490-496) **Study Design:** Case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 91.14 (51.85) IQR (25th, 75th): (54, 114) **Copollutant (correlation):** SO_2: r = 0.71 NO_2: r = 0.73	**Increment:** 10 µg/m^3 **Odds Ratio (Lower CI, Upper CI) lag:** Nonaccidental: Bidirectional referent days: 7 days: 1.000 (0.9988, 1.002) 0-1 ma 7 and 14 days: 1.002 (1.000, 1.004) 0-1 ma 7, 14, and 21 days: 1.003 (1.001, 1.005) 0-1 ma Unidirectional referent days: 7 days: 1.015 (1.012, 1.018) 0-1 ma 7 and 14 days: 1.017 (1.015, 1.019) 0-1 ma 7, 14, and 21 days: 1.019 (1.012, 1.021) 0-1 ma Bidirectional referent days (7, 14, and 21 days): Cardiovascular: 1.004 (1.001, 1.007) 0-1 ma COPD: 1.006 (0.999, 1.013) 0-1 ma Nonaccidental: PM_{10}+SO_2: 0.997 (0.994, 1.025) 0-1 ma PM_{10}+NO_2: 0.997 (0.994, 1.025) 0-1 ma PM_{10}+SO_2+NO_2: 0.995 (0.992, 1.025) 0-1 ma
Reference: Kan et al. (2005, 087561) **Period of Study:** Apr 2003-May 2003 **Location:** Beijing, China	**Outcome:** Mortality: Severe acute respiratory syndrome (SARS) **Study Design:** Time-series **Statistical Analyses:** Poisson, GAM, smoothing spline **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 149.1 (8.1) **Range (Min, Max):** (34, 246) **Copollutant:** SO_2 NO_2	**Increment:** 10 µg/m^3 **Relative Risk (Lower CI, Upper CI) lag:** 0.99 (0.96-1.03) 0 1.00 (0.97-1.04) 1 1.02 (0.98-1.06) 2 1.04 (0.99-1.09) 3 1.06 (1.00-1.11) 4 1.06 (1.00-1.12) 5 1.05 (0.98-1.12) 6
Reference: Kan et al. (2007, 091267) **Period of Study:** Mar 2004-Dec 2005 **Location:** Shanghai, China	**Outcome (ICD10):** Mortality: Total (nonaccidental) (A00-R99) Cardiovascular (I00-I99) Respiratory (J00-J98) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, penalized splines **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 107.9 (2.39) µg/m^3 **Range (Min, Max):** (22.0, 403.0) **Copollutant (correlation):** PM_{10} $PM_{2.5}$: r = 0.84 $PM_{10-2.5}$: r = 0.88 O_3: r = 0.21	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** PM_{10} Total: 0.16% (0.02, 0.30) 0-1 Cardiovascular: 0.31% (0.10, 0.53) 0-1 Respiratory: 0.33% (-0.08, 0.75) 0-1

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Kan et al. (2008, 156621) **Period of Study:** Jan 2001-Dec 2004 **Location:** Shanghai, China	**Outcome:** Mortality: Total (nonaccidental) (A00-R99) Cardiovascular (I00-I99) Respiratory (J00-J98) **Study Design:** Time-series **Statistical Analyses:** Poisson GLM, natural splines **Age Groups:** All ages; 0-4 yr 5-44 yr 45-64 yr ≥ 65 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** Warm season: 87.4 (1.8) Cool season: 116.7 (2.8) Entire period: 102.0 (1.7) **Range (Min, Max):** NR **Copollutant (correlation):** SO_2 NO_2 O_3	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Nonaccidental Warm season: 0.21 (0.09, 0.3) 0-1 Cool season: 0.26 (0.22, 0.30) 0-1 Entire period: 0.25 (0.14, 0.37) 0-1 Female: 0.33 (0.18, 0.48) 0-1 Male: 0.17 (0.03, 0.32) 0-1 5-44: 0.04 (-0.52, 0.59) 0-1 45-64: 0.17 (-0.11, 0.45) 0-1 ≥ 65: 0.26 (0.15, 0.38) 0-1 Cardiovascular Warm season: 0.22 (-0.14, 0.58) 0-1 Cool season: 0.25 (0.05, 0.45) 0-1 Entire period: 0.27 (0.10, 0.44) 0-1 Respiratory Warm season: -0.28 (-0.93, 0.38) 0-1 Cool season: 0.58 (0.25, 0.92) 0-1 Entire period: 0.27 (-0.01, 0.56) 0-1 Stratified by Educational Attainment Nonaccidental: Low: 0.33 (0.19, 0.47) 0-1 High: 0.18 (0.01, 0.36) 0-1 Cardiovascular: Low: 0.30 (0.10, 0.51) 0-1 High: 0.23 (-0.03, 0.50) 0-1 Respiratory: Low: 0.36 (0.00, 0.72) 0-1 High: 0.02 (-0.43, 0.47) 0-1
Reference: Keatinge and Donaldson (2006, 087536) **Period of Study:** 1991-2002 **Location:** London, England	**Outcome:** Mortality: Total (nonaccidental) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM **Age Groups:** ≥ 65 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR **Copollutant:** O_3 SO_2	**Increment:** 10 µg/m^3 **Mortality per 106 (Lower CI, Upper CI) lag:** PM_{10}+Temp: 2.1 (0.9, 3.3) 0-2 avg PM_{10}+Temp+Acclim: 1.6 (0.4, 2.8) 0-2 avg PM_{10}+Temp+Acclim+Acclim x T: 1.5 (0.3, 2.6) 0-2 avg PM_{10}+Temp+Acclim+Acclim x T+Sun: 1.4 (0.2, 2.5) 0-2 avg PM_{10}+Temp+Acclim+Acclim x T+Sun+Wind: 0.8 (-0.4, 1.9) 0-2 avg PM_{10}+Temp+Acclim+Acclim x T+Sun+Wind+Abs. Humid.: 0.8 (-0.3, 1.9) 0-2 avg PM_{10}+Temp+Acclim+Acclim x T+Sun+Wind+Abs. Humid.+ Rain: 0.9 (-0.3, 2.0) 0-2 avg PM_{10}+Temp+Abs. Humid.: 1.9 (0.7, 3.1) 0-2 avg
Reference: Kettunen et al. (2007, 091242) **Period of Study:** 1998-2004 **Location:** Helsinki, Finland	**Outcome (ICD10):** Mortality: Stroke (I60-I61, I63-I64) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, penalized thin-plate splines **Age Groups:** ≥ 65	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Median (SD) unit:** Cold Season: 16.3 Warm Season: 16.5 **Range (Min, Max):** Cold Season: (3.1, 136.7) Warm Season: (3.3, 67.4) **Copollutant:** $PM_{2.5}$ $PM_{10-2.5}$ UFP O_3 CO NO_2	**Increment:** Cold Season: 13.8 µg/m^3 Warm Season: 9.8 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Cold Season -0.56% (-3.32, 2.29) 0 -0.93% (-3.55, 1.75) 1 -1.68% (-4.30, 1.00) 2 -1.53% (-4.14, 1.14) 3 Warm Season 10.89% (0.95, 21.81) 0 8.56% (-0.88, 18.90) 1 2.06% (-6.76, 11.71) 2 -2.89% (-11.32, 6.34) 3

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Kim et al. (2003, 155899) **Period of Study:** Jan 1995-Dec 1999 **Location:** Seoul, Korea	**Outcome (ICD10):** Mortality: Nonaccidental (all except S01-S99, T01-T98) Cardiovascular (I00-I52) Respiratory (J00-J98) Cerebrovascular (I60-I69) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 69.19 (10.36) IQR (25th, 75th): (44.82, 87.95) **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** All cause: 2.8% (1.8, 3.7) 0 2.8% (1.9, 3.7) 1 1.4% (0.5, 2.3) 2 3.7% (2.1, 5.4) distributed lag (6-day) Respiratory: 8.3% (4.3, 12.5) 0 6.4% (2.7, 10.2) 1 6.5% (2.7, 10.4) 2 13.9% (6.8, 21.5) distributed lag (6-day) Pneumonia: 11.6% (4.2, 19.6) 0 9.0% (2.1, 16.3) 1 7.7% (0.8, 15.2) 2 17.1% (4.1, 31.7) distributed lag (6-day) COPD: 4.2% (-1.2, 10.0) 0 3.5% (-1.5, 8.9) 1 1.4% (-3.7, 6.8) 2 12.2% (2.5, 22.9) distributed lag (6-day) Cardiovascular: 2.0% (-0.9, 5.0) 0 3.3% (0.6, 6.2) 1 2.9% (0.1, 5.8) 2 4.4% (-0.6, 9.6) distributed lag (6-day) Myocardial infarction: 2.6% (-2.3, 7.8) 0 5.8% (1.0, 10.7) 1 5.5% (0.7, 10.6) 2 4.9% (-3.4, 13.9) distributed lag (6-day) Cerebrovascular: 3.2% (0.8, 5.5) 0 3.1% (0.9, 5.3) 1 2.4% (0.1, 4.6) 2 6.3% (2.3, 10.5) distributed lag (6-day) Ischemic stroke: -0.6% (-5.6, 4.7) 0 0.6% (-4.2, 5.7) 1 -0.1% (-4.9, 5.1) 2 10.3% (1.0, 20.4) distributed lag (6-day)
Reference: Kim et al. (2004, 087417) **Period of Study:** Jan 1997-Dec 2001 **Location:** Seoul, Korea	**Outcome:** Mortality: Nonaccidental **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 68.23 (36.36) µg/m^3 IQR (25th, 75th): (42.56, 84.67) **Copollutant (correlation):** NR	**Increment:** 42.11 µg/m^3 **Relative Risk (Lower CI, Upper CI) lag:** 1.021 (1.009, 1.035)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Le Tertre et al. (2005, 087560) **Period of Study:** NR **Location:** 21 European cities (APHEA-2)	**Outcome:** Mortality: Nonaccidental (<800) **Study Design:** Time-series **Statistical Analyses:** Empirical Bayes **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR **Copollutant:** NO_2	**Increment:** 1.0 µg/m^3 **β coefficient (SE) lag:** Athens: 0.001311 (0.0003) Barcelona: 0.000575 (0.0002) Basel: 0.000462 (0.0005) Birmingham: 0.000305 (0.0003) Budapest: -0.000248 (0.0005) Cracow: 0.000155 (0.0004) Erfurt: -0.000465 (0.0004) Geneva: -0.000059 (0.0005) Helsinki: 0.000389 (0.0004) London: 0.000591 (0.0002) Lyon: 0.001554 (0.0005) Madrid: 0.000372 (0.0003) Milan: 0.000901 (0.0002) Paris: 0.000411 (0.0003) Prague: 0.000097 (0.0002) Rome: (0.001333 (0.0003) Stockholm: 0.000479 (0.0009) Tel Aviv: 0.000522 (0.0003) Teplice: 0.000876 (0.0004) Torino: 0.000938 (0.0002) Zurich: 0.000365 (0.0004) Toulouse: NR (NR) Overall: 0.00055 (0.000098)
Reference: Lee et al. (2007, 093042) **Period of Study:** Jan 2000-Dec 2004 **Location:** Seoul, Korea	**Outcome (ICD10):** Mortality: Nonaccidental (A00-R99) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** w/ Asian dust days: 70.00 (47.80) w/o Asian dust days: 65.77 (33.60) Asian dust days only: 188.49 (142.85) **Copollutant:** CO NO_2 SO_2 O_3	**Increment:** 41.49 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Model with Asian Dust Days 0.7% (0.2, 1.3) 1-3 Model without Asian dust days 1.0% (0.2, 1.8) 1-3
Reference: Lee and Shaddick (2007, 156685) **Period of Study:** Jan 1993-Dec 1997 **Location:** Cleveland, Ohio Detroit, Michigan Minneapolis, Minnesota Pittsburgh, Pennsylvania	**Outcome (ICD10):** Mortality: Nonaccidental **Study Design:** Time-series **Statistical Analyses:** 1. Bayesian, penalized spline 2. Likelihood, penalized spline **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR	**Increment:** 10 µg/m^3 **Relative Risk (Lower CI, Upper CI) lag:** Constant model Cleveland: 1.0049 1 Detroit: 1.0046 1 Minneapolis: 1.0052 1 Pittsburgh: 1.0045 1
Reference: Martins et al. (2004, 087457) **Period of Study:** Jan 1997-Dec 1999 **Location:** São Paulo, Brazil	**Outcome (ICD10):** Mortality: Respiratory (J00-J99) **Study Design:** Time-series **Statistical Analyses:** Poisson GLM, natural cubic splines **Age Groups:** ≥ 60	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** Cerqueira Cesar: 42.5(22.9) Santa Amaro: 49.6(32.1) Central: 52.1(23.5) Penha: 40.4(23.8) Santana: 72.6(24.5) Sao Miguel Paulista: 68.6(31.0) **Range (Min, Max):** NR	The study does not present quantitative results.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Nawrot et al. (2007, 098619) **Period of Study:** Jan 1997-Dec 2003 **Location:** Flanders, Belgium	**Outcome:** Mortality: Nonaccidental (<800) Cardiovascular (390-459) Respiratory (460-519) **Study Design:** Time-series **Statistical Analyses:** Main analysis: Segmented regression models Sensitivity analysis: Poisson GAM, LOESS **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Median (SD) unit:** Winter: 43.3(0.88) Spring: 39.5(0.88) summer: 37.7(0.91) Fall: 37.2(0.88) **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** Main analysis: NR Sensitivity analysis: 10 $\mu g/m^3$ **% Increase (Lower CI, Upper CI) lag:** Highest season-specific PM_{10} quartile vs. the lowest season-specific PM_{10} quartile Summer: 7.8% (6.1, 9.6) Spring: 6.3% (4.7, 7.8) Fall: 2.2% (0.58, 3.8) Winter: 1.4% (0.06, 2.9) Warm months (Jun, Jul, Aug): 7.9% (6.2, 9.6) Cold months (Dec, Jan, Feb): 1.5% (0.22, 3.3) Intermediate months (Mar, Apr, May, Sep, Oct, Nov): 4.2% (2.9, 5.6) Warmer Periods (Apr-Sep) Nonaccidental: 1.5% (1.1, 2.0) 0 Respiratory: 2.0% (0.6, 3.7) 0 Cardiovascular: 1.8% (1.1, 2.4) 0

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: O'Neill et al. (2004, 087429) **Period of Study:** 1996-1998 1994-1995 **Location:** Mexico City, Mexico	**Outcome:** Mortality: Nonaccidental **Study Design:** Time-series **Statistical Analyses:** Poisson, natural cubic spline **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Range**: Hi-Vol: 46.3-164.0 TEOM: 48.2-107.5 Predicted: 30.2-162.4 Impactor: 58.4 **Range (Min, Max):** Xalostoc Hi-Vol: (40.0, 335.0) TEOM: (16.5, 291.2) Predicted: (60.6, 320.0) Tlalnepantla Hi-Vol: (25.0, 264.0) TEOM: (10.4, 275.9) Predicted: (17.7, 175.0) Merced Hi-Vol: (17.0, 266.0) TEOM: (9.4, 318.7) Predicted: (12.3, 160.8) Cerro de la Estrella Hi-Vol: (15.0, 292.0) TEOM: (13.7, 268.3) Predicted: (11.2, 154.4) Pedregal (1996-1998) Hi-Vol: (5.0, 226.0) TEOM: (7.8, 264.4) Predicted: (-0.5, 86.3) Pedregal (1994-1995) Hi-Vol: (24.0, 114.0) TEOM: (8.7, 152.5) Impactor: (15.0, 154.0) Predicted: (3.9, 75.9)	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** TEOM 0.04% (-0.12, 0.20) 0 -0.02% (-0.18, 0.13) 1 -0.01% (-0.27, 0.25) 2 -0.03% (-0.19, 0.13) 3 -0.03% (-0.19, 0.13) 4 -0.05% (-0.21, 0.11) 5 0.05% (-0.25, 0.35) 0-5 Predicted -0.05% (-0.29, 0.19) 0 0.09% (-0.16, 0.34) 1 -0.12% (-0.43, 0.20) 2 -0.02% (-0.26, 0.21) 3 -0.14% (-0.37, 0.09) 4 -0.05% (-0.28, 0.18) 5 0.00% (-0.39, 0.38) 0-5 Sierra-Anderson High Volume Air Sampler 0.02% (-0.29, 0.32) 0 0.13% (-0.27, 0.54) 1 0.21% (-0.10, 0.52) 2 0.53% (0.07, 0.99) 3 0.11% (-0.20, 0.41) 4 0.38% (0.07, 0.70) 5 GAM: 2 LOESS terms, default convergence 1.68% (0.45, 2.93) 0 -0.36% (-1.56, 0.86) 1 -0.21% (-1.40, 1.00) 2 -0.18% (-1.40, 1.05) 3 1.31% (0.08, 2.55) 4 1.49% (0.25, 2.73) 5 1.77% (-0.26, 3.83) 0-5 Parametric: cubic splines 5 df 1.45% (0.09, 2.83) 0 -0.71% (-2.06, 0.67) 1 -0.59% (-1.95, 0.79) 2 -0.70% (-2.09, 0.71) 3 0.92% (-0.46, 2.32) 4 1.17% (-0.19, 2.55) 5 1.17% (-1.54, 3.95) 0-5 10 df 1.60% (0.20, 3.02) 0 -0.80% (-2.18, 0.60) 1 -0.73% (-2.11, 0.68) 2 -1.05% (-2.49, 0.40) 3 0.64% (-0.79, 2.10) 4 1.05% (-0.36, 2.48) 5 0.51% (-2.60, 3.71) 0-5 2 df 1.79% (0.48, 3.11) 0 -0.09% (-1.38, 1.22) 1 0.10% (-1.18, 1.40) 2 0.20% (-1.10, 1.52) 3 1.60% (0.30, 2.91) 4 1.72% (0.43, 3.04) 5 1.90% (-0.36, 4.21) 0-5
Reference: O'Neill et al. (2005, 098094) **Period of Study:** 1996-1998 1996-1999 **Location:** Mexico City and Monterrey, Mexico	**Outcome:** Mortality: Nonaccidental Cardiovascular (390-460) Respiratory (460-520) Other-causes **Study Design:** Time-series **Statistical Analyses:** Poisson, natural cubic splines **Age Groups:** All ages, 0-15, ≥ 65	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** Mexico City: 75.8 (31.4) Monterrey: 50.0 (23.5) **Range (Min, Max):** Mexico City: (18.0, 233.9) Monterrey: (6.2, 230.8) **Copollutant:** O_3	The study focuses on the temperature-mortality relationship and only includes PM_{10} as a covariate in models.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: O'Neill et al. (2008, 192314) **Period of Study:** Jan 1998-Dec 2002 **Location:** Mexico City, Mexico Santiago, Chile São Paulo, Brazil	**Outcome:** **Study Design:** Time-series **Covariates:** Temperature, day of week, temporal trends, sex **Statistical Analysis:** Poisson regression **Statistical Package:** S-Plus **Age Groups:** Adults over 21 yr	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD) µg/m³:** Mexico City: 53.8 (24.9) São Paulo: 48.9 (21.9) Santiago: 78.7 (33.0) **Range (Min, Max):** Mexico City: 1.08-192.2 São Paulo: 12.0-171.3 Santiago: 8.0-218.6 **Copollutant:** NR	**Increment:** 10 µg/m³ **Percent increase (95% CI) in all-cause adult mortality (>22yrs) by educational level and sex** **Mexico City** All Adults, Concurrent Day None: 0.76 (0.17-1.36) Primary: 0.27 (-0.19-0.72) Secondary: 0.19 (-0.19-0.57) ≥ 12 yr: 0.83 (0.03-1.63) All Adults, Lag 1 None: 0.62 (0.02-1.22) Primary: 0.62 (0.17-1.08) Secondary: 0.29 (-0.09-0.90) ≥ 12 yr: 0.58 (-0.21-1.38) All Adults, Distributed Lags 0-5 None: 0.91 (-0.07-1.89) Primary: 0.48 (-0.27-1.24) Secondary: 0.27 (-0.36-0.90) ≥ 12 yr: 0.75 (-0.49-2.02) All Adults, df (yr) None: 5.4 Primary: 6.0 Secondary: 6.0 ≥ 12 yr: 3.0 Women, Concurrent Day None: 0.65 (-0.08-1.38) Primary: 0.48 (-0.13-1.09) Secondary: 0.35 (-0.16-0.86) ≥ 12 yr: 1.64 (0.69-2.59) Women, Lag 1 None: 0.62 (-0.12-1.36) Primary: 1.03 (0.42-1.64) Secondary: 0.59 (0.08-1.11) ≥ 12 yr: 1.79 (0.84-2.75) Women, Distributed Lags 0-5 None: 0.46 (-0.74-1.68) Primary: 1.39 (0.42-2.36) Secondary: 0.51 (-0.30-1.33) ≥ 12 yr: 1.71 (0.61-2.83) Women, df (yr) None: 5.4 Primary: 4.4 Secondary: 4.8 ≥ 12 yr: 1.0 Men, Concurrent Day None: 0.75 (-0.21-1.72) Primary: 0.52 (-0.11-1.15) Secondary: 0.56 (0.08-1.05) ≥ 12 yr: 1.20 (0.25-2.17) Men, Lag 1 None: 0.45 (-0.51-1.42) Primary: 0.70 (0.06-1.34) Secondary: 0.47 (-0.02-0.95) ≥ 12 yr: 0.74 (-0.22-1.70) Men, Distributed Lags 0-5 None: 1.24 (-0.25-2.75) Primary: 0.65 (-0.39-1.69) Secondary: 0.88 (0.11-1.66) ≥ 12 yr: 1.07 (-0.41-2.57) Men, df (yr) None: 3.8 Primary: 5.6 Secondary: 4.6 ≥ 12 yr: 3.8 **São Paulo** All Adults, Concurrent Day None: 0.77 (-0.28-1.82) Primary: 1.27 (0.78-1.76) Secondary: 0.93 (-0.07-1.94) ≥ 12 yr: 2.93 (2.00-2.88) All Adults, Lag 1 None: 0.70 (-0.34-1.76) Primary: 1.32 (0.83-1.82) Secondary: 1.91 (0.58-2.60) ≥ 12 yr: 2.20 (1.27-3.15)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			All Adults, Distributed Lags 0-5 None: 0.76 (-0.91-2.46) Primary: 1.34 (0.55-2.14) Secondary: 1.91 (0.35-2.60) ≥ 12 yr: 2.20 (1.27-3.15) All Adults, df (yr) None: 4.0 Primary: 4.0 Secondary: 2.8 ≥ 12 yr: 1.6 Women, Concurrent Day None: 1.93 (0.87-3.00) Primary: 1.72 (1.04-2.41) Secondary: 0.85 (-0.21-1.92) ≥ 12 yr: 1.84 (0.56-3.13) Women, Lag 1 None: 1.41 (0.34-2.48) Primary: 1.64 (0.96-2.33) Secondary: 1.43 (0.36-2.50) ≥ 12 yr: 2.27 (0.99-3.56) Women, Distributed Lags 0-5 None: 2.00 (0.40-3.63) Primary: 2.05 (0.96-3.14) Secondary: 1.61 (0.07-3.17) ≥ 12 yr: 3.35 (1.49-5.25) Women, df (yr) None: 2.4 Primary: 3.6 Secondary: 1.4 ≥ 12 yr: 0.8 Men, Concurrent Day None: -0.43 (-2.15-1.32) Primary: 1.36 (0.71-2.02) Secondary: 1.74 (0.77-2.72) ≥ 12 yr: 2.81 (1.71-3.92) Men, Lag 1 None: -0.44 (-2.17-1.33) Primary: 1.44 (0.79-2.10) Secondary: 1.52 (0.55-2.49) ≥ 12 yr: 1.48 (0.38-2.59) Men, Distributed Lags 0-5 None: -0.30 (-3.09-2.56) Primary: 1.67 (0.65-2.70) Secondary: 1.06 (-0.34-2.49) ≥ 12 yr: 3.18 (1.60-4.79) Men, df (yr) None: 4.4 Primary: 3.2 Secondary: 0.8 ≥ 12 yr: 1.2 **Santiago** All Adults, Concurrent Day None: 1.44 (0.53-2.36) Primary: 0.06 (-0.21-0.34) Secondary: 0.42 (0.06-0.78) ≥ 12 yr: 1.32 (0.60-2.05) All Adults, Lag 1 None: 2.08 (1.16-30.1) Primary: 0.53 (0.25-0.81) Secondary: 0.55 (0.19-0.91) ≥ 12 yr: 1.31 (0.59-2.04) All Adults, Distributed Lags 0-5 None: 3.18 (1.60-4.78) Primary: 0.58 (0.10-1.06) Secondary: 1.10 (0.48-1.73) ≥ 12 yr: 2.00 (0.93-3.07) All Adults, df (yr) None: 3.6 Primary: 5.6 Secondary: 4.0 ≥ 12 yr: 1.6 Women, Concurrent Day None: 0.91 (-0.06-1.89) Primary: 0.31 (-0.06-0.68) Secondary: 0.84 (0.33-1.36) ≥ 12 yr: 0.60 (-0.32-1.52) Women, Lag 1

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			None: 1.58 (0.58-2.58) Primary: 0.79 (0.42-1.17) Secondary: 0.76 (0.25-1.28) ≥ 12 yr: 0.53 (-0.39-1.45) Women, Distributed Lags 0-5 None: 1.15 (-0.48-2.80) Primary: 1.05 (0.41-1.69) Secondary: 1.29 (0.40-2.19) ≥ 12 yr: 1.06 (-0.27-2.41) Women, df (yr) None: 2.6 Primary: 4.8 Secondary: 4.4 ≥ 12 yr: 1.0 Men, Concurrent Day None: 0.05 (-1.02-1.12) Primary: -0.11 (-0.5-0.28) Secondary: 0.18 (-0.31-0.68) ≥ 12 yr: 1.52 (0.70-2.35) Men, Lag 1 None: 0.61 (-0.44-1.68) Primary: 0.23 (-0.16-0.62) Secondary: 0.49 (0.00-0.98) ≥ 12 yr: 1.03 (0.21-1.86) Men, Distributed Lags 0-5 None: 2.08 (0.28-3.91) Primary: 0.16 (-0.50-0.82) Secondary: 1.27 (0.43-2.12) ≥ 12 yr: 1.98 (0.76-3.20) Men, df (yr) None: 2.8 Primary: 4.8 Secondary: 4.4 ≥ 12 yr: 1.6
			Percent increase (95% CI) in all-cause adult mortality (≥65yrs) by educational level and sex
			Mexico City All Adults, Concurrent Day None: 0.41 (-0.25-1.08) Primary: 0.40 (-0.15-0.95) Secondary: 0.50 (-0.01-1.01) ≥ 12 yr: 1.51 (0.39-2.63) All Adults, Lag 1 None: 0.20 (-0.47-0.87) Primary: 0.80 (0.24-1.36) Secondary: 0.60 (0.09-1.12) ≥ 12 yr: 1.09 (-0.02-2.22) All Adults, Distributed Lags 0-5 None: 0.27 (-0.83-1.38) Primary: 0.99 (0.07-1.91) Secondary: 0.30 (-0.56-1.16) ≥ 12 yr: 1.83 (0.09-3.59) All Adults, df (yr) None: 5.6 Primary: 5.4 Secondary: 6.0 ≥ 12 yr: 3.2 Women, Concurrent Day None: 0.49 (-0.30-1.29) Primary: 0.39 (-0.33-1.11) Secondary: 0.52 (-0.16-1.20) ≥ 12 yr: 1.29 (0.12-2.48) Women, Lag 1 None: 0.73 (-0.07-1.54) Primary: 1.24 (0.52-1.97) Secondary: 0.55 (-0.13-1.23) ≥ 12 yr: 1.50 (0.32-2.70) Women, Distributed Lags 0-5 None: 0.75 (-0.56-2.08) Primary: 1.43 (0.29-2.59) Secondary: 0.06 (-1.01-1.15) ≥ 12 yr: 1.48 (0.10-2.87) Women, df (yr) None: 5.4 Primary: 4.2 Secondary: 4.8

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			≥ 12 yr: 0.6 Men, Concurrent Day None: 0.90 (-0.23-2.04) Primary: 0.37 (-0.40-1.16) Secondary: 0.78 (0.07-1.49) ≥ 12 yr: 1.66 (0.30-3.04) Men, Lag 1 None: -0.15 (-1.27-0.98) Primary: 0.26 (-0.53-1.05) Secondary: 0.93 (0.22-1.65) ≥ 12 yr: 0.95 (-0.41-2.32) Men, Distributed Lags 0-5 None: 0.80 (-0.95-2.58) Primary: 0.29 (-0.99-1.58) Secondary: 1.06 (-0.08-2.21) ≥ 12 yr: 1.76 (-0.35-3.91) Men, df (yr) None: 3.8 Primary: 5.6 Secondary: 4.6 ≥ 12 yr: 3.8 **São Paulo** All Adults, Concurrent Day None: 0.60 (-0.48-1.70) Primary: 0.59 (1.00-2.19) Secondary: 1.21 (-0.01-2.44) ≥ 12 yr: 2.80 (1.67-3.94) All Adults, Lag 1 None: 0.62 (-0.47-1.72) Primary: 1.48 (0.89-2.07) Secondary: 2.31 (1.08-3.55) ≥ 12 yr: 2.52 (1.40-3.66) All Adults, Distributed Lags 0-5 None: 0.91 (-0.84-2.69) Primary: 1.73 (0.79-2.67) Secondary: 3.25 (1.39-5.16) ≥ 12 yr: 3.63 (2.01-5.29) All Adults, df (yr) None: 4.0 Primary: 3.8 Secondary: 2.6 ≥ 12 yr: 1.6 Women, Concurrent Day None: 1.82 (0.71-2.94) Primary: 1.84 (1.05-2.64) Secondary: 0.62 (-0.55-1.81) ≥ 12 yr: 1.00 (-0.27-2.29) Women, Lag 1 None: 1.36 (0.25-2.49) Primary: 1.76 (0.97-2.56) Secondary: 1.57 (0.39-2.76) ≥ 12 yr: 1.39 (0.12-2.68) Women, Distributed Lags 0-5 None: 1.80 (0.12-3.51) Primary: 1.97 (0.73-3.22) Secondary: 1.89 (0.19-3.61) ≥ 12 yr: 2.53 (0.70-4.40) Women, df (yr) None: 2.4 Primary: 3.4 Secondary: 1.2 ≥ 12 yr: 0.8 Men, Concurrent Day None: -0.67 (-2.50-1.19) Primary: 1.82 (1.00-2.65) Secondary: 2.46 (1.31-3.63) ≥ 12 yr: 1.73 (0.47-3.00) Men, Lag 1 None: -0.59 (-2.42-1.26) Primary: 1.59 (0.78-2.41) Secondary: 2.64 (1.49-3.80) ≥ 12 yr: 0.89 (-0.35-2.15) Men, Distributed Lags 0-5 None: 1.50 (-1.52-4.60) Primary: 2.46 (1.20-3.74) Secondary: 2.24 (0.56-3.95) ≥ 12 yr: 1.45 (-0.34-3.29)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Men, df (yr) None: 4.6 Primary: 3.0 Secondary: 0.8 ≥ 12 yr: 1.0 **Santiago** All Adults, Concurrent Day None: 1.49 (0.54-2.45) Primary: 0.28 (-0.03-0.59) Secondary: 0.58 (0.13-1.04) ≥ 12 yr: 2.32 (1.50-3.15) All Adults, Lag 1 None: 2.20 (1.24-3.17) Primary: 0.74 (0.43-1.05) Secondary: 0.64 (0.20-1.11) ≥ 12 yr: 2.20 (1.36-3.04) All Adults, Distributed Lags 0-5 None: 3.21 (1.54-4.90) Primary: 0.92 (0.38-1.46) Secondary: 1.46 (0.67-2.25) ≥ 12 yr: 4.02 (2.78-5.27) All Adults, df (yr) None: 3.8 Primary: 5.2 Secondary: 4.0 ≥ 12 yr: 1.8 Women, Concurrent Day None: 1.39 (0.41-2.39) Primary: 0.4 (0.01-0.8) Secondary: 0.91 (0.29-1.53) ≥ 12 yr: 0.87 (-0.02-1.78) Women, Lag 1 None: 1.83 (0.83-2.85) Primary: 0.98 (0.58-1.38) Secondary: 0.73 (0.11-1.35) ≥ 12 yr: 0.76 (-0.15-1.68) Women, Distributed Lags 0-5 None: 2.47 (0.85-4.11) Primary: 1.2 (0.52-1.88) Secondary: 1.71 (0.65-2.78) ≥ 12 yr: 0.87 (-0.02-1.78) Women, df (yr) None: 2.4 Primary: 4.8 Secondary: 4.4 ≥ 12 yr: 0.6 Men, Concurrent Day None: 0.54 (-0.51-1.61) Primary: 0.34 (-0.12-0.80) Secondary: 0.25 (-0.40-0.91) ≥ 12 yr: 1.97 (1.09-2.86) Men, Lag 1 None: 0.84 (-0.21-1.91) Primary: 0.43 (-0.03-0.89) Secondary: 0.61 (-0.04-1.26) ≥ 12 yr: 1.57 (0.67-2.46) Men, Distributed Lags 0-5 None: 2.41 (0.64-4.22) Primary: 0.80 (0.02-1.59) Secondary: 1.58 (0.45-2.71) ≥ 12 yr: 2.99 (1.66-4.33) Men, df (yr) None: 2.0 Primary: 4.4 Secondary: 4.4 ≥ 12 yr: 1.8

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Peng et al. (2005, 087463) **Period of Study:** 1987-2000 **Location:** 100 U.S. cities (NMMAPS)	**Outcome:** Mortality: Nonaccidental **Study Design:** Time-series **Statistical Analyses:** Bayesian semiparametric hierarchical models **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Median (SD) unit:** 27.1 **Range (Min, Max):** (13.2, 48.7) **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Winter: -0.4% (-0.30, 0.21) 0 0.15% (-0.08, 0.39) 1 0.10% (-0.13, 0.33) 2 Spring: 0.32% (0.08, 0.56) 0 0.14% (-0.14, 0.42) 1 0.05% (-0.21, 0.32) 2 Summer: 0.13% (-0.11, 0.37) 0 0.36% (0.11, 0.61) 1 -0.03% (-0.27, 0.21) 2 Fall: 0.05% (-0.16, 0.25) 0 0.14% (-0.06, 0.34) 1 0.13% (-0.08, 0.35) 2 All Seasons: 0.09% (-0.01, 0.19) 0 0.19% (0.10, 0.28) 1 0.08% (-0.03, 0.19) 2 **PM10 only (45 cities):** Winter: 0.15% (-0.16, 0.45) 1 Spring: 0.13% (-0.21, 0.48) 1 Summer: 0.30% (-0.10, 0.69) 1 Fall: 0.07% (-0.23, 0.37) 1 **PM10 + O3 (45 cities):** Winter: 0.18% (-0.16, 0.52) 1 Spring: 0.10% (-0.30, 0.49) 1 Summer: 0.33% (-0.14, 0.81) 1 Fall: 0.08% (-0.25, 0.41) 1 **PM10 + O3 (45 cities):** Winter: 0.13% (-0.24, 0.49) 1 Spring: 0.1% 9(-0.18, 0.56) 1 Summer: 0.28% (-0.13, 0.70) 1 Fall: -0.01% (-0.34, 0.31) 1 **PM10 + NO2 (45 cities):** Winter: 0.21% (-0.18, 0.60) 1 Spring: 0.19% (-0.17, 0.54) 1 Summer: 0.34% (0.01, 0.68) 1 Fall: 0.13% (-0.12, 0.39) 1
Reference: Penttinen et al. (2004, 087432) **Period of Study:** 1988-1996 **Location:** Helsinki, Finland	**Outcome:** Mortality: Total (nonaccidental) (<800) Cardiovascular (390-459) Respiratory (460-519) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups:** 15-64 yr 65-74 yr ≥ 75 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Median (SD) unit:** 21 µg/m^3 **Range (Min, Max):** (0.2, 213) **Copollutant (correlation):** O_3: r = -0.09 NO_2: r = 0.50 CO: r = 0.45 SO_2: r = 0.61 TSP: r = 0.72	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Total (nonaccidental) -0.23% (-1.47, 1.01) 0 0.88% (-0.32, 2.08) 1 0.11 (-0.51, 0.73) 0-3 avg Cardiovascular -1.22% (-3.00, 0.56) 0 0.63% (-1.09, 2.35) 1 0.08% (-0.96, 0.81) 0-3 avg Respiratory 3.94% (0.01, 7.87) 0 3.96% (0.11, 7.81) 1 2.13% (0.03, 4.22) 0-3 avg
Reference: Qian et al. (2007, 093054) **Period of Study:** 2001-2004 **Location:** Wuhan, China	**Outcome:** Mortality: Total (nonaccidental) (<800) Cardiovascular (390-459) Stroke (430-438) Cardiac Diseases (390-398) Respiratory (460-519) Cardiopulmonary **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, natural splines **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 141.8 3 **Range (Min, Max):** (24.8, 477.8) **Copollutant (correlation):** NO_2 SO_2 O_3	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Nonaccidental 0.36% (0.19, 0.53) 0 0.28% (0.12, 0.45) 1 0.43% (0.24, 0.62) 0-1 0.08% (-0.15, 0.31) 0-4 <45 yr 0.28% (-0.26, 0.82) 0 0.45% (-0.06, 0.96) 1 0.53% (-0.08, 1.13) 0-1 0.41% (-0.31, 1.13) 0-4 ≥ 45 yr 0.36% (0.19, 0.54) 0 0.27% (0.10, 0.44) 1 0.42% (0.22, 0.62) 0-1 0.05% (-0.18, 0.29) 0-4 <65 yr

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
	<45 yr		0.20% (-0.08, 0.49) 0 0.25% (-0.03, 0.52) 1 0.33% (0.01, 0.66) 0-1 0.01% (-0.38, 0.39) 0-4
	≥ 45 yr		≥ 65 yr 0.41% (0.21, 0.61) 0 0.30% (0.10, 0.49) 1 0.46% (0.24, 0.69) 0-1 0.10% (-0.16, 0.37) 0-4
	<65 yr		
	≥ 65 yr		
			Cardiovascular 0.51% (0.28, 0.75) 0 0.35% (0.12, 0.58) 1 0.58% (0.31, 0.84) 0-1 0.35% (0.05, 0.66) 0-4 <45 yr 0.59% (-0.62, 1.82) 0 0.93% (-0.22, 2.08) 1 1.07% (-0.27, 2.42) 0-1 1.15% (-0.40, 2.72) 0-4 ≥ 45 yr 0.51% (0.27, 0.75) 0 0.33% (0.10, 0.56) 1 0.56% (0.30, 0.83) 0-1 0.33% (0.02, 0.63) 0-4 <65 yr 0.27% (-0.23, 0.76) 0 0.30% (-0.16, 0.77) 1 0.42% (-0.12, 0.97) 0-1 0.43% (-0.19, 1.06) 0-4 ≥ 65 yr 0.57% (0.31, 0.83) 0 0.36% (0.11, 0.61) 1 0.61% (0.32, 0.90) 0-1 0.33% (0.00, 0.67) 0-4
			Stroke 0.44% (0.16, 0.72) 0 0.41% (0.14, 0.68) 1 0.58% (0.27, 0.89) 0-1 0.45% (0.09, 0.81) 0-4 <45 yr 1.18% (-0.45, 2.83) 0 1.66% (0.11, 3.24) 1 1.91% (0.10, 3.75) 0-1 2.72% (0.58, 4.89) 0-4 ≥ 45 yr 0.42% (0.14, 0.70) 0 0.37% (0.10, 0.65) 1 0.55% (0.23, 0.86) 0-1 0.39% (0.03, 0.76) 0-4 <65 yr 0.26% (-0.35, 0.87) 0 0.38% (-0.20, 0.96) 1 0.48% (-0.19, 1.16) 0-1 0.57% (-0.21, 1.35) 0-4 ≥ 65 yr 0.49% (0.17, 0.80) 0 0.41% (0.11, 0.72) 1 0.61% (0.26, 0.96) 0-1 0.42% (0.02, 0.83) 0-4
			Cardiac 0.49% (0.08, 0.89) 0 0.28% (-0.11, 0.67) 1 0.49% (0.04, 0.94) 0-1 0.22% (-0.29, 0.74) 0-4 <45 yr 0.25% (-1.64, 2.17) 0 0.56% (-1.22, 2.38) 1 0.61% (-1.47, 2.74) 0-1 -0.42% (-2.80, 2.02) 0-4 ≥ 45 yr 0.49% (0.09, 0.91) 0 0.27% (-0.12, 0.66) 1 0.48% (0.03, 0.94) 0-1 0.25% (-0.27, 0.77) 0-4

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			<65 yr 0.00% (-0.89, 0.90) 0 0.12% (-0.73, 0.98) 1 0.13% (-0.86, 1.13) 0-1 0.05% (-1.08, 1.20) 0-4 ≥ 65 yr 0.60% (0.17, 1.03) 0 0.32% (-0.10, 0.74) 1 0.57% (0.09, 1.06) 0-1 0.26% (-0.29, 0.82) 0-4 Respiratory 0.71% (0.20, 1.23) 0 0.63% (0.13, 1.13) 1 0.86% (0.28, 1.44) 0-1 0.19% (-0.48, 0.87) 0-4 <45 yr 1.74% (-1.28, 4.86) 0 2.52% (-0.30, 5.42) 1 2.95% (-0.41, 6.42) 0-1 3.47% (-0.61, 7.73) 0-4 ≥ 45 yr 0.69% (0.18, 1.21) 0 0.58% (0.09, 1.08) 1 0.81% (0.23, 1.39) 0-1 0.13% (-0.54, 0.80) 0-4 <65 yr 0.06% (-1.30, 1.43) 0 -0.53% (-1.83, 0.79) 1 -0.32% (-1.84, 1.22) 0-1 -0.72% (-2.47, 1.05) 0-4 ≥ 65 yr 0.79% (0.27, 1.31) 0 0.76% (0.26, 1.26) 1 0.99% (0.41, 1.57) 0-1 0.30% (-0.38, 0.98) 0-4 Cardiopulmonary 0.46% (0.23, 0.69) 0 0.35% (0.13, 0.57) 1 0.53% (0.28, 0.79) 0-1 0.11% (-0.19, 0.42) 0-4 <45 yr 0.71% (-0.48, 1.92) 0 1.26% (0.14, 2.4) 1 1.39% (0.06, 2.74) 0-1 1.41% (-0.18, 3.03) 0-4 ≥ 45 yr 0.45% (0.23, 0.68) 0 0.32% (0.10, 0.54) 1 0.51% (0.25, 0.77) 0-1 0.08% (-0.23, 0.38) 0-4 <65 yr 0.14% (-0.34, 0.61) 0 0.15% (-0.30, 0.61) 1 0.23% (-0.30, 0.76) 0-1 0.11% (-0.52, 0.74) 0-4 ≥ 65 yr 0.53% (0.28, 0.78) 0 0.39% (0.15, 0.63) 1 0.60% (0.32, 0.88) 0-1 0.11% (-0.22, 0.45) 0-4 **Two-pollutant Models** Nonaccidental PM_{10}+NO_2: 0.14% (-0.07, 0.36) 0 PM_{10}+SO_2: 0.37% (0.20, 0.55) 0 PM_{10}+O_3: 0.34% (0.17, 0.51) 0 Cardiovascular PM_{10}+NO_2: 0.34% (0.04, 0.63) 0 PM_{10}+SO_2: 0.53% (0.28, 0.77) 0 PM_{10}+O_3: 0.50% (0.26, 0.74) 0 Stroke PM_{10}+NO_2: 0.28% (-0.07, 0.63) 0 PM_{10}+SO_2: 0.49% (0.21, 0.78) 0 PM_{10}+O_3: 0.44 (0.16, 0.72) 0

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Cardiac PM_{10}+NO_2: 0.24% (-0.27, 0.75) 0 PM_{10}+SO_2: 0.43 (0.01, 0.84) 0 PM_{10}+O_3: 0.44% (0.03, 0.85) 0 Respiratory PM_{10}+NO_2: 0.46% (-0.19, 1.12) 0 PM_{10}+SO_2: 0.64% (0.11, 1.18) 0 PM_{10}+O_3: 0.67% (0.15, 1.20) 0 Cardiopulmonary PM_{10}+NO_2: 0.26% (-0.02, 0.55) 0 PM_{10}+SO_2: 0.46% (0.23, 0.70) 0 PM_{10}+O_3: 0.44% (0.21, 0.67) 0
Reference: Qian et al. (2008, 156894) **Period of Study:** Jul 2001-Jun 2004 **Location:** Wuhan, China	**Outcome:** Mortality: Total (nonaccidental) (<800) Cardiovascular (390-459) Stroke (430-438) Cardiac diseases (390-398, 410-429) Respiratory (460-519) Cardiopulmonary (390-459, 460-519) **Study Design:** Time-series **Statistical Analyses:** Poisson GLM, natural splines and penalized splines **Age Groups:** All ages <65 yr ≥ 65 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** Normal temperature: 145.7 (64.6) Low temperature: 117.3 (49.5) High temperature: 96.3 (27.9) **Range (Min, Max):** NR **Copollutant (correlation):** Normal temperature: NO_2: r = 0/72 SO_2: r = 0.59 O_3: r = 0.06 Low temperature: NO_2: r = 0.83 SO_2: r = 0.74 O_3: r = 0.19 High temperature: NO_2: r = 0.68 SO_2: r = 0.15 O_3: r = 0.65	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Nonaccidental: Normal: All ages: 0.36 (0.17, 0.56) 0-1 <65: 0.23 (-0.10, 0.56) 0-1 ≥ 65: 0.51 (0.18, 0.64) 0-1 PM_{10}+NO_2: 0.07 (-0.17, 0.30) 0-1 PM_{10}+SO_2: 0.27 (0.06, 0.47) 0-1 PM_{10}+O_3: 0.38 (0.18, 0.58) 0-1 Low: All ages: 0.62 (-0.09, 1.34) 0-1 <65: 1.78 (0.52, 3.05) 0-1 ≥ 65: 0.22 (-0.61, 1.05) 0-1 PM_{10}+NO_2: 0.24 (-0.49, 0.97) 0-1 PM_{10}+SO_2: 0.45 (-0.27, 1.17) 0-1 PM_{10}+O_3: 0.72 (0.00, 1.44) 0-1 High: All ages: 2.20 (0.74, 3.68) 0-1 <65: 2.34 (-0.09, 4.83) 0-1 ≥ 65: 2.14 (0.42, 3.89) 0-1 PM_{10}+NO_2: 1.87 (0.42, 3.35) 0-1 PM_{10}+SO_2: 2.12 (0.67, 3.60) 0-1 PM_{10}+O_3: 2.15 (0.55, 3.77) 0-1 Cardiovascular: Normal: All ages: 0.39 (0.11, 0.66) 0-1 <65: 0.17 (-0.40, 0.73) 0-1 ≥ 65: 0.44 (0.14, 0.74) 0-1 PM_{10}+NO_2: 0.11 (-0.23, 0.45) 0-1 PM_{10}+SO_2: 0.27 (-0.02, 0.55) 0-1 PM_{10}+O_3: 0.42 (0.15, 0.70) Low: All ages: 0.72 (-0.25, 1.70) 0-1 <65: 2.63 (0.67, 4.63) 0-1 ≥ 65: 0.24 (-0.84, 1.32) 0-1 PM_{10}+NO_2: 0.37 (-0.62, 1.38) 0-1 PM_{10}+SO_2: 0.50 (-0.47, 1.49) 0-1 PM_{10}+O_3: 0.82 (-0.16, 1.80) 0-1 High: All ages: 3.28 (1.24, 5.37) 0-1 <65: 4.32 (0.10, 8.71) 0-1 ≥ 65: 3.03 (0.77, 5.34) 0-1 PM_{10}+NO_2: 3.00 (0.95, 5.09) 0-1 PM_{10}+SO_2: 3.20 (1.16, 5.29) 0-1 PM_{10}+O_3: 3.71 (1.50, 5.96) 0-1 Stroke: Normal: All ages: 0.38 (0.06, 0.70) <65: 0.17 (-0.53, 0.88) 0-1 ≥ 65: 0.43 (0.07, 0.79) 0-1 PM_{10}+NO_2: 0.09 (-0.31, 0.49) 0-1 PM_{10}+SO_2: 0.31 (-0.03, 0.64) 0-1 PM_{10}+O_3: 0.38 (0.05, 0.71) 0-1 Low: All ages: 0.67 (-0.50, 1.85) 0-1 <65: 2.85 (0.34, 5.42) 0-1 ≥ 65: 0.11 (-1.22, 1.45) 0-1 PM_{10}+NO_2: 0.29 (-0.90, 1.51) 0-1 PM_{10}+SO_2: 0.53 (-0.65, 1.73) 0-1

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			$PM_{10}+O_3$: 0.69 (-0.48, 1.87) 0-1 High: All ages: 2.35 (-0.03, 4.78) 0-1 <65: 4.54 (-0.79, 10.16) 0-1 ≥ 65: 1.83 (-0.83, 4.57) $PM_{10}+NO_2$: 2.05 (-0.34, 4.49) 0-1 $PM_{10}+SO_2$: 2.31 (-0.07, 4.74) 0-1 $PM_{10}+O_3$: 2.77 (0.25, 5.35) 0-1 Cardiac: Normal: All ages: 0.32 (-0.14, 0.79) 0-1 <65: -0.04 (-1.07, 1.01) 0-1 ≥ 65: 0.40 (-0.10, 0.91) 0-1 $PM_{10}+NO_2$: 0.02 (-0.57, 0.60) 0-1 $PM_{10}+SO_2$: 0.11 (-0.38, 0.61) 0-1 $PM_{10}+O_3$: 0.41 (-0.06, 0.89) 0-1 Low: All ages: 0.50 (-1.10, 2.13) 0-1 <65: 1.79 (-1.65, 5.35) 0-1 ≥ 65: 0.19 (-1.55, 1.95) 0-1 $PM_{10}+NO_2$: 0.12 (-1.53, 1.80) 0-1 $PM_{10}+SO_2$: 0.14 (-1.48, 1.78) 0-1 $PM_{10}+O_3$: 0.72 (-0.90, 2.37) 0-1 High: All ages: 3.31 (-0.22, 6.97) 0-1 <65: 2.71 (-4.58, 10.56) 0-1 ≥ 65: 3.45 (-0.41, 7.46) 0-1 $PM_{10}+NO_2$: 3.01 (-0.54, 6.69) 0-1 $PM_{10}+SO_2$: 3.17 (-0.37, 6.84) 0-1 $PM_{10}+O_3$: 4.92 (0.96, 9.03) 0-1 Respiratory: Normal: All ages: 0.80 (0.25, 1.35) 0-1 <65: -0.35 (-1.85, 1.18) 0-1 ≥ 65: 0.93 (0.38, 1.50) 0-1 $PM_{10}+NO_2$: 0.30 (-0.39, 0.99) 0-1 $PM_{10}+SO_2$: 0.64 (0.07, 1.22) 0-1 $PM_{10}+O_3$: 0.84 (0.28, 1.41) 0-1 Low: All ages: 1.07 (-0.76, 2.95) 0-1 <65: -1.13 (-6.33, 4.35) 0-1 ≥ 65: 1.30 (-0.57, 3.20) 0-1 $PM_{10}+NO_2$: 0.44 (-1.46, 2.36) 0-1 $PM_{10}+SO_2$: 0.80 (-1.05, 2.69) 0-1 $PM_{10}+O_3$: 1.11 (-0.73, 2.99) 0-1 High: All ages: 1.15 (-3.54, 6.07) 0-1 <65: -3.42 (-15.82, 10.80) 0-1 ≥ 65: 1.76 (-3.03, 6.78) 0-1 $PM_{10}+NO_2$: 0.63 (-4.07, 5.55) 0-1 $PM_{10}+SO_2$: 1.03 (-3.66, 5.94) 0-1 $PM_{10}+O_3$: 2.66 (-2.44, 8.02) 0-1 Cardiopulmonary: Normal: All ages: 0.45 (0.19, 0.70) 0-1 <65: 0.07 (-0.47, 0.61) 0-1 ≥ 65: 0.53 (0.25, 0.81) 0-1 $PM_{10}+NO_2$: 0.15 (-0.17, 0.47) 0-1 $PM_{10}+SO_2$: 0.34 (0.07, 0.61) 0-1 $PM_{10}+O_3$: 0.43 (0.17, 0.70) 0-1 Low: All ages: 0.69 (-0.22, 1.61) 0-1 <65: 1.95 (0.04, 3.90) 0-1 ≥ 65: 0.43 (-0.57, 1.44) 0-1 $PM_{10}+NO_2$: 0.33 (-0.61, 1.27) 0-1 $PM_{10}+SO_2$: 0.50 (-0.42, 1.43) 0-1 $PM_{10}+O_3$: 0.76 (-0.16, 1.68) 0-1 High: All ages: 3.02 (1.03, 5.04) 0-1 <65: 3.49 (-0.66, 7.81) 0-1 ≥ 65: 2.91 (0.74, 5.12) 0-1 $PM_{10}+NO_2$: 2.70 (0.72, 4.73) 0-1 $PM_{10}+SO_2$: 2.95 (0.96, 4.97) 0-1 $PM_{10}+O_3$: 3.32 (1.16, 5.53) 0-1

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ren et al. (2006, 092824) **Period of Study:** Jan 1996-Dec 2001 **Location:** Brisbane, Australia	**Outcome:** Mortality: Nonaccidental Cardiovascular (390-448) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, cubic spline **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 15.84 **Range (Min, Max):** (2.5, 60) **Copollutant:** O_3	The study presents quantitative results associated with an incremental increase in temperature, not PM_{10}.
Reference: Roberts (2004, 087924) **Period of Study:** 1987-1994 **Location:** Cook County, Illinois Allegheny County, Pennsylvania	**Outcome:** Mortality: Nonaccidental (<800) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, smooth splines Poisson GLM, natural cubic splines **Age Groups:** ≥ 65 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Median (SD) unit:** Cook County Lower Temp.: 29.24 Middle Temp.: 30.03 Upper Temp.: 52.76 Allegheny County Lower Temp.: 16.50 Middle Temp.: 24.97 Upper Temp.: 55.42 Range (10th, 90th): Cook County Lower Tem.: (16.42, 46.42) Middle Temp.: (14.79, 56.33) Upper Temp.: (30.81, 82.81) Allegheny County Lower Temp.: (5.14, 34.54) Middle Temp.: (8.91, 57.91) Upper Temp.: (30.91, 88.99)	**Increment:** 10 µg/m^3 **% Increase (SE) lag:** GLM **Cook** α = 0.5 No Interaction: 0.288% (0.157) 0 Low Temp.: -0.272% (0.380) 0 Middle Temp.: 0.344% (0.165) 0 Upper Temp.: 0.281% (0.239) 0 No Interaction: 0.359% (0.149) 1 Low Temp.: -0.168% (0.372) 1 Middle Temp.: 0.361% (0.156) 1 Upper Temp.: 0.616% (0.250) 1 No Interaction: 0.465% (0.176) 0-1 ma Low Temp.: 0.043% (0.397) 0-1 ma Middle Temp.: 0.506% (0.184) 0-1 ma Upper Temp.: 0.464% (0.256) 0-1 ma No Interaction: 0.633% (0.214) 0-3 ma Low Temp.: 0.365% (0.419) 0-3 ma Middle Temp.: 0.638% (0.222) 0-3 ma Upper Temp.: 0.718% (0.295) 0-3 ma α = 1 No Interaction: 0.117% (0.157) 0 Low Temp.: -0.351% (0.406) 0 Middle Temp.: 0.161% (0.165) 0 Upper Temp.: 0.096% (0.264) 0 No Interaction: 0.141% (0.150) 1 Low Temp.: -0.366% (0.397) 1 Middle Temp.: 0.161% (0.156) 1 Upper Temp.: 0.301% (0.278) 1 No Interaction: 0.260% (0.181) 0-1 ma Low Temp.: -0.163% (0.431) 0-1 ma Middle Temp.: 0.305% (0.188) 0-1 ma Upper Temp.: 0.207% (0.291) 0-1 ma No Interaction: 0.289% (0.225) 0-3 ma Low Temp.: 0.014% (0.459) 0-3 ma Middle Temp.: 0.311% (0.231) 0-3 ma Upper Temp.: 0.301% (0.334) 0-3 ma α = 2 No Interaction: 0.060% (0.158) 0 0 Low Temp.: -0.464% (0.486) 0 0 Middle Temp.: 0.115% (0.168) 0 0 Upper Temp.: -0.022% (0.319) 0 0 No Interaction: 0.101% (0.152) 1 Low Temp.: -0.432% (0.484) 1 Middle Temp.: 0.089% (0.160) 1 Upper Temp.: 0.455% (0.327) 1 No Interaction: 0.129% (0.184) 0-1 ma Low Temp.: -0.320% (0.546) 0-1 ma Middle Temp.: 0.157% (0.193) 0-1 ma Upper Temp.: 0.130% (0.346) 0-1 ma No Interaction: 0.090% (0.236) 0-3 ma Low Temp.: -0.319% (0.572) 0-3 ma Middle Temp.: 0.105% (0.244) 0-3 ma Upper Temp.: 0.193% (0.412) 0-3 ma

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Allegheny α = 0.5 No Interaction: 0.078% (0.209) 0 Low Temp.: -0.759% (0.643) 0 Middle Temp.: 0.207% (0.216) 0 High Temp.: -0.367% (0.364) 0 No Interaction: 0.189% (0.206) 1 Low Temp.: -0.335% (0.691) 1 Middle Temp.: 0.293% (0.215) 1 High Temp.: -0.171% (0.349) 1 No Interaction: 0.224% (0.246) 0-1 ma Low Temp.: -0.753% (0.763) 0-1 ma Middle Temp.: 0.353% (0.253) 0-1 ma High Temp.: -0.142% (0.382) 0-1 ma No Interaction: 0.526% (0.300) 0-3 ma Low Temp.: 0.050% (0.733) 0-3 ma Middle Temp.: 0.688% (0.310) 0-3 ma High Temp.: -0.043% (0.436) 0-3 ma α = 1 No Interaction: 0.078% (0.211) 0 Low Temp.: -0.694% (0.656) 0 Middle Temp.: 0.214% (0.219) 0 High Temp.: -0.533% (0.430) 0 No Interaction: 0.179% (0.207) 1 Low Temp.: -0.283% (0.718) 1 Middle Temp.: 0.273% (0.217) 1 High Temp.: -0.221% (0.396) 1 No Interaction: 0.221% (0.249) 0-1 ma Low Temp.: -0.731% (0.794) 0-1 ma Middle Temp.: 0.348% (0.258) 0-1 ma High Temp.: -0.253% (0.447) 0-1 ma No Interaction: 0.464% (0.309) 0-3 ma Low Temp.: 0.056% (0.780) 0-3 ma Middle Temp.: 0.626% (0.319) 0-3 ma High Temp.: -0.356% (0.516) 0-3 ma α = 2 No Interaction: 0.034% (0.217) 0 Low Temp.: -1.059% (0.715) 0 Middle Temp.: 0.162% (0.230) 0 High Temp.: -0.233% (0.489) 0 No Interaction: 0.130% (0.214) 1 Low Temp.: -0.189% (0.800) 1 Middle Temp.: 0.157% (0.226) 1 High Temp.: 0.070% (0.471) 1 No Interaction: 0.183% (0.260) 0-1 ma Low Temp.: -0.918% (0.907) 0-1 ma Middle Temp.: 0.279% (0.273) 0-1 ma High Temp.: -0.001% (0.526) 0-1 ma No Interaction: 0.270% (0.331) 0-3 ma Low Temp.: -0.105% (0.898) 0-3 ma Middle Temp.: 0.394% (0.346) 0-3 ma High Temp.: -0.287% (0.615) 0-3 ma **GAM** **Cook** α = 0.5 No Interaction: 0.438% (0.151) 0 Low Temp.: -0.178% (0.364) 0 Middle Temp.: 0.439% (0.163) 0 Upper Temp.: 0.627% (0.197) 0 No Interaction: 0.495% (0.144) 1 Low Temp.: -0.114% (0.361) 1 Middle Temp.: 0.460% (0.151) 1 Upper Temp.: 0.938% (0.208) 1 No Interaction: 0.710% (0.169) 0-1 ma Low Temp.: 0.151% (0.379) 0-1 ma Middle Temp.: 0.686% (0.180) 0-1 ma Upper Temp.: 0.952% (0.214) 0-1 ma No Interaction: 0.923% (0.203) 0-3 ma Low Temp.: 0.532% (0.402) 0-3 ma Middle Temp.: 0.855% (0.210) 0-3 ma Upper Temp.: 1.289% (0.251) 0-3 ma α = 1 No Interaction: 0.190% (0.154) 0

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Low Temp.: -0.338% (0.414) 0 Middle Temp.: 0.242% (0.162) 0 Upper Temp.: 0.161% (0.230) 0 No Interaction: 0.239% (0.146) 1 Low Temp.: -0.283% (0.406) 1 Middle Temp.: 0.248% (0.152) 1 Upper Temp.: 0.453% (0.244) 1 No Interaction: 0.353% (0.174) 0-1 ma Low Temp.: -0.074% (0.437) 0-1 ma Middle Temp.: 0.388% (0.182) 0-1 ma Upper Temp.: 0.345% (0.251) 0-1 ma No Interaction: 0.453% (0.213) 0-3 ma Low Temp.: 0.190% (0.460) 0-3 ma Middle Temp.: 0.455% (0.219) 0-3 ma Upper Temp.: 0.557% (0.294) 0-3 ma α = 2 No Interaction: 0.071% (0.157) 0 0 Low Temp.: -0.534% (0.478) 0 0 Middle Temp.: 0.132% (0.165) 0 0 Upper Temp.: 0.011% (0.264) 0 0 No Interaction: 0.099% (0.150) 1 Low Temp.: -0.467% (0.472) 1 Middle Temp.: 0.109% (0.156) 1 Upper Temp.: 0.329% (0.278) 1 No Interaction: 0.168% (0.180) 0-1 ma Low Temp.: -0.371% (0.525) 0-1 ma Middle Temp.: 0.216% (0.188) 0-1 ma Upper Temp.: 0.116% (0.290) 0-1 ma No Interaction: 0.149% (0.227) 0-3 ma Low Temp.: -0.291% (0.557) 0-3 ma Middle Temp.: 0.174% (0.233) 0-3 ma Upper Temp.: 0.210% (0.340) 0-3 ma **Allegheny** α = 0.5 No Interaction: 0.245% (0.203) 0 Low Temp.: -0.727% (0.648) 0 Middle Temp.: 0.314% (0.216) 0 High Temp.: 0.308% (0.287) 0 No Interaction: 0.446% (0.199) 1 Low Temp.: -0.307% (0.701) 1 Middle Temp.: 0.469% (0.211) 1 High Temp.: 0.556% (0.285) 1 No Interaction: 0.522% (0.237) 0-1 ma Low Temp.: -0.646% (0.761) 0-1 ma Middle Temp.: 0.567% (0.251) 0-1 ma High Temp.: 0.640% (0.307) 0-1 ma No Interaction: 0.977% (0.282) 0-3 ma Low Temp.: 0.307% (0.733) 0-3 ma Middle Temp.: 1.027% (0.296) 0-3 ma High Temp.: 1.001% (0.352) 0-3 ma α = 1 No Interaction: 0.107% (0.209) 0 Low Temp.: -0.819% (0.699) 0 Middle Temp.: 0.229% (0.219) 0 High Temp.: -0.214% (0.350) 0 No Interaction: 0.223% (0.205) 1 Low Temp.: -0.316% (0.751) 1 Middle Temp.: 0.295% (0.216) 1 High Temp.: 0.002% (0.341) 1 No Interaction: 0.267% (0.246) 0-1 ma Low Temp.: -0.797% (0.840) 0-1 ma Middle Temp.: 0.372% (0.257) 0-1 ma High Temp.: 0.035% (0.372) 0-1 ma No Interaction: 0.534% (0.302) 0-3 ma Low Temp.: 0.029% (0.810) 0-3 ma Middle Temp.: 0.660% (0.314) 0-3 ma High Temp.: 0.071% (0.431) 0-3 ma

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			α = 2 No Interaction: 0.061% (0.214) 0 Low Temp.: -1.048% (0.749) 0 Middle Temp.: 0.206% (0.226) 0 High Temp.: -0.332% (0.419) 0 No Interaction: 0.145% (0.211) 1 Low Temp.: -0.278% (0.816) 1 Middle Temp.: 0.210% (0.223) 1 High Temp.: -0.105% (0.394) 1 No Interaction: 0.180% (0.256) 0-1 ma Low Temp.: -1.028% (0.931) 0-1 ma Middle Temp.: 0.298% (0.269) 0-1 ma High Temp.: -0.114% (0.441) 0-1 ma No Interaction: 0.275% (0.324) 0-3 ma Low Temp.: -0.384% (0.915) 0-3 ma Middle Temp.: 0.436% (0.338) 0-3 ma High Temp.: -0.366% (0.513) 0-3 ma
Reference: Roberts (2004, 087924) **Period of Study:** 1987-1994 **Location:** Cook County, Illinois Allegheny County, Pennsylvania	**Outcome:** Mortality: Nonaccidental **Study Design:** Time-series **Statistical Analyses:** Poisson GLM **Age Groups:** ≥ 65 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** Max = 89	The study does not present quantitative results.
Reference: Roberts (Roberts, 2005, 087992) **Period of Study:** Cook County: 1987-2000. Allegheny County: 1987-1998 **Location:** Cook County, Illinois Allegheny County, Pennsylvania	**Outcome:** Mortality: Nonaccidental **Study Design:** Time-series **Statistical Analyses:** Poisson **Age Groups:** ≥ 65 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** NR **β (SE) lag:** Standard Model Cook County 0.000127 (0.000264) 0 -0.000042 (0.000249) 1 -0.000441 (0.000246) 2 Allegheny County 0.000693 (0.000437) 0 0.000356 (0.000423) 1 0.000524 (0.000415) 2 Moving Total Model Cook County 0.000150 (0.000187) k = 2 -0.000047 (0.000153) k = 3 0.000009 (0.000133) k = 4 Allegheny County 0.000633 (0.000310) k = 2 0.000542 (0.000255) k = 3 0.000598 (0.000351) k = 4
Reference: Roberts (2006, 089762) **Period of Study:** 1987-2000 **Location:** Cook County, Illinois Suffolk County, Massachusetts (NMMAPS)	**Outcome:** Mortality: Nonaccidental **Study Design:** Time-series **Statistical Analyses:** Poisson GLM **Age Groups:** ≥ 65 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** Cook County: 33.7 (19.4) Suffolk County: 25.9 (11.8) Range (10th, 90th): Cook County: (13.4, 58.1) Suffolk County: (14.0, 41.7) **Copollutant (correlation):** Cook County CO: r = 0.30 NO_2: r = 0.53 SO_2: r = 0.45 O_3: r = 0.44 Suffolk County CO: r = 0.33 NO_2: r = 0.43 SO_2: r = 0.23 O_3: r = 0.36	**Increment:** Cook County: 19.4 µg/m^3 Suffolk County: 14.0 µg/m^3 **% Increase (SD) lag:** Cook County Standard Model: 0.49% (0.25) 0 Proposed Model: 0.29% (0.16) 0 Standard Model: 0.67% (0.25) 0-2 avg Proposed Model: 0.49% (0.25) 0-2 avg Suffolk County Standard Model: 0.88% (1.27) 0 Proposed Model: 0.85% (0.84) 0 Standard Model: 1.60% (0.71) 0-2 avg Proposed Model: 1.35% (0.73) 0-2 avg

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Roberts and Martin (2006, 097799) **Period of Study:** 1987-2000 **Location:** Cook County, Illinois (NMMAPS)	**Outcome:** Mortality: Nonaccidental **Study Design:** Time-series **Statistical Analyses:** Dose-response 1. Piecewise linear relationship (no-threshold) with change point at 25 µg/m^3 and 50 µg/m^3 2. Piecewise linear relationship (threshold), exposure below 25 µg/m^3 no effect, and exposures above 50 µg/m^3 having a different effect then exposures between 25 µg/m^3 and 50 µg/m^3 **Age Groups:** ≥ 65 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** NR **IQR (25th, 75th):** (23.9, 45.4) Suffolk County: (14.0, 41.7) **Copollutant (correlation):** NR	The study does not present quantitative results.
Reference: Roberts and Martin (2006, 088670) **Period of Study:** 1987-2000 **Location:** 109 U.S. cities (NMMAPS)	**Outcome:** Mortality: Nonaccidental Cardiorespiratory **Study Design:** Time-series **Statistical Analyses:** Poisson 2-stage Bayesian hierarchical model **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** NR **IQR (25th, 75th):** NR **Copollutant (correlation):** NR	**Increment**: NR **β x 1000 (SE x 1000) lag:** Nonaccidental Model 1 Base df: 0.079 (0.050) 0 Double df: 0.044 (0.046) 0 Half df: 0.107 (0.052) 0 Base df: 0.180 (0.044) 1 Double df: 0.149 (0.047) 1 Half df: 0.254 (0.048) 1 Base df: 0.059 (0.056) 2 Double df: 0.024 (0.056) 2 Half df: 0.143 (0.054) 2 Model 2 Base df: 0.115 (0.037) 0-2 ma Double df: 0.107 (0.034) 0-2 ma Half df: 0.145 (0.039) 0-2 ma Cardio-respiratory Model 1 Base df: 0.103 (0.068) 0 Double df: 0.056 (0.067) 0 Half df: 0.134 (0.066) 0 Base df: 0.232 (0.060) 1 Double df: 0.179 (0.067) 1 Half df: 0.309 (0.059) 1 Base df: 0.210 (0.078) 2 Double df: 0.144 (0.075) 2 Half df: 0.305 (0.079) 2 Model 2 Base df: 0.168 (0.047) 0-2 ma Double df: 0.140 (0.044) 0-2 ma Half df: 0.196 (0.051) 0-2 ma **Notes:** Model 1 uses current day's mortality count, while Model 2 uses a 3-day moving total mortality count.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Roberts and Martin (2007, 156917) **Period of Study:** 1987-2000 **Location:** 8 U.S. cities and >100 U.S. cities (NMMAPS)	**Outcome:** Mortality: Total (nonaccidental) Cardiorespiratory **Study Design:** Time-series **Statistical Analyses:** Poisson **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR	**Increment:** 10 µg/m^3 **β x 1000 (SE x 1000) lag:** 8 U.S. cities Distributed Lag Model: 0.229 0-2 Weighted Model: 0.315 0-2 Standard Model: 0.276 0 -0.062 1 0.476 2 90 U.S. cities Total (nonaccidental) Standard Model: 0.078 (0.039) 0 0.182 (0.037) 1 0.108 (0.036) 2 Moving Total Model: 0.131 (0.023) 0-2 Weighted Model: 0.274 (0.075) 0-2 Cardio-respiratory Standard Model: 0.096 (0.055) 0 0.232 (0.053) 1 0.226 (0.051) 2 Moving Total Model: 0.174 (0.032) 0-2 Weighted Model: 0.389 (0.105) 0-2 **Notes:** The 8 U.S. cities consist of Chicago, Cleveland, Denver, El Paso, Houston, Nashville, Pittsburgh, and Salt Lake City.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Roberts and Martin (2007, 156916) **Period of Study:** 1987-2000 **Location:** 10 U.S. cities (NMMAPS)	**Outcome:** Mortality: Nonaccidental **Study Design:** Time-series **Statistical Analyses:** Poisson **Age Groups:** ≥ 65 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** Anchorage: 27.32 Chicago: 36.95 Cleveland: 39.83 Detroit: 40.78 El Paso: 40.14 Minneapolis/St. Paul: 28.01 Pittsburgh: 35.09 Salt Lake City: 37.40 Seattle: 28.72 Spokane: 34.52 **Range (Min, Max):** NR	**Increment:** NR **β Coefficient (SE) lag:** Pooled Estimates Combined Model (Unconstrained Distributed Lag Model + Piecewise Linear Dose-Response Function) Change-point: 60 μg/m^3 Slope below: 0.00130 (0.00016) 0-5 Slope above: -0.00163 (0.00026) 0-5 Change-point: 30 μg/m^3 Slope below: 0.00014 (0.00039) 0-5 Slope above: -0.00003 (0.00015) 0-5 Piecewise Linear Dose-Response Model Change-point: 60 μg/m^3 Slope below: 0.00044 (0.00011) 3-day ma Slope above: -0.00077 (0.00020) 3- day ma Change-point: 30 μg/m^3 Slope below: 0.00022 (0.00026) 3-day ma Slope above: -0.00004 (0.00011) 3-day ma Polynomial Distributed Lag Model (degree 2) 0.00046 (0.00011) 0-5
Reference: Samoli et al. (2005, 087436) **Period of Study:** 1990-1997 **Location:** 22 European cities (APHEA-2)	**Outcome:** Mortality: All-cause (nonaccidental) (<800) Cardiovascular (390-459) Respiratory (460-519) **Study Design:** Time-series **Statistical Analyses:** Hierarchical modeling: 1. Poisson GAM, penalized splines 2. Multivariate modeling **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg Median (SD) unit: Range: (Stockholm: 14 μg/m^3 to Torino: 65 μg/m^3) Percentile (90th): Range: (Stockholm: 27 μg/m^3 to Torino: 129 μg/m^3) **Copollutant (correlation):** BS	The study does not present quantitative results.
Reference: Schwartz (2004, 078998) **Period of Study:** 1986-1993 **Location:** 14 U.S. cities	**Outcome:** Mortality: Nonaccidental (<800) **Study Design:** Case-crossover Time-series **Statistical Analyses:** Conditional logistic regression Poisson **Age Groups:** All ages **Notes:** Case days matched to referent days that had the same temperature.	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** 10 μg/m^3 **% Increase (Lower CI, Upper CI) lag:** Overall: Two stage: 0.36% (0.22, 0.50) 1 Single stage: 0.33% (0.19, 0.46) 1 More winter temperature lags: Two Stage: 0.39% (0.23, 0.56) 1 One stage: 0.32% (0.19, 0.46) 1 Time stratified with temperature matching: Two Stage: 0.39% (0.19, 0.58) 1 One Stage: 0.53% (0.34, 0.72) 1 Poisson regression: 0.40% (0.18, 0.62) 1

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Schwartz (2004, 053506) **Period of Study:** 1986-1993 **Location:** 14 U.S. cities	**Outcome:** Mortality: Nonaccidental (<800) **Study Design:** Case-crossover **Statistical Analyses:** Time-stratified conditional logistic regression **Age Groups:** All ages **Notes:** Case days matched to referent days based on concentration of gaseous air pollutants. Matched on the following conditions: 1. 24-h avg SO_2 within 1 ppb 2. Daily-maximum O_3 within 2 ppb 3. 24-h avg NO_2 within 1 ppb 4. 24-h avg CO within 0.03 ppm	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Median (SD) unit:** Range: 23-36 µg/m^3 IQR (25th, 75th): Range 25th: 17-24 µg/m^3 Range 75th: 31-57 µg/m^3 **Copollutant (correlation):** CO SO_2 NO_2 O_3	**Increment:** 10 µg/m^3 **β x 1000 (SE x 1000) lag:** Matched on CO: 0.527 (0.251) 0-1 avg Matched on O_3: 0.451 (0.170) 0-1 avg Matched on NO_2: 0.784 (0.185) 0-1 avg Matched on SO_2: 0.811 (0.175) 0-1 avg
Reference: Sharovsky et al. (2004, 156976) **Period of Study:** Jul 1996-Jun 1998 **Location:** São Paulo, Brazil	**Outcome:** Mortality: Myocardial infarction **Study Design:** Time-series **Statistical Analyses:** Poisson GAM **Age Groups:** ≥ 35 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 58.2 (25.8) **Range (Min, Max):** (23, 186) **Copollutant (correlation):** CO: r = 0.73 SO_2: r = 0.72	**Increment:** 10 µg/m^3 **β (SE) lag:** PM_{10}: 0.001 (0.001) PM_{10}+CO+SO_2: 0.0004 (0.0008)
Reference: Simpson et al. (2005, 087438) **Period of Study:** 1/1996-12/1999 **Location:** 4 Australian cities	**Outcome:** Mortality: Nonaccidental (<800) Cardiovascular (390-459) Respiratory (460-519) **Study Design:** Time-series meta-analysis **Statistical Analyses:** Poisson GAM, natural splines Poisson GLM, natural splines **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** Brisbane: 16.60 Sydney: 16.30 Melbourne: 18.20 **Range (Min, Max):** Brisbane: (2.6, 57.6) Sydney: (3.7, 75.5) Melbourne: (3.3, 51.9) **Copollutant:** $PM_{2.5}$ CO NO_2	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI)** **lag:** 0.2% (-0.8, 1.2)
Reference: Slaughter et al. (2005, 073854) **Period of Study:** Jan 1995-Dec 1999 **Location:** Spokane, Washington	**Outcome:** Mortality: Nonaccidental (<800) **Study Design:** Time-series **Statistical Analyses:** Poisson GLM, natural splines **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (9th, 95th):** (7.9, 41.9) µg/m^3 **Copollutant (correlation):** PM_{10} $PM_{10-2.5}$: r = 0.94 CO: r = 0.32	**Increment**: : 25 µg/m^3 **Relative Risk (Lower CI, Upper CI)** **lag:** 1.00 (0.97, 1.03) 1 0.98 (0.95, 1.01) 2 1.00 (0.97, 1.03) 3
Reference: Staniswalis et al. (2005, 087473) **Period of Study:** 1992-1995 **Location:** El Paso, Texas	**Outcome:** Mortality: Nonaccidental (<800) **Study Design:** Time-series **Statistical Analyses:** Poisson Principal component analysis (PCA) **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** (0.2, 133.4) **Notes:** The chemical composition and size distribution of PM was not available, therefore, the study used wind speed as a surrogate variable for the PM_{10} composition.	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI)** **lag:** Poisson regression: 1.7% 3 PCA: 24-hly measurements: 2.06% 3 Daily avg: 1.7% 3
Reference: Stafoggia et al. (2008, 157005) **Period of Study:** 1997-2004	**Outcome:** Mortality: Total (nonaccidental) (<800)	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD) unit:** Bologna: 50.4 (31.7)	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Cardiovascular All yr: 0.63% (0.31, 1.38) 0-1

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Location: 9 Italian cities	Cardiovascular (390-459) Respiratory (460-519) Other natural causes **Study Design:** Time-stratified case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups:** ≥ 35 yr	Florence: 37.5 (16.6) Mestre: 48.1 (26.8) Milan: 57.9 (38.0) Palermo: 36.2 (21.7) Pisa: 35.1 (14.9) Rome: 47.3 (19.9) Taranto: 59.8 (18.9) Turin: 71.5 (38.1) **Range (Min, Max):** NR **Copollutant (correlation):** NR	Winter: 0.15% (-0.29, 0.59) 0-1 Spring: 0.72% (-0.07, 1.52) 0-1 Summer: 2.90% (1.14, 4.69) 0-1 Fall: 1.37% (0.43, 2.32) 0-1 Apparent Temperature <50th Percentile: 0.31% (-0.06, 0.67) 0-1 50th-75th Percentile: 2.05% (0.47, 3.66) 0-1 >75th Percentile: 2.68% (1.20, 4.17) 0-1 Respiratory All yr: 0.98% (0.27, 1.70) 0-1 Winter: 0.41% (-0.67, 1.51) 0-1 Spring: 2.99% (1.18, 4.83) 0-1 Summer: 3.89% (0.19, 7.73) 0-1 Fall: 0.45% (-1.11, 2.03) 0-1 Apparent Temperature <50th Percentile: 0.54% (-0.47, 1.57) 0-1 50th-75th Percentile: 3.15% (0.64, 5.73) 0-1 >75th Percentile: 4.12% (0.44, 7.93) 0-1 Other natural causes All yr: 0.37% (0.09, 0.66) 0-1 Winter: 0.14% (-0.36, 0.63) 0-1 Spring: 0.29% (-0.47, 1.05) 0-1 Summer: 2.15% (0.90, 3.42) 0-1 Fall: 0.70% (-0.41, 1.83) 0-1 Apparent Temperature <50th Percentile: 0.07% (-0.27, 0.41) 0-1 50th-75th Percentile: 1.08% (-0.02, 2.19) 0-1 >75th Percentile: 2.30% (1.06, 3.56) 0-1 Total (nonaccidental) All yr: 0.53% (0.25, 0.80) 0-1 Winter: 0.20% (-0.08, 0.49) 0-1 Spring: 0.62% (0.14, 1.10) 0-1 Summer: 2.54% (1.31, 3.78) 0-1 Fall: 1.21% (0.37, 2.06) 0-1 Apparent Temperature <50th Percentile: 0.21% (-0.06, 0.47) 0-1 50th-75th Percentile: 1.60% (0.64, 2.57) 0-1 >75th Percentile: 2.55% (1.58, 3.52) 0-1 **β coefficient (SE) lag:** Linear interaction PM_{10} and Apparent Temperature Cardiovascular <50th Percentile: -0.000117 (0.000415) 0-1 50th-75th Percentile: 0.003445 (0.001407) 0-1 >75th Percentile: 0.002764 (0.001795) 0-1 Respiratory <50th Percentile: 0.001119 (0.000943) 0-1 50th-75th Percentile: -0.001120 (0.003480) 0-1 >75th Percentile: 0.005306 (0.004350) 0-1 Other natural causes <50th Percentile: 0.000411 (0.000383) 0-1 50th-75th Percentile: -0.001526 (0.001207) 0-1 >75th Percentile:

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			0.002564 (0.001958) 0-1 Total (nonaccidental) <50th Percentile: 0.000246 (0.000269) 0-1 50th-75th Percentile: 0.000584 (0.000880) 0-1 >75th Percentile: 0.002396 (0.001629) 0-1
Reference: Stölzel et al. (2007, 091374) **Period of Study:** Sep 1995-Aug 2001 **Location:** Erfurt, Germany	**Outcome:** Mortality: Total (nonaccidental) (<800) Cardio-respiratory (390-459, 460-519, 785, 786) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD) unit:** : 31.9 (23.2) IQR (25th, 75th): (16.5, 39.5) **Copollutant (correlation):** MC0.1-0.5: r = 0.85 MC0.01-2.5: r = 0.84 NO: r = 0.54 NO_2: r = 0.62 CO: r = 0.50	**Increment:** 23 µg/m^3 **Relative Risk (Lower CI, Upper CI) lag:** Total (nonaccidental) 1.004 (0.980 1.029) 0 1.004 (0.981 1.027) 1 0.998 (0.976 1.021) 2 0.984 (0.962 1.006) 3 0.993 (0.972 1.015) 4 0.990 (0.969 1.012) 5 Cardio-respiratory 1.007 (0.981 1.034) 0 1.006 (0.981 1.032) 1 0.996 (0.971 1.021) 2 0.977 (0.953 1.002) 3 0.994 (0.970 1.018) 4 0.993 (0.969 1.017) 5
Reference: Sullivan et al. (2003, 043156) **Period of Study:** 1985-1994 **Location:** Western Washington	**Outcome:** Out-of-hospital cardiac arrest **Study Design:** Case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups:** 19-79 Study Population: Out-of-hospital cardiac arrests: 1,206	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Median (SD) unit:** Lag 0: 28.05 Lag 1: 27.97 Lag 2: 28.40 **Range (Min, Max):** (7.38, 89.83) **Copollutant (correlation):** SO_2 CO **Notes:** Study used nephelometry to measure particles and equated the measurements to $PM_{2.5}$ concentrations.	**Increment: :** 16.51 µg/m^3 **Odds Ratio (Lower CI, Upper CI) lag:** Overall 1.05 (0.87, 1.27) 0 0.91 (0.75, 1.11) 1 1.03 (0.82, 1.28) 2

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Sunyer et al. (2002, 034835) **Period of Study:** 1985-1995 **Location:** Barcelona, Spain	**Outcome:** Mortality: Respiratory mortality **Study Design:** Case-crossover **Statistical Analyses:** Condition logistic regression **Age Groups:** >14 Study population: Asthmatic individuals: 5,610	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Median (SD) unit:** 61.2 **Range (Min, Max):** (17.3, 240.7) **Copollutant:** BS NO_2 O_3 SO_2 CO	**Increment:** 32.7 µg/m^3 **Odds Ratio (Lower CI, Upper CI) lag:** Asthmatic individuals with 1 ED visit 0.884 (0.672, 1.162) 0-2 avg Asthmatic individuals with >1 ED visit 1.084 (0.661, 1.778) 0-2 avg Asthma/COPD individuals with >1 ED visit 1.011 (0.746, 1.368) 0-2 avg
Reference: Touloumi et al. (2005, 087477) **Period of Study:** 1990-1997 **Location:** 7 European cities (London, Budapest, Stockholm, Zurich, Paris, Lyon, Madrid) (APHEA2)	**Outcome:** Mortality: Total (nonaccidental) (<800) Cardiovascular (390-459) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Median (SD) unit:** London: 25.1 Budapest: 40.2 Stockholm: 13.7 Zurich: 27.5 Paris: 22.2 Lyon: 38.5 µ Madrid: 33.4 IQR (25th, 75th): London: (20.3, 33.9) Budapest: (34.3, 45.8) Stockholm: (10.3, 19.1) Zurich: (19.2, 38.5) Paris: (16.0, 33.0) Lyon: (29.7, 50.4) Madrid: (27.6, 41.0) **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **β (x 1000) (SE (x 1000)):** Total (nonaccidental) No control: 0.4834 (0.1095) Reported Influenza Data Count ID: 0.4967 (0.1089) I1 ID: 0.4740 (0.1090) MI ID: 0.5019 (0.1096) RI-ID: 0.4735 (0.1091) SF ID: 0.6714 (0.1080) Estimated Influenza Data APHEA-2: 0.5550 (0.1076) I1 EID: 0.5640 (0.1073) MI EID: 0.5872 (0.1100) RI EID: 0.5872 (0.1074) SF EID: 0.6641 (0.1073) Cardiovascular No control: 0.8432 (0.1665) Reported Influenza Data Count ID: 0.8896 (0.1662) I1 ID: 0.8545 (0.1661) MI ID: 0.8693 (0.1674) RI-ID: 0.8649 (0.1665) SF ID: 1.0107 (0.1659) Estimated Influenza Data APHEA-2: 0.9389 (0.1654) I1 EID: 0.9485 (0.1648) MI EID: 1.0440 (0.1686) RI EID: 0.9718 (0.1653) SF EID: 1.0585 (0.1652) **Notes:** I1 = one indicator for all epidemics M1 = multiple indicators, one per epidemic R1 = indicators for intervals indicating the range of influenza counts SF = separate smooth function during epidemic periods.
Reference: Tsai et al. (2003, 050480) **Period of Study:** 1994-2000 **Location:** Kaohsiung, Taiwan	**Outcome:** Mortality: Total (nonaccidental) (<800) Respiratory (460-519) Circulatory (390-459) **Study Design:** Bidirectional case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 81.45 **Range (Min, Max):** (20.50, 232.00) **Copollutant:** SO_2 NO_2 CO O_3	**Increment:** 67.00 µg/m^3 **Odds Ratio (Lower CI, Upper CI) lag:** Total (nonaccidental) 1.000 (0.947, 1.056) 0-2 avg Respiratory 1.023 (0.829, 1.264) 0-2 avg Circulatory 0.971 (0.864, 1.092) 0-2 avg

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Vajanapoom et al. (2002, 042542) **Period of Study:** 1992-1997 **Location:** Bangkok, Thailand	**Outcome:** Mortality: Total (nonaccidental) (<800) Respiratory (460-519) Cardiovascular (390-459) Other-causes **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, LOESS **Age Groups:** All ages 55-64 yr 65-74 yr ≥ 75 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 68.0 (23.9) IQR (25th, 75th): (50.1, 80.7) **Copollutant (correlation):** NR	**Increment:** 30 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Total (nonaccidental) All ages: 2.3% (1.3, 3.3) 0-4 ma 55-64: 1.5% (-0.8, 3.9) 0-4 ma 65-74: 4.2% (2.0, 6.3) 0-4 ma ≥ 75: 3.9% (2.1, 5.6) 0-4 ma Cardiovascular All ages: 0.8% (-0.9, 2.4) 0 55-64: -2.5% (-6.3, 1.3) 0 65-74: 2.9% (-0.7, 6.5) 0 ≥ 75: 1.6% (-1.8, 5.0) 0 Respiratory All ages: 5.1% (0.6, 9.6) 0-2 ma 55-64: 1.4% (-11.3, 14.2) 0-2 ma 65-74: 2.8% (-9.5, 15.2) 0-2 ma ≥ 75: 10.2% (-0.1, 20.5) 0-2 ma Other-causes All ages: 2.4% (1.3, 3.5) 0-4 ma 55-64: 1.7% (-1.1, 4.5) 0-4 ma 65-74: 5.6% (3.1, 8.1) 0-4 ma ≥ 75: 3.7% (1.8, 5.6) 0-4 ma
Reference: Vedal et al. (2003, 039044) **Period of Study:** Jan 1994-Dec 1996 **Location:** Vancouver, British Columbia, Canada	**Outcome:** Mortality: Total (nonaccidental) (<800) Respiratory (460-519) Cardiovascular (390-459) **Study Design:** Time-series **Statistical Analyses: Poisson** GAM, LOESS **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 14.4 (5.9) **Range (Min, Max):** (4.1, 37.2) **Copollutant (correlation):** O_3: r = 0.48 SO_2: r = 0.76 NO_2: r = 0.84 CO: r = 0.71	The study does not present quantitative results
Reference: Venners et al. (2003, 089931) **Period of Study:** Jan 1995-Dec 1995 **Location:** Chongqing, China	**Outcome:** Mortality: Total (nonaccidental) (<800) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, cubic spline **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 146.8 **Range (Min, Max):** (44.7, 666.2) **Copollutant:** SO_2 **Notes:** PM_{10} was measured for only 7 mo of the study period.	**Increment:** 100 µg/m^3 **Relative Risk (Lower CI, Upper CI) lag:** 1.00 (0.93, 1.07) 0 0.98 (0.91, 1.04) 1 1.00 (0.93, 1.07) 2 0.96 (0.90, 1.03) 3 0.97 (0.90, 1.03) 4 0.99 (0.93, 1.06) 5
Reference: Vichit-Vadakan et al. (2008, 157095) **Period of Study:** Jan 1999-Dec 2003 **Location:** Bangkok, Thailand	**Outcome (ICD10):** Mortality: Nonaccidental (A00-R99) Cardiovascular (I00-I99) Ischemic heart diseases (I20-I25) Stroke (I60-I69) Conduction disorder (I44-I49) Respiratory (J00-J98) Lower Respiratory Infection (J10-J22) COPD (J40-J47) Asthma (J45-J46) Senility (R54) **Study Design:** Time-series **Statistical Analyses:** Poisson, natural cubic spline **Age Groups:** All ages 0-4 yr 5-44 yr 18-50 yr 45-64 yr ≥ 50 yr ≥ 65 yr ≥ 75 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 52.1 (20.1) **Range (Min, Max):** (21.3, 169.2) **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **% Excess Risk (Lower CI, Upper CI) lag:** Cause-specific mortality: Nonaccidental: 1.3% (0.8, 1.7) 0-1 Cardiovascular: 1.9% (0.8, 3.0) 0-1 Ischemic heart disease: 1.5% (-0.4, 3.5) 0-1 Stroke: 2.3% (0.6, 4.0) 0-1 Conduction disorders: -0.%3 (-5.9, 5.6) 0-1 Cardiovascular: ≥ 65 1.8 (0.2, 3.3) 0-1 Respiratory: All ages: 1.0 (-0.4, 2.4) 0-1 ≤ 1: 14.6 (2.9, 27.6) 0-1 ≥ 65: 1.3 (-0.8, 3.3) 0-1 LRI: <5: 7.7 (-3.6, 20.3) 0-1 COPD: 1.3 (-1.8, 4.4) 0-1 Asthma: 7.4 (1.1, 14.1) 0-1 Senility: 1.8 (0.7, 2.8) 0-1 Age-specific for nonaccidental 0-4: 0.2 (-2.0, 2.4) 0-1 5-44: 0.9 (0.2, 1.7) 0-1 18-50: 1.2 (0.5, 1.9) 0-1 45-64: 1.1 (0.4, 1.9) 0-1 ≥ 50: 1.4 (0.9, 1.9) 0-1

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			≥ 65: 1.5 (0.9, 2.1) 0-1 ≥ 75: 2.2 (1.3, 3.0) 0-1 Sex-specific for nonaccidental Male: 1.2 (0.7, 1.7) 0-1 Female: 1.3 (0.7, 1.9) 0-1 Nonaccidental 1.2 (0.8, 1.6) 0 0.9 (0.6, 1.3) 1 0.9 (0.5, 1.3) 2 0.8 (0.4, 1.2) 3 0.3 (-0.1, 0.7) 4 1.3 (0.8, 1.7) 0-1 1.4 (0.9, 1.9) 0-4 Cardiovascular 1.5 (0.5, 2.6) 0 1.7 (0.7, 2.7) 1 1.6 (0.6, 2.6) 2 0.8 (-0.1, 1.8) 3 -0.1 (-1.1, 0.9) 4 1.9 (0.8, 3.0) 0-1 1.9 (0.6, 3.2) 0-4 Respiratory 1.0 (-0.3, 2.3) 0 0.8 (-0.5, 2.0) 1 1.1 (-0.1, 2.3) 2 1.3 (0.1, 2.6) 3 0.7 (-0.6, 1.9) 4 1.0 (-0.4, 2.4) 0-1 1.9 (1.2, 2.6) 0-4 ≥ 65 1.5 (0.9, 2.0) 0 1.1 (0.6, 1.7) 1 1.1 (0.6, 1.6) 2 1.2 (0.6, 1.7) 3 0.7 (0.2, 1.2) 4 1.5 (0.9, 2.1) 0-1 1.9 (1.2, 2.6) 0-4 **Sensitivity analysis:** Nonaccidental (df): 3: 1.3 (0.9, 1.8) 4: 1.2 (0.8, 1.7) 6: 1.3 (0.8, 1.7) 6, with SO_2: 1.2 (0.8, 1.7) 6, with NO_2: 1.0 (0.2, 1.8) 6, with O_3: 1.1 (0.6, 1.7) 9: 1.1 (0.7, 1.6) 12: 1.1 (0.6, 1.5) 15: 1.2 (0.7, 1.6) Cardiovascular (df): 3: 1.8 (0.8, 2.7) 4: 1.6 (0.7, 2.6) 6: 1.7 (0.7, 2.7) 6, with SO_2: 2.0 (0.9, 3.3) 6, with NO_2: 2.3 (0.2, 4.3) 6, with O_3: 1.8 (0.5, 3.2) 9: 1.7 (0.6, 2.8) 12: 1.8 (0.7 to 3.0) 15: 2.2 (0.9, 3.4)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Villeneuve et al. (2003, 055051) **Period of Study:** 1986-1999 **Location:** Vancouver, Canada	**Outcome:** Mortality: Nonaccidental (<800) Cardiovascular (401-440) Respiratory (460-519) Cancer (140-239) **Study Design:** Time-series **Statistical Analyses:** Poisson, natural splines **Age Groups:** ≥ 65 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** Daily 14.0 Every 6th Day 19.6 **Range (Min, Max):** Daily (3.8, 52.2) Every 6th Day (3.5, 63.0) **Copollutant:** SO_2 CO NO_2 O_3 $PM_{2.5}$ $PM_{10-2.5}$	**Increment:** 15.4 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Nonaccidental 3.7% (-0.5, 8.0) 0-2 avg 2.6% (-0.9, 6.1) 0 2.7% (-0.7, 6.2) 1 1.9% (-1.4, 5.3) 2 Cardiovascular 3.4% (-2.7, 9.8) 0-2 avg 5.1% (0.0, 10.4) 0 1.3% (-3.8, 6.7) 1 0.6% (-4.3, 5.7) 2 Respiratory PM_{10} 0.1% (-9.5, 10.8) 0-2 avg 1.0% (-7.5, 10.4) 0 0.4% (-7.7, 9.3) 1 -1.3% (-8.9, 7.1) 2 Cancer 1.2% (-6.9, 10.1) 0-2 avg -2.5% (-8.8, 4.3) 0 2.3% (-4.6, 9.6) 1 3.3% (-3.7, 10.8) 2
Reference: Welty et al. (2008, 157134) **Period of Study:** 1987-2000 **Location:** Chicago, Illinois	**Outcome:** Mortality: Total (nonaccidental) **Study Design:** Time-series **Statistical Analyses:** Poisson-Gibbs Sampler Bayesian Distributed Lag Model **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **% Excess Risk (Lower CI, Upper CI) lag:** Poisson-Gibbs Sampler 0.17% (0.01, 0.34) 3 -0.24% (-0.73, 0.23) 0-14 Unconstrained: -0.19% (-0.86, 0.48) 0-14 Bayesian Distributed Lag Model -0.21% (-0.86, 0.41) 0-14
Reference: Welty and Zeger (2005, 087484) **Period of Study:** 1987-2000 **Location:** 100 U.S. cities (NMMAPS)	**Outcome:** Mortality: Total (nonaccidental) (<800) **Study Design:** Time-series **Statistical Analyses:** Bayesian hierarchical model **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **% Increase (SE) lag:** Distributed Lag Model: Seasonally-Temporally Varying Temperature variables: 0, 1-2, 1-7, 1-14 S(t, 1 × yr): 0.229 (0.053) 1 S(t, 2 × yr): 0.220 (0.053) 1 S(t, 4 × yr): 0.187 (0.050) 1 S(t, 8 × yr): 0.178 (0.049) 1 Temperature variables: 0, 1-2, 1-7, 1-14, 0×1-2, 0×1-7, 1-2 × 1-7 S(t, 1 × yr): 0.195 (0.048) 1 S(t, 2 × yr): 0.200 (0.051) 1 S(t, 4 × yr): 0.176 (0.050) 1 S(t, 8 × yr): 0.149 (0.050) 1 Distributed Lag Model: Nonlinear Temperature variables: 0, 1-2, 1-7, 1-14 S(t, 4 × yr): 0.239 (0.053) 1 Temperature variables: 0, 1-2, 1-7, 1-14, 0×1-2, 0×1-7, 1-2 × 1-7 S(t, 4 × yr): 0.172 (0.045) 1 Temperature variables: S(0,2), S(1-2,2), S(1-7,2), S(1-14,2) S(t, 4 × yr): 0.186 (0.046) 1 Temperature variables: S(0,2), S(1-2,2), S(1-7,2), S(1-14,2), S(0×1-2,2), S(0×1-7,2), S(1-2 × 1-7,2) S(t, 4 × yr): 0.189 (0.047) 1

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Temperature variables: S(0,4), S(1-2,4), S(1-7,4), S(1-14,4) S(t, 4 × yr): 0.175 (0.046) 1 Temperature variables: S(0,4), S(1-2,4), S(1-7,4), S(1-14,4), S(0×1-2,4), S(0×1-7,4), S(1-2 × 1-7,4) S(t, 4 × yr): 0.190 (0.048) 1 Temperature variables: 0, 1-2, 1-7 S(t, 4 × yr): 0.252 (0.053) 1 Temperature variables: 0, 1-2, 1-7, 0×1-2, 0×1-7, 1-2 × 1-7 S(t, 4 × yr): 0.186 (0.044) 1 Temperature variables: S(0,2), S(1-2,2), S(1-7,2) S(t, 4 × yr): 0.198 (0.046) 1 Temperature variables: S(0,2), S(1-2,2), S(1-7,2), S(0×1-2,2), S(0×1-7,2), S(1-2 × 1-7,2) S(t, 4 × yr): 0.201 (0.047) 1 Temperature variables: S(0,4), S(1-2,4), S(1-7,4) S(t, 4 × yr): 0.189 (0.045) 1 Temperature variables: S(0,4), S(1-2,4), S(1-7,4), S(0×1-2,2), S(0×1-7,4), S(1-2 × 1-7,2) S(t, 4 × yr): 0.205 (0.047) 1 Temperature variables: S(0,4), S(1-2,4) S(t, 4 × yr): 0.250 (0.045) 1 Temperature variables: S(0,4), S(1-2,4), S(0×1-2,4) S(t, 4 × yr): 0.253 (0.044) 1 Temperature variables: S(0,4) S(t, 4 × yr): 0.220 (0.045) 1 **Notes:** 0 indicates current-day temperature 1-r indicates avg of lag 1 through lag r temperature S (, ρ) indicates a natural spline smooth with ρ degrees of freedom. S (t, α x yr) indicates the natural spline smooth of time with degrees of freedom equal to α x (number of yr of data).

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Wong et al. (2007, 098391) **Period of Study:** Jan 1998-Dec 1998 **Location:** Hong Kong, China	**Outcome:** Mortality: Total (nonaccidental) (<800) Cardiorespiratory (390-519) **Study Design:** Main analysis: Time-series **Sensitivity analysis:** Case-crossover, case-only **Statistical Analyses:** Main analysis: Poisson GAM **Sensitivity analysis:** Conditional logistic regression **Age Groups:** ≥ 30 yr; ≥ 65 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 48.1 (24.3) **Range (Min, Max):** (15.5, 140.5) **Copollutant:** NO_2 SO_2 O_3	**Increment:** 10 µg/m^3 **% Excess Risk (Lower CI, Upper CI) lag:** Main Analysis Nonaccidental Smokers: ≥ 301: .80% (0.35, 3.26) 0 1.77% (0.46, 3.11) 2 ≥ 65: 3.20% (1.36, 5.07) 0 2.42% (0.73, 4.13) 2 Never-smokers ≥ 30: -0.37% (-2.23, 1.52) 0 -0.03% (-1.72, 1.66) 2 ≥ 65P -0.70% (-2.81, 1.46) 0 -0.13% (-2.04, 1.80) 2 Cardiorespiratory Smokers ≥ 30: 1.43% (-0.86, 3.78) 0 2.32% (0.24, 4.44) 2 ≥ 65: 2.98% (0.47, 5.55) 0 2.61% (0.31, 4.95) 2 Never-smokers ≥ 30: 0.02% (-2.75, 2.87) 0 -0.79% (-3.33, 1.82) 2 ≥ 65: 0.25% (-2.62, 3.19) 0 -0.66% (-3.29, 2.04) 2 Sensitivity Analysis Poisson Regression Nonaccidental ≥ 30: 1.81% (0.21, 3.44) 0 1.93% (0.32, 3.56) 2 1.99% (0.14, 3.87) 0-3 ≥ 65: 2.31% (0.37, 4.29) 0 2.16% (0.20, 4.15) 2 2.57% (0.30, 4.89) 0-3 Cardiorespiratory ≥ 30: 1.04% (-1.45, 3.59) 0 2.18% (-0.35, 4.77) 2 1.66% (-1.24, 4.64) 0-3 ≥ 65: 1.69% (-0.93, 4.37) 0 2.44% (-0.23, 5.18) 2 2.30% (-0.80, 5.50) 0-3 Case-only: Logistic Regression Nonaccidental ≥ 30: 1.79% (0.21, 3.37) 0 1.94% (0.33, 3.56) 2 ≥ 65: 2.30% (0.42, 4.17) 0 2.16% (0.26, 4.07) 2 Cardiorespiratory ≥ 30: 1.01% (-1.37, 3.40) 0 2.16% (-0.28, 4.61) 2 ≥ 65: 1.65% (-0.96, 4.27) 0 2.42% (-0.27, 5.12) 2 Case-crossover Nonaccidental ≥ 30: 2.54% (0.35, 4.78) 0 1.35% (-0.81, 3.56) 2 ≥ 65: 3.96% (1.37, 6.63) 0 2.20% (-0.35, 4.81) 2 Cardiorespiratory ≥ 30: 0.48% (-2.74, 3.80) 0 3.24% (-0.03, 6.61) 2 ≥ 65: 2.17% (-1.40, 5.86) 0 3.43% (-0.13, 7.13) 2
Reference: Wong et al. (2007, 093278) **Period of Study:** Jan 1998-Dec 1998	**Outcome:** Mortality: Total (nonaccidental) (<800)	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 48.1 (24.3)	**Increment:** 10 µg/m^3 **% Excess Risk (Lower CI, Upper CI) lag:** Nonaccidental

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Location: Hong Kong, China	Cardiorespiratory (390-519) **Study Design:** Main analysis: Time-series **Sensitivity analysis:** Case-only **Statistical Analyses:** Main analysis: Poisson GAM, natural cubic spline **Sensitivity analysis:** Logistic regression **Age Groups:** ≥ 30 yr; ≥ 65 yr	**Range (Min, Max):** (15.5, 140.5) **Copollutant:** NO_2 SO_2 O_3	Exercise ≥ 30: 0.13% (-1.16, 1.44) 1 ≥ 65: 0.24% (-1.16, 1.67) 1 Never-exercise ≥ 30: 1.04% (0.07, 2.02) 1 ≥ 65: 1.26% (0.27, 2.27) 1 Cardio-respiratory Exercise ≥ 30: 0.46% (-1.43, 2.39) 1 ≥ 65: 0.30% (-1.65, 2.29) 1 Never-exercise ≥ 30: 0.97% (-0.36, 2.32) 1 ≥ 65: 0.98% (-0.45, 2.43) 1 Difference in % Excess Risk (Exercise vs. Never-Exercise) Nonaccidental Poisson Regression ≥ 30: -2.86% (-4.03 to -1.67) 1 ≥ 65: -3.06% (-4.37 to -1.74) 1 Case-only ≥ 30: -2.91% (-4.04 to -1.77) 1 ≥ 65: -3.12% (-4.38 to -1.84) 1 Cardiorespiratory Poisson regression ≥ 30: -2.55% (-4.32 to -0.75) 1 ≥ 65: -2.64% (-4.48 to -0.76) 1 Case-only ≥ 30: -2.63% (-4.32 to -0.92) 1 ≥ 65: -2.73% (-4.50 to -0.92) 1 Adjusted Case-only Nonaccidental Sex ≥ 30: -2.88% (-1.73 to -4.01) 1 ≥ 65: -3.09% (-1.82 to -4.35) 1 Education ≥ 30: -2.94% (-1.80 to -4.07) 1 ≥ 65: -3.18% (-1.90 to -4.44) 1 Job ≥ 30: -2.88% (-1.74 to -4.02) 1 ≥ 65: -3.11% (-1.83 to -4.37) 1 Smoking ≥ 30: -2.82% (-1.66 to -3.96) 1 ≥ 65: -2.97% (-1.68 to -4.25) 1 Illness time ≥ 30: -2.94% (-1.80 to -4.07) 1 ≥ 65: -3.16% (-1.88 to -4.42) 1 Cardiorespiratory Sex ≥ 30: -2.61% (-0.89 to -4.29) 1 ≥ 65: -2.71% (-0.90 to -4.48) 1 Education ≥ 30: -2.58% (-0.85 to -4.27) 1 ≥ 65: -2.77% (-0.95 to -4.54) 1 Job ≥ 30: -2.68% (-0.96 to -4.37) 1 ≥ 65: -2.68% (-0.88 to -4.46) 1 Smoking ≥ 30: -2.46% (-0.73 to -4.17) 1 ≥ 65: -2.50% (-0.68 to -4.29) 1 Illness Time ≥ 30: -2.63% (-0.91 to -4.32) 1 ≥ 65: -2.73% (-0.92 to -4.51) 1

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Case-only by Exercise Group (Never as Reference) Nonaccidental ≥ 30 Low: -3.34% (-5.77 to -0.85) 1 Moderate: -6.32% (-8.55 to -4.03) 1 High: -1.74% (-3.06 to -0.40) 1 ≥ 65 Low: -3.79% (-6.67 to -0.82) 1 Moderate: -7.78% (-10.39 to -5.10) 1 High: -1.77% (-3.21 to -0.31) 1 Cardiorespiratory ≥ 30 Low: -3.95% (-7.77, 0.04) 1 Moderate: -8.50% (-11.84 to -5.02) 1 High: -0.62% (-2.58, 1.38) 1 ≥ 65 Low: -3.97% (-8.17, 0.43) 1 Moderate: -9.42% (-13.00 to -5.69) 1 High: -0.68% (-2.71, 1.38) 1
Reference: Wong et al. (2002, 025436) **Period of Study:** 1995-1998 **Location:** Hong Kong, China	**Outcome:** Mortality: Respiratory (461-519) COPD (490-496) Pneumonia & Influenza (480-487) Cardiovascular (390-459) IHD (410-414) Cerebrovascular (430-438) **Study Design:** Time-series **Statistical Analyses:** Poisson **Age Groups:** ≥ 30 yr; ≥ 65 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 51.53 (24.79) **Range (Min, Max):** (14.05, 163.79) **Copollutant (correlation):** NO_2: r = 0.780 SO_2: r = 0.344 O_3: r = 0.538	**Increment:** 10 µg/m^3 **Relative Risk (Lower CI, Upper CI) lag:** Respiratory 1.008 (1.001 to 1.014) 1 COPD 1.017 (1.002, 1.033) 0-3 Pneumonia & Influenza 1.007 (0.999, 1.015) 2 Cardiovascular 1.003 (0.998, 1.016) 2 IHD 1.013 (1.001, 1.025) 0-3 Cerebrovascular 1.007 (0.998, 1.016) 2 Respiratory PM_{10}+SO_2+O_3+NO_2: 1.005 (0.992, 1.010) 1 COPD PM_{10}+SO_2+O_3+NO_2: 0.991 (0.968, 1.015) 0-3 PM_{10}+O_3+NO_2: 0.993 (0.970, 1.016) 0-3 Pneumonia & Influenza PM_{10}+SO_2+O_3+NO_2: 1.002 (0.991, 1.013) 2 IHD 0.994 (0.978, 1.009) 0-3

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Wong et al. (2008, 157152) **Period of Study:** Bangkok: 1999-2003 Hong Kong: 1996-2002 Shanghai & Wuhan: 2001-2004 **Location:** Bangkok, Thailand Hong Kong, Shanghai, and Wuhan, China	**Outcome (ICD10):** Mortality: Natural causes (A00-R99) Cardiovascular (I00-I99) Respiratory (J00-J98) **Study Design:** Time-series **Statistical Analyses:** Poisson GLM, natural splines **Age Groups:** All ages ≥ 65 yr ≥ 75 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** Bangkok: 52.0 Hong Kong: 51.6 Shanghai: 102.0 Wuhan: 141.8 **Range (Min, Max):** Bangkok: (21.3, 169.2) Hong Kong: (13.7, 189.0) Shanghai: (14.0, 566.8) Wuhan: (24.8, 477.8) **Copollutant:** NO_2 SO_2 O_3	**Increment:** 10 µg/m^3 **% Excess Risk (Lower CI, Upper CI) lag:** Random Effects (4 cities) Natural causes: 0.55% (0.26, 0.85) 0-1 Cardiovascular: 0.58% (0.22, 0.93) 0-1 Respiratory: 0.62% (0.22, 1.02) 0-1 Random Effects (3 Chinese cities) Natural causes: 0.37% (0.21, 0.54) 0-1 Cardiovascular: 0.44% (0.19, 0.68) 0-1 Respiratory: 0.60% (0.16, 1.04) 0-1 Sensitivity Analysis Random Effects (4 cities) Omit PM_{10}>95th: 0.53% (0.27, 0.78) 0-1 Omit PM_{10}>75th: 0.53% (0.29, 0.78) 0-1 Omit PM_{10}>180 µg/m^3: 0.65% (0.24, 1.06) 0-1 Omit stations with high traffic source: 0.55% (0.26, 0.85) 0-1 Warm season-dichotomous variables: 0.86% (0.11, 1.60) 0-1 Add temperature at lag 1-2 days: 0.51% (0.23, 0.79) 0-1 Add temperature at lag 3-7 days: 0.35% (0.14, 0.57) 0-1 Daily PM_{10} defined by centering: 0.54% (0.26, 0.82) 0-1 Natural spline with (8, 4, 4f: 0.54% (0.26, 0.81) 0-1 Penalized spline: 0.52% (0.26, 0.77) 0-1 Random Effects (3 Chinese cities) Omit PM_{10}>95th: 0.47% (0.21, 0.73) 0-1 Omit PM_{10}>75th: 0.55% (0.24, 0.85) 0-1 Omit PM_{10}>180 µg/m^3: 0.46% (0.15, 0.76) 0-1 Omit stations with high traffic source: 0.38% (0.20, 0.57) 0-1 Warm season-dichotomous variables: 0.43% (0.10, 0.76) 0-1 Add temperature at lag 1-2 days: 0.36% (0.18, 0.53) 0-1 Add temperature at lag 3-7 days: 0.25% (0.10, 0.40) 0-1 Daily PM_{10} defined by centering: 0.37% (0.21, 0.53) 0-1 Natural spline with (8, 4, 4f: 0.36% (0.23, 0.49) 0-1 Penalized spline: 0.34% (0.23, 0.45) 0-1
Reference: Wong et al. (2008, 157151) **Period of Study:** Jan 1996-Dec 2002 **Location:** Hong Kong	**Outcome (ICD10):** Mortality: Nonaccidental (A00-T99 Z00-Z99) Cardiovascular (I00-I99) Respiratory (J00-J98) **Study Design:** Time-series **Statistical Analyses:** Poisson GLM, natural splines **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** 51.6 (25.3) **Range (Min, Max):** (13.5, 188.5) **Copollutant:** NO_2 SO_2 O_3	**Increment:** 10 µg/m^3 **% Excess Risk (Lower CI, Upper CI) lag:** Nonaccidental: Low SDI 0.37 (-0.10, 0.84) 0 0.40 (-0.04, 0.84) 1 0.14 (-0.28, 0.57) 2 -0.12 (-0.55, 0.30) 3 -0.14 (-0.56, 0.28) 4 Middle SDI 0.70 (0.34, 1.07) 0 0.48 (0.14, 0.82) 1 0.35 (0.02, 0.68) 2 0.18 (-0.14, 0.51) 3 0.17 (-0.16, 0.50) 4 High SDI 0.22 (-0.29, 0.73) 0 0.46 (-0.01, 0.94) 1 0.29 (-0.17, 0.75) 2 -0.05 (-0.51, 0.40) 3 -0.06 (-0.51, 0.40) 4 All areas

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			0.45 (0.19, 0.72) 0 0.40 (0.15, 0.64) 1 0.22 (-0.02, 0.45) 2 0.00 (-0.24, 0.23) 3 0.03 (-0.20, 0.26) 4 Cardiovascular: Low SDI 0.14 (-0.77, 1.06) 0 0.64 (-0.21, 1.49) 1 0.24 (-0.58, 1.07) 2 -0.27 (-1.09, 0.55) 3 0.01 (-0.80, 0.83) 4 Middle SDI 0.66 (0.00, 1.34) 0 0.49 (-0.13, 1.12) 1 0.80 (0.20, 1.40) 2 0.65 (0.06, 1.25) 3 0.52 (-0.07, 1.12) 4 High SDI 0.83 (-0.08, 1.75) 0 0.89 (0.04, 1.75) 1 0.12 (-0.70, 0.95) 2 -0.09 (-0.91, 0.73) 3 0.04 (-0.77, 0.86) 4 All areas 0.52 (0.05, 1.00) 0 0.58 (0.14, 1.03) 1 0.43 (0.00, 0.86) 2 0.14 (-0.28, 0.57) 3 0.23 (-0.20, 0.65) 4 Respiratory: Low SDI 0 0.69 (-0.44, 1.82) 0 1 0.55 (-0.50, 1.61) 1 2 0.36 (-0.66, 1.39) 2 3 -0.24 (-1.25, 0.78) 3 4 -0.17 (-1.17, 0.85) 4 Middle SDI 0.31 (-0.50, 1.13) 0 0.77 (0.01, 1.53) 1 0.85 (0.12, 1.59) 2 0.66 (-0.07, 1.39) 3 0.69 (-0.03, 1.42) 4 High SDI 0.27 (-0.85, 1.40) 0 0.72 (-0.32, 1.78) 1 1.46 (0.45, 2.47) 2 0.70 (-0.30, 1.71) 3 0.48 (-0.52, 1.48) 4 All areas 0.39 (-0.20, 0.99) 0 0.70 (0.15, 1.26) 1 0.89 (0.36, 1.42) 2 0.45 (-0.08, 0.98) 3 0.43 (-0.10, 0.96) 4 High SDI vs. Middle SDI Nonaccidental: 0.23 (-0.25, 0.72) 0-1 Cardiovascular: 0.49 (-0.40, 1.40) 0-1 Respiratory: 0.49 (-0.58, 1.58) 0-1 High SDI vs. Low SDI Nonaccidental: 0.12 (-0.42, 0.67) 0-1 Cardiovascular: 0.82 (-0.20, 1.86) 0-1 Respiratory: -0.15 (-1.39, 1.10) 0-1 Trend Test Nonaccidental: 0.04 (-0.15, 0.22) 0-1 Cardiovascular: 0.27 (-0.07, 0.61) 0-1 Respiratory: -0.04 (-0.46, 0.37)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			0-1 SDI = Social Deprivation Index. The higher the SDI the lower the SES of the individual.
Reference: Yang et al. (2004, 055603)	**Outcome:** Mortality:	**Pollutant:** PM_{10}	**Increment:** 31.43 µg/m^3
Period of Study: 1994-1998	Nonaccidental (<800)	**Averaging Time:** 24-h avg	**Odds Ratio (Lower CI, Upper CI) lag:**
Location: Taipei, Taiwan	Circulatory (390-459)	**Mean (SD):** 51.99	Nonaccidental
	Respiratory (460-519)	**Range (Min, Max):** (13.71, 211.30)	0.995 (0.971, 1.020) 0
	Study Design: Bi-directional case-crossover	**Copollutant:** SO_2 NO_2 CO O_3	Respiratory
	Statistical Analyses: Conditional logistic regression		0.986 (0.906, 1.074) 0
	Age Groups: All ages		Circulatory
			0.988 (0.942, 1.035)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Zanobetti et al. (2003, 042812) **Period of Study:** 1990-1997 **Location:** 10 European cities (APHEA2)	**Outcome:** Mortality: Nonaccidental (<800) Circulatory (390-459) Respiratory (460-519) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM **Age Groups:** 15-64 yr 65-74 yr ≥ 75 yr	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** Athens: 42.7 (12.9) Budapest: 41 (9.1) Lodz: 53.5 (15.5) London: 28.8 (13.7) Madrid: 37.8 (17.7) Paris: 22.5 (11.5) Prague: 76.2 (45.7) Rome: 58.7 (17.4) Stockholm: 15.5 (7.9) Tel Aviv: 50.3 (57.5) **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Cardiovascular 0.69% (0.31, 1.08) 0-1 avg 40-day distributed lag 1.99% (1.44, 2.54) 4th degree 1.97% (1.38, 2.55) Unrestricted Respiratory 0.74% (-0.17, 1.66) 0-1 avg 40-day distributed lag 4.21% (1.70, 6.79) 4th degree 4.20% (1.08, 7.42) Unrestricted Unrestricted distributed lags Cardiovascular 1.34% (0.89, 1.79) 20 1.72% (1.20, 2.25) 30 1.97% (1.38, 2.55) 40 Respiratory 1.71% (-0.65, 4.12) 20 2.62% (0.19, 5.11) 30 4.20% (1.08, 7.42) 40 40-day lags Nonaccidental 15-64 -0.25% (-0.87, 0.36) 4th degree -0.01 (-0.76, 0.75) Unrestricted 65-74 0.78% (0.23, 1.33) 4th degree 0.74% (0.02, 1.45) Unrestricted ≥ 75 1.84% (0.92, 2.78) 4th degree 1.94% (1.07, 2.81) Unrestricted Cardiovascular 65-74 2.06% (1.05, 3.09) 4th degree 1.62 (0.54, 2.70) Unrestricted ≥ 75 2.35% (1.42, 3.29) 4th degree 2.52% (1.57, 3.48) Unrestricted Respiratory ≥ 75 4.57% (1.25, 7.99) 4th degree 4.52% (0.89, 8.28) Unrestricted

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Zeka et al. (2005, 088068) **Period of Study:** Jan 1989-Dec 2000 **Location:** 20 U.S. cities	**Outcome (ICD10):** Mortality: All-cause (nonaccidental) (V01-Y98) Heart Disease (I01-I51) IHD (I20-I25) Myocardial infarction (I21, I22) Dysrhythmias (I46-I49) Heart failure (I50) Stroke (I60-I69) Respiratory (J00-J99) Pneumonia (J12-J18) COPD (J40-J44, J47) **Study Design:** Time-stratified case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups:** All ages	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** Birmingham: 31.9 (18.0) µg/m^3 Boulder: 22.1 (11.3) Caton: 26.6 (11.5) Chicago: 33.7 (16.4) Cincinnati: 31.4 (13.9) Cleveland: 37.5 (18.7) Colorado Springs: 24.0 (13.2) Columbus: 28.5 (12.5) Denver: 28.5 (12.8) Detroit: 32.1 (17.7) Honolulu: 15.9 (6.8) Minneapolis: 24.7 (12.3) Nashville: 30.1 (12.1) New Haven: 25.4 (14.4) Pittsburgh: 30.2 (18.5) Provo: 33.7 (22.2) Seattle: 26.4 (14.7) Salt lake City: 35.0 (20.8) µ Terra Haute: 29.2 (14.6) µ Youngstown: 30.8 (13.9) **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Single-lag model All-Cause (nonaccidental) 0.20% (0.08, 0.32) 0 0.35% (0.21, 0.49) 1 0.24% (0.14, 0.34) 2 Respiratory 0.34% (-0.07, 0.75) 0 0.52% (0.15, 0.89) 1 0.51% (0.16, 0.86) 2 COPD -0.06% (-0.63, 0.51) 0 0.43% (-0.14, 1.00) 1 0.39% (-0.16, 0.94) 2 Pneumonia 0.50% (0.09, 1.09) 0 0.59% (-0.12, 1.30) 1 0.82% (0.25, 1.39) 2 Heart disease 0.12% (-0.06, 0.30) 0 0.30% (0.12, 0.48) 1 0.37% (0.17, 0.57) 2 IHD 0.19% (-0.03, 0.41) 0 0.41% (0.19, 0.63) 1 0.43% (0.10, 0.76) 2 Myocardial Infarction 0.36% (-0.05, 0.77) 0 0.17% (-0.18, 0.52) 1 0.13% (-0.22, 0.48) 2 Heart Failure 0.17% (-0.63, 0.97) 0 -0.01% (-0.81, 0.79) 1 0.78% (-0.004, 1.56) 2 Dysrhythmias -0.23% (-1.41, 0.95) 0 0.37% (-0.47, 1.21) 1 0.33% (-0.55, 1.21) 2 Stroke 0.09% (-0.49, 0.60) 0 0.41% (-0.02, 0.84) 1 0.14% (-0.27, 0.55) 2 Unconstrained distributed lag model All-cause (nonaccidental) 0.45% (0.25, 0.65) 0-3 Respiratory 0.87% (0.38, 1.36) 0-3 COPD 0.43% (-0.35, 1.21) 0-3 Pneumonia 1.24% (0.46, 2.02) 0-3 Heart Disease 0.50% (0.25, 0.75) 0-3 IHD 0.65% (0.32, 0.98) Myocardial Infarction 0.36% (-0.25, 0.97) 0-3 Heart Failure 0.60% (-0.50, 1.70) 0-3 Dysrhythmias 0.20% (-1.03, 1.43) 0-3 Stroke 0.46% (-0.13, 1.05) 0-3
Reference: Zeka et al. (2006, 088749) **Period of Study:** Jan 1989-Dec 2000 **Location:** 20 U.S. cities	**Outcome (ICD10):** Mortality: All-cause (nonaccidental) (V01-Y98) Heart Disease (I01-I51) Myocardial infarction (I21, I22) Stroke (I60-I69) Respiratory (J00-J99) **Study Design:** Time-stratified case-	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg **Mean (SD):** Birmingham: 31.9 (18.0) µg/m^3 Boulder: 22.1 (11.3) Caton: 26.6 (11.5) Chicago: 33.7 (16.4) Cincinnati: 31.4 (13.9) Cleveland: 37.5 (18.7) Colorado Springs: 24.0 (13.2)	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag: All-cause (nonaccidental)** Male: 0.46% (0.28, 0.64) 1-2 avg Female: 0.37% (0.17, 0.57) 1-2 avg White: 0.40% (0.22, 0.58) 1-2 avg Black: 0.37% (-0.02, 0.76) 1-2 avg **Age:** <65: 0.25% (0.01, 0.49) 1-2 avg 75: 0.23% (-0.06, 0.52) 1-2 avg

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
	crossover **Statistical Analyses:** Conditional logistic regression **Age Groups:** All ages <65 yr 65-75 yr >75 yr	Columbus: 28.5 (12.5) Denver: 28.5 (12.8) Detroit: 32.1 (17.7) Honolulu: 15.9 (6.8) Minneapolis: 24.7 (12.3) Nashville: 30.1 (12.1) New Haven: 25.4 (14.4) Pittsburgh: 30.2 (18.5) Provo: 33.7 (22.2) Seattle: 26.4 (14.7) Salt lake City: 35.0 (20.8) Terra Haute: 29.2 (14.6) Youngstown: 30.8 (13.9) **Range (Min, Max):** NR **Copollutant (correlation):** NR	>75: 0.64% (0.44, 0.84) 1-2 avg **Educational Attainment:** Low (<8 yr): 0.62% (0.29, 0.95) 1-2 avg Medium (8-12 yr): 0.36% (0.12, 0.60) 1-2 avg High (>12 yr): 0.27% (-0.004, 0.54) 1-2 avg **Location of Death:** In hospital: 0.22% (0.04, 0.40) 1-2 avg Out of hospital: 0.71% (0.51, 0.91) 1-2 avg **Season:** Winter: 0.28% (0.04, 0.52) 1-2 avg Summer: 0.19% (-0.22, 0.60) 1-2 avg Transition (spring/fall): 0.49% (0.25, 0.73) 1-2 avg **Respiratory** Male: 0.71% (0.004, 1.42) 0-3 Female: 1.04% (0.33, 1.75) 0-3 White: 0.88% (0.33, 1.43) 0-3 Black: 0.71% (-0.56, 1.98) 0-3 **Age:** <65: 0.94% (-0.31, 2.19) 0-3 65-75: 0.87% (-0.25, 1.99) 0-3 >75: 0.88% (0.17, 1.59) 0-3 **Educational Attainment:** Low (<8 yr): 0.82% (-0.32, 1.96) 0-3 Medium (8-12 yr): 0.88% (0.12, 1.64) 0-3 High (>12 yr): 0.88% (-0.04, 1.80) 0-3 **Location of Death:** In hospital: 0.78% (0.17, 1.39) 0-3 Out of hospital: 1.09% (0.25, 1.93) 0-3 **Season:** Winter: -0.007% (-0.87, 0.86) 0-3 Summer: 0.69% (-0.68, 2.06) 0-3 Transition (spring/fall): 1.57% (0.86, 2.28) 0-3 **Heart Disease** Male: 0.54% (0.23, 0.85) 2 Female: 0.46% (0.15, 0.77) 2 White: 0.50% (0.25, 0.75) 2 Black: 0.64% (0.13, 1.15) 2 **Age:** <65: 0.04% (-0.45, 0.53) 2 65-75: 0.60% (0.13, 1.07) 2 >75: 0.65% (0.30, 1.00) 2 **Educational Attainment:** Low (<8 yr): 0.72% (0.23, 1.21) 2 Medium (8-12 yr): 0.38% (0.07, 0.69) 2 High (>12 yr): 0.54% (0.13, 0.95) 2 **Location of Death:** In hospital: 0.15% (-0.14, 0.44) 2 Out of hospital: 0.93% (0.60, 1.26) 2 **Season:** Winter: 0.41% (-0.002, 0.82) 2 Summer: 0.52 (0.03, 1.01) 2 Transition (spring/fall): 0.56% (0.13, 0.99) 2

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Myocardial Infarction Male: 0.21% (-0.40, 0.82) 0 Female: 0.59% (0.08, 1.10) 0 White: 0.24% (-0.27, 0.75) 0 Black: 0.99% (0.05, 1.93) 0 <65: 0.12% (-0.76, 1.00) 0 65-75: 0.92% (0.21, 1.63) 0 >75: 0.16% (-0.58, 0.90) 0 **Educational Attainment:** Low (<8 yr): 0.33% (-0.83, 1.49) 0 Medium (8-12 yr): 0.79% (0.28, 1.30) 0 High (>12 yr): -0.13% (-0.82, 0.56) 0 **Location of Death:** In hospital: 0.34% (-0.11, 0.79) 0 Out of hospital: 0.48% (-0.23, 1.19) 0 **Season:** Winter: 0.32% (-0.37, 1.01) 0 Summer: 0.30% (-0.82, 1.42) 0 Transition (spring/fall): 0.38% -0.31, 1.07) 0 **Stroke** Male: 0.11% (-0.58, 0.80) 1 Female: 0.59% (-0.04, 1.22) 1 White: 0.48% (0.01, 0.95) 1 Black: 0.13% (-0.87, 1.13) 1 **Age:** <65: 0.09% (-1.09, 1.27) 1 65-75: -0.46% (-1.42, 0.50) 1 >75: 0.80% (0.27, 1.33) 1 **Educational Attainment:** Low (<8 yr): 0.07% (-1.44, 1.58) 1 Medium (8-12 yr): 0.29% (-0.32, 0.90) 1 High (>12 yr): 0.52% (-0.28, 1.32) 1 **Location of Death:** In hospital: 0.06% (-0.49, 0.61) 1 Out of hospital: 0.87% (0.05, 1.69) 1 **Season:** Winter: -0.09% (-0.93, 0.75) 1 Summer: 0.67% (-0.31, 1.65) 1 Transition (spring/fall): 0.51% (-0.20, 1.22) 1 **Contributing causes of disease: All-cause** Secondary pneumonia present: 0.67% (0.16, 1.18) 1-2 avg Secondary pneumonia absent: 0.34% (0.16, 0.52) 1-2 avg Secondary heart failure present: 0.42% (0.01, 0.83) 1-2 avg Secondary heart failure absent: 0.37% (0.19, 0.55) 1-2 avg Secondary stroke present: 0.85% (0.30, 1.40) 1-2 avg Secondary stroke absent: 0.32% (0.14, 0.50) 1-2 avg Diabetes present: 0.57% (0.02, 1.12) 1-2 avg Diabetes absent: 0.34% (0.14, 0.54) 1-2 avg **Respiratory** Secondary pneumonia present: 1.28% (-0.33, 2.89) 0-3 Secondary pneumonia absent: 0.78% (0.15, 1.41) 0-3 Secondary heart failure present: 1.48% (0.07, 2.89) 0-3 Secondary heart failure absent:

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			0.79% (0.26, 1.32) 0-3 Secondary stroke present: 1.95% (-0.11, 4.01) 0-3 Secondary stroke absent: 0.80% (0.29, 1.31) 0-3 Diabetes present: 1.96% (-0.22, 4.14) 0-3 Diabetes absent: 0.82% (0.31, 1.33) 0-3 Heart Disease Secondary pneumonia present: 0.66% (-0.63, 1.95) 2 Secondary pneumonia absent: 0.49% (0.27, 0.71) 2 Secondary stroke present: 0.73% (-0.05, 1.51) 2 Secondary stroke absent: 0.48% (0.24, 0.72) 2 Diabetes present: 0.34% (-0.42, 1.10) 2 Diabetes absent: 0 .52% (0.28, 0.76) 2 Myocardial Infarction Secondary pneumonia present: 1.54% (-1.05, 4.13) 0 Secondary pneumonia absent: 0.42% (0.05, 0.79) 0 Secondary stroke present: 0.50% (-1.38, 2.38) 0 Secondary stroke absent: 0.36% (-0.05, 0.77) 0 Diabetes present: 0.70% (-0.38, 1.78) 0 Diabetes absent: 0.41% (0.04, 0.78) 0 Stroke Secondary pneumonia present: 1.74% (0.35, 3.13) 1 Secondary pneumonia absent: 0.29% (-0.16, 0.74) 1 Secondary heart failure present: 1.01% (-0.77, 1.79) 1 Secondary heart failure absent: 0.38% (-0.05, 0.81) 1 Diabetes present: 1.02% (-0.53, 2.57) 1 Diabetes absent: 0.37% (-0.08, 0.82) 1

[1]All units expressed in μg/m^3 unless otherwise specified.

Table E-17. Short-term exposure-mortality - $PM_{10-2.5}$.

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Burnett et al. (2004, 086247) **Period of Study:** 1981-1999 **Location:** 12 Canadian cities	**Outcome:** Mortality: Nonaccidental (<800) **Study Design:** Time-series **Statistical Analyses:** 1. Poisson, natural splines 2. Random effects regression model **Age Groups:** All ages	**Pollutant:** P10-2.5 **Averaging Time:** 24-h avg **Mean (SD):** 11.4 **Range (Min, Max):** NR **Copollutant:** NO_2 O_3 SO_2 CO PM_{10} $PM_{2.5}$ **Note:** PM_{10} measurement calculated as the sum of $PM_{2.5}$ and $PM_{10-2.5}$ measurements.	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** 1981-1999 $PM_{10-2.5}$: 0.31% (-0.66, 1.33) 1 $PM_{10-2.5}$+NO_2: 0.65% (-0.23, 1.59) 1
Reference: Kan et al. (2007, 091267) **Period of Study:** Mar 2004-Dec 2005 **Location:** Shanghai, China	**Outcome (ICD10):** Mortality: Total (nonaccidental) (A00-R99) Cardiovascular (I00-I99) Respiratory (J00-J98) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, penalized splines **Age Groups:** All ages	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** 56.4 (1.34) **Range (Min, Max):** (8.3, 235.0) **Copollutant (correlation):** PM_{10}: r = 0.88 $PM_{2.5}$: r = 0.48 O_3: r = 0.07	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI)** **lag:** Total: 0.12% (-0.13, 0.36) 0-1 Cardiovascular: 0.34% (-0.05, 0.73) 0-1 Respiratory: 0.40% (-0.34, 1.13) 0-1
Reference: Kettunen et al. (2007, 091242) **Period of Study:** 1998-2004 **Location:** Helsinki, Finland	**Outcome (ICD10):** Mortality: Stroke (I60-I61, I63-I64) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, penalized thin-plate splines **Age Groups:** ≥ 65 yr	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 24-h avg **Median (SD) unit:** Cold Season: 6.7 Warm Season: 8.4 **Range (Min, Max):** Cold Season: (0.0, 101.4) Warm Season: (0.0, 42.0) **Copollutant:** O_3, CO, NO_2 PM_{10} $PM_{2.5}$ UFP	**Increment:** Cold Season: 8.3 µg/m^3 Warm Season: 5.7 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Cold Season: -1.04% (-6.63, 4.89) 0 -2.49% (-7.57, 2.88) 1. -4.93% (-9.99, 0.41) 2 -4.33% (-9.32, 0.93) 3 Warm Season: 7.05% (-1.88, 16.80) 0 4.38% (-4.26, 13.81) 1: -1.19% (-9.45, 7.84) 2 1.42% (-6.79, 10.34) 3
Reference: Klemm et al. (2004, 056585) **Period of Study:** Aug 1998-Jul 2000 **Location:** Fulton and DeKalb counties, Georgia (ARIES)	**Outcome:** Mortality: Nonaccidental (<800) Cardiovascular (390-459) Respiratory (460-519) Cancer (140-239) **Study Design:** Time-series **Statistical Analyses:** Poisson GLM, natural cubic splines **Age Groups:** <65 yr, ≥ 65 yr	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** 9.69 (3.94) **Range (Min, Max):** (1.71, 25.17) **Copollutant:** $PM_{2.5}$ O_3 NO_2 CO SO_2 Acid EC OC SO_4 Oxygenated Hydrocarbons Nonmethane hydrocarbons NO_3	**Increment:** NR **β (SE)** **lag:** Quarterly Knots: 0.00433 (0.00333) 0-1 Monthly Knots: 0.00617 (0.00360) 0-1 Biweekly Knots: 0.00516 (0.00381) 0-1

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Perez et al. (2008, 156020) **Period of Study:** Mar 2003-Dec 2005 **Location:** Barcelona, Spain	**Outcome:** Respiratory mortality **Study Design:** Cohort **Covariates:** Temperature, humidity **Statistical Analysis:** autoregressive Poisson regression models **Statistical Package:** NR **Age Groups:** All deaths	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 24 h **Mean (SD) Unit:** 14.0 (9.5) $\mu g/m^3$ **Range (Min, Max):** 0.1, 93.1 **Copollutant:** $PM_{2.5}$-1, PM1	**Increment:** 10 $\mu g/m^3$ **Odds Ratio (95%CI) Lag** Single Pollutant Model Avg L0-1: 1.000 (0.944-1.060), p = 0.991 L1: 1.002 (0.955-1.052), p = 0.931 L2: 1.070 (1.023-1.118), p = 0.003 Multi-pollutant Model Avg L0-1: 1.002 (0.937-1.071), p = 0.958 L1: 0.998 (0.943-1.056), p = 0.0.936 L2: 1.033 (0.980-1.089), p = 0.226
Reference: Perez et al. (2008, 156020) **Period of Study:** Mar 2003-Dec 2005 **Location:** Barcelona, Spain	**Outcome:** Cardiovascular mortality **Study Design:** Cohort **Covariates:** Temperature, humidity **Statistical Analysis:** Autoregressive Poisson regression models **Statistical Package:** NR **Age Groups:** All deaths	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 24 h **Mean (SD) Unit:** 14.0 (9.5) $\mu g/m^3$ **Range (Min, Max):** 0.1, 93.1 **Copollutant:** $PM_{2.5}$-1, PM1	**Increment:** 10 $\mu g/m^3$ **Odds Ratio (95%CI) Lag** Avg L0-1: 1.054 (1.019-1.089), p = 0.002 L1: 1.059 (1.031-1.072), p = 0.000 L2: 1.044 (1.017-1.072), p = 0.001 Multi-pollutant Model Avg L0-1: 1.053 (1.013-1.094), p = 0.009 L1: 1.059 (1.026-1.094), p = 0.001 L2: 1.044 (1.012-1.078), p = 0.007
Reference: Perez et al. (2008, 156020) **Period of Study:** Mar 2003-Dec 2005 **Location:** Barcelona, Spain	**Outcome:** Cerebrovascular mortality **Study Design:** Cohort **Covariates:** Temperature, humidity **Statistical Analysis:** Autoregressive Poisson regression models **Statistical Package:** NR **Age Groups:** All deaths	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 24 h **Mean (SD) Unit:** 14.0 (9.5) $\mu g/m^3$ **Range (Min, Max):** 0.1, 93.1 **Copollutant:** $PM_{2.5}$-1, PM1	**Increment:** 10 $\mu g/m^3$ **Odds Ratio (95%CI) Lag** Avg L0-1: 1.087 (1.018-1.161), p = 0.013 L1: 1.086 (1.030-1.145), p = 0.002 L2: 1.051 (0.997-1.108), p = 0.064 Multi-pollutant Model Avg L0-1: 1.103 (1.022-1.191), p = 0.011 L1: 1.098 (1.030-1.171), p = 0.004 L2: 1.076 (1.010-1.146), p = 0.023
Reference: Slaughter et al. (2005, 073854) **Period of Study:** Jan 1995-Dec 1999 **Location:** Spokane, Washington	**Outcome:** Mortality: Nonaccidental (< 800) **Study Design:** Time-series **Statistical Analyses:** Poisson GLM, natural splines **Age Groups:** All ages	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 24-h avg **Mean (SD) unit:** NR **Range (9th, 95th):** NR **Copollutant (correlation):** PM1: r = 0.19 $PM_{2.5}$: r = 0.31 PM_{10}: r = 0.94 CO: r = 0.32	This study does not present quantitative results for $PM_{10-2.5}$.
Reference: Stieb et al. (2002, 025205) **Period of Study:** Publication dates of studies: 1985-Dec 2000 Mortality series: 1958-1999 **Location:** 40 cities (11 Canadian cities, 19 U.S. cities, Santiago, Amsterdam, Erfurt, 7 Korean cities)	**Outcome:** Mortality: All-cause (nonaccidental) **Study Design:** Meta-analysis **Statistical Analyses:** Random effects model **Age Groups:** All ages	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** NR **Mean (SD):** NR **Range (Min, Max):** NR **Copollutant:** Varied between studies: $PM_{2.5}$, O_3, SO_2, NO_2, CO	**Increment:** 13.0 $\mu g/m^3$ **% Increase (Lower CI, Upper CI) lag:** Single-pollutant models: 10 studies $PM_{10-2.5}$: 1.2% (0.5, 1.9) Multipollutant models: 6 studies $PM_{10-2.5}$: 0.9% (-0.3, 2.0)

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Villeneuve et al. (2003, 055051) **Period of Study:** 1986-1999 **Location:** Vancouver, Canada	**Outcome:** Mortality: Nonaccidental (<800) Cardiovascular (401-440) Respiratory (460-519) Cancer (140-239) **Study Design:** Time-series **Statistical Analyses:** Poisson, natural splines **Age Groups:** ≥ 65	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** Daily: 6.1 Every 6th Day 8.3 **Range (Min, Max):** Daily: (0.0, 72.0) Every 6th Day: (0.7, 35.0) **Copollutant:** $PM_{2.5}$ PM_{10} SO_2 CO NO_2 O_3	**Increment:** 11.0 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Nonaccidental 1.4% (-2.5, 5.4) 0-2 avg 1.0% (-1.9, 4.0) 0 -1.1% (-4.0, 1.8) 1 2.0% (-1.0, 5.1) 2 Cardiovascular 5.9% (-0.2, 12.4) 0-2 avg 5.9% (1.1, 10.8) 0 1.4% (-3.3, 6.4) 1 2.2% (-2.0, 6.7) 2 Respiratory -1.0% (-9.8, 8.8) 0-2 avg -1.5% (-9.4, 7.1) 0 -1.5% (-8.4, 6.0) 1 0.1% (-6.4, 6.9) 2 Cancer 4.4% (-3.6, 13.1) 0-2 avg 3.1% (-2.9, 9.4) 0 -1.0% (-6.9, 5.3) 1 4.0% (-2.1, 10.4) 2
Reference: Wilson et al. (2007, 157149) **Period of Study:** 1995-1997 **Location:** Phoenix, Arizona	**Outcome:** Mortality: Cardiovascular **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, nonparametric smoothing spline **Age Groups:** >25	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **% Excess Risk (Lower CI, Upper CI) lag:** Central Phoenix: 2.4% (-1.2, 6.1) 0-5 ma Middle Phoenix: 3.8% (0.3, 7.5) 0-5 ma 3.4% (1.0, 5.8) 1 3.0% (0.7, 5.4) 2 Outer Phoenix: 1.6% (-1.9, 5.2) 0-5 ma

[1]All units expressed in µg/m^3 unless otherwise specified.

Table E-18. Short-term exposure-mortality - $PM_{2.5}$ (including PM components/sources).

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Basu et al. (2008, 098716) **Period of Study:** May 1999-Sept 2003 **Location:** 9 California counties	**Outcome (ICD10):** Mortality: Nonaccidental (V01-Y98) **Study Design:** (1) Main analysis: Case-crossover (2) Sensitivity analysis: Time-series **Statistical Analyses:** (1) Main analysis: conditional logistic regression (2) Sensitivity analysis: Poisson GAM **Age Groups:** All ages	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SE) unit:** Contra Costa: 8.6 Fresno: 7.6 Kern: 11.3 Los Angeles: 19.8 Orange: 17.0 Riverside: 28.4 Sacramento: 8.8 San Diego: 13.4 Santa Clara: 10.8 IQR (25th, 75th): Contra Costa: (5.8, 10.1) Fresno: (3.8, 9.8) Kern: (8.0, 13.5) Los Angeles: (14.7, 23.3) Orange: (11.8, 21.0) Riverside: (17.9, 36.1) Sacramento: (5.8, 10.1) San Diego: (10.3, 15.8) Santa Clara: (7.2, 13.8) **Copollutant (correlation):** PM_{10} r = 0.45 O_3 (1hr) r = 0.28 O_3 (8hr) r = 0.22 CO r = 0.45 NO_2 r = 0.43	The study does not provide results quantitatively.
Reference: Dominici et al. (2007, 097361) **Period of Study:** PM_{10}: 1987-2000 $PM_{2.5}$: 1999-2000 **Location:** 100 U.S. counties (NMMAPS)	**Outcome:** Mortality: All-cause (nonaccidental) Cardiorespiratory Other-cause **Study Design:** Time-series **Statistical Analyses:** 2-stage Bayesian hierarchical model **Age Groups:** All ages	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** 1999-2000: All-cause: 0.29% (0.01, 0.57) 1 Cardiorespiratory: 0.38% (-0.07, 0.82) 1
Reference: Dominici et al. (2007, 099135) **Period of Study:** 2000-2005 **Location:** 72 U.S. counties representing 69 communities	**Outcome:** Total mortality **Study Design:** Time-series **Statistical Analyses:** 2-stage Bayesian hierarchical model **Age Groups:** All ages	**Pollutant:** $PM_{2.5}$, Nickel, speciated fine PM, and Vanadium **Averaging Time:** Annual avg **Mean (SD):** NR **Range (Min, Max):** NR **Copollutant (correlation):** NR	The study does not provide results quantitatively. **Note:** The study investigated whether county-specific short-term effects of PM_{10} on mortality are modified by long-term county-specific nickel or vanadium $PM_{2.5}$ concentrations.
Reference: Franklin et al. (2007, 091257) **Period of Study:** 1997-2002 **Location:** 27 U.S. communities	**Outcome:** Mortality: All-cause (nonaccidental (<800) Cardiovascular (390-429) Respiratory (460-519) Stroke (430-438) **Study Design:** Time-stratified case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups:** All ages	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** 15.7 µg/m^3 **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** All-cause (nonaccidental): 0.67% (-0.12, 1.46) 0 1.21% (0.29, 2.14) 10.82% (0.02, 1.63) 0-1 Respiratory: 1.31% (-0.10, 2.73) 0 1.78% (0.20, 3.36) 1 1.67% (0.19, 3.16) 0-1 Cardiovascular: 0.34% (-0.61, 1.28) 0 0.94% (-0.14, 2.02) 1. 0.54% (-0.47, 1.54) 0-1 Stroke: 0.62% (-0.69, 1.94) 0 1.03% (0.02, 2.04) 1. 0.67% (-0.23, 1.57) 0-1

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
			Age≥ 75: All cause: 1.66% (0.62, 2.70) 1 Respiratory: 1.85% (0.27, 3.44) 1 Cardiovascular: 1.29% (0.15, 2.42) 1 Stroke: 1.52% (0.37, 2.67) 1 Age<75: All cause: 0.62% (-0.30, 1.55) 1 Respiratory: 1.53% (-0.67, 3.74) 1 Cardiovascular: 0.26% (-1.04, 1.56) 1 Stroke: -0.78% (-2.32, 0.76) 1 Male: All cause: 1.06% (0.07, 2.06) 1 Respiratory: 1.90% (0.14, 3.65) 1 Cardiovascular: 0.52% (-0.63, 1.66) 1 Stroke: 0.79% (-0.42, 2.02) 1 Female: All cause: 1.34% (0.40, 2.27) 1 Respiratory: 1.57% (-0.22, 3.35) 1 Cardiovascular: 1.30% (0.14, 2.46) 1 Stroke: 0.79% (-0.51, 2.09) 1 East: ll cause: 1.95% (0.50, 3.40)1 Respiratory: 2.66% (0.33, 5.00) 1 Cardiovascular: 1.52% (0.06, 2.98) 1 Stroke: 1.16% (-0.40, 2.73) 1 West: All cause: 0.05% (-1.80, 1.89) 1 Respiratory: 0.67% (-2.00, 3.34) 1| Cardiovascular: 0.11% (-2.03, 2.24) 1| Stroke: 0.94% (-0.38, 2.26) 1 $PM_{2.5}$>15 μg/m^3: All cause: 1.10% (-0.43, 2.64) 1 Respiratory: 1.42% (-0.84, 3.68) 1 Cardiovascular: 0.88% (-0.87, 2.62) 1 Stroke: 0.91% (-0.28, 2.10) 1 $PM_{2.5}$≤ 15 μg/m^3: All cause: 1.41% (-0.49, 3.30) 1 Respiratory: 2.46% (-0.49, 5.42) 1 Cardiovascular: 1.09% (-1.15, 3.32) 1 Stroke: 1.36% (-0.56, 3.27) 1 Effect of A/C at percentile of air conditioning prevalence: 25th percentile (45% prevalence of A/C): All cause: 1.50% (0.13, 2.88) 1 Respiratory: 2.27% (0.27, 4.27) 1 Cardiovascular: 1.04% (-0.54, 2.63) 1 Stroke: 1.04% (-0.44, 2.53) 1 75th percentile (80% prevalence of A/C): All cause: 0.85% (-0.64, 2.35) 1 Respiratory: 1.04% (-1.29, 3.37) 1 Cardiovascular: 0.81% (-0.93, 2.61) 1 Stroke: 1.03% (-0.76, 2.83) 1 Effect of A/C at percentile of air conditioning prevalence in cities with summer peaking $PM_{2.5}$ concentrations: 25th percentile (45% prevalence of A/C): All cause: 1.01% (-0.30, 2.32) 1 Respiratory: 0.76% (-1.38, 2.90) 1 Cardiovascular: 0.43% (-0.86, 1.72) 1 Stroke: -0.18% (-2.08, 1.73) 1 75th percentile (77% prevalence of A/C): All cause: -0.55% (-1.95, 0.85) 1

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
			Respiratory: -2.08% (-4.47, 0.31) 1 Cardiovascular: -1.02% (-2.44, 0.41) 1 Stroke: 0.69% (-1.19, 2.57) 1
Reference: Franklin et al. (2008, 097426) **Period of Study:** 2000-2005 **Location:** 25 U.S. communities	**Outcome (ICD10):** Mortality: Nonaccidental (V01-Y98) Respiratory (J00-J99) Cardiovascular (I01-I52) Stroke (I60-J69) **Study Design:** Time-series **Statistical Analyses:** 1st stage: Poisson, cubic spline 2nd stage: Random effects meta-analysis **Age Groups:** All ages	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Range Mean (SD):** Winter: 9.6-34.4 Spring: 6.7-27.6 Summer: 7.6-26.0 Fall: 9.5-32.1 **Range (Min, Max):** NR **Copollutant:** Al, As, Br, Cr, EC, Fe, K, Mn, Na^+, Ni, NO_3^-, NH_4, OC, Pb, Si, SO_4^{2-}, V, Zn	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Nonaccidental: 0.74% (0.41, 1.07) 0-1 Cardiovascular: 0.47% (0.02, 0.92) 0-1 Respiratory: 1.01% (-0.03, 2.05) 1-2 Stroke: 0.68% (-0.21, 1.57) 0-1 Winter: 0.15% (-0.42, 0.72) 0-1 Spring: 1.88% (1.29, 2.48) 0-1 Summer: 0.99% (0.35, 1.68) 0-1 Fall: 0.19% (-0.25, 0.64) 0-1 West: 0.51% (0.10, 0.92) 0-1 East & Central: 0.92% (0.44, 1.39) 0-1 % Increase per 10 µg/m^3 increase in $PM_{2.5}$ for an IQR increase in species to $PM_{2.5}$ mass proportion Univariate analysis Al: 0.58% As: 0.55% Br: 0.38 Cr: 0.33% EC: 0.06% Fe: 0.12% K: 0.41% Mn: 0.14% Na+: 0.20% Ni: 0.37% NO_3-: -0.49% NH4: 0.04% OC: -0.02% Pb: 0.17% Si: 0.41% SO_4^{2-}: 0.51% V: 0.30% Zn: 0.23% Multivariate (1) Al: 0.79% Ni: 0.34% SO_4^{2-}: 0.75% Multivariate (2) Al: 0.61% Ni: 0.35% As: 0.58%
Reference: Holloman et al. (2004, 087375) **Period of Study:** 1999-2001 **Location:** 7 North Carolina counties	Outcome (ICD10): Mortality: Cardiovascular (I00-I99) **Study Design:** Time-series **Statistical Analyses:** 3-stage Bayesian hierarchical model **Age Groups:** >16	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI)** **lag:** 2.5% (-3.9 to 9.6) 0 4.0% (-3.3 to 12.2) 1 11.4% (2.8-19.8) 2 -1.1% (-7.5 to 5.2) 3

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Hopke et al. (2006, 088390) **Period of Study:** Washington, DC: Aug 1988-Dec 1997. Phoenix, Arizona: Mar 1995-Jun 1998 **Location:** Washington, DC and surrounding counties Phoenix, Arizona	**Outcome:** Mortality: Total (nonaccidental) Cardiovascular Cardiovascular-Respiratory **Study Design:** Source-apportionment **Statistical Analyses:** Receptor modeling **Age Groups:** All ages	**Pollutant:** Source-apportioned $PM_{2.5}$: Washington, DC: Soil Traffic Secondary Sulfate Nitrate Residual Oil Wood Smoke Sea Salt Incinerator Primary Coal Phoenix, Arizona: Crustal Traffic Vegetation and Wood Burning Secondary Sulfate Metals Sea Salt Primary Coal **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR **Copollutant (correlation):** NR	The study does not present quantitative results.
Reference: Ito et al. (2006, 088391) **Period of Study:** Aug 1988-Dec 1997 **Location:** Washington, DC and surrounding counties	**Outcome:** Mortality: Total (nonaccidental) Cardiovascular Cardiovascular-Respiratory **Study Design:** Time-series Source-apportionment **Statistical Analyses:** Poisson GLM, natural splines **Age Groups:** All ages	**Pollutant:** Source-apportioned $PM_{2.5}$: Soil Traffic Secondary Sulfate Nitrate Residual Oil Wood Smoke Sea Salt Incinerator Primary Coal **Averaging Time:** 24-h avg **Mean (SD):** 17.8 (8.7) **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** $PM_{2.5}$ = 28.7 µg/m^3 $PM_{2.5}$ Sources 5-95th = Not reported **% Increase (Lower CI, Upper CI) lag:** Secondary sulfate (variance-weighted mean percent excess mortality) 6.7% (1.7, 11.7) 3 Primary coal-related $PM_{2.5}$ (mean percent excess mortality) 5.0% (1.0, 9.1) 3 Residual oil (mean percent excess mortality) 2.7% (-1.1, 6.5) 2 Traffic-related $PM_{2.5}$ (mean percent excess mortality) 2.6% (-1.6, 6.9) NR Soil-related $PM_{2.5}$ (mean percent excess mortality) 2.1% (-0.8, 4.9) NR **$PM_{2.5}$ Sensitivity analysis:** 2 df/yr: 7.9% (3.3, 12.6) 3 4 df/yr: 8.3% (3.7, 13.1) 3 8 df/yr: 8.3% (3.7, 13.2) 3 16 df/yr: 8.1% (3.1, 13.2) 3
Reference: Kan et al. (2007, 091267) **Period of Study:** Mar 2004-Dec 2005 **Location:** Shanghai, China	**Outcome (ICD10):** Mortality: Total (nonaccidental) (A00-R99) Cardiovascular (I00-I99) Respiratory (J00-J98) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, penalized splines **Age Groups:** All ages	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** 52.3 (1.57) **Range (Min, Max):** (2.0, 330.3) **Copollutant (correlation):** PM_{10}: r = 0.84 $PM_{10-2.5}$: r = 0.48 O_3: r = 0.31	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI)** **lag:** Total: 0.36% (0.11, 0.61) 0-1 Cardiovascular: 0.41% (0.01, 0.82) 0-1 Respiratory: 0.95% (0.16, 1.73) 0-1

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Kettunen et al. (2007, 091242) **Period of Study:** 1998-2004 **Location:** Helsinki, Finland	**Outcome (ICD10):** Mortality: Stroke (I60-I61, I63-I64) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, penalized thin-plate splines **Age Groups:** ≥ 65	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Median (SD) unit:** Cold Season: 8.2 Warm Season: 7.8 **Range (Min, Max):** Cold Season: (1.1, 69.5) Warm Season: (1.1, 41.5) **Copollutant:** O_3 CO NO_2 PM_{10} $PM_{10-2.5}$ UFP	**Increment:** Cold Season: 6.7 µg/m^3 Warm Season: 5.7 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Cold Season -0.19% (-3.77, 3.51) 0 -0.17% (-3.73, 3.52) 1 0.59% (-2.95, 4.26) 2 0.46% (-3.10, 4.15) 3 Warm Season 6.86% (0.37, 13.78) 0 7.40% (1.33, 13.84) 1 4.01% (-1.79, 10.14) 2 -1.72% (-7.38, 4.29) 3
Reference: Klemm et al. (2004, 056585) **Period of Study:** Aug 1998-Jul 2000 **Location:** Fulton and DeKalb counties, Georgia (ARIES)	**Outcome:** Mortality: Nonaccidental (<800) Cardiovascular (390-459) Respiratory (460-519) Cancer (140-239) **Study Design:** Time-series **Statistical Analyses:** Poisson GLM, natural cubic splines **Age Groups:** <65 ≥ 65	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** 19.62 (8.32) **Range (Min, Max):** (5.29, 48.01) **Copollutant:** $PM_{10-2.5}$ O_3 NO_2 CO SO_2 Acid EC OC SO_4 Oxygenated Hydrocarbons Nonmethane hydrocarbons NO_3	**Increment:** NR **β (SE) lag:** Quarterly Knots: $PM_{2.5}$: 0.00398 (0.00161) 0-1 Monthly Knots: $PM_{2.5}$: 0.00544 (0.00184) 0-1 Biweekly Knots: $PM_{2.5}$: 0.00369 (0.00201) 0-1
Reference: Lippmann et al. (2006, 091165) **Period of Study:** 2000-2003 **Location:** 60 U.S. cities (NMMAPS)	**Outcome:** Mortality: Nonaccidental (<800) **Study Design:** Time-series **Statistical Analyses:** Poisson GLM **Age Groups:** All ages	**Pollutant:** Speciated Fine PM: Al, Ar, Cr, Cu, EC, Fe, Mn, Ni, Nitrate, OC, Pb, Se, Si, Sulfate, V, Zn **Averaging Time:** Annual avg **Mean (SD):** R **Range (Min, Max):** NR	The study does not present quantitative results.
Reference: Mar et al. (2005, 087566) **Period of Study:** 1995-1997 **Location:** Phoenix, Arizona	**Outcome:** Mortality: Nonaccidental (<800) Cardiovascular (390-448) **Study Design:** Time-series **Statistical Analyses:** Poisson GLM **Age Groups:** ≥ 65	**Pollutant:** Source-apportioned $PM_{2.5}$: Soil Traffic Secondary Sulfate Nitrate Residual Oil Wood Smoke Sea Salt Incinerator Primary Coal **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR	**Increment:** $PM_{2.5}$ Sources 5-95th = NR **% Increase (median percent excess risk) lag:** Secondary sulfate: 16.0% 0 Traffic: 13.2% 1 Copper (Cu) smelter: 12.0% 0 Sea salt: 10.2% 5 Biomass/wood combustion: 8.6% 3

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Ostro et al. (2006, 087991) **Period of Study:** Jan 1999-Dec 2002 **Location:** 9 California counties (CALFINE)	**Outcome (ICD10):** Mortality: Total mortality (respiratory, cardiovascular, ischemic heart disease, diabetes) Respiratory (J00-J98) Cardiovascular (I00-I99) Ischemic heart disease (I20-I25) Diabetes (E10-E14) **Study Design:** Time-series **Statistical Analyses:** Poisson, natural splines and penalized splines **Age Groups:** All ages >65 yr	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** Contra Costa: 14 Fresno: 23 Kern: 22 Los Angeles: 21 Orange: 21 Riverside: 29 Sacramento: 14 Santa Clara: 15 San Diego: 16 **Range (Min, Max):** Contra Costa: (1, 77) Fresno: (1, 160) Kern: (1, 155) Los Angeles: (4, 85) Orange: (4, 114) Riverside: (2, 120) Sacramento: (1, 108) Santa Clara: (2, 74) San Diego: (0, 66) **Copollutant (correlation):** NO_2 r = 0.56 CO r = 0.60 O_3 (1h) r = -0.14 O_3 (8h) r = -0.22	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Penalized splines All ages: All-cause: 0.2% (-0.2, 0.7) 2 0.6% (0.2, 1.0) 0-1 Cardiovascular: 0.3% (-0.1, 0.7) 2 0.6% (0.0, 1.1) 0-1 Respiratory: 1.3% (0.1, 2.6) 2 2.2% (0.6, 3.9) 0-1 >65: All-cause: 0.2% (-0.2, 0.7) 2 0.7% (0.2, 1.1) 0-1 Ischemic heart disease: 0.3% (-0.5, 1.0) 0-1 Males: 0.5% (-0.2, 1.2) 0-1 Females: 0.8% (0.3, 1.3) 0-1 Whites: 0.8% (0.2, 1.3) 0-1 Blacks: 0.1% (-0.9, 1.2) 0-1 Hispanics: 0.8% (-0.1, 1.6) 0-1 In hospital: 0.6% (-0.1, 1.3) 0-1 Out of hospital: 0.6% (0.1, 1.1) 0-1 High school graduates: 0.4% (0.0, 0.8) 0-1 Non-high school graduates: 0.9% (-0.1, 1.9) 0-1 Natural splines All cause 4 df: 0.5% (-0.1, 1.1) 0-1 8 df: 0.4% (-0.1, 0.9) 0-1 12 df: 0.3% (-0.1, 0.7) 0-1 Cardiovascular 4 df: 0.4% (-0.2, 0.9) 0-1 8 df: 0.1% (-0.5, 0.6) 0-1 12 df: 0.0% (-0.6, 0.6) 0-1 Respiratory 4 df: 2.1% (0.2, 4.1) 0-1 8 df: 1.6% (-0.5, 3.6) 0-1 12 df: 1.3% (-0.3, 2.9) 0-1 >65 All cause 4 df: 0.7% (0.0, 1.3) 0-1 8 df: 0.4% (-0.1, 0.9) 0-1 12 df: 0.3% (-0.1, 0.8) 0-1

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Ostro et al. (2007, 091354) **Period of Study:** $PM_{2.5}$ speciation analysis: Jan 2000-Dec 2003. $PM_{2.5}$ analysis: Jan 1999-Dec 2003 **Location:** 6 California counties (2000-2003). 9 California counties (1999-2003) (CALFINE)	**Outcome (ICD10):** Mortality: Total (nonaccidental) mortality Respiratory (J00-J98) Cardiovascular (I00-I99) **Study Design:** Time-series **Statistical Analyses:** Poisson, natural splines **Age Groups:** >65	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** 2000-2003: 19.28 1999-2003: 18.6 **Range (Min, Max): NR** **Copollutant (correlation):** EC: r = 0.53 OC: r = 0.62 NO_3: r = 0.65 SO_4: r = 0.32 Al: r = 0.02 Br: r = 0.54 Ca: r = 0.23 Cl: r = 0.15 Cu: r = 0.23 Fe: r = 0.38 K: r = 0.52 Mn: r = 0.21 Ni: r = 0.11 Pb: r = 0.27 S: r = 0.35 Si: r = 0.16 Ti: r = 0.24 V: r = 0.20 Zn: r = 0.51	**Increment:** 14.6 µg/m^3 **% Increase (Lower CI, Upper CI)** **lag:** Cardiovascular 1.6% (0.0, 3.1) 3 **Notes:** The study does not present all estimates quantitatively.
Reference: Ostro et al. (2008, 097971) **Period of Study:** Jan 2000-Dec 2003 **Location:** 6 California counties	**Outcome (ICD10):** Mortality: Cardiovascular (I00-I99) **Study Design:** Time-series **Statistical Analyses:** Poisson, natural cubic splines and natural splines **Age Groups:**	**Pollutant:** $PM_{2.5}$, EC, OC, NO_3, SO_4, Ca, Cl, Cu, Fe, K, S, Si, Ti, Zn **Averaging Time:** 24-h avg **Mean (SD):** $PM_{2.5}$: 19.28 EC: 0.966 OC: 7.129 NO_3: 5.415 SO_4: 1.908 Ca: 0.080 Cl: 0.094 Cu: 0.007 Fe: 0.124 K: 0.117 S: 0.648 Si: 0.168 Ti: 0.009 Zn: 0.012 **Range (95th):** $PM_{2.5}$: 46.91 EC: 2.57 OC: 15.91 NO_3: 17.46 SO_4: 5.18 Ca: 0.20 Cl: 0.41 Cu: 0.02 Fe: 0.34 K: 0.26 S: 1.70 Si: 0.43 Ti: 0.02 Zn: 0.04	The study does not present quantitative results.
Reference: Perez et al. (2008, 156020) **Period of Study:** Mar 2003-Dec 2005 **Location:** Barcelona, Spain	**Outcome:** Respiratory mortality **Study Design:** Cohort **Covariates:** Temperature, humidity **Statistical Analysis:** Autoregressive Poisson regression models **Statistical Package:** NR **Age Groups:** All deaths	**Pollutant:** $PM_{2.5-1}$ **Averaging Time:** 24 h **Mean (SD) Unit:** 5.5 (3.8) µg/m^3 **Range (Min, Max):** 0.6, 45.5 **Copollutant:** $PM_{10-2.5}$, PM_1	**Increment:** 10 µg/m^3 **Odds Ratio (95%CI) lag** Avg L0-1: 0.998 (0.849-1.174), p = 0.981 L1: 1.014 (0.886-1.161), p = 0.838 L2: 1.295 (1.141-1.470), p = 0.000 Multi-pollutant Model Avg L0-1: 0.987 (0.806-1.208), p = 0.898 L1: 1.022 (0.859-1.214), p = 0. L2: 1.206 (1.028-1.416), p = 0.022

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Perez et al. (2008, 156020) **Period of Study:** Mar 2003-Dec 2005 **Location:** Barcelona, Spain	**Outcome:** Cardiovascular mortality **Study Design:** Cohort **Covariates:** Temperature, humidity **Statistical Analysis:** Autoregressive Poisson regression models **Statistical Package:** NR **Age Groups:** All deaths	**Pollutant:** $PM_{2.5-1}$ **Averaging Time:** 24 h **Mean (SD) Unit:** 5.5 (3.8) µg/m^3 **Range (Min, Max):** 0.6, 45.5 **Copollutant:** $PM_{10-2.5}$, PM_1	**Increment:** 10 µg/m^3 **Odds Ratio (95%CI) lag** Avg L0-1: 1.100 (1.002-1.207), p = 0.046 L1: 1.112 (1.031-1.200), p = 0.006 L2: 1.078 (0.999-1.163), p = 0.052 Multi-pollutant Model Avg L0-1: 0.994 (0.885-1.116), p = 0.920 L1: 0.984 (0.892-1.086), p = 0.754 L2: 0.981 (0.891-1.079), p = 0.688
Reference: Perez et al. (2008, 156020) **Period of Study:** Mar 2003-Dec 2005 **Location:** Barcelona, Spain	**Outcome:** Cerebrovascular mortality **Study Design:** Cohort **Covariates:** Temperature, humidity **Statistical Analysis:** Autoregressive Poisson regression models **Statistical Package:** NR **Age Groups:** All deaths	**Pollutant:** $PM_{2.5-1}$ **Averaging Time:** 24 h **Mean (SD) Unit:** 5.5 (3.8) µg/m^3 **Range (Min, Max):** 0.6, 45.5 **Copollutant:** $PM_{10-2.5}$, PM_1	**Increment:** 10 µg/m^3 **Odds Ratio (95%CI) lag** Avg L0-1: 1.083 (0.897-1.307), p = 0.406 L1: 1.121 (0.964-1.303), p = 0.140 L2: 0.984 (0.841-1.152), p = 0.839 Multi-pollutant Model Avg L0-1: 0.899 (0.712-1.135), p = 0.371 L1: 0.905 (0.743-1.102), p = 0.321 L2: 0.868 (0.711-1.060), p = 0.165
Reference: Rainham et al. (2005, 088676) **Period of Study:** 1981-1999 **Location:** Toronto, Canada	**Outcome:** Mortality: Total (nonaccidental) (<800) Cardiorespiratory (390-459 480-519) Other-causes **Study Design:** Time-series **Statistical Analyses:** Poisson GLM, natural splines **Age Groups:** All ages	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** All yr: 17.0 (8.7) Winters (Dec-Feb): 17.2 (6.8) Summers (Jun-Aug): 18.8 (10.2) **Range (Min, Max):** NR **Copollutant:** CO NO_2 SO_2 O_3	**Increment:** NR **% Increase (Lower CI, Upper CI) lag:** Winter and Winter Synoptic Events Winter Total: 0.998% (0.997, 1.000) 2 Cardiorespiratory: 0.998 (0.996, 1.000) 2 Other: 0.998% (0.996, 1.000) 2 Dry Moderate Total: 1.001% (0.996, 1.007) 1 Cardiorespiratory: 1.005 (0.998, 1.011) 1 Other: 0.997% (0.989, 1.006) 0 Dry Polar Total: 0.998% (0.995, 1.001) 2 Cardiorespiratory: 0.995 (0.991, 0.999) 2 Other: 1.002% (0.998, 1.005) 1 Moist Moderate Total: 0.998% (0.993, 1.002) 2 Cardiorespiratory: 1.003 (0.995, 1.010) 1 Other: 0.997% (0.991, 1.004) 1 Moist Polar Total: 1.001% (0.998, 1.005) 1 Cardiorespiratory: 1.002 (0.997, 1.007) 2 Other: 1.003% (0.999, 1.007) 0 Moist Tropical Total: 1.007% (0.965, 1.203) 0 Cardiorespiratory: 1.123 (1.031, 1.224) 2 Other: 1.248% (1.123, 1.387) 0 Transition Total: 1.003% (0.996, 1.009) 1 Cardiorespiratory: 0.996 (0.987, 1.004) 0 Other: 0.997% (0.990, 1.004) 0 Summer and summer Synoptic Events Summer Total: 1.000% (1.000, 1.001) 0 Cardiorespiratory: 1.001 (1.000, 1.002) 0

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
			Other: 1.001% (1.000, 1.002) 0 Dry Moderate Total: 1.001% (0.999, 1.002) 2 Cardiorespiratory: 1.002 (0.999, 1.004) 2 Other: 0.999% (0.997, 1.002) 0 Dry Polar Total: 1.002% (0.999, 1.005) 2 Cardiorespiratory: 0.996 (0.991, 1.000) 0 Other: 1.003% (0.999, 1.007) 2 Dry Tropical Total: 1.016% (1.006, 1.027) 0 Cardiorespiratory: 1.017 (1.005, 1.030) 2 Other: 1.017% (1.003, 1.031) 0 Moist Moderate Total: 1.002% (1.000, 1.004) 2 Cardiorespiratory: 1.003 (0.999, 1.006) 2 Other: 1.004% (1.001, 1.006) 0 Moist Polar Total: 1.005% (0.998, 1.011) 1 Cardiorespiratory: 1.008 (0.997, 1.018) 0 Other: 1.003% (0.995, 1.011) 1 Moist Tropical Total: 0.999% (0.997, 1.001) 2 Cardiorespiratory: 0.996 (0.993, 1.000) 2 Other: 0.998% (0.995, 1.001) 1 Transition Total: 1.005% (0.996, 1.014) 1 Cardiorespiratory: 1.007 (0.994, 1.020) 1 Other: 1.002% (0.996, 1.008) 2

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Rosenthal et al. (2008, 156925) **Period of Study:** Jul 2002-Jul 2006 **Location:** Indianapolis, Indiana	**Outcome:** Non-Dead on Arrival (DOA) Out-of-Hospital Cardiac Arrests (OHCA) Witnessed non-DOA OHCA **Study Design:** Case-crossover **Statistical Analyses:** Time-stratified conditional logistic regression **Age Groups:** All ages Study Population: Non-DOA OHCA: 1,374 Witnessed non-DOA OHCA: 511	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg Hourly **Mean (SD):** NR IQR (25th, 75th): All non-DOA All heart rhythms: (9.4, 19.5) OHCA: (9.6, 19.5) Referents: (9.3, 19.5) Asystole: (9.2, 19.4) OHCA: (9.2, 19.7) Asystole: (9.2, 19.2) Witnessed non-DOA hourly All heart rhythms: (8.8, 20.7) OHCA: (8.8, 21.9) Referents: (8.8, 20.4) Asystole: (8.5, 19.8) OHCA: (9.4, 21.3) Referents: (8.3, 19.1) **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **Hazard Ratio (Lower CI, Upper CI) lag:** Out-of-Hospital non-DOA Cardiac Arrests All 1.02 (0.94, 1.11) 0 1.00 (0.92, 1.08) 1 0.98 (0.90, 1.06) 2 1.00 (0.92, 1.08) 3 1.02 (0.92, 1.12) 0-1 avg 1.01 (0.91, 1.12) 0-2 avg 1.02 (0.91, 1.14) 0-3 avg Asystole 1.03 (0.91, 1.17) 0 1.00 (0.89, 1.13) 1 1.01 (0.90, 1.13) 2 0.98 (0.87, 1.10) 3 1.03 (0.90, 1.18) 0-1 avg 1.05 (0.90, 1.22) 0-2 avg 1.04 (0.88, 1.22) 0-3 avg Vfib 1.08 (0.92, 1.28) 0 1.02 (0.87, 1.21) 1 0.96 (0.80, 1.14) 2 1.10 (0.93, 1.31) 3 1.06 (0.88, 1.28) 0-1 avg 1.01 (0.82, 1.25) 0-2 avg 1.05 (0.83, 1.32) 0-3 avg PEA 0.92 (0.77, 1.08) 0 0.98 (0.83, 1.15) 1 0.96 (0.82, 1.14) 2 0.95 (0.82, 1.10) 3 0.96 (0.80, 1.17) 0-1 avg 0.98 (0.80, 1.21) 0-2 avg 0.98 (0.78, 1.21) 0-3 avg Witnessed Out-of-Hospital non-DOA Cardiac Arrests (lag represents h in which or h before OHCA occurred) All: 1.12 (1.01, 1.25) 0 White: 1.18 (1.03, 1.35) 0 60-75: 1.25 (1.05, 1.49) 0 Asystole: 1.22 (1.01, 1.59) 0
Reference: Schwartz et al. (2002, 025312) **Period of Study:** 1979-Late 1980's **Location:** 6 U.S. cities	**Outcome:** Mortality: Total (nonaccidental) (<800) **Study Design:** Time-series **Statistical Analyses:** Hierarchical modeling: 1. Poisson GAM, LOESS 2. Multivariate modeling **Age Groups:** All ages	**Pollutant:** $PM_{2.5}$, $PM_{2.5}$ sources (Traffic, Coal, Residual Oil) **Averaging Time:** 24-h avg **Mean (SD):** $PM_{2.5}$ Range: (Madison: 11.3 to Steubenville: 30.5) Traffic Range: (Steubenville: 1.5 to Boston: 4.8) Coal Range: (Madison: 4.9 to Steubenville: 19.2) Residual Oil Range: (Boston: 0.5 to Steubenville: 0.9) **Range (Min, Max):** NR	The study does not present quantitative results.

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Simpson et al. (2005, 087438) **Period of Study:** Jan 1996-Dec 1999 **Location:** 4 Australian cities	**Outcome:** Mortality: Nonaccidental (<800) Cardiovascular (390-459) Respiratory (460-519) **Study Design:** Time-series meta-analysis **Statistical Analyses:** Poisson GAM, natural splines Poisson GLM, natural splines **Age Groups:** All ages	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** Brisbane: $PM_{2.5}$: 7.50 Sydney: $PM_{2.5}$: 9.00 Melbourne: $PM_{2.5}$: 9.30 Perth: $PM_{2.5}$: 9.0 µg/m^3 **Range (Min, Max):** Brisbane: $PM_{2.5}$: (1.9, 19.7) Sydney: $PM_{2.5}$: (2.4, 35.3) Melbourne: $PM_{2.5}$: (2.7, 35.1) Perth: $PM_{2.5}$: (2.8, 37.3) **Copollutant:** CO, NO_2	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** $PM_{2.5}$ 0.9% (-0.7, 2.5)
Reference: Slaughter et al. (2005, 073854) **Period of Study:** Jan 1995-Dec 1999 **Location:** Spokane, Washington	**Outcome:** Mortality: Nonaccidental (<800) **Study Design:** Time-series **Statistical Analyses:** Poisson GLM, natural splines **Age Groups:** All ages	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (9th, 95th):** $PM_{2.5}$: (4.2, 20.2) **Copollutant (correlation):** $PM_{2.5}$: r = 0.95 PM_{10}: r = 0.62 $PM_{10-2.5}$: r = 0.31 CO: r = 0.62	**Increment:** $PM_{2.5}$: 10 µg/m^3 PM_{10}: 25 µg/m^3 **Relative Risk (Lower CI, Upper CI) lag:** $PM_{2.5}$ (0.97, 1.04) 1 0.99 (0.96, 1.03) 2 1.00 (0.97, 1.03) 3
Reference: Stieb et al. (2002, 025205) **Period of Study:** Publication dates of studies: 1985-Dec 2000 Mortality series: 1958-1999 **Location:** 40 cities (11 Canadian cities, 19 U.S. cities, Santiago, Amsterdam, Erfurt, 7 Korean cities)	**Outcome:** Mortality: All-cause (nonaccidental) **Study Design:** Meta-analysis **Statistical Analyses:** Random effects model **Age Groups:** All ages	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **Mean (SD):** NR **Range (Min, Max):** NR **Copollutant:** Varied between studies: O_3 SO_2 NO_2 CO	**Increment:** $PM_{2.5}$: 18.3 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Single-pollutant models 18 studies $PM_{2.5}$: 2.0% (1.2, 2.7) Multipollutant models 8 studies $PM_{2.5}$: 1.3% (0.6, 1.9)
Reference: Sullivan et al. (2003, 043156) **Period of Study:** 1985-1994 **Location:** Western Washington	**Outcome:** Out-of-hospital cardiac arrest **Study Design:** Case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups:** 19-79 Study Population: Out-of-hospital cardiac arrests: 1,206	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Median (SD) unit:** PM_{10} Lag 0: 28.05 Lag 1: 27.97 Lag 2: 28.40 **Range (Min, Max):** PM_{10}: (7.38, 89.83) **Copollutant (correlation):** SO_2, CO **Notes:** Study used nephelometry to measure particles and equated the measurements to $PM_{2.5}$ concentrations.	**Increment:** PM_{10}: 16.51 µg/m^3 $PM_{2.5}$: 13.8 µg/m^3 **Odds Ratio (Lower CI, Upper CI) lag:** Overall PM_{10} 1.05 (0.87, 1.27) 0 0.91 (0.75, 1.11) 1 1.03 (0.82, 1.28) 2 $PM_{2.5}$ 0.94 (0.88, 1.01) 0 0.94 (0.88, 1.02) 1 1.00 (0.93, 1.08) 2 $PM_{2.5}$: Stratified by subject characteristics ≤ 55 0.95 (0.76, 1.18) 0 0.89 (0.71, 1.12) 1 0.95 (0.75, 1.20) 2 >55 0.94 (0.88, 1.02) 0 0.95, (0.88, 1.03) 1 1.01 (0.93, 1.10) 2 Male 0.95 (0.87, 1.03) 0 0.96 (0.88, 1.04) 1 1.01 (0.93, 1.10) 2 Female 0.93 (0.82, 1.06) 0 0.92 (0.80, 1.07) 1 0.98 (0.83, 1.15) 2 White

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
			0.93 (0.86, 1.01) 0 0.95 (0.88, 1.03) 1 1.03 (0.95, 1.12) 2 Non-White 1.09 (0.88, 1.36) 0 0.96 (0.75, 1.22) 1 0.88 (0.68, 1.14) 2 Current Smoker 1.05 (0.92, 1.19) 0 0.98 (0.86, 1.12) 1 1.06 (0.92, 1.22) 2 Nonsmoker 0.93 (0.85, 1.01) 0 0.93 (0.85, 1.02) 1 0.97 (0.89, 1.07) 2 Drinker 1.13 (0.92, 1.39) 0 1.15 (0.94, 1.41) 1 1.16 (0.92, 1.45) 2 Nondrinker 0.94 (0.86, 1.03) 0 0.93 (0.85, 1.02) 1 1.00 (0.92, 1.10) 2 Activity Level-Unrestricted 0.96 (0.89, 1.03) 0 0.96 (0.89, 1.04) 1 1.01 (0.93, 1.10) 2 Activity Level-Limited 0.82 (0.56, 1.20) 0 0.70 (0.45, 1.09) 1 0.97 (0.65, 1.43) 2 $PM_{2.5}$: Stratified by disease state Heart disease 0.95 (0.87, 1.04) 0 0.97 (0.89, 1.07) 1 1.06 (0.96, 1.16) 2 Ischemic Heart Disease 0.91 (0.80, 1.04) 0 0.97 (0.84, 1.11) 1 1.09 (0.95, 1.26) 2 Active Angina 0.98 (0.81, 1.20) 0 1.07 (0.88, 1.31) 1 1.08 (0.89, 1.32) 2 Congestive Heart Failure 0.91 (0.80, 1.03) 0 0.99 (0.87, 1.13) 1 1.11 (0.97, 1.26) 2 Supraventricular tachycardia 1.41 (0.97, 2.04) 0 1.55 (1.07, 2.25) 1 1.23 (0.84, 1.82) 2 Bradycardia 0.97 (0.64, 1.46) 0 1.29 (0.85, 1.96) 1 1.30 (0.84, 2.01) 2 Asthma (0.80, 1.27) 0 0.92 (0.71, 1.19) 1 0.93 (0.71, 1.22) 2 COPD 1.00 (0.86, 1.17) 0 1.04 (0.88, 1.23) 1 1.08 (0.92, 1.28) 2 $PM_{2.5}$: Persons with prior recognized heart disease stratified by smoking status All heart disease Current smoker 1.08 (0.92, 1.26) 0 1.06 (0.89, 1.26) 1 1.29 (1.06, 1.55) 2 Nonsmoker 0.91 (0.82, 1.02) 0 0.94 (0.84, 1.05) 1 0.99 (0.88, 1.11) 2 Ischemic Heart Disease

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
			Current smoker 1.06 (0.84, 1.34) 0 0.99 (0.75, 1.30) 1 1.39 (1.04, 1.86) 2 Nonsmoker 0.86 (0.73, 1.02) 0 0.93 (0.78, 1.11) 1 0.99 (0.83, 1.18) 2 Active Angina Current smoker 1.28 (0.88, 1.86) 0 1.26 (0.79, 2.01) 1 1.57 (0.99, 2.48) 2 Nonsmoker 0.87 (0.68, 1.12) 0 0.93 (0.72, 1.21) 1 0.91 (0.70, 1.17) 2 Congestive Heart Failure Current smoker 1.00 (0.79, 1.28) 0 1.03 (0.78, 1.35) 1 1.46 (1.10, 1.96) 2 Nonsmoker 0.88 (0.76, 1.03) 0 0.96 (0.82, 1.12) 1 0.99 (0.84, 1.17) 2 Supraventricular tachycardia Current smoker 12.80 (1.05, 156.57) 0 2.56 (0.82, 7.99) 1 1.15 (0.46, 2.86) 2 Nonsmoker 1.19 (0.74, 1.90) 0 1.35 (0.87, 2.10) 1 1.15 (0.73, 1.82) 2 Bradycardia Nonsmoker 0.84 (0.14, 4.95) 0 0.42 (0.03, 5.34) 1 0.51 (0.05, 5.79) 2 Nonsmoker 0.99 (0.63, 1.55) 0 1.42 (0.90, 2.24) 1 1.39 (0.88, 2.20) 2
Reference: Thurston et al. (2005, 097949) **Period of Study:** Washington, DC: Aug 1988-Dec 1997. Phoenix, Arizona: 1995-1997 **Location:** Washington, DC and surrounding counties Phoenix, Arizona	**Outcome:** Mortality: Total (nonaccidental) (<800) Cardiovascular (390-448) **Study Design:** Time-series Source-apportionment **Statistical Analyses:** Poisson GLM, natural splines **Age Groups:** Washington, DC: All ages Phoenix, Arizona: ≥ 65	**Pollutant:** $PM_{2.5}$, and source apportioned $PM_{2.5}$: Crustal Traffic Secondary SO_4 Secondary NO_3 Wood Oil Salt Incinerator **Averaging Time:** 24-h avg **Median (SD) unit:** NR **Range (Min, Max):** NR **Copollutant:** $PM_{2.5}$ species (Na, Mg, Al, Si, P, S, Cl, K, Ca, Sc, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Ga, Ge, As, Se, Br, Rb, Sr, Y, Zr, Mo, Rh, Pd, Ag, Cd, Sn, Sb, Te, I, Cs, Ba, La, W, Au, Hg, Pb, OC, EC)	**Increment:** 10 µg/m^3 **% Increase:** Total (nonaccidental): Secondary sulfate: Phoenix: 5.2% Washington, DC: 3.8% Motor vehicles: Phoenix: 0.9% Washington, DC: 4.2%

Study	Design & Methods	Concentrations1	Effect Estimates (95% CI)
Reference: Villeneuve et al. (2003, 055051) **Period of Study:** 1986-1999 **Location:** Vancouver, Canada	**Outcome:** Mortality: Nonaccidental (<800) Cardiovascular (401-440) Respiratory (460-519) Cancer (140-239) **Study Design:** Time-series **Statistical Analyses:** Poisson, natural splines **Age Groups:** ≥ 65	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** Daily $PM_{2.5}$: 7.9 Every 6th Day $PM_{2.5}$: 11.6 **Range (Min, Max):** Daily $PM_{2.5}$: (2.0, 32.0) Every 6th Day $PM_{2.5}$: (1.8, 43.0) **Copollutant:** SO_2 CO NO_2 O_3	**Increment:** $PM_{2.5}$ (Daily): 9.0 µg/m^3 $PM_{2.5}$ (6th Day): 15.7 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Nonaccidental $PM_{2.5}$ (Daily) -0.1% (-5.1, 5.2) 0-2 avg -0.1% (-4.1, 4.1) 0 -0.3% (-4.2, 3.7) 1 0.5% (-3.3, 4.4) 2 $PM_{2.5}$ (6th Day) -2.8% (-7.5, 2.1) 0 2.0% (-2.6, 7.0) 1 4.5% (-0.3, 9.5) 2 Cardiovascular $PM_{2.5}$ (Daily) 1.5% (-6.1, 9.7) 0-2 avg 4.3% (-1.7, 10.7) 0 -1.0% (-7.0, 5.4) 1 -0.5% (-6.5, 5.9) 2 $PM_{2.5}$ (6th Day) -1.5% (-8.9, 6.5) 0 -2.0% (-9.3, 5.8) 1 3.0% (-4.2, 10.8) 2 Respiratory $PM_{2.5}$ (Daily) -0.7% (-13.1, 13.4) 0-2 avg 6.7% (-3.7, 18.3) 0 -3.0% (-12.8, 7.9) 1 -5.8% (-15.2, 4.7) 2 $PM_{2.5}$ (6th Day) 10.0% (-4.7, 26.8) 0 8.3% (-5.4, 24.0) 1 0.3% (-12.4, 14.9) 2 Cancer $PM_{2.5}$ (Daily) -0.3% (-9.4, 9.8) 0-2 avg -4.5% (-11.2, 2.8) 0 2.7% (-5.0, 11.0) 1 2.5% (-5.1, 10.7) 2 $PM_{2.5}$ (6th Day) -5.1% (-13.8, 4.5) 0 -0.3% (-9.7, 11.0) 1 0.2% (-9.1, 10.4) 2
Reference: Wilson et al. (2007, 157149) **Period of Study:** 1995-1997 **Location:** Phoenix, Arizona	**Outcome:** Cardiovascular **Study Design:** Time-series **Statistical Analyses:** Poisson GAM, nonparametric smoothing spline **Age Groups:** >25	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **% Excess Risk (Lower CI, Upper CI) lag:** Central Phoenix: 11.5% (2.8, 20.9) 0-5 ma 6.6% (1.1, 12.5) 1 2.0% (-3.2, 7.5) 2 Middle Phoenix: 2.9% (-4.9, 11.4) 0-5 ma 6.4% (1.1, 11.9) 2 Outer Phoenix: 1.6% (-6.2, 10.0) 0-5 ma

[1]All units expressed in µg/m^3 unless otherwise specified.

Table E-19. Short-term exposure-mortality - other PM size fractions.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Perez et al. (2008, 156020) **Period of Study:** Mar 2003-Dec 2005 **Location:** Barcelona, Spain	**Outcome:** Respiratory mortality **Study Design:** Cohort **Covariates:** Temperature, humidity **Statistical Analysis:** Autoregressive Poisson regression models **Statistical Package:** NR **Age Groups:** All deaths	**Pollutant:** PM_1 **Averaging Time:** 24 h **Mean (SD) Unit:** 20.0 (10.3) µg/m^3 **Range (Min, Max):** 1.9, 80.1 **Copollutant:** $PM_{10-2.5}$, $PM_{2.5-1}$	**Increment:** 10 µg/m^3 **Odds Ratio (95%CI) lag** Avg L0-1: 1.005 (0.960-1.053), p = 0.824 L1: 1.012 (0.969-1.056), p = 0.599 L2: 1.042 (0.998-1.087), p = 0.063 Multi-pollutant Model Avg L0-1: 1.007 (0.957-1.059), p = 0.799 L1: 1.008 (0.961-1.058), p = 0.739 L2: 1.010 (0.963-1.059), p = 0.678
Reference: Perez et al. (2008, 156020) **Period of Study:** Mar 2003-Dec 2005 **Location:** Barcelona, Spain	**Outcome:** Cardiovascular mortality **Study Design:** Cohort **Covariates:** temperature, Humidity **Statistical Analysis:** Autoregressive Poisson regression models **Statistical Package:** NR **Age Groups:** All deaths	**Pollutant:** PM_1 **Averaging Time:** 24 h **Mean (SD) Unit:** 20.0 (10.3) µg/m^3 **Range (Min, Max):** 1.9, 80.1 **Copollutant:** $PM_{10-2.5}$, $PM_{2.5-1}$	**Increment:** 10 µg/m^3 **Odds Ratio (95%CI) lag** Avg L0-1: 1.028 (1.000-1.057), p = 0.054 L1: 1.029 (1.003-1.056), p = 0.030 L2: 1.023 (0.996-1.050), p = 0.091 Multi-pollutant Model Avg L0-1: 1.025 (0.995-1.057), p = 0.688 L1: 1.028 (1.000-1.058), p = 0.053 L2: 1.024 (0.995-1.053), p = 0.110
Reference: Perez et al. (2008, 156020) **Period of Study:** Mar 2003-Dec 2005 **Location:** Barcelona, Spain	**Outcome:** Cerebrovascular mortality **Study Design:** Cohort **Covariates:** Temperature, humidity **Statistical Analysis:** Autoregressive Poisson regression models **Statistical Package:** NR **Age Groups:** All deaths	**Pollutant:** PM_1 **Averaging Time:** 24 h **Mean (SD) Unit:** 20.0 (10.3) µg/m^3 **Range (Min, Max):** 1.9, 80.1 **Copollutant:** $PM_{10-2.5}$, $PM_{2.5-1}$	**Increment:** 10 µg/m^3 **Odds Ratio (95%CI) lag** Avg L0-1: 1.037 (0.981-1.097), p = 0.202 L1: 1.056 (1.003-1.113), p = 0.039 L2: 1.020 (0.968-1.075), p = 0.460 Multi-pollutant Model Avg L0-1: 1.042 (0.981-1.107), p = 0.179 L1: 1.063 (1.004-1.124), p = 0.035 L2: 1.034 (0.976-1.095), p = 0.255
Reference: Slaughter et al. (2005, 073854) **Period of Study:** Jan 995-Dec 1999 **Location:** Spokane, Washington	**Outcome:** Mortality: Nonaccidental (<800) **Study Design:** Time-series **Statistical Analyses:** Poisson GLM, natural splines **Age Groups:** All ages	**Pollutant:** PM_1 **Averaging Time:** 24-h avg **Mean (SD):** NR Range (9th, 95th) PM_1: (3.3, 17.6) **Copollutant (correlation):** PM_1 $PM_{2.5}$: r = 0.95 PM_{10}: r = 0.50 $PM_{10-2.5}$: r = 0.19 CO: r = 0.63	This study does not present quantitative results for PM_1.
Reference: Stölzel et al. (2007, 091374) **Period of Study:** Sept 1995-Aug 2001 **Location:** Erfurt, Germany	**Outcome:** Mortality: Total (nonaccidental) (<800) Cardio-respiratory (390-459, 460-519, 785, 786) **Study Design:** Time-series **Statistical Analyses:** Poisson GAM **Age Groups:** All ages	**Pollutant:** $MC_{0.1-0.5}$, $MC_{0.01-2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** $MC_{0.1-0.5}$: 17.6 (14.8) $MC_{0.01-2.5}$: 22.3 (19.2) IQR (25th, 75th): $MC_{0.1-0.5}$: (8.4, 21.5) $MC_{0.01-2.5}$: (10.5, 27.3) **Copollutant (correlation):** $MC_{0.1-0.5}$ NO: r = 0.52 NO_2: r = 0.60 CO: r = 0.58 $MC_{0.01-2.5}$ NO: r = 0.51 NO_2: r = 0.58 CO: r = 0.57	**Increment:** $MC_{0.1-0.5}$: 13.1 µg/m^3 $MC_{0.01-2.5}$: 16.8 µg/m^3 **Relative Risk (Lower CI, Upper CI) lag:** Total (nonaccidental) $MC_{0.1-0.5}$ 1.010 (0.986 1.034) 0 1.006 (0.983 1.029) 1 1.007 (0.985 1.029) 2 0.994 (0.973 1.016) 3

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			1.002 (0.981 1.023) 4 0.997 (0.976 1.018) 5 $MC_{0.01\text{-}2.5}$ 1.007 (0.985 1.030) 0 1.005 (0.984 1.026) 1 1.003 (0.983 1.023) 2 0.989 (0.970 1.009) 3 1.002 (0.982 1.022) 4 0.998 (0.979 1.018) 5 Cardio-respiratory MC0.1-0.5 1.004 (0.977 1.031) 0 1.004 (0.979 1.029) 1 1.001 (0.978 1.026) 2 0.991 (0.967 1.014) 3 1.000 (0.977 1.023) 4 1.000 (0.976 1.023) 5 MC0.01-2.5 1.001 (0.977 1.026) 0 0.999 (0.976 1.022) 1 0.998 (0.976 1.021) 2 0.985 (0.964 1.007) 3 1.001 (0.980 1.022) 4 1.003 (0.981 1.024) 5

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Yamazaki et al. (2007, 090748) **Period of Study:** 1995-1998 **Location:** Hong Kong, China	**Outcome:** Mortality: Intracerebral hemorrhage (431) Ischaemic stroke (434) **Study Design:** Time-stratified case-crossover **Statistical Analyses:** Conditional logistic regression **Age Groups:** ≥ 65	**Pollutant:** PM7 **Averaging Time:** 1-h avg **Mean (SD):** Warmer Months (Apr-Sep): 40.3 Colder Months (Oct-Mar): 39.4 **Range (Min, Max):** NR **Copollutant (correlation):** Warmer Months NO_2: r = 0.46-0.63 Ox: r = -0.14 to 0.20 Colder Months NO_2: 0.42-0.79 Ox: r = -0.36 to -0.14	**Increment:** 30 µg/m^3 **Odds Ratio (Lower CI, Upper CI) lag:** 24-h avg concentrations Intracerebral hemorrhage Warmer months: 1.041 (0.984, 1.102) 0 Colder months: 1.005 (0.951, 1.061) 0 Ischaemic stroke Warmer months: 1.027 (0.993, 1.062) 0 Colder months: 1.005 (0.973, 1.039) 0 Exposure measured jointly as 24-h and 1-h mean concentrations Warmer months Intracerebral hemorrhage 1-h with 200 µg/m^3 threshold: 2.397 (1.476, 3.892) 2 h 24-h: 1.019 (0.960, 1.082) 0 Ischaemic stroke 1-h with 200 µg/m^3 threshold: 1.051 (0.750, 1.472) 2 h 24-h: 1.018 (0.983, 1.055) 0 Warmer months Intracerebral hemorrhage 1-h with 200 µg/m^3 threshold: 0.970 (0.712, 1.322) 2 h 24-h: 1.015 (0.958, 1.075) 0 Ischaemic stroke 1-h with 200 µg/m^3 threshold: 1.040 (0.855, 1.265) 2 h 24-h: 1.003 (0.968, 1.039) 0

[1]All units expressed in µg/m^3 unless otherwise specified.

E.4. Long-Term Exposure and Cardiovascular Outcomes

Table E-20. Long-term exposure - cardiovascular morbidity outcomes - PM_{10}.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Baccarelli et al. (2008, 157984) **Period of Study:** 1995-2005 **Location:** Italy (Lombardy region)	**Outcome (ICD9 and ICD10):** Deep Vein Thrombosis (DVT) Prothrombin time (PT) Activated partial thromboplastin time (aPTT) **Age Groups:** 18-84yrs **Study Design:** Case-control (DVT outcome) Cross-sectional (PT and aPTT outcomes) **N:** 871 cases 1210 controls (randomly selected from friends and nonblood relatives of cases Frequency matched by age to cases) **Statistical Analyses:** Unconditional logistic regression (DVT outcome) Linear regression (PT and aPTT outcomes) **Covariates:** Sex, area of residence, education, factor V Leiden or G20210A prothrombin mutation, current use of oral contraceptives or hormone therapy (Variables controlled using penalized regression splines with 4 df) age, BMI, day of yr (for seasonality), index date, ambient temperature **Season:** covariate **Dose-response Investigated?** Yes **Statistical Package:** STATA v9.0 and R v2.2.0	**Pollutant:** PM_{10} **Averaging Time:** 1 yr (immediately preceding the diagnosis date for cases or the date of examination for controls) assessed other averaging periods presented in supplements (90 days, 180 days, 270 days, 2 yr) **Mean (SD):** NR **Percentiles:** NR **Range (Min, Max):** Range for tertiles of exposure: 1: 12.0-44.2 2: 44.3-48.1 3: 48.2-51.5 **Monitoring Stations:** Monitors from 53 sites exposure assigned by dividing area into 9 regions **Copollutant (correlation):** NR	**PM Increment:** 10 $\mu g/m^3$ **Effect Estimate [Lower CI, Upper CI]: Estimated changes of PT associated with PM_{10}:** Among DVT cases: -0.12 (-0.23, 0.00), p = 0.04 Among Controls: -0.06 (-0.11, 0.00) , p = 0.04 **Estimated changes of aPTT associated with PM_{10}:** Among Controls: -0.09 (-0.19, 0.01) , p = 0.07 Among DVT cases: 0.01 (-0.03, 0.04) , p = 0.78 **Risk of DVT associated with PM_{10} (avg of 1 yr preceding diagnosis/exam date): |** **All subjects:** 1.70 (1.30, 2.23), p < 0.001 **Sex:** Male: 2.07 (1.50, 2.84) , p < 0.001 Female: 1.40 (1.02, 1.92) , p = 0.04 P for interaction: p = 0.02 **Age:** 18-35yrs: 1.57 (1.11, 2.24), p = 0.01 36-50yrs: 1.97 (1.41, 2.77) , p < 0.001 51-84yrs: 1.54 (0.90, 2.63) , p = 0.12 P for interaction: p = 0.99**Premenopausal women with current use of oral contraceptives:** No: 1.53 (0.86, 2.72) , p = 0.14 Yes: 0.87 (0.46, 1.67), p = 0.68 P for interaction: p = 0.11**Postmenopausal women with current use of hormone therapy:** No: 1.60 (0.72, 3.54), p = 0.24 Yes: 0.85 (0.29, 2.45), p = 0.76 P for interaction: p = 0.27**Current use of oral contraceptive or hormone replacement therapy:** No: 1.64 (1.05, 2.57), p = 0.03 Yes: 0.97 (0.58, 1.61), p = 0.89 P for interaction: p = 0.048 **Body Mass Index:** 13.3-22.0: 1.47 (0.97, 2.23), p = 0.07; 22.1-24.9: 1.72 (1.17, 2.54), p = 0.006 25.0-53.3: 1.83 (1.03, 3.24), p = 0.04 P for interaction: p = 0.37 **Education:** Elementary/middle school: 1.93 (1.35, 2.76), p < 0.001 High school: 1.72 (1.24, 2.39), p = 0.001 College: 1.35 (0.74, 2.45), p = 0.33 P for interaction: p = 0.21 **Deficiencies of natural anticoagulant proteins:** None: 1.66 (1.26, 2.18), p < 0.001 Any: 2.56 (0.91, 7.18), p = 0.07 P for interaction: p = 0.41 **Factor V Leiden or G20210A prothrombin mutation:** None: 1.69 (1.27, 2.23), p < 0.001 Any: 1.79 (1.05, 3.05), p = 0.03 P for interaction: p = 0.83 **Hyperhomocysteinemia:**

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			No: 1.66 (1.26, 2.19), p < 0.001 Yes: 2.19 (1.33, 3.61), p = 0.002 P for interaction: p = 0.25 **Any cause of thrombophilia:** No: 1.59 (1.19, 2.13), p = 0.002 Yes: 1.96 (1.34, 2.87), p < 0.001 P for interaction: p = 0.27 **Year of diagnosis:** 1995-97: 1.61 (1.06, 2.46), p = 0.03 1998-00: 1.34 (0.90, 1.99), p = 0.15 2001-05: 2.14 (1.04, 4.39), p = 0.04 P for interaction: p = 0.12 **Risk of DVT associated with PM_{10} over varying averaging times:** 90 days: 0.91 (0.80, 1.03), p = 0.12 180 days: 0.96 (0.82, 1.13), p = 0.63 270 days: 1.26 (1.01, 1.57), p = 0.04 365 days: 1.70 (1.30, 2.23), p = 0.0001 2 yr: 1.47 (1.01, 2.14), p = 0.04 **Risk of DVT associated with PM_{10} (yr preceding diagnosis/exam date) sensitivity analysis to evaluate the effect of different methods for adjusting for long-term trends: Handling of long-term time trends:** Ignored: 1.13 (0.89, 1.42), p = 0.31 Dummy variable for each yr: 1.78 (1.31, 2.44), p = 0.0003 Linear term: 1.32 (1.02, 1.69), p = 0.03 Penalized spline, 2 df: 1.54 (1.19, 2.00), p = 0.001 Penalized spline, 3 df: 1.64 (1.26, 2.14), p = 0.0002 Penalized spline, 4 df: 1.70 (1.30, 2.23), p = 0.0001 Penalized spline, 5 df: 1.70 (1.29, 2.22), p = 0.0002 Penalized spline, 6 df: 1.66 (1.26, 2.19), p = 0.0003 Penalized spline, 7 df: 1.60 (1.21, 2.13), p = 0.001 Penalized spline, 8 df: 1.55 (1.15, 2.10), p = 0.004
Reference: Baccarelli et al. (2009, 188183) **Period of Study:** Jan 1995-Sept 2005 **Location:** Lombardia Region, Italy	**Outcome:** Deep Vein Thrombosis **Study Design:** Case-control **Covariates:** Age, Sex, area of residence, BMI, education, medication use **Statistical Analysis:** Logistic regression **Statistical Package:** Stata	**Pollutant:** PM_{10} Risk of DVT measured with regards to distance of residence from major road. Specific levels of PM_{10} not given.	**Increment:** NA **Relative Risk (95%CI) of DVT** All subjects, age-adjusted: 1.33 (1.03-1.71), p = 0.03 All subjects, adjusted for covariates: 1.47 (1.10-1.96), p = 0.008 All subjects, adjusted for covariates and background PM_{10} exposure: 1.47 (1.11-1.96), p = 0.008

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Calderon-Garciduenas et al. (2008, 156317) **Period of Study:** Children recruited between Jul 2003 and Dec 2004 **Location:** Mexico (northeast or southwest Mexico city or Polotitlan)	**Outcome (ICD9 and ICD10):** Plasma Endothelin-1 (ET-1) and pulmonary arterial pressure (PAP) **Age Groups:** 6-13 yr 7.9 ± 1.3 yr **Study Design:** Cross-sectional **N:** 81 children **Statistical Analyses:** Analysis of variance by parametric one-way analysis of variance and the Newman-Keuls multiple comparison post test, Pearson's correlation **Covariates:** Doesn't appear to have performed multivariable analyses However, collected information on age, place and length of residency, daily outdoor time, household cooking methods, parents' occupational history, family history of atopic illnesses and respiratory disease, and personal history of otolaryngologic and respiratory symptoms **Season:** No **Dose-response Investigated?** No **Statistical Package:** STATA v8.3, or GraphPad Software, Inc.	**Pollutant:** PM_{10} ($\mu g/m^3$) Exposures assessed quantitatively in Mexico City only No monitors in Polotitlan **Averaging Time:** 1, 2, and 7 days before the exam Pollutant concentrations between 0700 and 1900 h were used for the estimates **Mean (SD):** Presented only in figures **Percentiles:** NR **Range (Min, Max):** Presented only in figures **Monitoring Stations:** 4 (2 in northeast and 2 in southwest Mexico City) Residence and school within 5 mi of one of these monitors) **Copollutant (correlation):** O_3	**PM Increment:** NA **Effect Estimate [Lower CI, Upper CI]:** No health effects models with measured PM concentrations were presented Used city of residence to assign exposure No multivariable analyses presented Authors presented (statistically significantly) elevated ET-1 levels among children residing in both areas of Mexico City as compared to Polotitlan (control city): Mean ± SE (pg/mL) Control: 1.23 ± 0.06 Southwest Mexico City: 2.40 ± 0.14 Northeast Mexico City: 2.09 ± 0.10 Mexico City (overall): 2.24 ± 0.12 Authors presented (statistically significantly) elevated PAP levels among children residing in both areas of Mexico City as compared to Polotitlan (control city): Mean ± SE (mmHg) Control: 14.6 ± 0.4 Southwest Mexico City: 16.7 ± 0.6 Northeast Mexico City: 18.6 ± 0.9 Mexico City (overall): 17.3 ± 0.5 Correlation between ET-1 and time spent outdoors: r = 0.31, p = 0.0012 Correlation between PAP and time spent outdoors: r = 0.42, p = 0.0008

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Diez Roux et al. (2008, 156401) **Period of Study:** Baseline data collected Jun 2000-Aug 2002 Exposure assessed retrospectively between Aug 1982 and baseline date **Location:** USA (6 field centers: Baltimore, MD Chicago, IL Forsyth Co, NC Los Angeles, CA New York, NY St. Paul, MN	**Outcome (ICD9 and ICD10):** Three measures of subclinical atherosclerosis (common carotid intimal-medial thickness (CIMT), coronary artery calcification, and ankle-brachial index (ABI)) **Age Groups:** 44-84 yr (MESA cohort) **Study Design:** Cross-sectional retrospective cohort **N:** 5172 for coronary calcium analysis 5037 for CIMT analysis 5110 for ABI analysis **Statistical Analyses:** Generalized Additive Models (Binomial regression: presence of calcification Linear regression: CIMT, ABI, amount of calcium among persons with non-zero calcification) **Covariates:** Age, sex, race/ethnicity, socioeconomic factors, cardiovascular risk factors (BMI, hypertension, high density lipoprotein and low density lipoprotein cholesterol, smoking, diabetes, diet, physical activity models presented with and without adjustment for cardiovascular RFs) **Season:** NA **Dose-response Investigated?** No **Statistical Package:** NR	**Pollutant:** PM_{10} ($\mu g/m^3$) **Averaging Time:** 20-yr imputed mean **Mean (SD):** 34.1 (7.5) **Percentiles:** NR **Range (Min, Max):** NR **Monitoring Stations:** A spatio-temporal model was used to predict monthly $PM_{2.5}$ exposures based on the geographic location of each participant's residence. **Copollutant (correlation with 20-yr imputed mean):** PM_{10} 20-yr observed mean r = 0.93 $PM_{2.5}$ 20-yr imputed mean r = 0.73 PM_{10} 2001 imputed mean r = 0.75 PM_{10} 2001 observed mean r = 0.80 $PM_{2.5}$ 2001 mean r = 0.86	**PM Increment:** 21.0 $\mu g/m^3$ (approx. 10th-90th percentile) **Effect Estimate [Lower CI, Upper CI]:** **CIMT:** Relative difference (95% CI): 1.01 (1.00, 1.02) Adj. for additional CVD RFs: 1.02 (1.00, 1.03) **ABI:** Mean difference (95% CI): 0.002 (-0.005, 0.009) Adj. for additional CVD RFs: 0.001 (-0.006, 0.009) **Coronary calcium:** Relative prevalence (95% CI): 1.02 (0.96, 1.07) Adj. for additional CVD RFs: 1.02 (0.96, 1.08) **Coronary calcium (in those with calcium):** Relative difference (95% CI): 0.98 (0.84, 1.13) Adj. for additional CVD RFs: 1.01 (0.86, 1.18) Found no clear heterogeneity by age, sex, lipid status, smoking status, diabetes status, BMI, education or study site.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Maheswaran et al. (2005, 088683) **Period of Study:** 1994-1998 **Location:** Sheffield, United Kingdom	**Outcome (ICD9 and ICD10):** Stroke mortality (ICD9: 430-438) and Emergency hospital admissions (ICD10: I60-I69) **Age Groups:** ≥ 45 yr **Study Design:** Small area ecological cross-sectional **N:** 1030 census enumeration districts (CEDs) 108 CEDs excluded from PM analyses due to artifacts in the modeled emissions data. The analysis was based on 2979 deaths, 5122 admissions and a population of 199,682 **Statistical Analyses:** Poisson regression **Covariates:** Age, sex, socioeconomic deprivation, and smoking prevalence (some models also included age-by-deprivation interaction) **Season:** NA **Dose-response Investigated?** Yes, examined quintiles of exposure **Statistical Package:** SAS	**Pollutant:** PM_{10} ($\mu g/m^3$) **Averaging Time:** 5-yr avg **Mean (SD):** Presented mean values and ranges for each quintile of exposure: 1: 16.0 (<16.8) 2: 17.5 (≥ 16.8, <18.2) 3: 18.8 (≥ 18.2, <19.3) 4: 19.8 (≥ 19.3, <20.6) 5: 23.3 (≥ 20.6) **Monitoring Stations:** Used air pollution model incorporating point, line and grid sources of pollution and meteorological data. **Copollutant (correlation):** CO (r = 0.82) NO_X (r = 0.87)	**PM Increment:** NA **Effect Estimate [Lower CI, Upper CI]:** **Rate Ratios (95%CI) for stroke mortality adjusted for overdispersion by quintile of PM_{10} level** Adjusted for sex and age: 1: 1 (ref) 2: 0.95 (0.84, 1.08) 3: 1.12 (0.99, 1.27) 4: 1.16 (1.03, 1.32) 5: 1.39 (1.23, 1.58) Adjusted for sex, age, deprivation, and smoking: 1: 1 (ref) 2: 0.94 (0.83, 1.07) 3: 1.08 (0.94, 1.24) 4: 1.12 (0.97, 1.29) 5: 1.33 (1.14, 1.56) **Rate Ratios (95%CI) for emergency hospital admissions because of stroke by quintile of PM_{10} level** Adjusted for sex and age: 1: 1 (ref) 2: 1.06 (0.95, 1.17) 3: 1.10 (0.99, 1.23) 4: 1.25 (1.12, 1.38) 5: 1.40 (1.26, 1.55) Adjusted for sex, age, deprivation, and smoking: 1: 1 (ref) 2: 1.01 (0.91, 1.13) 3: 0.98 (0.87, 1.10) 4: 1.08 (0.96, 1.22) 5: 1.13 (0.99, 1.29) **Rate Ratios (95%CI) for stroke mortality in relation to spatially smoothed (using a 1-km radius) modeled outdoor air pollution quintiles** Adjusted for sex, age, socioeconomic deprivation, age by deprivation interaction, and smoking prevalence: 1: 1 (ref) 2: 0.86 (0.75, 0.98) 3: 1.05 (0.92, 1.21) 4: 1.03 (0.89, 1.19) 5: 1.24 (1.05, 1.47) **Rate Ratios (95%CI) for emergency hospital admissions because of stroke in relation to spatially smoothed modeled outdoor air pollution quintiles** Adjusted for sex, age, socioeconomic deprivation, age by deprivation interaction, and smoking prevalence: 1: 1 (ref) 2: 1.05 (0.94, 1.17) 3: 1.07 (0.95, 1.20) 4: 1.06 (0.94, 1.20) 5: 1.15 (1.01, 1.31)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Maheswaran et al. (2005, 090769) **Period of Study:** 1994-1998 **Location:** Sheffield, United Kingdom	**Outcome (ICD9 and ICD10):** Coronary Heart Disease (CHD) mortality (ICD9: 410-414) and Emergency hospital admissions (ICD10: I20-I25) **Age Groups:** ≥ 45 yr **Study Design:** Small area ecological cross-sectional **N:** 1030 census enumeration districts (CEDs) 108 CEDs excluded from PM analyses due to artifacts in the modeled emissions data. Results based on 6857 deaths, 11407 hospital admissions and 199,682 people aged ≥ 45 yr **Statistical Analyses:** Poisson regression **Covariates:** Age, sex, socioeconomic deprivation, and smoking prevalence (some models also included age-by-deprivation interaction) **Season:** NA **Dose-response Investigated?** Yes, examined quintiles of exposure **Statistical Package:** SAS	**Pollutant:** PM_{10} ($\mu g/m^3$) **Averaging Time:** 5-yr avg **Mean (SD):** Presented mean values and ranges for each quintile of exposure: 1: 16.0 (<16.8) 2: 17.5 (≥ 16.8, <18.2) 3: 18.8 (≥ 18.2, <19.3) 4: 19.8 (≥ 19.3, <20.6) 5: 23.3 (≥ 20.6) **Monitoring Stations:** Study used an air pollution model incorporating points, lines, and grids as sources of pollution, and meteorological data. **Copollutant (correlation):** CO (r = 0.82) NO_X (r = 0.87)	**PM Increment:** NA **Effect Estimate [Lower CI, Upper CI]:** **Rate Ratios (95%CI) for CHD mortality in relation to modeled outdoor air pollution quintiles, adjusted for overdispersion** Adjusted for sex and age: 1: 1 (ref) 2: 1.06 (0.98, 1.16) 3: 1.10 (1.01, 1.21) 4: 1.23 (1.13, 1.35) 5: 1.30 (1.19, 1.43) Adjusted for sex, age, deprivation, and smoking: 1: 1 (ref) 2: 1.03 (0.94, 1.12) 3: 1.00 (0.90, 1.11) 4: 1.08 (0.98, 1.20) 5: 1.08 (0.96, 1.20) Adjusted for sex, age, deprivation, and smoking (spatially smoothed using a 1km radius): 1: 1 (ref) 2: 0.97 (0.89, 1.07) 3: 1.00 (0.90, 1.10) 4: 1.03 (0.93, 1.15) 5: 1.07 (0.96, 1.21) **Rate Ratios (95%CI) for emergency hospital admissions from CHD in relation to modeled outdoor air pollution quintiles** Adjusted for sex and age: 1: 1 (ref) 2: 1.08 (0.98, 1.19) 3: 1.11 (1.01, 1.22) 4: 1.17 (1.07, 1.29) 5: 1.36 (1.23, 1.50) Adjusted for sex, age, deprivation, and smoking: 1: 1 (ref) 2: 1.03 (0.93, 1.13) 3: 0.96 (0.86, 1.07) 4: 0.97 (0.87, 1.08) 5: 1.01 (0.90, 1.14) Adjusted for sex, age, deprivation, and smoking (spatially smoothed using a 1km radius): 1: 1 (ref) 2: 1.01 (0.92, 1.11) 3: 1.04 (0.93, 1.15) 4: 0.97 (0.87, 1.08) 5: 1.07 (0.95, 1.20)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: O'Neill et al. (2007, 156006) **Period of Study:** 2000-2004 **Location:** USA (6 field centers: Baltimore, MD Chicago, IL Forsyth Co, NC Los Angeles, CA New York, NY St. Paul, MN	**Outcome (ICD9 and ICD10):** Creatinine adjusted urinary albumin excretion Assessed 2 ways: continuous log urinary albumin/creatine ration (UACR) and clinically defined micro- or macro-albuminuria (UACR ≥ 25 mg/g) vs. normal levels **Age Groups:** 44-84 yr **Study Design:** Cross-sectional analyses and prospective cohort analyses **N:** 3901 participants free of clinical CVD at baseline **Statistical Analyses:** At baseline: multiple linear regression (continuous outcome) Binomial regression (dichotomous outcome) 3-yr change: repeated measures model with random subject effects (estimate 3-yr change in log UACR by levels of exposure) **Covariates:** Age, gender, race, BMI, cigarette status, ETS, percent dietary protein For repeated measures models: time Time x PM_{10} **Season:** NA **Dose-response Investigated?** Yes, examined quartiles of exposure **Statistical Package:** SAS	**Pollutant:** PM_{10} **Averaging Time:** Avg of previous month, avg of previous 2 mo (recent exposures) 20-yr directly monitored PM_{10} avg, 20-yr imputed PM_{10} avg (longer-term exposures) **Mean (SD):** Previous 20 yr: 34.7 (7.0) Previous month: 27.5 (7.9) **Percentiles:** NR **Range (Min, Max):** NR **Monitoring Stations:** NR (used closest monitor to residence to assign exposure 20-yr imputed PM_{10} was derived using a space-time model) **Copollutant (correlation):** $PM_{2.5}$	**PM Increment:** 10 µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** **Adjusted mean differences in log UACR (mg/g) per increase in PM_{10} among participants seen at baseline** **Previous 30 days** Full sample: -0.42 (-0.085, 0.002) Within 10 km: -0.023 (-0.079, 0.034) **Previous 60 days** Full sample: -0.056 (-0.106 to -0.005) Within 10 km: -0.040 (-0.106, 0.025) **20 yr PM_{10} (nearest monitors)** Full sample: -0.019 (-0.072, 0.033) Within 10 km: 0.009 (-0.067, 0.085) **Imputed 20 yr exposure** Full sample: -0.002 (-0.038, 0.035) Within 10 km: 0.016 (-0.033, 0.066) **Adjusted relative prevalence of microalbuminuria vs. high-normal and normal levels (below 25 mg/g) per increase in PM_{10} among participants without macroalbuminuria during the baseline visit** Previous 30 days: 0.88 (0.76, 1.02) Previous 60 days: 0.83 (0.70, 0.99) 20 yr PM_{10} (nearest monitors): 0.92 (0.77, 1.08) Imputed 20 yr exposure: 0.98 (0.87, 1.10) **Adjusted mean 3-yr change (SE) in log UACR (mg/g) by quartiles of 1982-2002 exposure to PM_{10} from ambient monitors among participants seen in 2000-20004** **Full sample** Quartile: 18.5 to <29.3: 0.147 (0.024) 29.3 to <33.1: 0.159 (0.024) 33.1 to <36.3: 0.163 (0.024) 36.3 to 55.7: 0.174 (0.023) p-trend: 0.42 **Within 10 km** Quartile: 18.5 to <29.3: 0.159 (0.030) 29.3 to <33.1: 0.155 (0.031) 33.1 to <36.3: 0.167 (0.028) 36.3 to 55.7: 0.152 (0.036) p-trend: 0.99 Interactions with either 20 yr or shorter-term PM exposure were not significant ($p < 0.01$) by gender, age, city, race/ethnicity or study site.
Reference: Puett et al, (2008, 156891) **Period of Study:** 1992-2002 **Location:** Northeastern metropolitan U.S.	**Outcome:** Nonfatal myocardial infarction **Study Design:** Cohort **Covariates:** Age in months, state of residence, yr and season **Statistical Analysis:** Cox proportional hazard **Statistical Package:** SAS **Age Groups:** 30-55	**Pollutant:** PM_{10} **Averaging Time:** 3-, 12-, 24-, 36- and 48-mo ma **Mean (SD) Unit:** NR **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **Hazard Ratio, 95% CI, 12 month ma** 0.94 (0.77-1.15)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Rosenlund et al. (2006, 114678) **Period of Study:** 1992-1994 **Location:** Stockholm County, Sweden	**Outcome (ICD9 and ICD10):** Myocardial infarction (MI) **Age Groups:** 45-70 yr **Study Design:** Case-control **N:** 1397 cases 1870 controls **Statistical Analyses:** Logistic regression (main analysis) Also performed multinomial logistic regression to assess cases as nonfatal, fatal in the hospital within 28 days, and out-of-hospital death within 28 days with all controls as reference **Covariates:** Age, sex, and hospital catchment area (frequency matched variables) Smoking, physical inactivity, diabetes, SES Also assessed but did not include hypertension, BMI, job strain, diet, passive smoking, alcohol consumption, coffee intake, and occupational exposure to motor exhaust and other combustion products **Season:** NA **Dose-response Investigated?** No **Statistical Package:** STATA v8.2	**Pollutant:** PM_{10} (modeled traffic-related pollution; also modeled $PM_{2.5}$, but since the PM correlation was high (r = 0.998) only PM_{10} results were presented) ($\mu g/m^3$) **Averaging Time:** 30 yr (PM only assessed during 2000, thus assumed constant levels during 1960-2000) **Median (5th-95th percentile):** **Cases:** 2.6 (0.5-6.0) **Controls:** 2.4 (0.6-5.9) **Range (Min, Max):** NR **Monitoring Stations:** NR **Copollutant (correlation):** NO_2 (r = 0.93) CO (r = 0.66) SO_2	**PM Increment:** 5 $\mu g/m^3$ (5th to 95th percentile distribution among controls) **Effect Estimate [Lower CI, Upper CI]:** Association of 30-yr avg exposure to air pollution from traffic with MI Logistic regression All cases: 1.00 (0.79, 1.27) Multinomial logistic regression Nonfatal cases: 0.92 (0.71, 1.19) Fatal cases: 1.39 (0.94, 2.07) In-hospital death: 1.21 (0.75, 1.94) Out-of-hospital death: 1.84 (1.00, 3.40) After adjustment for heating-related SO_2, the estimate for fatal MI was 1.40 (0.86-2.26) for PM_{10}.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Zanobetti & Schwartz (2007, 091247) **Period of Study:** 1985-1999 **Location:** 21 U.S. cities (Birmingham, Alabama Boulder, Colorado Canton, Ohio Chicago, Illinois Cincinnati, Ohio Cleveland, Ohio Colorado Springs, Colorado Columbus, Ohio Denver, Colorado Detroit, Michigan Honolulu, Hawaii Houston, Texas Minneapolis-St. Paul, Minnesota Nashville, Tennessee New Haven, Connecticut Pittsburgh, Pennsylvania Provo-Orem, Utah Salt Lake City, Utah Seattle, Washington Steubenville, Ohio and Youngstown, Ohio)	**Outcome (ICD9 and ICD10):** Death, subsequent myocardial infarction (MI ICD9 codes 410.0-410.9), and a first admission for congestive heart failure (CHF ICD9 code 428) **Age Groups:** ≥ 65 yr **Study Design:** Cohort **N:** 196,000 persons discharged alive following an acute MI **Statistical Analyses:** Cox's Proportional Hazards Regression Meta-regression for city-specific results **Covariates:** Age, sex, race, type of MI, number of days of coronary care and intensive care, previous diagnoses for atrial fibrillation, and secondary or previous diagnoses for COPD, diabetes, and hypertension, and for season of initial event (time period, and, sex, race, and type of MI were treated as stratification variables) **Season:** Assessed as a confounder **Dose-response Investigated?** No **Statistical Package:** NR	**Pollutant:** PM_{10} **Averaging Time:** Yearly avg of pollution for that yr and lags up to the 3 previous yr (distributed lag) **Mean (SD):** 28.8 (all cities SD not reported) **Percentiles:** 10, 50, and 90 percentiles listed individually for each city (Table 2) **Range (Min, Max):** NR **Monitoring Stations:** NR (obtained data from the U.S. EPA Aerometric Information Retrieval System) **Copollutant (correlation):** None	**PM Increment:** 10 µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** Hazard ratio (95%CI) for an increase in PM for the yr of failure and for the distributed lag from the yr of failure up to 3 previous yr **Death** PM_{10} annual: 1.11 (1.05, 1.19), p = 0.001 Distributed lag model Lag 0: 1.04 (0.96, 1.14), p = 0.336 Lag 1: 1.07 (0.99, 1.14), p = 0.070 Lag 2: 1.14 (1.10, 1.18), p = 0.000 Lag 3: 1.06 (0.99, 1.12), p = 0.077 Sum lags 0-3: 1.34 (1.14, 1.52), p = 0.000 **CHF** PM_{10} annual: 1.11 (1.03, 1.21), p = 0.009 Distributed lag model Lag 0: 1.09 (1.01, 1.18), p = 0.030 Lag 1: 1.09 (1.01, 1.19), p = 0.038 Lag 2: 1.13 (1.02, 1.25), p = 0.014 Lag 3: 1.04 (0.97, 1.12), p = 0.260 Sum lags 0-3: 1.41 (1.19, 1.66), p = 0.000 **2nd MI** PM_{10} annual: 1.17 (1.05, 1.31), p = 0.003 Distributed lag model Lag 0: 1.09 (0.92, 1.30), p = 0.325 Lag 1: 1.12 (0.97, 1.30), p = 0.108 Lag 2: 1.15 (1.08, 1.23), p = 0.000 Lag 3: 1.01 (0.94, 1.09), p = 0.783 Sum lags 0-3: 1.43 (1.12, 1.82), p = 0.005 Hazard Ratio (95%CI) for an increase in PM (sum of the previous 3 yr distributed lag) for the sensitivity analyses **Death** Subjects with follow-up starting after 2nd MI: 1.33 (1.15, 1.55), p = 0.000 Subjects admitted between 1985-1996: 1.45 (1.26, 1.68), p = 0.000 2nd cohort definition (yr defined at time of MI): 1.29 (1.15, 1.44), p = 0.000 **CHF** Subjects with follow-up starting after 2nd MI: 1.42 (1.22, 1.65), p = 0.000 Subjects admitted between 1985-1996: 1.51 (1.26, 1.81), p = 0.000 **2nd MI** Subjects admitted between 1985-1996: 1.62 (1.23, 2.13), p = 0.001 **Note:** Age and sex effect modification results presented in Fig 1 Used meta-regression to examine predictors of heterogeneity across city and found that most predictors were not significant modifiers of PM (Table 7)

[1]All units expressed in µg/m^3 unless otherwise specified.

Table E-21. Long-term effects-cardiovascular- $PM_{2.5}$ (including PM components/sources).

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Allen et al. (2009, 156209) **Period of Study:** Oct 2000-Sep 2002 (exposure averaging period) outcome assessed in 2002 **Location:** 5 U.S. communities (Chicago, Illinois Forsyth County, North Carolina Los Angeles, California Northern Manhattan and the Bronx, New York and St. Paul, Minnesota) part of MESA (Multi-ethnic Study of Atherosclerosis)	**Outcome (ICD9 and ICD10):** Abdominal aortic calcium (AAC), a marker of systemic atherosclerosis (quantitative measure of interest was the Agatston score) **Age Groups:** 46-88 yr **Study Design:** Cross-sectional **N:** 1,147 participants (sensitivity analysis among 1,269 participants) **Statistical Analyses:** 2-part modeling approach: 1) Modeled relative risk of having any AAC using a log link and a Gaussian error model Sensitivity analysis used modified Poisson regression with robust error variance 2) Multiple linear regression of the log-transformed AAC Agatston score (among those with AAC>0) Sensitivity analysis modeled all participants by adding 1 prior to log-transforming **Covariates:** Age, gender, race/ethnicity, BMI, smoking status, pack-yr of smoking, diabetes, education, annual income, blood lipid concentration, blood pressure, and medications Assessed impact of gender, age, diabetes, obesity, use of lipid-lowering medications, education, income, race/ethnicity, and employment status on heterogeneity of effects (or in sensitivity analyses) **Season:** NA **Dose-response Investigated?** NR **Statistical Package:** SAS v9.1	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 2-yr averaging period (Oct 2000-Sep 2002) **Mean (SD):** 15.8 (3.6) $\mu g/m^3$ **Percentiles:** NR **Range (Min, Max):** 10.6-24.7 $\mu g/m^3$ **Monitoring Stations:** All monitors with 1) the objective of "population exposure," "regional transport," or "general/background;) and 2) at least 50% data reporting in each of 8 3-month periods over the averaging time Used monitors located within 50 km of a study participant's residence **Copollutant (correlation):** Assessed traffic by roadway proximity	**PM Increment:** 10 $\mu g/m^3$ **Effect Estimate [Lower CI, Upper CI]:** Results for fully adjusted models under different participant inclusion, employment status, and roadway proximity criteria. **Presence/Absence of Calcium RR (95% CI)** Inclusion criteria: <10yrs at address: 1.04 (0.89, 1.22) ≥ 10yrs at address: 1.06 (0.96, 1.16) ≥ 10yrs at address & <10km from monitor: 1.08 (0.98, 1.18) ≥ 20yrs at address: 1.10 (0.99, 1.22) ≥ 20yrs at address & <10km from monitor: 1.11 (1.00, 1.24) <10yrs at address & employed: 1.02 (0.87, 1.20) ≥ 20yrs at address & employed: 1.07 (0.89, 1.27) <10yrs at address & not employed: 1.10 (1.00, 1.22) ≥ 20yrs at address & not employed: 1.16 (1.02, 1.31) <10yrs at address & near major road: 0.85 (0.69, 1.05) ≥ 20yrs at address & not near major road: 1.10 (0.99, 1.23) **Log-transformed Agatston Score (Agatston >0)** **% Change (95% CI)** Inclusion criteria: <10yrs at address: -6.6 (-64.0, 50.9) ≥ 10yrs at address: 8.0 (-29.7, 45.7) ≥ 10yrs at address & <10km from monitor: 19.7 (-19.6, 58.9) ≥ 20yrs at address: 14.4 (-32.8, 61.7) ≥ 20yrs at address & <10km from monitor: 24.6 (-24.6, 73.8) <10yrs at address & employed: 29.1 (-25.7, 83.8) ≥ 20yrs at address & employed: 43.8 (-32.4, 119.9) <10yrs at address & not employed: -15.1 (-66.3, 36.1) ≥ 20yrs at address & not employed: -14.1 (-72.6, 44.4) <10yrs at address & near major road: 34.0 (-44.2, 112.1) ≥ 20yrs at address & not near major road: 3.9 (-39.9, 47.8) **Log-transformed Agatston Score (all)** **% Change (95% CI)** Inclusion criteria: <10yrs at address: -8.5 (-81.3, 64.2) ≥ 10yrs at address: 40.7 (-11.5, 92.8) ≥ 10yrs at address & <10km from monitor: 60.7 (5.9, 115.4) ≥ 20yrs at address: 64.1 (-1.73, 129.9) ≥ 20yrs at address & <10km from monitor: 79.2 (10.1, 148.3) <10yrs at address & employed: 33.5 (-35.9, 102.9) ≥ 20yrs at address & employed: 55.8 (-37.2, 148.7) <10yrs at address & not employed: 54.8 (-23.8, 133.4) ≥ 20yrs at address & not employed: 89.3 (-3.7, 182.3) <10yrs at address & near major road: -30.6 (-141.3, 80.1) ≥ 20yrs at address & not near major

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			road: 51.3 (-8.3, 110.8) **Exploratory/sensitivity analyses (also presented in figures):** **Detectable AAC RR (95%CI):** Among women: 1.14 (1.00, 1.30) Among persons >65yrs: 1.10 (1.01, 1.19) Among users of lipid-lowering medications: 1.14 (1.00, 1.30) Among Hispanics: 1.22 (1.03, 1.45) Imputing missing covariates among residentially stable participants: 1.08 (0.98, 1.19) **Agatston score % change (95%CI):** Among Hispanics: 64 (-4, 133) Among persons earning >$50,000: 72 (5, 139) **Agatston score including those with Agatston = 0** **% change (95%CI):** Fully adjusted model: 41 (-12, 93) Among persons >65yrs: 75 (8, 143) Among diabetics: 149 (29, 270) Among users of lipid-lowering medications: 121 (25, 217) Among Hispanics: 141 (45, 236) Imputing missing **Covariates:** 49 (1.3, 100.1)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Auchincloss et al. (2008, 156234) **Period of Study:** Jul 2000-Aug 2002 **Location:** 6 U.S. communities (Baltimore City and Baltimore County, Maryland Chicago, Illinois Forsyth County, North Carolina Los Angeles, California Northern Manhattan and the Bronx, New York and St. Paul, Minnesota) part of MESA (Multi-ethnic Study of Atherosclerosis)	**Outcome (ICD9 and ICD10):** Blood pressure: systolic (SBP), diastolic (DBP), mean arterial (MAP), pulse pressure (PP) Avg of 2nd and 3rd BP measurement used for analyses **Age Groups:** 45-84 yr **Study Design:** Cross-sectional (Multi-Ethnic Study of Atherosclerosis baseline examination) **N:** 5,112 persons (free of clinically apparent cardiovascular disease) **Statistical Analyses:** Linear regression Secondary analyses used log binomial models to fit a binary hypertension outcome **Covariates:** Age, sex, race/ethnicity, per capita family income, education, BMI, diabetes status, cigarette smoking status, exposure to ETS, high alcohol use, physical activity, BP medication use, meteorology variables, and copollutants Examined site as a potential confounder and effect modifier Heterogeneity of effects also examined by traffic-related exposures, age, sex, type 2 diabetes, hypertensive status, cigarette use **Season:** Adjusted for temperature and barometric pressure to adjust for seasonality (because seasons vary by the study sites) Also performed sensitivity analyses adjusting for season to examine the potential for residual confounding not accounted for by weather variables **Dose-response Investigated?** Assessed nonlinear relationships-no evidence of strong threshold/nonlinear effects for $PM_{2.5}$ **Statistical Package:** NR	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 5 exposure metrics constructed: prior day, avg of prior 2 days, prior 7 days, prior 30 days, and prior 60 days **Mean (SD):** Prior day: 17.0 (10.5) Prior 2 days: 16.8 (9.3) Prior 7 days: 17.0 (6.9) Prior 30 days: 16.8 (5.0) Prior 60 days: 16.7 (4.4) **Percentiles:** NR **Range (Min, Max):** NR **Monitoring Stations:** Used monitor nearest the participant's residence to calculate exposure metrics **Copollutant (correlation):** SO_2 NO_2 CO Traffic-related exposures (straight-line distance to a highway; total road length around a residence)	**PM Increment:** 10 $\mu g/m^3$ (approx. equivalent to difference between 90th and 10th percentile for prior 30 day mean) **Effect Estimate [Lower CI, Upper CI]:** Adjusted mean difference (95% CI) in PP and SBP (mmHg) per 10 $\mu g/m^3$ increase in $PM_{2.5}$ (avg for the prior 30 days) **Pulse Pressure** Adjustment variables: Person-level **Covariates:** 1.04 (0.25, 1.84) Person-level cov., weather: 1.12 (0.28, 1.97) Person-level cov., weather, gaseous copollutants: 2.66 (1.61, 3.71) Person-level cov., study site: 0.93 (-0.04, 1.90) Person-level cov., study site, weather: 1.11 (0.01, 2.22) Person-level cov., study site, weather, gaseous copollutants: 1.34 (0.10, 2.59) **Systolic Blood Pressure** Adjustment variables: Person-level **Covariates:** 0.66 (-0.41, 1.74) Person-level cov., weather: 0.99 (-0.15, 2.13) Person-level cov., weather, gaseous copollutants: 2.8 (1.38, 4.22) Person-level cov., study site: 0.86 (-0.45, 2.17) Person-level cov., study site, weather: 1.32 (-0.18, 2.82) Person-level cov., study site, weather, gaseous copollutants: 1.52 (-0.16, 3.21) **Additional results:** Associations became stronger with longer averaging periods up to 30 days. For example: Adjusted (personal covariates and weather) mean differences in PP: Prior day: -0.38 (-0.76, 0.00) Prior 2 days: -0.22 (-0.65, 0.21) Prior 7 days: 0.52 (-0.08, 1.11) Prior 30 days: 1.12 (0.28, 1.97) Prior 60 days: 1.08 (0.11, 2.05) (Pattern held for additional adjustments and for SBP results. Therefore, only results for 30-day mean differences were presented) **Additional results (not presented):** None of DBP results were statistically significant. Rresults for MAP were similar to SBP, though weaker and generally not significant Effect modification: associations between $PM_{2.5}$ and BP were stronger for persons taking medications, with hypertension, during warmer weather, in the presence of high NO_2, residing ≤ 300m from a highway, and surrounded by a high density of roads (Fig 1) Associations were not modified for age, sex, diabetes, cigarette smoking, study site, high levels of CO or SO_2, season , nor residence ≤ 400m fro a highway **Note:** supplementary material available on-line

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Calderón-Garcidueñas et al. (2009, 192107) **Period of Study:** Sept 2004-Jan 2005 **Location:** Mexico City and Polotitlan, Mexico	**Outcome:** Flow cytometry **Study Design:** Panel **Covariates:** NR **Statistical Analysis:** Pearson's Correlation **Statistical Package:** Stata **Age Groups:** 9.7 ± 1.2 yr	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 1-, 2- and 7-day avg **Mean (SD) Unit:** 35.89 ± 0.93 $\mu g/m^3$ **Range (Min, Max):** NR **Copollutant:** PM_{10}, O_3	**Increment:** NR **Flow cytometry results and their statistical significance in control vs. exposed children** CD3 Exposed: 62.9±1.8 Control: 67.1±1.7 P = 0.1 CD4 Exposed: 39.3±1.3 Control: 38.2±1.4 P = 0.57 CD8 Exposed: 24.0±0.95 Control: 27.3±1.0 P = 0.02 CD4/CD8 Exposed: 1.7±0.14 Control: 1.4±0.07 P = 0.09 CD3-/CD19+ Exposed: 11.8±1.0 Control: 14.8±1.0 P = 0.04 CD56+ Exposed: 11.5±1.2 Control: 12.4±1.5 P = 0.63 CD56+/CD3-NK Exposed: 14.0±9.5 Control: 7.0±2.7 P = 0.003 HLA-DR+ Exposed: 27.5±4.2 Control: 17.0±2.4 P = 0.04 mCD14+ Exposed: 66.5±2.3 Control: 80.6±1.8 P = <0.001 CD14/CD69 Exposed: 0.20±0.07 Control: 1.0±0.26 P = <0.001 CD4/CD69 Exposed: 0.08±0.03 Control: 3.1±0.65 P = <0.001

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Diez Roux et al. (2008, 156401) **Period of Study:** Baseline data collected Jun 2000-Aug 2002 Exposure assessed retrospectively between Aug 1982 and baseline date **Location:** USA (6 field centers: Baltimore, MD Chicago, IL Forsyth Co, NC Los Angeles, CA New York, NY St. Paul, MN	**Outcome (ICD9 and ICD10):** Three measures of subclinical atherosclerosis (common carotid intimal-medial thickness (CIMT), coronary artery calcification, and ankle-brachial index (ABI)) **Age Groups:** 44-84 yr **Study Design:** Cross-sectional **N:** 5172 for coronary calcium analysis 5037 for CIMT analysis 5110 for ABI analysis **Statistical Analyses:** Generalized Additive Models (Binomial regression: presence of calcification Linear regression: CIMT, ABI, amount of calcium) **Covariates:** Age, sex, race/ethnicity, socioeconomic factors, cardiovascular risk factors (BMI, hypertension, high density lipoprotein and low density lipoprotein cholesterol, smoking, diabetes, diet, physical activity Models presented with and without adjustment for cardiovascular RFs) **Season:** NA **Dose-response Investigated?** No **Statistical Package:** NR	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 20-yr imputed mean **Mean (SD):** 21.7 (5.0) **Percentiles:** NR **Range (Min, Max):** NR **Monitoring Stations:** NR Long-term exposure to PM estimated based on residential history reported retrospectively all addresses geocoded ambient AP obtained from U.S. EPA **Copollutant (correlation):** PM_{10} 20-yr observed mean r = 0.64 PM_{10} 20-yr imputed mean r = 0.73 PM_{10} 2001 mean r = 0.43 $PM_{2.5}$ 2001 mean r = 0.64 Due to high correlation among PM exposures, only results of mean 20-yr exposures are reported.	**PM Increment:** 12.5 $\mu g/m^3$ (approx. 10th-90th percentile) **Effect Estimate [Lower CI, Upper CI]:** **CIMT:** Relative difference (95% CI): 1.01 (1.00, 1.01) Adj. for additional CVD RFs: 1.01 (1.00, 1.02) 1.02 **ABI:** Mean difference (95% CI): 0.000 (-0.006, 0.006) Adj. for additional CVD RFs: -0.001 (-0.006, 0.006) **Coronary calcium:** Relative prevalence (95% CI): 1.01 (0.96, 1.05) Adj. for additional CVD RFs: 1.01 (0.96, 1.06) 1.02 **Coronary calcium (in those with calcium):** Relative difference (95% CI): 0.99 (0.88, 1.12) Adj. for additional CVD RFs: 1.01 (0.89, 1.14)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Hoffman et al. (2007, 091163) **Period of Study:** 2000-2003 **Location:** Ruhr area of Germany (3 large cities: Essen, Mulheim, and Bochum)	**Outcome (ICD9 and ICD10):** Coronary artery calcification (CAC) **Age Groups:** 45-74 yr **Study Design:** Cross-sectional **N:** 4494 participants **Statistical Analyses:** Linear regression (outcome = natural logarithm of CAC score + 1) Logistic regression (outcome = CAC score above/below the age- and gender-specific 75th percentile) **Covariates:** City and area of residence, age, sex, education, smoking, ETS, physical inactivity, waist-to-hip ratio, diabetes, blood pressure, and lipids (and household income in a subset) **Season:** NA **Dose-response Investigated?** Yes, PM was also categorized into quartiles for analyses **Statistical Package:** NR	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 1 yr (2002, midpoint of the study) **Mean (SD):** Total: 22.8 (1.5) High traffic exposure (≤ 100m): 22.9 (1.4) Low traffic exposure (>100m): 22.8 (1.5) **Percentiles:** Q1: 21.54 Q2: 22.59 Q3: 23.75 10th-90th percentile: 3.91 **Range (Min, Max):** NR **Monitoring Stations:** Daily mean $PM_{2.5}$ values for 2002 were estimated with the EURAD model using data from official emission inventories, meteorological information, and regional topographical data. **Copollutant (correlation):** None (Traffic was assessed using distance to roadways) Correlation between modeled daily avg of $PM_{2.5}$ and measured $PM_{2.5}$: 0.86-0.88, depending on season.	**PM Increment:** 3.91 µg/m^3 (10th-90th percentile) **Effect Estimate [Lower CI, Upper CI]:** **Percent change (95%CI) in CAC associated with an increase in** $PM_{2.5}$ Unadjusted: 12.7 (-7.0, 36.4) Model 1 (adjusted for distance to major road): 12.3 (-7.3, 35.9) Model 2 (model 1 + city and area of residence): 29.7 (0, 68.3) Model 3 (model 2 + age, sex, education): 24.2 (0, 55.1) Model 4 (model 3 + smoking, ETS, physical inactivity, waist-to-hip ratio): 17.9 (-5.3, 46.7) Model 5 (model 4 + diabetes, blood pressure, LDL, HDL, triglycerides): 17.2 (-5.6, 45.5) **Adjusted ORs (95%CI) for the association between the top quarter of PM exposure vs. the low quarter of PM exposure and a CAC score above the age- and sex-specific 75th percentiles** All: 1.22 (0.96, 1.54) No CHD: 1.22 (0.95, 1.57) Men: 1.09 (0.78, 1.53) Women: 1.34 (0.97, 1.87) Age <60 yr: 1.18 (0.83, 1.68) Age >60 yr: 1.27 (0.93, 1.75) Nonsmokers: 1.17 (0.89, 1.53) Current smokers: 1.30 (0.83, 2.05) Educational level Low: 1.16 (0.86, 1.57) Medium: 1.30 (0.83, 2.05) High: 1.62 (0.81, 3.25) **Additional notes:** No clear dose-response relationship demonstrated when exposure assessed in quartiles (Fig 2) Participants who had not been working full-time during the last 5 yr showed stronger effects, with possible dose-response between $PM_{2.5}$ and CAC (results presented in Fig 3)
Reference: Hoffman et al. (2006, 091162) **Period of Study:** Dec 2000-Jul 2003 **Location:** Ruhr area of Germany (2 large cities: Essen, Mulheim)	**Outcome (ICD9 and ICD10):** Clinically manifest CHD (defined as self-reported history of a 'hard' coronary event, i.e. myocardial infarction or application of a coronary stent or angioplasty or bypass surgery) **Age Groups:** 45-75 yr **Study Design:** Cross-sectional (German Heinz Nixdorf RBCALL study) **N:** 3399 participants **Statistical Analyses:** Multivariable logistic regression **Covariates:** Sex, diabetes, hypertension, smoking status, ETS, educational level, physical activity, BMI, triglycerides, age, cigarettes smoked per day, WHR, LDL, HDL, HbAlc, indicator variable for cities, indicator variable for living in northern part of cities. **Statistical Package:** SAS v8.2	**Pollutant:** $PM_{2.5}$ (µg/m^3) **Averaging Time:** Yearly mean estimated with model for yr 2002 (on a spatial scale of 5 km) **Mean (SD):** Total: 23.3 (1.4) High traffic: 23.4 (1.4) Low traffic: 23.3 (1.4) **Percentiles:** NR **Range (Min, Max):** NR **Monitoring Stations:** NR **Copollutant (correlation):** None (Traffic was assessed using distance to roadways)	**Effect Estimate [Lower CI, Upper CI]:** Model 1: $PM_{2.5}$ + high traffic exposure 0.92 (0.36, 2.39) Model 2: model 1 + age, sex 0.83 (0.31, 2.27) Model 3: model 2 + education, diabetes, HbAlc, BMI, WHR, smoking status, ETS, physical activity, city, area of residence 0.56 (0.16, 2.01) Model 4: model 3 + hypertension, lipids 0.55 (0.14, 2.11) Modeled vs. Measured: r = 0.86-0.88, depending on season

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Hoffmann et al, (2009, 190376) **Period of Study:** 2000-2003 **Location:** Ruhr area, Germany	**Outcome:** Peripheral Arterial Disease **Study Design:** **Covariates:** Height, weight, medication use, diabetes, physical activity level, smoking, socioeconomic status, education, population density **Statistical Analysis:** NR **Statistical Package:** NR **Age Groups:** 45-75 yr	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily **Mean (SD) Unit:** 22.96 (0.85) **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** 3.91 µg/m^3 **Odds Ratio (95%CI) for prevalence of peripheral arterial disease** 0.87 (0.57-1.34)
Reference: Kunzli et al. (2005, 087387) **Period of Study:** 1998-2003 **Location:** Los Angeles Basin	**Outcome (ICD9 and ICD10):** Carotid intima-media thickness (CIMT) **Age Groups:** Less than 40 yr excluded Mean age = 59.2 ± 9.8 **Study Design:** Cross-sectional **N:** 798 participants **Statistical Analyses:** Linear regression **Covariates:** Age, sex, education, income, smoking, ETS, blood pressure, LDL cholesterol, treatment with antihypertensives or lipid-lowering medications **Season:** NA **Dose-response Investigated?** Yes, assessed $PM_{2.5}$ in quartiles **Statistical Package:** NR	**Pollutant:** $PM_{2.5}$ (µg/m^3) **Averaging Time:** GIS/geostatics model to estimate 'long-term mean ambient concentrations of $PM_{2.5}$' derived from data collected in 2000, including data from 23 state and local monitoring stations. **Mean (SD):** 20.3 ± 2.6 **Percentiles:** NR **Range (Min, Max):** 5.2, 26.9 **Monitoring Stations:** 23 monitors **Copollutant (correlation):** None	**PM Increment:** 10 µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** Percent change (95%CI) in CIMT associated with an increase in $PM_{2.5}$ concentration Based on a linear model with log intima-media thickness as dependent variable **Total population:** Unadjusted: 5.9 (1.0, 10.9) , p = 0.018 Adjusted for age, sex, education, income: 4.4 (0.0, 9.0) , p = 0.056 Adjusted for above + smoking, ETS, multivitamins, alcohol: 4.2 (-0.2, 8.9) , p = 0.064 **Among Females ≥ 60 yr:** Unadjusted: 19.2 (8.8, 30.5) , p = 0.001 Adjusted for age, sex, education, income: 15.7 (5.7, 26.6) , p = 0.002 Adjusted for above + smoking, ETS, multivitamins, alcohol: 13.8 (4.0, 24.5) , p = 0.002 **Among those taking lipid-lowering therapy:** Unadjusted: 15.8 (2.1, 31.2) , p = 0.024 Adjusted for age, sex, education, income: 13.3 (0, 28.5) , p = 0.031 Adjusted for above + smoking, ETS, multivitamins, alcohol: 13.3 (-0.3, 28.8) , p = 0.060 **For the observed contrast between lowest and highest exposure:** Approximately 20 µg/ m^3 → 12.1% (2.0-231%) increase in CIMT. Among nonsmokers: 6.6% (1.0-12.3%). The estimate was small and not significant in current and former smokers. Women: In the range of 6-9% per 10 µg/m^3 Unadjusted means of CIMT across quartiles of exposure were 734, 753, 758, and 774 µm Adjusted means trend across exposure groups, p = 0.041 Stratified results presented in figures
Reference: Miller et al. (2007, 090130) **Period of Study:** 1994-2003 **Location:** 36 U.S. metropolitan areas (Women's Health Initiative)	**Outcome (ICD9 and ICD10):** First cardiovascular event (myocardial infarction, coronary revascularization, stroke, and death from either coronary heart disease [categorized as "definite" or "possible"] or cerebrovascular disease) **Age Groups:** 50-79 yr (median age at	**Pollutant:** $PM_{2.5}$ (µg/m^3) **Averaging Time:** Annual avg concentration in 2000 (used to represent long-term exposure) **Mean (SD):** Individual exposure: 13.5 (3.7) Citywide avg exposure: 13.5 (3.3)	**PM Increment: 10** µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** Estimated Hazards Ratio (95%CI) for the time to the first cardiovascular event or death associated with an increase in $PM_{2.5}$ Any cardiovascular event (first event) Overall: 1.24 (1.09, 1.41)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
	enrollment: 63) **Study Design:** Cohort (median follow-up of 6 yr) **N:** 65,893 postmenopausal women without previous cardiovascular disease **Statistical Analyses:** Cox-proportional hazards regression **Covariates:** Age, race/ethnicity, smoking status, the number of cigarettes smoked per day, the number of yr of smoking, systolic blood pressure, education level, household income, BMI, and presence or absence of diabetes, hypertension, or hypercholesterolemia (also evaluated ETS, occupation, physical activity, diet, alcohol consumption, waist circumference, waist-to-hip ratio, medical history, medications, and presence or absence of a family history of cardiovascular disease as possible confounders in extended models) **Season:** NA **Dose-response Investigated?** **Statistical Package:** SAS v8.0, STATA v8.0	Median: 13.4 **Percentiles:** Quintile ranges: 1: 3.4, 10.9 2: 11.0, 12.4 3: 12.5, 14.2 4: 14.3, 16.4 5: 16.5, 28.3 IQR: 11.6-18.3 10th-90th Personal: 9.1-18.3 City-wide: 9.3-17.8 **Range (Min, Max):** Personal exposure: 3.4, 28.3 Citywide exposure: 4.0, 19.3 **Monitoring Stations:** 573 monitors The nearest monitor to the location of each residence was used to assign exposure (monitor within 30 mi of residence Median of 20 monitors per city (range: 4-78)) **Copollutant (correlation):** PM_{10} SO_2 NO_2 CO O_3	Between cities: 1.15 (0.99, 1.32) Within cities: 1.64 (1.24, 2.18) Coronary heart disease (first event): Overall: 1.21 (1.04, 1.42) Between cities: 1.13 (0.95, 1.35) Within cities: 1.56 (1.11, 2.19) Cerebrovascular disease (first event): Overall: 1.35 (1.08, 1.68) Between cities: 1.20 (0.94, 1.54) Within cities: 2.08 (1.28, 3.40) MI (first event): Overall: 1.06 (0.85, 1.34) Between cities: 0.97 (0.75, 1.25) Within cities: 1.52 (0.91, 2.51) Coronary revascularization (first event): Overall: 1.20 (1.00, 1.43) Between cities: 1.14 (0.93, 1.39) Within cities: 1.45 (0.98, 2.16) Stroke (first event): Overall: 1.28 (1.02, 1.61) Between cities: 1.12 (0.87, 1.45) Within cities: 2.08 (1.25, 3.48) Any death from cardiovascular cause: Overall: 1.76 (1.25, 2.47) Between cities: 1.63 (1.10, 2.40) Within cities: 2.28 (1.10, 4.75) Coronary heart disease death (definite diagnosis): Overall: 2.21 (1.17, 4.16) Between cities: 2.22 (1.06, 4.62) Within cities: 2.17 (0.60, 7.89) Coronary heart disease death (possible diagnosis): Overall: 1.26 (0.62, 2.56) Between cities: 1.20 (0.54, 2.63) Within cities: 1.57 (0.29, 8.51) Cerebrovascular disease death: Overall: 1.83 (1.11, 3.00) Between cities: 1.58 (0.90, 2.78) Within cities: 2.93 (1.03, 8.38) Estimated Hazard Ratios for cardiovascular events associated with an increase in $PM_{2.5}$ according to selected characteristics (presented adjusted H and adjusted H including adjustment for city) Any cardiovascular event: H: 1.24 (1.09, 1.41) H (city): 1.69 (1.26, 2.27) Household income <$20,000: H: 1.30 (1.10, 1.53) H (city): 1.75 (1.28, 2.40) Household income $20,000-49,999: H: 1.23 (1.08, 1.41) H (city): 1.69 (1.25, 2.27) Household income ≥ $50,000: H: 1.20 (1.02, 1.40) 6 H (city): 1.66 (1.22, 2.26) P for trend: HR: p = 0.34 HR (city): p = 0.54 Education: Not high-school graduate: H: 1.40 (1.11, 1.75) H (city): 1.88 (1.32, 2.67) Education: High school grad/trade school/GED: H: 1.33 (1.14, 1.55) H (city): 1.79 (1.32, 2.44) Education: Some college or associate degree: H: 1.26 (1.09, 1.44)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			H (city): 1.74 (1.29, 2.34) Education: Bachelor's degree or higher: H: 1.11 (0.94, 1.31) H (city): 1.54 (1.13, 2.10) P for trend: H: p = 0.07 H (city): p = 0.15 Age <60 yr: H: 1.21 (0.84, 1.73) H (city): 1.66 (1.05, 2.61) Age 60-69 yr: H: 1.14 (0.93, 1.39) H (city): 1.53 (1.09, 2.14) Age ≥ 70 yr: H: 1.34 (1.11, 1.63) H (city): 1.85 (1.34, 2.56) P for trend: H: p = 0.20 H (city): p = 0.20 Current smoker: H: 1.68 (1.06, 2.66) H (city): 2.28 (1.33, 3.92) Former smoker: H: 1.24 (1.01, 1.52) H (city): 1.71 (1.23, 2.39) Never smoked: H: 1.18 (0.99, 1.40) H (city): 1.60 (1.16, 2.21) Living with smoker currently: H: 1.28 (0.84, 1.97) H (city): 1.65 (0.99, 2.76) Living with smoker formerly: H: 1.18 (1.00, 1.38) H (city): 1.59 (1.16, 2.16) Living with smoker never: H: 1.39 (1.07, 1.80) H (city): 1.90 (1.31, 2.78) BMI <22.5: H: 0.99 (0.80, 1.21) H (city): 1.35 (0.96, 1.88) BMI 22.5-24.7: H: 1.16 (0.96, 1.40) H (city): 1.58 (1.14, 2.19) BMI 24.8-27.2: H: 1.24 (1.05, 1.45) H (city): 1.69 (1.24, 2.30) BMI 27.3-30.9: H: 1.38 (1.18, 1.61) H (city): 1.88 (1.38, 2.56) BMI >30.9: H: 1.35 (1.12, 1.64) H (city): 1.84 (1.33, 2.55) P for trend: H: p = 0.003 H (city): p = 0.007 Waist-to-hip ratio <0.74: H: 1.07 (0.90, 1.29) H (city): 1.45 (1.05, 2.00) Waist-to-hip ratio 0.74-0.77: H: 1.12 (0.95, 1.31) H (city): 1.51 (1.11, 2.06) Waist-to-hip ratio 0.78-0.80: H: 1.24 (1.07, 1.44) H (city): 1.68 (1.23, 2.27) Waist-to-hip ratio 0.81-0.86: H: 1.30 (1.13, 1.50) H (city): 1.76 (1.30, 2.38) Waist-to-hip ratio >0.86: H: 1.29 (1.11, 1.50) H (city): 1.75 (1.29, 2.37) Waist circumference <73 cm: H: 1.05 (0.86, 1.27) H (city): 1.43 (1.02, 1.99) Waist circumference 73-78 cm: H: 1.20 (1.02, 1.41) H (city): 1.63 (1.19, 2.23) Waist circumference 79-85 cm: H: 1.22 (1.05, 1.41) H (city): 1.66 (1.22, 2.24) Waist circumference 86-95 cm: H: 1.33 (1.15, 1.53) H (city): 1.80 (1.33, 2.43) Waist circumference >95 cm: H: 1.27 (1.07, 1.51) H (city): 1.73 (1.26, 2.36) P for trend: H: p = 0.06 H (city): p = 0.07 Hormone-replacement therapy-Current Use: H: 1.33 (1.09, 1.61) H (city): 1.85 (1.32, 2.58) Hormone-replacement therapy-No Current Use: H: 1.16 (0.98, 1.39)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			H (city): 1.57 (1.14, 2.17) Diabetes-yes: H: 0.96 (0.67, 1.37) H (city): 1.24 (0.78, 1.96) Diabetes-no: H: 1.28 (1.12, 1.47) H (city): 1.75 (1.30, 2.36) Hypertension-yes: H: 1.22 (1.02, 1.45) H (city): 1.65 (1.09, 2.27) Hypertension-no: H: 1.26 (1.05, 1.51) H (city): 1.74 (1.25, 2.40) Hypercholesterolemia-yes: H: 1.25 (0.94, 1.67) H (city): 1.71 (1.15, 2.54) Hypercholesterolemia-no: H: 1.23 (1.07, 1.42) H (city): 1.69 (1.25, 2.28) Family history of CVD- yes: H (city): 1.80 (1.32, 2.44) Family history of CVD- no: H: 1.07 (0.83, 1.37) H (city): 1.46 (1.00, 2.12) Time lived in current state: ≥ 20 yr: H: 1.21 (1.06, 1.39) H (city): 1.66 (1.23, 2.23) Time lived in current state: 10-19 yr: H: 1.39 (1.12, 1.72)' H (city): 1.97 (1.40, 2.79) Time lived in current state: ≤ 9 yr: H: 1.54 (1.06, 2.26) H (city): 2.24 (1.39, 3.59) Health insurance coverage-yes: H: 1.22 (1.07, 1.39) H (city): 1.71 (1.27, 2.30) Health insurance coverage-no: H: 1.82 (0.81, 4.10) H (city): 2.65 (1.12, 6.28) Time spent outdoors: <30 min: H: 1.09 (0.86, 1.39) H (city): 1.56 (1.05, 2.31) Time spent outdoors: ≥ 30 min H: 1.26 (1.05, 1.50) H (city): 1.82 (1.29, 2.57)
Reference: O'Neill et al. (2007, 156006) **Period of Study:** 2000-2004 **Location:** USA (6 field centers: Baltimore, MD Chicago, IL Forsyth Co, NC Los Angeles, CA New York, NY St. Paul, MN	**Outcome (ICD9 and ICD10):** Creatinine adjusted urinary albumin excretion Assessed 2 ways: continuous log urinary albumin/creatine ration (UACR) and clinically defined micro- or macro-albuminuria (UACR ≥ 25 mg/g) vs. normal levels **Age Groups:** 44-84 yr **Study Design:** Prospective cohort analyses (MESA cohort) **N:** 3901 participants, free of clinical CVD at baseline **Statistical Analyses:** Multiple linear regression (continuous outcome) Binomial regression (dichotomous outcome) **Covariates:** Age, gender, race, BMI, cigarette status, ETS, percent dietary protein **Season:** NA **Dose-response Investigated?** Yes, examined quartiles of exposure **Statistical Package:** SAS	**Pollutant:** $PM_{2.5}$ ($\mu g/m^3$) **Averaging Time:** Avg of previous month, avg of previous 2 mo (recent exposures) 20-yr imputed $PM_{2.5}$ avg (longer-term exposures) **Mean (SD):** Previous month: 16.5 (4.8) **Percentiles:** NR **Range (Min, Max):** NR **Monitoring Stations:** NR (used closest monitor to residence to assign value for recent exposures 20-yr $PM_{2.5}$ exposures were imputed using a space-time model.) **Copollutant (correlation):** PM_{10}	**PM Increment:** 10 $\mu g/m^3$ **Effect Estimate [Lower CI, Upper CI]:** **Adjusted mean differences in log UACR (mg/g) per increase in $PM_{2.5}$ among participants seen at baseline** **Previous 30 days** Full sample: -0.017 (-0.087, 0.052) Within 10 km: 0.026 (-0.067, 0.119) **Previous 60 days** Full sample: -0.040 (-0.121, 0.042) Within 10 km: -0.013 (-0.122, 0.097) **Imputed 20 yr exposure** Full sample: 0.002 (-0.048, 0.052) Within 10 km: -0.012 (-0.076, 0.053) **Adjusted relative prevalence of microalbuminuria vs. high-normal and normal levels (below 25 mg/g) per increase in $PM_{2.5}$ among participants without macroalbuminuria during the baseline visit** Previous 30 days: 0.94 (0.77, 1.16) Previous 60 days: 0.90 (0.71, 1.14) Imputed 20 yr exposure: 0.98 (0.84, 1.14)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Solomon et al. (2003, 156994) **Period of Study:** Exposures measures 1966-1969 Health endpoints assessed via questionnaire, yr not reported but apparently 30 yr after exposure assessment (given the 30 yr residency requirement) **Location:** United Kingdom	**Outcome (ICD9 and ICD10):** Ischemic heart disease (a self-reported history of medically diagnosed angina or heart attack) **Age Groups:** 45 yr and older **Study Design:** Cross-sectional **N:** 1,166 women **Statistical Analyses:** Log linear modeling **Covariates:** Smoking, passive smoking in childhood, tenancy, social class, worked in industry with respiratory hazard, childhood hospital admission for chest problem, diabetes, BMI **Season:** NA **Dose-response Investigated?** No **Statistical Package:** STATA	**Pollutant:** Black smoke ($\mu g/m^3$) **Averaging Time:** Exposure measures performed 1966-1969 women had to live within 5 miles of their current address for the past 30 yr to be included **Mean (SD):** 11 wards with pollution measures were categorized into high (mean >120 $\mu g/m^3$) and low (mean <50 $\mu g/m^3$) exposure categories when classified according to their black smoke levels during 1966-69 SD not reported **Percentiles:** NR **Range (Min, Max):** NR **Monitoring Stations:** NR **Copollutant (correlation):** SO_2 (health results not presented)	**PM Increment:** Categorical **Effect Estimate [Lower CI, Upper CI]:** Association of particulate pollution in place of residence and ischemic heart disease Low (ref): 1.0 High: 1.0 (0.7, 1.4)

[1]All units expressed in $\mu g/m^3$ unless otherwise specified.

E.5. Long-Term Exposure and Respiratory Outcomes

Table E-22. Long-term exposure - respiratory morbidity outcomes - PM_{10}.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ackermann-Liebrich et al. (1997, 077537) **Period of Study:** 1991-1993 **Location:** Switzerland (Aarau, Basel, Davos, Geneva, Lugano, Montana, Payerne, Wald)	**Outcome:** Pulmonary function **Age Groups:** 18-60 yr **Study Design:** Cross-sectional **N:** 9651 people **Statistical Analyses:** Regression analysis **Covariates:** Age, sex, height, weight, education level, nationality, workplace exposure **Season:** NR **Dose-response Investigated?** No **Statistical Package:** NR	**Pollutant:** PM_{10} **Averaging Time:** Continuously measured, 12-mo. avg. used **Mean (SD):** 21.2 (7.4) **Range:** (10.1-33.4) **Copollutant (correlation):** SO_2: r = 0.93 NO_2: r = 0.91 O_3: r = -0.55 Summer Daytime O_3: r = 0.31 Excess O_3: r = 0.67 Altitude: r = -0.77	**PM Increment:** 10 µg/m^3 **Regression Coefficient β (Lower CI, Upper CI) for air pollutants as predictors of pulmonary function** FVC: -0.0345 (-0.0407 to -0.0283) p < 0.001 FEV_1: -0.0160 (-0.0225 to -0.0095) p < 0.001 **Percent Change (Lower CI, Upper CI) associated with increase in avg annual air pollution concentration** Healthy Never-smokers FVC: -3.39 p < 0.001 FEV_1: -1.59 p < 0.001 All Never-smokers FVC: -3.14 p < 0.001 FEV_1: -1.06 p < 0.001 Former Smokers FVC: -3.03 p < 0.001 FEV_1: -0.42 Current Smokers FVC: -3.21 p < 0.001 FEV_1: -1.35 p < 0.001 All FVC: -3.14 p < 0.001 FEV_1: -1.03 p < 0.001 Long-term Residents FVC: -3.16 p < 0.001 FEV_1: -0.96 p < 0.001
Reference: Avol et al. (2001, 020552) **Period of Study:** 1993-1998 **Location:** Southern California	**Outcome:** FVC, FEV_1, MMEF, PEFR **Age Groups:** 10 yr **Study Design:** cohort **N:** 110 **Statistical Analyses:** Linear regression **Covariates:** Sex, race, cohort entry yr, annual avg change in height, weight, BMI **Dose-response Investigated?** No	**Pollutant:** PM_{10} **Averaging Time:** 24-h PM_{10} avgd over 1994 **Mean (SD):** 15.0-66.2	**PM Increment:** 10 µg/m^3 **Mean Change (Lower CI, Upper CI)** FVC: -1.8 (-9.1, 5.5) FEV_1: -6.6 (-13.5, 0.3) MMEF: -16.6 (-32.1 to -1.1) PEFR: -34.9 (-59.8 to -10.0)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Bayer-Oglesby et al. (2005, 086245) **Period of Study:** 1992-2001 **Location:** Switzerland (Lugano, Zurich, Bern, Geneva, Anieres, Biel, Langnau, Payerne, & Montana)	**Outcome:** Respiratory symptoms (chronic cough, bronchitis, cold, dry cough, conjunctivitis, wheeze, sneezing, asthma, & hay fever) **Age Groups:** 6-15 yr **Study Design:** Cross-sectional **N:** 9,591 children **Statistical Analyses:** Logistic regression models **Covariates:** Age, sex, nationality, parental education, number of siblings, farming status, low birth weight, breast feeding, smoking, family history of asthma, bronchitis and/or atopy, mother who smokes, indoor humidity, mode of cooking & heating, carpeting, pets, removal of carpets/pets for health reasons, completed questionnaire & month, days max temperature <0°C, mother's belief of association between environmental exposures & respiratory health **Dose-response Investigated?** Yes **Statistical Package:** STATA	**Pollutant:** PM_{10} **Averaging Time:** 12-mo avg **Mean (SD):** NR **Range (Min, Max):** NR **Monitoring Stations**: 9 **Copollutant (correlation):** NR	**PM Increment:** 10 µg/m^3 "Fig 2 shows that declining levels of PM_{10} were associated with declining prevalence of chronic cough, bronchitis, common cold, nocturnal dry cough, and conjunctivitis symptoms. For wheezing, sneezing, asthma, and hay fever, no significant association could be seen with declining PM_{10} levels." "Fig 3 illustrates that, on an aggregate level, across regions the mean change in PM_{10} levels (r pearson = 0.81, p = 0.008). The strongest decline of adjusted prevalence of nocturnal dry cough was observed in Geneva, Lugano, and Anieres, where the strongest reduction of PM_{10} had also been achieved."
Reference: Burr et al. (2004, 087809) **Period of Study:** 3 wk in Jul and Jan 1997 and 2 wk in Nov 1996 and Apr 1997 **Location:** North Wales, England	**Outcome:** Self-report of symptoms only for wheeze, cough, phlegm, rhinitis, and itchy eyes. **Age Groups:** all **Study Design:** Repeated measures **N:** 386 persons in congested streets and 425 in the uncongested streets in 1996/1997. Of these, 165 and 283 completed the second phase of the study.	**Pollutant:** PM_{10} **Averaging Time:** Mean hourly concentrations **Mean (SD):** SD NR Congested streets - 1996-97 35.2 1998-99 27.2 Uncongested Streets 1996-97 11.6 1998-99 8.2 **Monitoring Stations**: 1 in congested street and 1 in uncongested	**Percent change PM10 in congested streets: 22.7** **Percent change PM10 in uncongested streets: 28.9** Uncongested street sampling site was 20 m from the congested street sampler. The opening of the by-pass produced a reduction in pollution in the congested streets. The health effects of these changed is likely to be greater for nasal and ocular symptoms than for lower respiratory symptoms. Uncertainty about the causality arises from low response rates and conflicting trends in respiratory and nasal symptoms.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Calderón-Garcidueñas et al. (2006, 091253) **Period of Study:** 1999, 2000 **Location:** Southwest Mexico City & Tlaxcala, Mexico	**Outcome:** Hyperinflation, interstitial markings-measured by chest radiograph, and lung function-FVC, FEV_1, PEF, FEF25-75, measured using spirometry tests **Age Groups:** 5-13 yr **Study Design:** Cohort **N:** 249 (total), 230 (Southwest Mexico City), 19 (Tlaxcala) **Statistical Analyses:** Bayes test, Spearman rank correlation, multiple regression **Covariates:** Age, sex **Dose-response Investigated?** No **Statistical Package:** SAS 8.2	**Pollutant:** PM_{10} **Averaging Time:** 1 yr **Mean (SD):** Mexico City 1999-48 2000-45 Tlaxacala: 1994-2000: <NAAQS std **Monitoring Stations**: Southwest Mexico City-2 Tlxacala-periodic air monitoring data **Copollutant:** O_3	**PM Increment:** NR **% Change:** % of children with FEV_1 <80% expected value: Mexico City (n = 77): 7.8% Tlaxacala (n = 19): 0% % children with hyperinflation: Mexico City: 65.6% No hyperinflation: 79 Mild: 72 Moderate: 56 Severe: 23 Tlaxacala: 5.3% No hyperinflation: 18 Mild: 1 Moderate: 0 Severe: 0 % children with interstitial markings: Mexico City: 52.6% Number with: No interstitial markings: 19 Mild: 0 Moderate: 0 Severe: 0 Tlaxacala: 0% No interstitial markings: 109 Mild: 112 Moderate: 9 Severe: 0
Reference: Calderon-Garcidueñas, et al. (2003, 156316) **Period of Study:** Jan 1999-Jun 2000 **Location:** Mexico City, Tuxpam, and Tlaxcala, Mexico	**Outcome:** Respiratory system changes **Age Groups:** 5-17 yr **Study Design:** Case-control of subjects examined for this study **N:** 174 cases, 27 controls, children **Statistical Analyses:** Chi-square test with Yates correction, Spearman's rank correlation test. **Dose-response Investigated?** No **Statistical Package:** SAS 8.2	**Pollutant:** PM_{10} **Averaging Time:** 12 h (daytime 08: 00-20: 00) and nighttime (20: 00-08: 00) **Mean (SD):** Mexico City Day/Night Jan-Jun 1999 76.0/50.0 Jul-Dec 1999 42.8/22.5 Jan-Jun 2000 75.2/47.5	Daily ambient exposure of children to a complex mixture of air pollutants produces significant chest X-ray abnormalities, a decrease in predicted values of FEF_{25-75}, FEF_{75}, and the FEV_1/FVC ratio in association with interstitial marking on chest X-rays, a mild restrictive pattern by spirometry, peripheral blood abnormalities, and an imbalance of serum cytokines.
Reference: Cavanagh et al. (2007, 189802) **Period of Study:** Mar-Aug 2004 **Location:** Christchurch, New Zealand	**Outcome:** A clinical study of excretion of 1-hydroypyrene (1-OHP) as a marker of PAH exposure **Age Groups:** Non-smoking males aged 12-18 yr **Study Design:** Comparison of 2 high pollution events and 2 low pollution events **N:** 89 male students in a boarding school **Statistical Analyses:** Wilcoxon signed rank test for paired observations, Mann-Whitney U test **Season:** Winter **Dose-response Investigated?** No	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** Fall Low Outdoor 19 Indoor NA Winter I Outdoor 43 Indoor 38 Winter II Outdoor 72 Indoor 84 Winter Low Outdoor 12 Indoor 16 **Monitoring Stations**: One inside the boarding house, and one outside	Urinary 1-OHP were raised after high-pollutions events. Peaks were slightly higher than for U.S. non-smokers of similar ages and slightly lower than for German non-smokers of similar ages. Urinary 1-OHP was slightly higher in asthmatics compared to non-asthmatics. There were no indoor sources of PAHs (wood-burning stoves, tobacco smoke). Diet is another source of PAHs, but all students ate in the boarding house. These results suggest 1-OHP could be used as a biomarker of ambient air pollution.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Downs et al. (2007, 092853) **Period of Study:** 1991, 2002 **Location:** Switzerland	**Outcome:** FEV_1, FEV_1 as % of FVC, FEF25-75 **Age Groups:** 18-60 yr **Study Design:** Prospective Cohort **N:** 4742 people **Statistical Analyses:** Linear random effects models **Covariates:** Age, sex, height, parental smoking, season, education, nationality, occupational exposure, smoking (status, pack-yr), atopy, BMI **Dose-response Investigated?** Yes-linear fit best **Statistical Package:** SAS 9.1, STATA 8.2, R 2.4	**Pollutant:** PM_{10} **Averaging Time:** Annual **Mean:** Mean interval exposure: 238 $\mu g/m^3$/yr **Percentiles:** 25th: 197 75th: 287	**PM Increment:** 10 $\mu g/m^3$ reduction in annual mean Percent / absolute reduction in annual decline in lung function over 11-yr period (95% CI): Annual decline in FEV_1 reduced by 9% / 3.1 mL (0.03-6.2) Annual decline in FEF_{25-75} reduced by 16% / 11.3 mL/second (4.3-18.2) Annual decline in FEV_1 as a percentage of FVC of 0.06 (0.01-0.12) A reduction in interval exposure of 109 µg per m^3 cubic meter-yr (equivalent to a reduction of 10 $\mu g/m^3$ in the annual avg during the mean follow-up time of 10.9 yr) was associated with: A reduction of 6.9 mL (95% CI, 2.1 to 11.7) in the annual decline in FEV_1 A 22% reduction in the annual decline in FEF25-75 (i.e., by 14.0 mL per second 95% CI, 3.1 to 24.8)
Reference: Gauderman et al. (2000, 012531) **Period of Study:** 1993-1997 **Location:** Southern California	**Outcome:** FVC, FEV_1, MMEF, FEF75 **Age Groups:** Fourth, seventh, or tenth graders **Study Design:** Cohort **N:** 3035 subjects **Statistical Analyses:** Linear regression **Covariates:** Height, weight, BMI, asthma, smoking, exercise, room temperature, barometric pressure **Dose-response Investigated?** Yes **Statistical Package:** SAS	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg PM_{10} **Mean (SD):** PM_{10} 51.5 **Copollutant (correlation):** $PM_{2.5}$ r = 0.96 O_3 r = -0.32 $PM_{10-2.5}$ r = 0.92 NO_2 r = 0.65 Inorg. Acid r = 0.68	PM_{10} **Increment:** 51.5 $\mu g/m^3$ **% Change (Lower CI, Upper CI)** PM_{10}-4th grade FVC -0.58 (-1.14 to -0.02) FEV_1 -0.85 (-1.59 to -0.10) MMEF -1.32 (-2.43 to -0.20) FEF_{75} -1.63 (-3.14 to -0.11) PM_{10}-7th grade FVC -0.45 (-1.03, 0.13) FEV_1 -0.44 (-1.10, 0.23) MMEF -0.48 (-2.51, 1.59) FEF_{75} -0.50 (-2.26, 1.29) PM_{10}-10th grade FVC 0.07 (-0.99, 1.13) FEV_1 -0.46 (-1.84, 0.94) MMEF -0.71 (-4.87, 3.63) FEF_{75} -1.54 (-5.61, 2.71)
Reference: Gauderman et al. (2002, 026013) **Period of Study:** 1996-2000 **Location:** Southern California	**Outcome:** Lung function development: FEV_1, maximal midexpiratory flow (MMEF) **Age Groups:** Fourth grade children (avg age = 9.9 yr) **Study Design:** Cohort study **N:** 1678 children, 12 communities **Statistical Analyses:** Mixed model linear regression **Covariates:** Height, BMI, doctor-diagnosed asthma and cigarette smoking in previous yr, respiratory illness and exercise on day of test, interaction of each of these variables with sex, barometric pressure, temperature at test time, indicator variables for field technician and spirometer **Dose-response Investigated?** Yes **Statistical Package:** SAS (10)	**Pollutant:** PM_{10} **Averaging Time:** Annual 24-h avg **Mean (SD):** The avg levels were presented in an online data supplement (Fig E1) **Monitoring Stations**: 12 **Copollutant (correlation):** O_3 (10 AM to 6 PM) r = 0.13 O_3 r = -0.37 NO_2 r = 0.64 Acid vapor r = 0.79 $PM_{2.5}$ r = 0.95 $PM_{10-2.5}$ r = 0.95 EC r = 0.86 OC r = 0.97	**PM Increment:** 51.5 $\mu g/m^3$ Association Estimate: None of the pulmonary function tests had a statistically significant correlation with PM_{10} FEV_1 r = -0.12 p = 0.63 MMEF r = -0.22 p = 0.30

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Gauderman et al. (2004, 056569) **Period of Study:** Air pollution data ascertainment: 1994-2000. Spirometry testing: Spring 2001-Spring 2003 **Location:** 12 Communities in Southern California	**Outcome:** Lung function FVC, FEV_1, MMEF (Maximal midexpiratory flow rate) **Age Groups:** Children, Avg age 10 yr **Study Design:** Prospective Cohort Study **N:** 12 Communities 2,034 Children 24,972 child-months **Statistical Analyses:** Linear regression of changes in sex-and-community specific lung growth function and PM **Covariates:** Random effect for communities **Season:** ALL (except for $PM_{2.5}$) **Dose-response Investigated?** No **Statistical Package:** SAS	**Pollutant:** PM_{10} **Averaging Time:** 24-h measurements over each yr used to create annual avg Mean: Means are presented in figures only. **Range (Min, Max):** ~15, ~65 **Monitoring Stations**: 12 **Copollutant (correlation):** O_3: r = 0.18 NO_2: r = 0.67 $PM_{2.5}$: r = 0.95 EC: r = 0.85 OC: r = 0.97	**PM Increment:** Most to least polluted community Range: PM_{10}: 51.4 µg/m^3 EC: 1.2 µg/m^3 OC: 10.5 µg/m^3 Difference in Lung Growth [Lower CI, Upper CI]: FVC -60.2 (-190.6 to 70.3) FEV_1 -82.1 (-176.9 to 12.8) MMEF -154.2 (-378.3 to 69.8) EC: FVC -77.7 (-166.7 to 11.3) FEV_1 -87.9 (-146.4 to -29.4) MMEF -165.5 (-323.4 to -7.6) OC: FVC -58.6 (-196.1 to 78.8) FEV_1 -86.2 (-185.6 to 13.3) MMEF -151.2 (-389.4 to 87.1) Correlation with % below 80% predicted Lung function (p-value) PM_{10}: 0.66 (0.02) EC: 0.74 (0.006)
Reference: Gauderman et al. (2007, 090121) **Period of Study:** 1993-2004 **Location:** 12 Southern California Communities	**Outcome:** pulmonary function tests FVC, FEV_1, MMEF/FEF25.75 **Age Groups:** Children (mean age 10 at recruitment, followed for 8 yr) **Study Design:** Cohort Study (Children's Health Study) **N:** 3677 children (1718 in cohort 1 recruited 1993 and 1959 in cohort 2 recruited 1996) 22686 pulmonary function tests. **Statistical Analyses:** Hierarchical mixed effects model with linear splines **Covariates:** Adjustments for height, height squared, BMI, BMI squared, present asthma status, exercise or respiratory illness on day of test, smoking in previous yr, field technician, traffic indicator (distance from freeway, distance from major roads), random effects for participant and community. **Dose-response Investigated?** no **Statistical Package:** SAS	**Pollutant:** PM_{10} **Monitoring Stations**: 1 in each community	**PM Increment:** 51.4 µg/m^3 Pollutant effect reported as difference in 8 yr lung function growth from least to most polluted community. Negative difference indicates growth deficits associated with exposure. For PM_{10} FEV growth deficit is -111

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Goss et al. (2004, 055624) **Period of Study:** 1999-2000 **Location:** USA	**Outcome:** Cystic Fibrosis pulmonary exacerbations, FEV_1 **Age Groups: >** 6 **Study Design:** Cohort **N:** 11484 patients **Statistical Analyses:** Logistic regression, t-tests, Mann-Whitney tests, Chi-squared tests, polytomous regression, multiple linear regression **Covariates:** Age, sex, lung function, weight, insurance status, pancreatic insufficiency, airway colonization, genotype, median household income by census tract, zipcode. **Dose-response Investigated?** No **Statistical Package:** STATA, SAS	**Pollutant:** PM_{10} **Averaging Time:** Annual mean of 24-h avg **Mean (SD):** 24.8(7.8) mg/m^3 Percentiles: 25th: 20.3 50th(Median): 24.0 75th: 28.9 **Monitoring Stations**: 626	**PM Increment:** 10 $\mu g/m^3$ **Odds Ratio Estimate [Lower CI, Upper CI]:** Odds of having 2 or more pulmonary exacerbations as compared to 1 or less in 2000 1.08 (1.02 -1.15) Odds of having 2 or more pulmonary exacerbations as compared to no exacerbations in 2000 1.09 (1.02 -1.17) Decrease in FEV_1 38ml(18-58)
Reference: Hanigan et al, (2008, 156518) **Period of Study:** Fire Season (Apr-Nov) from 1996-2005 **Location:** Darwin, Australia	**Outcome:** Respiratory admissions **Study Design:** Time-series **Covariates:** Race, age **Statistical Analysis:** Over-dispersed Poisson generalized linear models **Statistical Package:** R **Age Groups:** All	**Pollutant:** PM_{10} **Averaging Time:** Daily levels estimated from visibility data **Mean Unit:** *Only reported for 2005* 15.31 $\mu g/m^3$ **Range (Min, Max):** 6.93, 31.12 **Copollutant (correlation):** NR	**Increment:** 10 $\mu g/m^3$ **Percent Increase (95% CI)** *Full results reported visually in Fig 3* Total Respiratory Admissions 4.81 % (-1.04-11.01) Indigenous Respiratory Admissions, No Lag 9.40% (1.04-18.46) Non-Indigenous Respiratory Admissions, No Lag 3.14% (-2.99-9.66) Indigenous Respiratory Admissions, Lag 3 15.02% (3.73-27.54) Non-Indigenous Respiratory Admissions, Lag 3 0.67% (-7.55-9.61) Indigenous Asthma Admissions, Lag 1 16.27% (3.55-40.17) Non-Indigenous Asthma Admissions, Lag 1 8.54% (-5.60-24.80)
Reference: Ho et al. (2007, 093265) **Period of Study:** Oct 1995-Mar 1996 **Location:** Taiwan, Republic of China	**Outcome:** Asthma **Age Groups:** 10-17 yr **Study Design:** Screened junior high students for asthma, collected meteorological data to determine the relationship. **N:** 69,367 **Statistical Analyses:** Logistic regression model, the maximum likelihood estimation with Fisher's scoring algorithm, stepwise regression model, Wald statistic, Akaike criteria. GEE, GENMOD **Covariates:** Wind, barometric pressure, temperature, rain, humidity **Season:** Fall-spring **Dose-response Investigated?** No **Statistical Package:** SAS	**Pollutant:** PM_{10} **Averaging Time:** Monthly **Monitoring Stations**: 72	**Odds Ratio from stepwise regression model:** Females (n = 32, 648) 0.993 [0.990-0.997] Males: NS Higher PM_{10} concentration resulted in less asthma prevalence. However, a higher number of rain days seemed to reduce asthma prevalence Rain days might interact with PM_{10}.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Hong et al. (2004, 156565) **Period of Study:** 2001 **Location:** Kerinci, SP7, and Pelalawan, Indonesia	**Outcome:** Respiratory symptoms **Age Groups:** <12 yr **Study Design:** Disproportionate random sampling was used to select 100 households from each village. An interviewer interviewed all children through the caregiver/parent to obtain symptoms in the past 2 wk (cough, cold, phlegm) and the last 12 mo. **N:** 382 children **Statistical Analyses:** Chi-square test, analysis of variance, prevalence rates, adjusted odds ratios, multivariate adjusted odds ratios from multiple logistic regression models, allowing for clustering. **Covariates:** Age, gender, no. of children in household, household income, floor area of house, fuel for cooking, no. of smokers in household, personal and family medical history. **Dose-response Investigated?** No **Statistical Package:** SPSS STATA v.7	**Pollutant:** PM_{10} **Averaging Time:** 24-h measurements were taken daily from 2 wk before he field survey to 1 mo after the survey **Mean (SD):** Kerinci 102.9 (49.6) µg/m^3 SP7 73.7 (41.7) Pelalawan 26.1 (14.5) P<0.01 **Range (Min, Max):** Kerinci 25, 184 SP7 13, 138 Pelalawan 10, 66 **Monitoring Stations**: 3	**PM Increment:** Low (Pelalawan), Medium (SP7), & High (Kerinci) PM Exposure **Odds Ratios (95% CI) for Symptoms by village:** Cough/cold past 2 wks Pelalawan 1.00 SP7 2.03 (1.04, 3.96) Kerinci 3.17 (1.43, 7.07) Respiratory symptoms last 12 mo Pelalawan 1.00 SP7 1.15 (0.58, 2.26) Kerinci 1.42 (0.62, 3.25) Ever had rhinitis w/o flu Pelalawan 1.00 SP7 2.17 (0.57, 8.29) Kerinci 0.56 (0.11, 2.83) Ever had wheezing Pelalawan 1.00 SP7 0.85 (0.35, 2.08) Kerinci 1.18 (0.46, 3.01)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Horak et al. (2002, 034792) **Period of Study:** 1994-1997 **Location:** Lower Austria	**Outcome:** Lung function growth measured by changes in: 1. FVC (forced vital capacity) 2. FEV_1 3. MEF_{25}-75 (midexpiratory flow between 25-75% of the forced vital capacity) **Age Groups:** 2-3 grade schoolchildren (mean age = 8) **Study Design:** Prospective cohort with repeated measures **N:** 975 children **Statistical Analyses:** Linear regression GEE, nonstationary M-dependent correlation structure **Covariates:** Gender, atopy, ETS exposure, baseline lung function, first height, height difference, school site **Season:** Winter, summer **Dose-response Investigated?** No	**Pollutant:** PM_{10} **Mean (SD):** Winter: 21.0 (4.8) Summer: 17.4 (2.8) **Range (Min, Max):** Winter: 9.4-30.5 Summer: 11.7-28.9 **Monitoring Stations**: NR, stations were located in the immediate vicinity of each of the 8 elementary schools **Copollutant (correlation):** Winter O_3: (r = -0.581) SO_2 (r = 0.520) NO_2 (r = 0.595) Summer O_3 (r = -0.429) SO_2 (r = 0.335) NO_2 (r = 0.412)	**PM Increment:** 1 $\mu g/m^3$ Mean per unit increase in PM (p-value) **Outcome:** difference per day of FVC (mL/day) Summer: 0.001 (0.938) Winter: 0.008 (0.042) Controlling for temperature: Summer: -0.007 (0.417) Winter: -0.003 (0.599) Controlling for O_3: Summer: 0.001 (0.911) Winter: 0.010 (0.019) Controlling for NO_2: Summer: -0.018 (0.056) Winter: 0.015 (0.000) Controlling for SO_2: Summer: 0.005 (0.575) Winter: 0.004 (0.492) In non-asthmatic children: Summer: -0.003 (0.710) Winter: 0.009 (0.030) In group not exposed to ETS: Summer: 0.014 (0.154) Winter: 0.012 (0.0018) In group exposed to ETS: Summer: 0.022 (0.088) Winter: 0.003 (0.656) **Outcome:** difference per day of FEV_1 (mL/day) Summer: -0.023 (0.003) Winter: 0.001 (0.885) Controlling for temperature: Summer: -0.034 (0.000) Winter: -0.011 (0.016) Controlling for O_3: Summer: -0.022 (0.008) Winter: 0.004 (0.338) Controlling for NO_2: Summer: -0.038 (0.000) Winter: 0.011 (0.005) Controlling for SO_2: Summer: -0.022 (0.010) Winter: -0.005 (0.358) **Outcome:** difference per day MEF_{25-75} (mL/day) Summer: -0.090 (0.000) Winter: -0.008 (0.395) Controlling for temperature: Summer: -0.112 (0.000) Winter: -0.013 (0.295) Controlling for O_3: Summer: -0.087 (0.000) Winter: -0.008 (0.434) Controlling for NO_2: Summer: -0.102 (0.000) Winter: 0.005 (0.610) Controlling for SO_2: Summer: -0.095 (0.000) Winter: -0.011 (0.474)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Hwang et al. (2006, 088971) **Period of Study:** 2001 **Location:** Taiwan	**Outcome:** Peak expiratory flow rate (PEFR), Forced Expiratory Volume in 1 second (FEV_1), Forced Vital Capacity (FVC), Self reported "frequent coughing," Self reported "shortness of breath," Self reported " irritation of respiratory tract" **Age Groups:** 24-55 yr (mean = 40) **Study Design:** Cohort **N:** 120 men (60 traffic policemen and 60 controls) **Statistical Analyses:** ANOVA, odds ratios calculated from 2X2 table **Dose-response Investigated?** No	**Pollutant:** PM_{10} **Mean (SD):** 55.58 (16.57) Percentiles: 25th: 42.96 50th(Median): 53.81 75th: 70.37 **Range (Min, Max):** 29.36, 99.58 **Monitoring Stations**: 22 **Copollutant (correlation):** NO_X (r = 0.34) SO_2 (r = 0.58) CO (r = 0.27) O_3 (r = 0.28)	**PM Increment:** 10 µg/m^3 RR Estimate [Lower CI, Upper CI] Single pollutant model: 1.00 [0.99, 1.02] Controlling for NO_X: 0.99 [0.97, 1.00] Controlling for CO: 1.00 [0.99, 1.01] Controlling for O_3: 1.00 [0.99, 1.02]
Reference: Hwang et al, (2008, 134420) **Period of Study:** 2001-2003 **Location:** Taiwan	**Outcome:** Oral Cleft **Study Design:** Case-control **Covariates:** Maternal age, plurality, gestational age, population density and season of conception **Statistical Analysis:** Logistic regression **Age Groups:** Infants	**Pollutant:** PM_{10} **Averaging Time:** hourly **Mean (SD) Unit:** Avg: 54.83 ± 13.07 µg/m^3 Spring: 64.44 ± 16.21 µg/m^3 Summer: 39.11 ± 8.31 µg/m^3 Fall: 47.76 ± 11.77 µg/m^3 Winter: 68.00 ± 21.88 µg/m^3 **Range (Min, Max):** Avg: 20.75-78.05 µg/m^3 Spring: 23.33-94.33 µg/m^3 Summer: 17.33-60.00 µg/m^3 Fall: 21.00-72.00 µg/m^3 Winter: 21.33-116.00 µg/m^3 **Copollutant (correlation):** CO: -0.19 NO_X: 0.56 O_3: 0.39 SO_2: 0.50	**Increment:** 10 µg/m^3 **Odds Ratio (Min CI, Max CI);** Single Pollutant Model Month 1: 1.01 (0.96-1.06) Month 2: 1.00 (0.95-1.05) Month 3: 0.99 (0.95-1.05) Two Pollutant Model (O_3 + PM_{10}) Month 1: 0.99 (0.94-1.04) Month 2: 0.99 (0.94-1.04) Month 3: 0.98 (0.93-1.04) Two Pollutant Model (CO + PM_{10}) Month 1: 1.01 (0.96-1.06) Month 2: 1.00 (0.95-1.05) Month 3: 0.99 (0.95-1.05) Two Pollutant Model (NO_X + PM_{10}) Month 1: 1.02 (0.97-1.08) Month 2: 1.01 (0.95-1.07) Month 3: 1.01 (0.95-1.07) Three Pollutant Model (O_3 + CO + PM_{10}) Month 1: 0.99 (0.94-1.04) Month 2: 0.99 (0.94-1.04) Month 3: 0.99 (0.93-1.04) Three Pollutant Model (O_3 + NO_X + PM_{10}) Month 1: 1.00 (0.94-1.06) Month 2: 0.98 (0.92-1.05) Month 3: 1.00 (0.93-1.06)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ingle et al. (2005, 089014) **Period of Study:** May 2003-Apr 2004 **Location:** Jalgaon City, India	**Outcome:** Peak expiratory flow rate (PEFR), Forced Expiratory Volume in 1 second (FEV_1), Forced Vital Capacity (FVC), Self reported "frequent coughing," Self reported "shortness of breath," Self reported " irritation of respiratory tract" **Age Groups:** 24-55 yr (mean = 40) **Study Design:** Cohort **N:** 120 men (60 traffic policemen and 60 controls) **Statistical Analyses:** ANOVA, odds ratios calculated from 2X2 table **Dose-response Investigated?** No	**Pollutant:** PM_{10} **Mean (SD):** Location-specific means: Prabhat: 224 (27) Ajanta: 269 (41) Icchdevi: 229 (24) **Monitoring Stations**: 3	**OR Estimate [p-value]** Self reported frequent coughing 2.96 [p < 0.05] Self reported shortness of breath 1.22 [p < 0.05] Self reported irritation in respiratory tract 7.5 [p < 0.05] Observed/expected lung function p-value for difference between groups: FVC (L) Traffic policemen: 0.82 Controls: 0.99 Traffic policemen: Obs = 3.03 ± 1.7 Exp = 3.70 ± 2.8 Controls: Obs = 3.18 ± 0.91 Exp = 3.19 ± 1.71 FEV_1 (L) Traffic policemen: 0.73 Controls: 1.18 Traffic policemen: Obs = 2.27 ± 1.05 Exp = 3.08 ± 2.7 Controls: Obs = 3.61 ± 0.90 Exp = 3.06 ± 0.91 PEFR (L/s) Traffic policemen: 0.66 Controls: 0.92 Traffic policemen: Obs = 6.05 ± 2.15 Exp = 9.21 ± 0.47 Controls: Obs = 5.54 ± 1.85 Exp = 6.11 ± 2.31
Reference: Islam et al. (2007, 090697) **Period of Study:** 2006 **Location:** 12 California communities	**Outcome:** Respiratory symptoms, Asthma **Study Design:** Longitudinal study cohort **Statistical Analyses:** Cox proportional hazards regression **Age Groups:** 7-9 10-11 >11	**Pollutants:** PM_{10} **Averaging Time:** 24-h avg **Copollutants (correlation):** O_3 NO_2 EC OC	The study doesn't present quantitative results on PM_{10}.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Janssen et al. (2003, 133555) **Period of Study:** Apr 1997-Jul 1998 **Location:** Netherlands-24 schools	**Outcome:** Symptoms of asthma and allergic disease (asthma, conjunctivitis, hay fever, itchy rash, eczema, phlegm, bronchitis), skin prick test (SPT) reaction to allergens, lung function (forced vital capacity [FVC], forced expiratory volume in 1 second [FEV_1], and positive test for fall in $FEV_1 \geq 15\%$ after inhalation of maximal 23 mL hypertonic saline [BHR = bronchial hyper-responsiveness]) **Age Groups**: 7-12 yr old **Study Design:** Cohort **N:** 24 schools (see notes) **Statistical Analyses:** Multilevel model **Covariates:** Age, sex, non-Dutch nationality, cooking on gas, current parental smoking, current pet possession, parental education level, number of persons in the household, presence of an unvented water heater in kitchen, questionnaire not filled out by the mother, presence of mold stains in kitchen or living room or bedroom, parental respiratory symptoms, distance of home to motorway, cough or cold at time of lung function measurement, bronchitis or severe cold or flu in 3 wk preceding measurement, season **Dose-response Investigated?** No **Statistical Package**: MLwiN	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual **Mean (SD):** 20.5 µg/m^3 (2.2) **Percentiles:** 25th: 18.6 50th (Median): 20.4 75th: 22.1 **Range (Min, Max):** 17.3, 24.4	**PM Increment:** 'Difference between the maximum and the minimum of the exposure indicator' (3.5 µg/m^3) **RR Estimate [Lower CI, Upper CI] lag:** Current wheeze 1.51 (0.90, 2.53) Asthma ever 1.03 (0.59, 1.82) Current conjunctivitis 2.08 (1.17, 3.71) Hay fever ever 2.28 (1.13, 4.57) Current itchy rash 1.63 (0.91, 2.89) Eczema ever 1.31 (0.94, 1.83) Current phlegm 1.53 (0.74, 3.19) Current bronchitis 1.71 (0.84, 3.50) Elevated total IgE 1.45 (0.74, 2.84) Any allergen (spt reactivity) 1.33 (0.83, 2.11) Indoor allergens (spt reactivity) 1.17 (0.70, 1.94) Outdoor allergens (spt reactivity) 1.90 (1.06, 3.40) FVC < 85% predicted 0.54 (0.29, 1.00) FEV_1 < 85% predicted 0.88 (0.37, 2.09) BHR 0.93 (0.51, 1.68) **Notes:** Fig 1 of the article illustrates the association between exposures, including $PM_{2.5}$, and various respiratory symptoms among children with and without a positive SPT and positive BHR. In general, the association between $PM_{2.5}$ and respiratory symptoms were higher for children with a positive SPT or BHR, except for the outcome of current phlegm. This effect appeared to be the strongest for children with a positive BHR, particularly for current wheeze and current bronchitis. The authors also reported separate analyses for children with SPT reactivity for indoor and outdoor allergens, but did not report any clear differences between the two groups. The authors did report, in the text, that the OR of $PM_{2.5}$ exposure for children sensitized for outdoor allergens was 7.64 for current itchy rash ($p < 0.05$).

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Kan, et al. (2007, 091383) **Period of Study:** 1987-1992 **Location:** Four Communities in the U.S.: Forsyth County, North Carolina Jackson, Mississippi northwest suburbs of Minneapolis, Minnesota and Washington County, Maryland.	**Outcome:** FEV_1 and FVC **Age Groups:** Middle-aged (mean age was 54.2 yr) **Study Design:** Hierarchical regression **N:** 15,792 **Statistical Analyses:** SAS PROC MIXED **Covariates:** Distance to major roads, traffic exposure, age, ethnicity, sex, smoking, environmental tobacco smoke exposure, occupation, education, medical history, BMI. **Dose-response Investigated?** No **Statistical Package:** SPSS Version 11 for traffic density, SAS Version 9.1.2 for statistical analysis	**Pollutant:** PM_{10} **Averaging Time:** 24-h PM_{10} averaged over study period **PM Component:** Vehicle emissions **Monitoring Stations**: 0 **Copollutant:** NO_2 O_3	**RR Estimate (Lower CI, Upper CI):** (Note: for ARIC participants living <150 meters from major roads) Women FEV_1(mL) Age-adjusted model -29.5 (-52.2 to -6.9) Multivariate model -15.7 (-34.4 to -2.9) FVC (mL) Age-adjusted model -33.2 (-60.4 to -5.9) Multivariate model -24.2 (-46.2,-2.3) FEV_1/FVC (%) Age-adjusted model -0.1(-0.5,0.2) Multivariate model 0.1 (-0.3,0.4) Men FEV_1(mL) Age-adjusted model -38.4 (-76.7,0.6) Multivariate model -6.4 (-38.1,25.3) FVC (mL) Age-adjusted model -17.0(-62.0,28.0) Multivariate model 10.9(-24.7,46.5) FEV_1/FVC (%) Age-adjusted model -0.05 (-0.9,0.0) Multivariate model -0.3 (-0.7,0.2)
Reference: Kim et al. (2005, 087418) **Period of Study:** Mar and Dec 2000 **Location:** Incheon & Ganghwa, Korea	**Outcome:** Lung function (FEV_1, FVC) **Age Groups:** Middle school students **Study Design:** Panel **N:** 368 children **Statistical Analyses:** Generalized liner model **Covariates:** Gender, grade **Season:** Spring and fall **Dose-response Investigated?** No **Statistical Package:** SAS	**Pollutant:** PM_{10} **Averaging Time:** Monthly **Mean (SD):** Incheon Mar 64 Dec 54 Ganghwa Mar 64 Dec 53 **Range (Min, Max):** NR	**PM Increment:** NR **OR Estimate [Lower CI, Upper CI]:** "The present study showed that the values of FEV_1 and FVC were greater in Dec than in Mar for both male and female students at all academic yr…Because only the level of PM_{10} was significantly higher for Mar than for Dec in both areas, the authors suggest that decrements of pulmonary function in Mar for both areas are associated with the increased level of PM_{10}"
Reference: Kim et al. (2004, 087383) **Period of Study:** Mar-Jun (spring) 2001 Sep-Nov (fall) 2001 **Location:** Alameda County, CA	**Outcome:** Asthma, bronchitis **Age Groups:** Children (in grades 3-5) **Study Design:** Cross-sectional **N:** 1109 children, 871 (long term resident children), 462 (long term related females), 403 (long term related males) **Statistical Analyses:** 2-stage multiple logistic regression model **Covariates:** Respiratory illness before age of 2, household mold/moisture, pests, maternal history of asthma (for asthma) Season: Spring and fall **Dose-response Investigated?** Yes **Statistical Package:** SAS 8.2	**Pollutant:** PM_{10} **Averaging Time:** 9 wk **Mean (SD):** Study Avg 30 **Monitoring Stations**: 10 **Copollutant (correlation):** r2 is approximately 0.9 for all copollutants – BC, $PM_{2.5}$, NO_X, NO_2, NO (NO_X-NO_2)	**PM Increment:** 1.4 (IQR) **OR Estimate [Lower CI, Upper CI]:** Bronchitis All subjects: 1.03 [0.99, 1.07] LTR subjects: 1.02 [0.98, 1.07] LTR females: 1.04 [1.01, 1.09] LTR males: 1.01 [0.95, 1.06] Asthma All subjects: 1.02 [0.96, 1.09] LTR subjects: 1.04 [0.97, 1.12] LTR females: 1.09 [0.92, 1.29] LTR males: 1.02 [0.94, 1.10] Asthma excluding outlier school having a larger proportion of Hispanics All subjects: 1.06 [0.97, 1.16] LTR subjects: 1.08 [0.98, 1.19] LTR females: 1.09 [0.96, 1.24] LTR males: 1.08 [0.97, 1.19]

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Kumar et al. (2004, 089873) **Period of Study:** 1999-2001 **Location:** Mandi Gobindgarh and Morinda, Punjab State, northern India	**Outcome:** Chronic respiratory symptoms & Spirometric ventilatory defect **Age Groups:** >15 yr **Study Design:** Cross-sectional **N:** 3603 individuals **Statistical Analyses:** Logistic regression **Covariates:** Age, gender, migration, SES, smoking, type of cooking fuel use **Dose-response Investigated?** No	**Pollutant:** PM_{10} **Mean (SD):** Study town 112.8 (17.9) Reference town 75.8 (2.9)	**PM_{10} Increment:** Low vs. High OR (Lower CI, Upper CI) p-value Chronic respiratory symptoms Low 1.00 (ref) High 1.5 (1.2, 1.8) <0.001 Spirometric ventilatory defect Low 1.00 (ref) High 2.4 (2.0-2.9) <0.001
Reference: Leonardi et al. (2000, 010272) **Period of Study:** 1996 **Location:** 17 cities of Central Europe (Bulgaria, Czech Republic, Hungary , Poland, Romania, Slovakia)	**Outcome:** Immune biomarkers **Age Groups:** 9-11 **Study Design:** Cross-sectional **N:** 366 school children **Statistical Analyses:** Linear regression **Covariates:** Age, gender, parental smoking, laboratory of analysis, recent respiratory illness **Dose-response Investigated?** No **Statistical Package:** STATA	**Pollutant:** PM_{10} **Averaging Time:** Annual PM_{10} **Mean (SD):** PM_{10}: 65 (14) **Range (Min, Max):** PM_{10}: (41, 96) 5th, median, & 95th percentile PM_{10}: 41, 63, 90	**% Change (Lower CI, Upper CI)** **p-value** PM_{10} Neutrophils -5 (-33, 36) >.20 Total lymphocytes 20 (-6, 54); .150 B lymphocytes 42 (-3, 107); .067 Total T lymphocytes 30 (-2, 73); .072 CD4+ 28 (-10, 82); .177 CD8+ 29 (-5, 75); .097 CD4/CD8 7 (-20, 43) >.20 NK 33 (-10, 97); .157 Total IgG 11 (-10, 38) >.20 Total IgM 5 (-21, 39) >.20 Total IgA11 (-16, 46) >.20 Total IgE -8 (-62, 123) >.20
Reference: Lichtenfels et al, (2007, 097041) **Period of Study:** 2001-2003 **Location:** São Paulo, Brazil	**Outcome:** Secondary sex ratio **Study Design:** Retrospective Cohort **Covariates:** NR **Statistical Analysis:** Correlation Coefficient **Age Groups:** Infants	**Pollutant:** PM_{10} **Averaging Time:** Annual **Mean (SD) Unit:** 2001: 49.8 (10.5) $\mu g/m^3$ 2002: 48.5 (11.4) $\mu g/m^3$ 2003: 49.4 (14.4) $\mu g/m^3$ **Range (Min, Max):** 31.71-60.96 $\mu g/m^3$ **Copollutant (correlation):** NR	**Increment:** NR **Correlation Coefficient:** R2 = 0.7642, P = 0.13
Reference: Lubinski, et al. (2005, 087563) **Period of Study:** 1993-1997 **Location:** Poland	**Outcome:** Pulmonary function TLC: total lung capacity ITGV: interthoracic gas volume ITGV%TLC: ITGV percent total lung capacity Raw: airway resistance FVC: forced vital capacity FEV_1: forced expiratory volume, 1 second FEV_1%FVC: FEV_1 percent forced vital capacity PEF: peak expiratory flow FEF50: forced expiratory flow **Age Groups:** 18-23 males, healthy **Study Design:** Ecological cross-sectional study **N:** 1278 subjects **Statistical Analyses:** Multiple linear regression, ANOVA **Covariates:** Report unclear on whether or not there was covariate control, but may include NO_2 and SO_2 **Dose-response Investigated?** No	**Pollutant:** PM_{10} **Averaging Time:** 12 mo **Mean (SD):** A: Highest Pollution Region Katowice 67-125 Krakow 41-49 B: Moderate Pollution Region Bielsko-Biala 29-48 Opole 18-45 Lodz 23-38 Warsaw 35-45 Wroclaw 28-76 Zagan 5-35 C: Lowest Pollution Region Gizycko 5-18 Hel 12-18 Ostroda 23-33 Swinoujscie 7-16 Ustka 12-26 **Copollutant:** NO_2, SO_2	**PM Increment:** 1 $\mu g/m^3$ Slope, multiple regression TLC PM_{10}: -0.05 +SO_2: 0.03 +NO_2: -0.06 ITGV PM_{10}: 0.01 +SO_2: -0.07 +NO_2: -0.07 ITGV%TLC PM_{10}: -0.06 +SO_2: 0.08 +NO_2: 0.00 Raw PM_{10}: 0.075 +SO_2: -0.08 +NO_2: 0.127 FVC PM_{10}: 0.045 +SO_2: 0.045 +NO_2: -0.14 FEV_1 PM_{10}: 0.031 +SO_2: -0.08 +NO_2: -0.12 FEV_1%FVC PM_{10}: 0.00 +SO_2: -0.14 +NO_2: -0.048 PEF PM_{10}: -0.18 +SO_2: 0.056 +NO_2: -0.09 FEF50 PM_{10}: 0.031 +SO_2: -0.11 +NO_2: -0.04

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: McConnell et al. (1999, 007028) **Period of Study:** 1993 **Location:** Southern California	**Outcome:** Bronchitis, chronic cough, phlegm **Age Groups:** Children: 4th, 7th, & 10th graders **Study Design:** Cross-sectional **N:** 3676 people **Statistical Analyses:** Logistic regression **Covariates:** Age, sex, race, grade, health insurance **Dose-response Investigated?** Yes	**Pollutant:** PM_{10} **Averaging Time:** Yearly avg 24 h PM_{10} **Mean (SD):** 34.8 **Range (Min, Max):** 13.0, 70.7 **Copollutant (correlation):** NO_2 r = 0.74 O_3 r = 0.32 Acid r = 0.54 $PM_{2.5}$ r = 0.90 NO_2 r = 0.83 O_3 r = 0.50 Acid r = 0.71	**PM_{10} Increment:** 19 µg/m^3 Children w/ asthma Bronchitis: 1.4 (1.1,1.8) Phlegm: 2.1 (1.4, 3.3) Cough: 1.1 (0.8, 1.7) Children w/ wheeze, no asthma Bronchitis: 0.9 (0.7, 1.3) Phlegm: 0.9 (0.6, 1.4) Cough: 1.2 (0.9, 1.8) Children w/ no wheeze, no asthma Bronchitis: 0.7 (0.4, 1.0) Phlegm: 0.8 (0.6, 1.3) Cough: 0.9 (0.7, 1.2)
Reference: McConnell et al. (2003, 049490) **Period of Study:** 1993-1999 **Location:** 12 Southern CA communities	**Outcome:** Bronchitis symptoms **Age Groups:** 9-19 **Study Design:** Communities selected on basis of historic levels of criteria pollutants and low residential mobility. **N:** 475 children **Statistical Analyses:** 3 stage regression combined to give a logistic mixed effects model **Covariates:** Sex, ethnicity, allergies history, asthma history, SES, insurance status, current wheeze, current exposure to ETS, personal smoking status, participation in team sports, in utero tobacco exposure through maternal smoking, family history of asthma, amount of time routinely spent outside by child during 2-6 pm. **Dose-response Investigated?** No **Statistical Package:** SAS Glimmix macro	**Pollutant:** PM_{10} **Averaging Time:** 4-yr avg **Mean (SD):** .30.8(13.4) µg/m^3 **Range (Min, Max):** 15.7-63.5 PM Component: particulate OC and EC **Copollutant (correlation):** $PM_{2.5}$: r = 0.79 $PM_{10-2.5}$: r = 0.79 Inorganic acid: r = 0.72 Organic Acid: r = 0.59 EC: r = 0.71 OC: r = 0.70 NO_2: r = 0.20 O_3: r = 0.64	**PM Increment:** Between community range 47.8 µg/m^3 Between community unit 1 µg/m^3 Within community 1 µg/m^3 OR Estimate [Lower CI, Upper CI] Between community per range 1.72(0.93-3.20)| Between Community per unit 1.01(1.00-1.02)| Within community per unit 1.04(0.99-1.10)
Reference: McConnell et al. (2002, 023150) **Period of Study:** 1993-1998 **Location:** 12 communities in Southern California (grouped into either high and low pollution communities)	**Outcome:** Asthma (new diagnosis) **Age Groups:** 9-12 yr, 12-13 yr, 15-16 yr **Study Design:** Cohort **N:** 3535 **Statistical Analyses:** Multivariate proportion hazard model **Covariates:** Sex, age, ethnic origin, BMI, child history of allergies and asthma history, SES, maternal smoking, time spent outside, history of wheezing, ownership of insurance (yes/no), number and type of sports played **Dose-response Investigated?** Yes **Statistical Package:** SAS 8.1	**Pollutant:** PM_{10} **Averaging Time:** 4 yr **Mean (SD):** Low pollution communities: 21.6 (3.8) **High pollution communities:** 43.3 (12.0) **Percentiles:** Low pollution communities: 50th(Median): 20.8 High pollution communities: 50th(Median): 43.3 **Range (Min, Max):** Low pollution communities: 16.62, 27.3 High pollution communities: 33.5, 66.9 **Monitoring Stations:** 12 **Copollutant (correlation):** $PM_{2.5}$: r = 0.96 NO_2: r = 0.65 O_3	**RR Estimate [Lower CI, Upper CI] lag:** Low PM communities: 1.0 [ref] 0 sport 1.5 [1.0, 2.2] 1 sport 1.2 [0.7, 1.9] 2 sports 1.7 [0.9, 3.2] ≥ 3 sports High PM communities: 1.0 [ref] 0 sport 1.1 [0.7, 1.7] 1 sport 0.9 [0.5, 1.7] 2 sports 2.0 [1.1, 3.6] ≥3 sports **High vs. Low PM_{10} communities: 0.8 (0.6, 1.0)** **Incidence-N (incidence) number of sports:** Low PM communities: 49 (0.023) 0 54 (0.032) 1 22 (0.024) 2 13 (0.033) ≥3 High PM communities: 55 (0.021) 0 36 (0.021) 1 14 (0.018) 2 16 (0.033) ≥3

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: McConnell, et al. (2006, 180226) **Period of Study:** 1996-1999 **Location:** 12 Southern California communities	**Outcome:** Prevalence of bronchitic symptoms (yrly). **Age Groups:** 10-15-yr-old **Study Design:** Longitudinal cohort **N:** 475 asthmatic children **Statistical Analyses:** Multilevel logistic mixed effects models. **Covariates:** Age, second-hand smoke Personal smoking history Sex, race. **Dose-response Investigated?** No **Statistical Package:** SAS with GLIMMIX macro	**Pollutant:** PM_{10} **Averaging Time:** 365 days **Percentiles:** Community by yr (n = 48 = 12 communities · 4 yr) 25th: NR 50th(Median): 3.4 75th: NR **Range (Min, Max):** Community by yr (n = 48 = 12 communities · 4 yr): (0.89, 8.7) **Monitoring Stations**: 12 **Copollutant:** O_3, NO_2, EC, OC, Acid vapor (acetic and formic acid)	**PM Increment:** 6.1 µg/m^3 OR Estimate [Lower CI, Upper CI] PM_{10} Dog (n = 292): 1.60 [1.12: 2.30] No dog (n = 183): 0.89 [0.57: 1.39] PM_{10}*Dog interaction p-value: 0.02 Cat (n = 202): 1.47 [0.96: 2.24] No Cat (n = 273): 1.20 [0.83: 1.73] PM_{10}*Cat interaction p-value: 0.41 Neither pet (n = 112): 0.91 [0.53: 1.56] Cat only (n = 71): 0.84 [0.42: 1.66] Dog only (n = 161): 1.41 [0.91: 2.19] Both pets (n = 131): 1.89 [1.15: 3.10] Results suggest that dog ownership, a source of residential exposure to endotoxin, may worsen the severity of respiratory symptoms from exposure to air pollutants in asthmatic children.
Reference: Meng et al. (2007, 093275) **Period of Study:** Nov 2000 and Sep 2001 (collection of health data) **Location:** Los Angeles and San Diego counties	**Outcome:** Poorly controlled asthma vs. controlled asthma **Age Groups:** 18-64, 65+ **Study Design:** Long-term exposure study Comparison of cases and controls **N:** 1,609 adults (represented individuals age 18+ who reported ever having been diagnosed as having asthma by a physician and had their address successfully geocoded) **Statistical Analyses:** Logistic regression to evaluate associations between TD (traffic density) and annual avg air pollution concentrations and poorly controlled asthma. Used sample weights that adjusted for unequal probabilities of selection into the CHIS sample. **Covariates:** Age, sex, race/ethnicity, family federal poverty level, county, insurance status, delay in care for asthma, taking medications, smoking behavior, self-reported health status, employment, physical activity **Dose-response Investigated?** yes	**Pollutant:** PM_{10} **Averaging Time:** 24 h over 1 yr **Copollutant (correlation):** O_3: r = -0.72 NO_2: r = 0.83 $PM_{2.5}$: r = 0.84 CO: r = 0.42 TD: r = 0.14	**PM Increment:** Continuous data: per 10 µg/m^3 OR Estimate [Lower CI, Upper CI] lag: All Adults: 1.08 [0.82, 1.43] Non-Elederly Adults: 1.14 [0.84, 1.55] Elderly: 0.84 [0.41, 1.73] Women: 1.38 [0.99, 1.94]

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Millstein et al. (2004, 088629) **Period of Study:** Mar-Aug, 1995, and Sep 1995-Feb 1996 Data were taken from the Children's Health Study **Location:** Alpine, Atascadero, Lake Arrowhead, Lake Elsinore, Lancaster, Lompoc, Long Beach, Mira Loma, Riverside, San Dimas, Santa Maria, and Upland, CA	**Outcome:** Wheezing & asthma medication use (ICD9 NR) **Age Groups:** 4th grade students, mostly 9 yr at the time of the study **Study Design:** Cohort Study, stratified into 2 seasonal groups/ **N:** 2081 enrolled, 2034 provided parent-completed questionnaire. **Statistical Analyses:** Multilevel, mixed-effects logistic model. **Covariates:** Contagious respiratory disease, ambient airborne pollen and other allergens, temperature, sex, age race, allergies, pet cats, carpet in home, environmental tobacco smoke, heating fuel, heating system, water damage in home, education level of questionnaire signer, physician diagnosed asthma. **Season:** Mar-Aug, 1995, and Sep, 1995 to Feb, 1996 **Statistical Package:** GLIMMIX SAS 8.00 macro for generalized linear mixed models. **Lags Considered:** 14	**Pollutant:** PM_{10} **Averaging Time:** Monthly means for PM_{10}. **PM Component:** Nitric acid, formic acid, acetic acid **Monitoring Stations**: 1 central location in each community **Copollutant (correlation):** O_3: r = 0.76 NO_2: r = 0.39 $PM_{2.5}$: r = 0.91	**PM Increment:** IQR 13.39 µg/m^3 Odds Ratio [lower CI, Upper CI] Annual PM_{10}: 0.93 [0.67, 1.27] Mar-Aug PM_{10}: 0.91 [0.46, 1.80] Sep-Feb PM_{10}: 0.65 [0.40, 1.06]
Reference: Neuberger et al. (2004, 093249) **Period of Study:** Jun 1999-Jun 2000 **Location:** Austria (Vienna and a rural area near Linz)	**Outcome:** Questionnaire derived asthma score, and a 1-5 point respiratory health rating by parent **Age Groups:** 7-10 yr **Study Design:** Cross-sectional survey **N:** about 2000 children **Statistical Analyses:** Mixed models linear regression-used factor analysis to develop the "asthma score" **Covariates:** Pre-existing respiratory conditions, temperature, rainy days, # smokers in household, heavy traffic on residential street, gas stove or heating, molds, sex, age of child, allergies of child, asthma in other family members **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 4 week avg (preceding interview)	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Copollutant (correlation):** $PM_{2.5}$ (r = 0.94) in Vienna	**PM Increment:** 10 µg/m^3 **Change in mean associated unit increase in PM (p-value) lag** Respiratory Health score Vienna: 0.005 (p>0.05) lag 4 week avg Rural area: 0.008 (p>0.05) lag 4 week avg Asthma score Vienna: 0.006 (p>0.05) lag 4 week avg Rural area: -0.001 (p>0.05) lag 4 week avg
Reference: Oftedal et al. (2008, 093202) **Period of Study:** 2001-2002 **Location:** Oslo, Norway	**Outcome:** Lung function (PEF, FEF25%, FEF50%, FEV_1, FVC) **Age Groups:** 9-10 yr **Study Design:** Cross-sectional **N:** 1847 children **Statistical Analyses:** Linear regression **Covariates:** Height, age, BMI, birth weight, temperature, maternal smoking, sex **Dose-response Investigated?** Yes **Statistical Package:** SPSS, STATA, S-Plus **Lags Considered:** 1-3	**Pollutant:** PM_{10} **IQR:** PM_{10} in 1st yr of life: 10.3 PM_{10} lifetime: 5.8	**PM Increment:** Per IQR **β (Lower CI, Upper CI)** PM_{10} in 1st yr of life PEF -72.5 (-122.3 to -22.7) FEF25% -77.4 (-133.4 to -21.4) FEF50% -53.9 (-102.6. to -5.2) FEV_1 -6.7 (-24.1, 10.7) FVC 0.5 (-18.5, 19.6) PM_{10} lifetime exposure PEF -66.4 (-109.5 to -23.3) FEF25% -61.5 (-110.0 to -13.1) FEF50% -45.6 (-87.7 to -3.5) FEV_1 -7.3 (-22.4, 7.7) FVC -2.1 (-18.6, 14.4)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Parker et al. (2009, 192359) **Period of Study:** 1999-2005 **Location:** U.S.	**Outcome:** Respiratory allergy/hayfever **Study Design:** Cohort **Covariates:** Survey yr, age, family structure, usual source of care, health insurance, family income relative to federal poverty level, race/ethnicity **Statistical Analysis:** Logistic regression **Statistical Package:** SUDAAN **Age Groups:** 73,198 children aged 3-17 yr	**Pollutant:** PM_{10} **Averaging Time:** NR **Median:** 24.1 µg/m^3 **IQR:** 20.8-28.7 **Copollutant (correlation):** Summer O_3: 0.26 SO_2: -0.19 NO_2: 0.48 $PM_{2.5}$: 0.51 $PM_{10-2.5}$: 0.86	**Increment:** 10 µg/m^3 **Odds Ratio (95% CI)** Single Pollutant Model, variable N Adjusted: 1.04 (0.99-1.09)
Reference: Penard-Morand et al. (2005, 087951) **Period of Study:** Mar 1999-Oct 2000 Mean concentrations of NO_2, SO_2, PM_{10}, and O_3 were taken from Jan 1998-Dec 2000 **Location:** 6 French cities: Bordeaux, Clermont-Ferrand, Creteil, Marseille, Strasbourg, Reims.	**Outcome:** Flexural dermatitis Asthma (493) Rhinoconjunctivitis Atopic dermatitis Wheeze Allergic rhinitis Atopy EIB (exercise-induced bronchial reactivity) **Age Groups:** 9-11 yr **Study Design:** Cross-sectional **N:** 9615 Children (6672 complete examination and questionnaire info) **Statistical Analyses:** Logistic regression Marginal Model (GENMOD) **Covariates:** Age, Sex, Family history of allergy, Passive smoking Parental education **Season:** All Excluding end of spring and during summer for clinical examinations **Dose-response Investigated?** No **Statistical Package:** SAS	**Pollutant:** PM_{10} **Averaging Time:** 3 yr **Mean (SD):** Low concentrations: 26.9 High Concentrations: 23.8 **Range (Min, Max):** Low concentrations: 10-20 High concentrations: 21.5-29.5 **Copollutant (correlation):** \NO_2: r =.46 SO_2: r =.76 O_3: r = -.02 **Monitoring Stations**: 16	**PM Increment:** 10 µg/m^3 (IQR) **OR Estimate [Lower CI, Upper CI]:** EIB (during exam): 1.43 (1.02-2.01) Flexural dermatitis (during exam): 0.79 (0.59-1.07) Wheeze (past yr): 1.05 (0.72-1.54) Asthma (past yr): 1.23 (0.77-1.95) Rhinoconjunctivitis (past yr): 1.17 (0.86-1.59) Atopic dermatitis (past yr): 1.28 (0.96-1.71) Asthma (lifetime): 1.32 (0.96-1.81) Allergic rhinitis (lifetime): 1.32 (1.04-1.68) Atopic dermatitis (lifetime): 1.09 (0.88-1.36) Atopy (lifetime): 0.98(0.80-1.22) Pollen: 1.14 (0.85-1.53) Indoor: 0.91 (0.72-1.15) Moulds: 1.00 (0.53-1.88) Highest correlated pollutant adjustments: EIB (during exam): 1.16 (0.72-1.85) Flexural dermatitis (during exam): 0.93 0(.60-1.43) Wheeze (past yr): 1.31 (0.71-2.36) Asthma (past yr): 1.25 (0.66-2.37) Rhinoconjunctivitis (past yr): 1.22 (0.98-1.68) Atopic dermatitis (past yr): 1.63 (1.07-2.49) Asthma (lifetime): 1.11 (0.70-1.74) Allergic rhinitis (lifetime): 1.19 (0.94-1.59) Atopic dermatitis (lifetime): 1.47 (1.07-2.00) Atopy (lifetime): 0.93(0.69-1.26) Pollen: 1.30 (0.98-1.57) Indoor: .83 (0.63-1.12) Molds: 1.62 (0.64-4.09)
Reference: Peters et al., (1999, 087237) **Period of Study:** 1986-1990, 1994 **Location:** Southern California	**Outcome:** Asthma, cough, bronchitis, wheeze **Age Groups:** 4th, 7th, & 10th graders **Study Design:** Cohort **N:** 3676 children **Statistical Analyses:** Stepwise logistic regression **Covariates:** Community, grade, race, sex, height, BMI, asthma in parents, hay fever, health insurance, plants in home, mildew in home, passive smoke exposure, pest infestation, carpet, vitamin supplements, active smoking, pets, gas stove, air conditioner **Dose-response Investigated?** Yes	**Pollutant:** PM_{10} **Averaging Time:** 24-h PM_{10} averaged over 1994 **Mean based on data collected during 1986-1990, 1994:** Alpine 37.4, 21.3 Atascadero 28.0, 20.7 Lake Elsinore 59.5, 34.7 Lake Gregory 38.3, 24.2 Lancaster 47.0, 33.6 Lompoc 30.0, 13.0 Long Beach 49.5, 38.8 Mira Loma 84.9, 70.7 Riverside 84.9, 45.2 San Dimas 67.0, 36.7 Santa Maria 28.0, 29.2 Upland 75.6, 49.0	**PM Increment:** 25 µg/m^3 **OR (Lower CI, Upper CI) for respiratory illness** Based on 1986-1990 pollutant levels Ever asthma 0.93 (0.76, 1.13) Current asthma 1.09 (0.86, 1.37) Bronchitis 0.94 (0.74, 1.19) Cough 1.06 (0.93, 1.21) Wheeze 1.05 (0.89, 1.25) Based on 1994 pollutant levels Ever asthma 0.87 (0.67, 1.14) Current asthma 1.11 (0.81, 1.54) Bronchitis 0.90 (0.65, 1.26) Cough 1.14 (0.96, 1.35) Wheeze 1.01 (0.79, 1.29)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Pierse, et al. (2006, 088757) **Period of Study:** 2 yr (once in 1998 and once in 2001—surveys) **Location:** Leicestershire, UK	**Outcome:** Cough without a cold Night time cough Current wheeze **Age Groups:** 1-5 yr **Study Design:** Cross-sectional (cohorts) **N:** 4400 children **Statistical Analyses:** Binomial generalized linear models (compared with likelihood ratio tests) Spatial variograms (due to the spatial concerns) **Covariates:** Age, Gender Mother/father has asthma Coal heating the home, Smoking by household member in the home, Either parent continued education past 16 yr of age, Pre-term birth, Breast feeding, Gas cooking, Presence of pets, Number of cigarettes smoked by mother, Overcrowding, Single parenthood, Diet **Dose-response Investigated?** Yes (Fig. 2 shows evidence of dose-response effect based on surveys, states in discussion). **Statistical Package:** SAS 8.2 S-Plus 6.1	**Pollutant:** PM_{10} **Averaging Time:** Annual PM_{10} **Mean (SD):** 1998: 1.47 2001: 1.33 Percentiles: 25th: 1998 (.73) and 2001 (.8) 75th: 1998 (1.93) and 2001 (1.84)	**PM Increment:** 10 µg/m^3 (IQR) **Unadjusted OR estimates [Lower CI, Upper CI]:** Cough without cold (1998): 1.22 (1.10 to 1.36) Cough without cold (2001): 1.46 (1.27 to 1.68) Night-time cough (1998): 1.11 (1.01 to 1.23) Night-time cough (2001): 1.25 (1.09 to 1.43) Current wheeze (1998): 0.99 (0.89 to 1.10) Current wheeze (2001): 1.09 (0.93 to 1.30) **Adjusted OR Estimate [Lower CI, Upper CI]:** Cough without cold (1998): 1.21 (1.07 to 1.38) Cough without cold (2001): 1.56 (1.32 to 1.84) Night-time cough (1998): 1.06 (0.94 to 1.19) Night-time cough (2001): 1.25 (1.06 to 1.47) Current wheeze (1998): 0.99 (0.88 to 1.12) Current wheeze (2001): 1.28 (1.04 to 1.58) **When the child was originally asymptomatic in 1998:** **Unadjusted OR estimates [Lower CI, Upper CI]:** Cough without cold (2001): 1.68 (1.39 to 2.03) Night-time cough (2001): 1.21 (1.00 to 1.46) Current wheeze (2001): 1.22 (0.92 to 1.62) **Adjusted OR Estimate [Lower CI, Upper CI]:** Cough without cold (2001): 1.62 (1.31 to 2.00) Night-time cough (2001): 1.19 (0.96 to 1.47) Current wheeze (2001): 1.42 (1.02 to 1.97)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Qian et al. (2005, 093283) **Period of Study:** 1990-1992 **Location:** Forsythe, NC Minneapolis, MN Jackson, MS.	**Outcome:** FVC, FEV_1, FEV_1/FVC **Age Groups:** Middle aged (avg 56.8 yr) **Study Design:** Cross-sectional **N:** 10,240 people **Statistical Analyses:** Regression equations, multiple linear regression analyses **Covariates:** Smoking status, recent use of respiratory medication, current respiratory symptoms, chronic lung diseases, field center **Dose-response Investigated?** No **Statistical Package:** SAS software, version 9.1	**Pollutant:** PM_{10} **Averaging Time:** Annual **Mean (SD):** 27.9 (2.8) Percentiles: 25th: 25.8 50th(Median): 27.5 75th: 30.2 **Range** (Maximum-Minimum): 12.2 **Monitoring Stations**: 3 (Minneapolis, MN) 5 (Jackson, MS) and 9 (Forsythe, NC) **Copollutant:** O_3	**PM Increment:** 2.8 µg/m^3 (1 SD) Effect Estimate: In Never Smokers FVC ß = -0.0108, SE = 0.0026, p =.0001 FEV_1 ß = -0.0082, SE = 0.0029, p =.0047 FEV_1/FVC ß = -0.0024, SE = 0.0023, p =.2787 Smoking status Current n = 2377, FVC = -1.96, FEV_1 = -2.23, FEV_1/FVC = -0.94 Former n = 3858, FVC = -1.25, FEV_1 = -1.10, FEV_1/FVC = -0.30 Never n = 4005, FVC = -1.12, FEV_1 = -0.63, FEV_1/FVC = 0.06 Recent Use of Respiratory Medication Yes n = 424, FVC = -2.65, FEV_1 = -3.89, FEV_1/FVC = -3.00 No n = 9816, FVC = -1.41, FEV_1 = -1.20, FEV_1/FVC = -0.24 Current Respiratory Symptoms Yes n = 4340, FVC = -1.68, FEV_1 = -1.70, FEV_1/FVC = -0.63 No n = 5900, FVC = -1.05, FEV_1 = -0.63, FEV_1/FVC = 0.05 Chronic Lung Diseases Yes n = 1374, FVC = -1.95, FEV_1 = -2.31, FEV_1/FVC = -1.18 No n = 8866, FVC = -1.35, FEV_1 = -1.10, FEV_1/FVC = -0.19 Field Center Forsythe, NC n = 3504, FVC = -0.03, FEV_1 = 0.05, FEV_1/FVC = -0.33 Minneapolis, MN n = 3793, FVC = 0.50, FEV_1 = 0.54, FEV_1/FVC = -0.30 Jackson, MS n = 2943, FVC = -0.01, FEV_1 = 0.17, FEV_1/FVC = -0.32
Reference: Rios et al. (2004, 087800) **Period of Study:** 1998-2000 **Location:** the metropolitan area of Rio de Janiero, Brazil, Duque de Caxias (DC) and Seropedica (SR)	**Outcome:** Wheezing, asthma, cough at night **Age Groups:** 13-14 yr **Study Design:** Cohort **N:** 4064 students **Statistical Analyses:** Cchi-squared **Covariates:** Sex, type of school, time of residence, domestic smoking, residents per home **Dose-response Investigated?** Yes **Statistical Package:** EpiInfo	**Pollutant:** PM_{10} **Averaging Time:** Weekly measurements used to create annual PM estimate **Mean (SD):** DC 1998: 147 1999: 115 2000: 110 Total: 124 SR 1998: 37 1999: 31 2000: 37 Total: 35 **Monitoring Stations**: NR	**PM Increment:** High vs. Low Global Cut-Off Score %, p-val: DC Male: 15.0 Female: 22.3, p < .05† Private School: 16.6 Public School: 19.4, p < .05* <5yr residence: 20.9 >5yr residence: 16.8 No domestic smoking exposure: 17.6 Domestic smoking exposure: 20.4, p < .05† <5 residents per home: 18.4 5+ residents per home: 19.5 SR Male: 12.3 Female: 19.7, p < .05† Private School: 28.3, p < .05*† Public School: 14.7 <5yr residence: 10.8 >5yr residence: 16.5 No domestic smoking exposure: 14.8 Domestic smoking exposure: 18.3 <5 residents per home: 15.6 5+ residents per home: 17.4 **Notes:** The Global Cut-off Score encompasses replies to the asthma component of ISAAC's written questionnaire that establishes a cut-off from which is defined the presence of asthma for the Brazilian population. *Comparing the cities in the same controlled variable †Comparing the controlled variable in the same city

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Rojas-Martinez et al. (2007, 091064) **Period of Study:** 1996-1999 **Location:** Mexico City, Mexico	**Outcome:** Lung function: FEV_1, FVC, FEF25-75% **Age Groups:** Children 8 yr old at time of cohort recruitment **Study Design:** School-based "dynamic" cohort study **N:** 3170 children 14,545 observations **Statistical Analyses:** Three-level generalized linear mixed models with unstructured variance-covariance matrix **Covariates:** Age, body mass index, height, height by age, weekday spent outdoors, environmental tobacco smoke, previous-day mean air pollutant concentration, time since first test **Dose-response Investigated?** No **Statistical Package:** SA	**Pollutant:** PM_{10} **Averaging Time:** 6 mo **Mean (SD):** 6-mo averaging SD: NR Mean: 75.6 **Percentiles:** 6-mo averaging 25th: 55.8 50th(Median): 67.5 75th: 92.2 **Monitoring Stations**: 5 sites for PM_{10}, 10 for other pollutants **Copollutant:** O_3 NO_2	**PM Increment:** IQR 6-LC: 36.4 Slope [Lower CI, Upper CI] Girls One-pollutant model FVC: -39 [-47: -31] FEV: -29 [-36: -21] FEF25-75%: -17 [-36: 1] FEV_1/FVC: 0.12 [0.07: 0.17] Two-pollutant model: PM_{10}, 6-LC & O_3 FVC: -30 [-39: -22] FEV: -24 [-31: -16] FEF25-75%: -9 [-26: 9] FEV_1/FVC: 0.10 [0.06: 0.15] PM_{10}, 6-LC & NO_2 FVC: -21 [-30: -13] FEV: -17 [-25: -8] FEF25-75%: -23 [-43: -4] FEV_1/FVC: 0.07 [0.02: 0.13] Multipollutant model: PM_{10}, 6-LC, O_3, & NO_2 FVC: -14 [-23: -5] FEV: -11 [-20: -3] FEF25-75%: -7 [-27: 12] FEV_1/FVC: 0.08 [0.03: 0.13] Boys One-pollutant model FVC: -33 [-41: -25] FEV: -27 [-34: -19] FEF25-75%: -18 [-34: -2] FEV_1/FVC: 0.04 [-0.01: 0.09] Two-pollutant model: PM_{10}, 6-LC & O_3 FVC: -28 [-36: -19] FEV: -22 [-30: -15] FEF25-75%: -10 [-27: 7] FEV_1/FVC: 0.04 [-0.01: 0.09] FEV_1/FVC: 0.24 [0.13: 0.34] PM_{10}, 6-LC & NO_2 FVC: -16 [-26: -7] FEV: -19 [-27: -10] FEF25-75%: -26 [-44: -9] FEV_1/FVC: 0.005 [-0.06: 0.05] Multipollutant model PM_{10}, 6-LC, O_3, & NO_2 FVC: -12 [-22: -3] FEV: -15 [-23: -6] FEF25-75%: -12 [-30: 6] FEV_1/FVC: -0.002 [-0.06: 0.05]
Reference: Schikowski et al. (2005, 088637) **Period of Study:** 1985-1994 **Location:** Rhine-Ruhr Basin of Germany [Dortmund (1985, 1990), Duisburg (1990), Gelsenkirchen (1986, 1990), and Herne (1986)]	**Outcome:** Respiratory symptoms & pulmonary function **Age Groups:** Age 54-55 **Study Design:** Cross-sectional **N:** 4757 women **Statistical Analyses:** Linear & Logistic regressions, including random effects model **Covariates:** Age, smoking, SES, occupational exposure, form of heating, BMI, height **Season:** NR **Dose-response Investigated?** No **Statistical Package:** SAS **Lags Considered:** NR	**Pollutant:** PM_{10} **Averaging Time:** NR Min, P25, Median, Mean, P75, Max Annual Mean 35, 40, 43, 44, 47, 53 5-yr Mean 39, 43, 47, 48, 53, 56 **Monitoring Stations**: 7 **Copollutant (correlation):** NR	**PM Increment:** 7 $\mu g/m^3$ **OR (Lower CI, Upper CI) for asthma symptoms** Annual means Chronic bronchitis 1.00 (0.85, 1.18) Chronic cough 1.03 (0.87, 1.23) Frequent cough 1.01 (0.93, 1.10) COPD 1.37 (0.98, 1.92) $p < 0.1$ FEV_1 0.953 (0.916, 0.989) $p < 0.1$ FVC 0.966 (0.940, 0.992) $p < 0.1$ FEV_1/FVC 0.989 (0.978, 1.000) $p < 0.1$ Five yr means Chronic bronchitis 1.13 (0.95, 1.34) Chronic cough 1.11 (0.93, 1.31) Frequent cough 1.05 (0.94, 1.17) COPD 1.33 (1.03, 1.72) $p < 0.1$ FEV_1 0.949 (0.923, 0.975) $p < 0.05$ FVC 0.963 (0.945, 0.982) $p < 0.05$ FEV_1/FVC 0.989 (0.980, 0.997) $p < 0.1$
Reference: Schindler et al, (2009,	**Outcome:** Respiratory Symptoms	**Pollutant:** PM_{10}	**Increment:** 10 $\mu g/m^3$

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
191950) **Period of Study:** 1991-2002 **Location:** Switzerland	**Study Design:** Prospective Cohort **Statistical Analysis:** Logistic Regression Model **Age Groups:** Adults, 18-60 yr of age at start of study **Covariates:** Sex, age, level of education, Swiss citizenship, BMI, parental smoking, parental history of asthma/atopy, early respiratory infection, smoking status, pack yr, daily number of cigarettes, yr since smoking cessation, passive smoking in general/at work, occupational exposure to airbourne irritants	**Averaging Time:** Annual **Mean (SD) Unit:** **Range (Min, Max):** **Copollutant (correlation):** NR	**Odds Ratio (95%CI) of reporting symptoms at second interview** Entire Sample, New Reports Regular Cough: 0.77 (0.62-0.97) Regular Phlegm: 0.74 (0.56-0.99) Chronic Cough or Phlegm: 0.78 (0.62-0.98) Wheezing: 1.01 (0.74-1.39) Wheezing with Dyspnea: 0.70 (0.49-1.01) Wheezing without Cold: 1.06 (0.76-1.50) Entire Sample, Persistent Reports Regular Cough: 0.55 (0.39-0.78) Regular Phlegm: 0.82 (0.52-1.33) Chronic Cough or Phlegm: 0.67 (0.40-1.15) Wheezing: 0.50 (0.32-0.80) Wheezing with Dyspnea: 0.59 (0.30-1.23) Wheezing without Cold: 0.61- (0.35-1.12) Persistent Non-Smokers, New Reports Regular Cough: 0.86 (0.63-1.19) Regular Phlegm: 0.70 (0.49-0.99) Chronic Cough or Phlegm: 0.71 (0.52-0.99) Wheezing: 0.93 (0.60-1.46) Wheezing with Dyspnea: 0.77 (0.50-1.20) Wheezing without Cold: 1.11 (0.66-1.92) Persistent Non-Smokers, Persistent Reports Regular Cough: 0.28 (0.14-0.60) Regular Phlegm: 0.87 (0.43-1.84) Chronic Cough or Phlegm: 0.35 (0.16-0.81) Wheezing: 0.53 (0.28-1.08) Wheezing with Dyspnea: 0.76 (0.30-2012) Wheezing without Cold: 0.61 (0.26-1.52) **Gender-specific odds ratio (95%CI) of reporting symptoms at second interview** New Reports Regular Cough, p = 0.73 Men: 0.75 (0.53-1.06) Women: 0.81 (0.58-1.15) Regular Phlegm, p = 0.41 Men: 0.85 (0.60-1.20) Women: 0.68 (0.46-1.00) Chronic Cough or Phlegm: 0.36 Men: 0.87 (0.63-1.21) Women: 0.71 (0.51-0.97) Wheezing, p = 0.20 Men: 0.83 (0.57-1.20) Women: 1.20 (0.78-1.87) Wheezing with Dyspnea, p = 0.11 Men: 0.56 (0.36-0.87) Women: 1.00.57-1.842 Wheezing without Cold, p = 0.43 Men: 0.95 (0.63-1.42) Women: 1.25 (0.72-2.17) Persistent Reports Regular Cough, p = 0.02 Men: 0.75 (0.48-1.18) Women: 0.31 (0.17-0.56) Regular Phlegm, p = 0.33 Men: 0.65 (0.37-1.12) Women: 1.04 (0.47-2.34) Chronic Cough or Phlegm: 0.47 Men: 0.68 (0.39-1.20) Women: 0.47 (0.20-1.11) Wheezing, p = 0.29 Men: 0.34 (0.17-0.72)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Women: 0.57 (0.32-1.01) Wheezing with Dyspnea, p = 0.63 Men: 0.56 (0.16-1.95) Women: 0.37 (0.13-1.05) Wheezing without Cold, p = 0.57 Men: 0.34 (0.12-0.91) Women: 0.49 (0.21-1.15) **Odds Ratio (95%CI) of reporting symptoms at second interview with additional adjustment for annual outdoor PM exposure at baseline** Entire Sample Regular Cough, p = 0.0003 New Reports: 0.77 (0.61-0.97) Persistent Reports: 0.55 (0.39-0.78) Regular Phlegm, p = 0.13 New Reports: 0.77 (0.59-1.02) Persistent Reports: 0.79 (0.46-1.33) Chronic Cough or Phlegm, p = 0.02 New Reports: 0.78 (0.62-0.98) Persistent Reports: 0.64 (0.40-1.02) Wheezing, p = 0.002 New Reports: 0.91 (0.63-1.33) Persistent Reports: 0.47 (0.31-0.72) Wheezing with Dyspnea, p = 0.03 New Reports: 0.65 (0.43-0.98) Persistent Reports: 0.55 (0.28-1.10) Severe Wheezing, p = 0.28 New Reports: 0.96 (0.66-1.40) Persistent Reports: 0.62 (0.34-1.12) Non-Smokers Regular Cough, p < 0.001 New Reports: 0.87 (0.63-1.19) Persistent Reports: 0.29 (0.16-0.52) Regular Phlegm, p = 0.07 New Reports: 0.70 (0.50-0.99) Persistent Reports: 0.67 (0.34-1.33) Chronic Cough or Phlegm, p = 0.008 New Reports: 0.72 (0.52-0.99) Persistent Reports: 0.38 (0.17-0.84) Wheezing, p = 0.07 New Reports: 0.87 (0.52-1.48) Persistent Reports: 0.48 (0.25-0.91) Wheezing with Dyspnea, p = 0.36 New Reports: 0.76 (0.48-1.19) Persistent Reports: 0.70 (0.27-1.82) Severe Wheezing, p = 0.57 New Reports: 1.11 (0.64-1.93) Persistent Reports: 0.64 (0.26-1.54)
Reference: Sharma et al. (2004, 156974) **Period of Study:** Nov 2002-Apr 2003 **Location:** 3 sections in Kanpur City, India: 1) Indian Institute of Technology Kanpur (IITK) 2) Vikas Nagar (VN) 3) Juhilal Colony (JC)	**Outcome:** Lung function **Age Groups:** 20-55 yr **Study Design:** Cohort **N:** 91 people **Statistical Analyses:** Linear regression **Covariates:** NR **Season:** Fall, Winter, spring **Dose-response Investigated?** No **Statistical Package:** Microsoft Excel **Lags Considered:** 1-day lag & 5-day ma	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** IITK 184 (40) VN 295 (58) JC 293 (90) **PM Component:** Lead, Nickel, Cadmium, Chromium, Iron, Zinc Benzene soluble fraction (includes polycyclic aromatic hydrocarbons [PAHs]) **Copollutant (correlation):** ΔPEF = mean daily deviations in PEF PM_{10}-ΔPEF: (-0.52) PM_{10}-$PM_{2.5}$: (0.67) PM_{10}-PM_{10} (1-day lag): (0.45) PM_{10}-$PM_{2.5}$ (1-day lag): (0.46)	**PM Increment:** 1 μg/m^3 ΔPEF (difference or change in peak expiratory flow) -0.0318 L/min

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Tager et al. (2005, 087538) **Period of Study:** Apr 2000-Jun 2000, Feb 2001-Jun 2001, Feb 2002-Jun 2002 **Location:** Los Angeles, California San Francisco, California	**Outcome:** Lung Function (FEV_1, FVC, PEFR, FEF75, FEF25-75, FEF25-75/FVC ratio) **Age Groups:** 16-21+ y/o College Freshman **Study Design:** Retrospective cohort **N:** 255 students 108 Men (M) 147 Women (W) **Statistical Analyses:** Multivariate Linear Regression **Covariates:** Sex, height, weight, area of residence, age, race, ETS exposure, respiratory disease history **Dose-response Investigated?** No	**Pollutant:** PM_{10} **Averaging Time:** Cumulative lifetime exposure **Median**: Prior to 1987: M: 73 W: 71 1987 and later: M: 36 W: 34 Lifetime: M: 48 W: 45 **Range (Min, Max):** Prior to 1987: M: 34, 117 W: 31, 124 1987 and later: M: 18, 68 W: 20, 61 Lifetime: M: 21, 80 W: 18, 71 **Monitoring Stations**: Between 1 and 3 **Copollutant (correlation):** O_3 prior to 1987: r = 0.68 O_3 1987 and later: r = 0.81 O_3-Lifetime: r = 0.57	**PM Increment:** 1 $\mu g/m^3$ Parameter Estimates (SD) (Lifetime PM_{10}, Interaction PM_{10} FEF25-75/FVC) LnFEF75: M: -0.009 (0.0009), 0.009 (0.007) W: -0.010 (0.0007), 0.008 (0.0005)
Reference: Tamura et a. (2003, 087445) **Period of Study:** 1998-1999 **Location:** Bangkok, Thailand	**Outcome:** Non-specific respiratory disease (Chronic bronchitis, acute bronchitis, bronchial asthma, dyspnea and wheezing) **Age Groups:** Adults **Study Design:** Cross-sectional **N:** 1603 policemen **Statistical Analyses:** Multiple logistic regression **Covariates:** Age, smoking status **Dose-response Investigated?** Yes **Statistical Package:** SPSS	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** Heavily Polluted 80-190 Moderately Polluted 60-69 Control 59 **Monitoring Stations**: 13	**PM Increment:** Heavily Polluted vs. Moderately Polluted vs. Control Number and Prevalence (%) of respiratory disease among heavily polluted, moderately polluted, and control areas. **Heavily Polluted** Chronic bronchitis 16 (3.0) Acute bronchitis 19 (3.5) Bronchial asthma 5 (0.9) Dyspnea & wheezing 49 (9.2) Any 1 of above 69 (13.0) Persistent cough 11 (2.1) Persistent phlegm 27 (1.3) Cough & phlegm 6 (1.1) **Moderately Polluted** Chronic bronchitis 8 (2.4) Acute bronchitis 12 (9.0) Bronchial asthma 2 (0.6) Dyspnea & wheezing 23 (6.8) Any 1 of above 37 (10.9) Persistent cough 1 (0.3) Persistent phlegm 11 (3.3)| Cough & phlegm 1 (0.3) Control Chronic bronchitis 6 (1.9) Acute bronchitis 11 (3.3) Bronchial asthma 0 (0.0) Dyspnea & wheezing 23 (7.2) Any 1 of above 31 (9.4) Persistent cough 1 (0.3) Persistent phlegm 8 (2.4) Cough & phlegm 1 (0.3)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Wheeler and Ben-Schlomo (2005, 188766) **Period of Study:** 1995-1997 **Location:** England	**Outcome:** FEV_1 **Age Groups:** 16-79 yr **Study Design:** Data from Health Survey for England were coupled geographically with air pollution measurements on a 1 km grid. **N:** 26,426 households with 39,251 adults **Statistical Analyses:** Logistic regression, least squares regression **Covariates:** Age, sex, height, body mass index, smoking status, household passive smoke exposure, inhaler use in the previous 24-h, doctor diagnosis of asthma. **Dose-response Investigated?** No	**Pollutant:** PM_{10} **Averaging Time:** 1996 annual mean **Mean (SD):** 23.95 (3.58) **Range (Min, Max):** 17.87-43.37	**β (95%CI) for Height-age standardized FEV1 by ambient air quality index** p-value Male Good (ref) Poor -0.023 (-0.030 to -0.016) <0.001 Female Good (ref) Poor -0.019 (-0.026 to -0.013) <0.001
Reference: Zhang et al., (2002, 034814) **Period of Study:** 1993-1996 **Location:** 4 Chinese cities (urban and suburban location in each city): Guangzhou, Wuhan, Lanzhou, Chongqing	**Outcome:** Interview-self reports of symptoms: Wheeze (ever wheezy when having a cold) Asthma (diagnosis by doctor) Bronchitis (diagnosis by doctor), Hospitalization due to respiratory disease (ever) Persistent cough (coughed for at least 1 month per yr with or apart from colds) Persistent phlegm (brought up phlegm or mucus from the chest for at least 1 month per yr with or apart from colds) **Age Groups:** Elementary school students age range: 5.4-16.2 **Study Design:** Cross-sectional **N:** 7,557 returned questionnaires 7,392 included in first stage of analysis **Statistical Analyses:** 2-stage regression approach: Calculated odds ratios and 95% CIs of respiratory outcomes and covariates Second stage consisted of variance-weighted linear regressions that examined associations between district-specific adjusted prevalence rates and district-specific ambient levels of each pollutant. **Covariates:** Age, gender, breast-fed, house type, number of rooms, sleeping in own or shared room, sleeping in own or shared bed, home coal use, ventilation device used, homes smokiness during cooking, eye irritation during cooking, parental smoking, mother's education level, mother's occupation, father's occupation, questionnaire respondent, yr of questionnaire administration, season of questionnaire administration, parental asthma prevalence	**Pollutant:** PM_{10} **Averaging Time:** 2 yr **Mean (SD):** 151 (56) IQR: 87 **Range (Min, Max):** Gives range (max.-min.): 80 **Monitoring Stations**: 2 types: municipal monitoring stations over a period of 4 yr (1993-1996) Schoolyards of participating children over a period of 2 yr (1995-1996)	**PM Increment:** Interquartile range corresponded to 1 unit of change. **RR Estimate [Lower CI, Upper CI] lag:** Association between persistent phlegm and PM_{10}: 3.21 (1.55, 6.67) $p < 0.05$ Between and within city modeled ORs, scaled to interquartile range of concentrations for each pollutant. No associations between any type of respiratory outcome and PM_{10} When scaled to an increment of 50 $\mu g/m^3$ of PM_{10}, ORs were: Wheeze: 1.07 Asthma: 1.18 Bronchitis: 1.53 Hospitalization: 1.17 Persistent cough: 1.20 Persistent phlegm: 1.95

[1]All units expressed in $\mu g/m^3$ unless otherwise specified.

Table E-23. Long-term exposure - respiratory morbidity outcomes - $PM_{10-2.5}$.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Chattopadhyay et al. (2007, 147471) **Period of Study:** NR **Location:** Three different points in Kolkata, India: North, South, and Central	**Outcome:** pulmonary function tests (respiratory impairments) **Age Groups**: All ages **Study Design:** Cross-sectional **N:** 505 people studied for PFT total population of Kolkata not given **Statistical Analyses:** Frequencies **Covariates:** Meteorologic data (i.e. temperature, wind direction, wind speed, and humidity) **Dose-response Investigated?** No	**Pollutant:** PM<3.3-0.4 **Averaging Time:** 8 h **Mean (SD):** North Kolkata: 266.1 Central Kolkata: 435.3 South Kolkata: 449.1 Unit (i.e. $\mu g/m^3$): $\mu g/m^3$ **Monitoring Stations**: 1 **Copollutant (correlation):** PM_{10} PM<10-3.3	**PM Increment:** NR **Respiratory impairments (SD):** North Kolkata Male (n=137) Restrictive: 4 (2.92) Obstructive: 5 (3.64) Combined Res. And Obs.: 6 (4.37) Total: 15 (10.95) Female (n=152) Restrictive: 3 (1.97) Obstructive: 5 (3.28) Combined Res. And Obs.: 0 Total: 8 (5.26) Total (n=289) Restrictive: 7 (2.42) Obstructive: 10 (3.46) Combined Res. And Obs.: 6 (2.07) Total: 23 (7.96) Central Kolkata Male (n=44) Restrictive: 6 (13.63) Obstructive: 1 (2.27) Combined Res. And Obs.: 1 (2.27) Total: 8 (18.18) Female (n=50) Restrictive: 3 (6.00) Obstructive: 2 (4.00) Combined Res. And Obs.: 0 Total: 5 (10.00) Total (n=94) Restrictive: 9 (9.57) Obstructive: 3 (3.19) Combined Res. And Obs.: 1 (1.06) Total: 13 (13.82) South Kolkata Male (n=52) Restrictive: 1 (1.92) Obstructive: 2 (3.84) Combined Res. And Obs.: 3 (5.76) Total: 6 (11.53) Female (n=70) Restrictive: 2 (2.85) Obstructive: 1 (1.42) Combined Res. And Obs.: 0 Total: 3 (4.28) Total (n=122) Restrictive: 3 (2.45) Obstructive: 3 (2.45) Combined Res. And Obs.: 3 (2.45) Total: 9 (7.37)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Chattopadhyay et al. (2007, 147471) **Period of Study:** NR **Location:** Three different points in Kolkata, India: North, South, and Central	**Outcome:** Pulmonary function tests (respiratory impairments) **Age Groups**: All ages **Study Design:** Cross-sectional **N:** 505 people studied for PFT Total population of Kolkata not given **Statistical Analyses:** Frequencies **Covariates:** Meteorologic data (i.e. temperature, wind direction, wind speed, and humidity) **Dose-response Investigated?** No	**Pollutant:** PM<10-3.3 **Averaging Time:** 8 h **Mean (SD):** North Kolkata: 269.8 Central Kolkata: 679.2 South Kolkata: 460.1 **Monitoring Stations**: 1 **Copollutant (correlation):** PM_{10} PM<3.3-0.	**PM Increment:** NR **Respiratory impairments (SD):** North Kolkata Male (n=137) Restrictive: 4 (2.92) Obstructive: 5 (3.64) Combined Res. And Obs.: 6 (4.37) Total: 15 (10.95) Female (n=152) Restrictive: 3 (1.97) Obstructive: 5 (3.28) Combined Res. And Obs.: 0 Total: 8 (5.26) Total (n=289) Restrictive: 7 (2.42) Obstructive: 10 (3.46) Combined Res. And Obs.: 6 (2.07) Total: 23 (7.96) Central Kolkata Male (n=44) Restrictive: 6 (13.63) Obstructive: 1 (2.27) Combined Res. And Obs.: 1 (2.27) Total: 8 (18.18) Female (n=50) Restrictive: 3 (6.00) Obstructive: 2 (4.00) Combined Res. And Obs.: 0 Total: 5 (10.00) Total (n=94) Restrictive: 9 (9.57) Obstructive: 3 (3.19) Combined Res. And Obs.: 1 (1.06) Total: 13 (13.82) South Kolkata Male (n=52) Restrictive: 1 (1.92) Obstructive: 2 (3.84) Combined Res. And Obs.: 3 (5.76) Total: 6 (11.53) Female (n=70) Restrictive: 2 (2.85) Obstructive: 1 (1.42) Combined Res. And Obs.: 0 Total: 3 (4.28) Total (n=122) Restrictive: 3 (2.45) Obstructive: 3 (2.45) Combined Res. And Obs.: 3 (2.45) Total: 9 (7.37)
Reference: Dales et al., (2008, 156378) **Period of Study: Location:** Windsor, ON	**Outcome:** Pulmonary function and inflammation **Age Groups:** Grades 4-6 **Study Design:** Cross-sectional prevalence design **Statistical Analyses:** Multivariate linear regression **Covariates:** Ethnic background, smokers at home, pets at home, acute respiratory illness, medication use	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** Annual **Mean:** 7.25 5th: 6.02 95th: 8.23 **Copollutant:** SO_2 NO_2	**Increment:** Tertiles of exposure FEV_1: <7.04: 2.18 ± 0.01 7.04-7.53: 2.19 ± 0.02 >7.53: 2.14 ± 0.01 FVC: <7.04: 2.52 ± 0.02 7.04-7.53: 2.53 ± 0.02 >7.53: 2.48 ± 0.02 eNO: <7.04: 15.48 ± 0.63 7.04-7.53: 16.73 ± 0.76 >7.53: 16.59 ± 0.79

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Gauderman et al. (2000, 012531) **Period of Study:** 1993-1997 **Location:** Southern California	**Outcome:** FVC, FEV_1, MMEF, FEF75 **Age Groups:** Fourth, seventh, or tenth graders **Study Design:** Cohort **N:** 3035 subjects **Statistical Analyses:** Linear regression **Covariates:** Height, weight, BMI, asthma, smoking, exercise, room temperature, barometric pressure **Dose-response Investigated?** Yes **Statistical Package:** SAS	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 24-h avg PM_{10} & annual avg of 2-wk avg $PM_{2.5}$ **Mean (SD):** $PM_{10-2.5}$ 25.6 **Copollutant (correlation):** O_3 r = -0.29 NO_2 r = 0.44 Inorg. Acid r = 0.43	**Increment:** 25.6 µg/m^3 **% Change (Lower CI, Upper CI)** $PM_{10-2.5}$-4th grade FVC -0.57 (-1.20 to -0.06) FEV_1 -0.90 (-1.71 to -0.09) MMEF -1.37 (-2.57 to -0.15) FEF75 -1.62 (-3.24, 0.04) $PM_{10-2.5}$-7th grade FVC -0.35 (-1.02, 0.31) FEV_1 -0.49 (-1.21, 0.24) MMEF -0.64 (-2.83, 1.60) FEF75 -0.74 (-2.65, 1.20) $PM_{10-2.5}$-10th grade FVC -0.17 (-1.32, 0.99) FEV_1 -0.68 (-2.15, 0.81) MMEF -1.41 (-5.85, 3.25) FEF75 -2.32 (-6.60, 2.17)
Reference: Gauderman et al. (2002, 026013) **Period of Study:** 1996-2000 **Location:** Southern California	**Outcome:** Lung function development: FEV_1, maximal mid-expiratory flow (MMEF) **Age Groups:** Fourth grade children (avg age = 9.9 yr) **Study Design:** Cohort study **N:** 1678 children, 12 communities **Statistical Analyses:** Mixed model linear regression **Covariates:** Height, BMI, doctor-diagnosed asthma and cigarette smoking in previous yr, respiratory illness and exercise on day of test, interaction of each of these variables with sex, barometric pressure, temperature at test time, indicator variables for field technician and spirometer **Dose-response Investigated?** Yes **Statistical Package:** SAS (10)	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** Annual 24-h avg **Mean (SD):** The avg levels were presented in an online data supplement (Fig E1) **Monitoring Stations**: 12 **Copollutant (correlation):** O_3 (10 AM to 6 PM) r = 0.10 O_3 r = -0.31 NO_2 r = 0.46 Acid vapor r = 0.63 PM_{10} r = 0.95 $PM_{10-2.5}$ r = 0.81 EC r = 0.71 OC r = 0.96	**PM Increment:** 29.1 µg/m^3 Association Estimate: $PM_{10-2.5}$ was not correlated with any of the pulmonary function tests that were analyzed
Reference: Leonardi et al. (2000, 010272) **Period of Study:** 1996 **Location:** 17 cities of Central Europe (Bulgaria, Czech Republic, Hungary , Poland, Romania, Slovakia)	**Outcome:** Immune biomarkers **Age Groups:** 9-11 **Study Design:** Cross-sectional **N:** 366 school children **Statistical Analyses:** Linear regression **Covariates:** Age, gender, parental smoking, laboratory of analysis, recent respiratory illness **Dose-response Investigated?** No **Statistical Package:** STATA	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** Subtracting $PM_{2.5}$ from PM_{10} provides avg $PM_{10-2.5}$ **Mean (SD):** $PM_{10-2.5}$: 20 (5) **Range (Min, Max):** $PM_{10-2.5}$: (12, 38) 5th, median, & 95th percentile $PM_{10-2.5}$: 12, 19, 29	**% Change (Lower CI, Upper CI)** **p-value** $PM_{10-2.5}$ Neutrophils 1 (-27, 38) >.20 Total lymphocytes 8 (-15, 38) >.20 B lymphocytes 22 (-16, 76) >.20 Total T lymphocytes 2 (-25, 37) >.20 CD4+ -1 (-30, 41) >.20 CD8+ 3 (-25, 41) >.20 CD4/CD8 0 (-23, 30) >.20 NK 1 (-33, 51) >.20 Total IgG -3 (-21, 18) >.20 Total IgM 19 (-9, 55) >.20 Total IgA 16 (-12, 52) >.20 Total IgE -29 (-70, 70) >.20

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: McConnell et al. (2003, 049490) **Period of Study:** 1993-1999 **Location:** 12 Southern CA communities	**Outcome:** Bronchitic symptoms **Age Groups:** 9-19 **Study Design:** Communities selected on basis of historic levels of criteria pollutants and low residential mobility. **N:** 475 children **Statistical Analyses:** 3 stage regression combined to give a logistic mixed effects model **Covariates:** Sex, ethnicity, allergies history, asthma history, SES, insurance status, current wheeze, current exposure to ETS, personal smoking status, participation in team sports, in utero tobacco exposure through maternal smoking, family history of asthma, amount of time routinely spent outside by child during 2-6 pm. **Dose-response Investigated?** No **Statistical Package:** SAS Glimmix macro	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 4-yr avg **Mean (SD):** 17.0(6.4) **Range (Min, Max):** 10.2-35.0 **Copollutant (correlation):** $PM_{2.5}$: r = 0.24 PM_{10}: r = 0.79 Inorganic acid: r = 0.38 Organic Acid: r = 0.35 EC: r = 0.30 OC: r = 0.27 NO_2: r = -0.22 O_3: r = 0.29	**PM Increment:** Between community range 24.8 µg/m^3 Between community unit 1 µg/m^3 Within community 1 µg/m^3 OR Estimate [Lower CI, Upper CI] Between community per range 1.38(0.65-2.92) Between Community per unit 1.01(0.98-1.04) Within community per unit 1.02(0.95-1.10)
Reference: Millstein et al. (2004, 088629) **Period of Study:** Mar-Aug, 1995, and Sep 1995-Feb 1996 Data were taken from the Children's Health Study **Location:** Alpine, Atascadero, Lake Arrowhead, Lake Elsinore, Lancaster, Lompoc, Long Beach, Mira Loma, Riverside, San Dimas, Santa Maria, and Upland, CA	**Outcome:** Wheezing & asthma medication use **Age Groups:** 4th grade students, mostly 9 yr at the time of the study **Study Design:** Cohort Study, stratified into 2 seasonal groups/ **N:** 2081 enrolled, 2034 provided parent-completed questionnaire. **Statistical Analyses:** Multilevel, mixed-effects logistic model. **Covariates:** Contagious respiratory disease, ambient airborne pollen and other allergens, temperature, sex, age race, allergies, pet cats, carpet in home, environmental tobacco smoke, heating fuel, heating system, water damage in home, education level of questionnaire signer, physician diagnosed asthma. **Season:** Mar-Aug, 1995, and Sep, 1995 to Feb, 1996 **Statistical Package:** SAS 8.00 **Lags Considered:** 14	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** monthly **PM Component:** Nitric acid, formic acid, acetic acid **Monitoring Stations**: 1 central location in each community **Copollutant (correlation):** NO_2: r = 0.29 O_3: r = 0.77 $PM_{2.5}$: r = -0.08	**PM Increment:** IQR 11.44 µg/m^3 **Odds Ratio [lower CI, Upper CI]** Annual $PM_{10-2.5}$: 0.96 [0.74, 1.25] Mar-Aug $PM_{10-2.5}$: 0.93 [0.54, 1.59] Sep-Feb $PM_{10-2.5}$: 0.68 [0.46, 1.01]
Reference: (Parker et al., 2009, 192359) **Period of Study:** 1999-2005 **Location:** U.S.	**Outcome:** Respiratory allergy/hayfever **Study Design:** Cohort **Covariates:** Survey yr, age, family structure, usual source of care, health insurance, family income relative to federal poverty level, race/ethnicity **Statistical Analysis:** Logistic regression **Statistical Package:** SUDAAN **Age Groups:** 73,198 children aged 3-17 yr	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** NR **Median:** 11.2 µg/m^3 **IQR:** 8.2-15.2 **Copollutant (correlation):** Summer O_3: 0.16 SO_2: -0.33 NO_2: 0.29 $PM_{2.5}$: 0.02 PM_{10}: 0.86	**Increment:** 10 µg/m^3 **Odds Ratio (95% CI)** Single Pollutant Model, variable N Adjusted: 1.01 (0.95-1.07) Single Pollutant Model, constant N Adjusted: 1.13 (1.04-1.46) Multi-pollutant Model: 1.16 (1.06-1.24)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Zhang et al. (2002, 034814) **Period of Study:** 1993-1996 **Location:** 4 Chinese cities (urban and suburban location in each city): Guangzhou, Wuhan, Lanzhou, Chongqing	**Outcome:** Interview-self reports of symptoms: Wheeze (ever wheezy when having a cold) Asthma (diagnosis by doctor) Bronchitis (diagnosis by doctor), Hospitalization due to respiratory disease (ever) Persistent cough (coughed for at least 1 month per yr with or apart from colds) Persistent phlegm (brought up phlegm or mucus from the chest for at least 1 month per yr with or apart from colds) **Age Groups:** Elementary school students age range: 5.4-16.2 **Study Design:** Cross-sectional **N:** 7,557 returned questionnaires 7,392 included in first stage of analysis **Statistical Analyses:** 2-stage regression approach: Calculated odds ratios and 95% CIs of respiratory outcomes and covariates Second stage consisted of variance-weighted linear regressions that examined associations between district-specific adjusted prevalence rates and district-specific ambient levels of each pollutant. **Covariates:** Age, gender, breast-fed, house type, number of rooms, sleeping in own or shared room, sleeping in own or shared bed, home coal use, ventilation device used, homes smokiness during cooking, eye irritation during cooking, parental smoking, mother's education level, mother's occupation, father's occupation, questionnaire respondent, yr of questionnaire administration, season of questionnaire administration, parental asthma prevalence	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 2 yr **Mean (SD):** 59 (28) **Percentiles:** 25th: NR 50th(Median): NR 75th: NR IQR: 42 **Range (Min, Max):** Gives range (max.-min.): 80 **Monitoring Stations**: 2 types: municipal monitoring stations over a period of 4 yr (1993-1996) Schoolyards of participating children over a period of 2 yr (1995-1996)	**PM Increment:** Interquartile range corresponded to 1 unit of change. **RR Estimate [Lower CI, Upper CI] lag:** Association between bronchitis and $PM_{10-2.5}$: 2.20 (1.14, 4.26) $p < 0.05$ Association between persistent cough and $PM_{10-2.5}$: 1.46 (1.12, 1.90) $p < 0.05$ Between and within city associations: Bronchitis: 3.18 (between city) Persistent phlegm (between city): 2.78 When scaled to an increment of 50 $\mu g/m^3$ of $PM_{10-2.5}$ associations (ORs) between respiratory outcome and $PM_{10-2.5}$ were: Wheeze: 1.14 Asthma: 1.34 Bronchitis: 2.56 Hospitalization: 1.58 Persistent cough: 1.57 Persistent phlegm: 3.45

[1]All units expressed in $\mu g/m^3$ unless otherwise specified.

Table E-24. Long-term exposure - respiratory morbidity outcomes - $PM_{2.5}$ (including PM components/sources).

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Annesi-Maesano et al.(2007, 091348) **Period of Study:** Mar 1999-Oct 2000 **Location:** France (Bordeaux, Clermont-Ferrand, Creteil, Marseille, Strasbourg,, & Reims)	**Outcome:** EIB, Flexural atopic dermatitis, asthma, rhiniconjuctivitis, allergic rhinitis **Age Groups:** Children mean 10.4 ± 0.7 yr **Study Design:** Semi-individual design **N:** 5338 **Statistical Analyses:** Logistic regression **Covariates:** Age, sex, family history of allergy, passive smoking **Season:** NR **Dose-response Investigated?** No **Statistical Package:** SAS	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 5-day mean (Mon.-Fri.) over a 13-wk to 24-wk span Residential Proximity Level **Mean (SD):** Low conc: 8.7 High conc: 20.7 **Range (Min, Max):** Low conc: (1.6, 12.2) High conc: (12.5, 54.0) City Level **Mean (SD):** Low conc: 9.6 High conc: 23.0 **Range (Min, Max):** Low conc: (4.7, 12.7) High conc: (13.0, 54.5)	**PM Increment:** High vs. Low **Allergic and respiratory morbidity OR Estimate (Lower CI, Upper CI)** Proximity Level EIB (C) 1.35 (1.10, 1.67) Fl. Atopic dermatitis (C) 2.51 (2.06, 3.06) Asthma (P) 1.11 (0.88, 1.39) Atopic asthma (P) 1.43 (1.07, 1.91) Non-atopic asthma (P) 0.73 (0.49, 1.07) Rhiniconjunctivitis (P) 0.94 (0.77, 1.15) Atopic dermatitis (P) 1.05 (0.88, 1.27) Asthma (L) 1.00 (0.82, 1.22) Allergic Rhinitis (L) 1.09 (0.93, 1.27) Atopic dermatitis (L) 0.94 (0.82, 1.09) City Level EIB (C) 1.43 (1.15, 1.78) Fl. Atopic dermatitis (C) 2.06 (1.69, 2.51) Asthma (P) 1.31 (1.04, 1.66) Atopic asthma (P) 1.58 (1.17, 2.14) Non-atopic asthma (P) 1.00 (0.68, 1.49) Rhiniconjunctivitis (P) 0.98 (0.80, 1.20) Atopic dermatitis (P) 1.08 (0.90, 1.30) Asthma (L) 1.09 (0.89, 1.33) Allergic Rhinitis (L) 1.13 (0.97, 1.33) Atopic dermatitis (L) 0.95 (0.82, 1.09) Notes: C = Current P = Past yr L = Lifetime Allergic sensitization OR Estimate (Lower CI, Upper CI) Proximity Level All allergens 1.19 (1.04, 1.36) Indoor allergens 1.29 (1.11, 1.50) Outdoor allergens 1.02 (0.85, 1.23) Moulds 1.13 (0.78, 1.65) City Level All allergens 1.32 (1.15, 1.51) Indoor allergens 1.51 (1.29, 1.76) Outdoor allergens 1.06 (0.88, 1.28) Molds 1.00 (0.69, 1.46)
Reference: Bakke et al. (2004, 156246) **Period of Study:** Jan 1989-Jun 2002 **Location:** One of Norway's major construction companies	**Outcome:** Spirometric measurements **Age Groups:** All ages, mean = 39 yr **Study Design:** Cohort **N:** 651 male construction workers **Statistical Analyses:** Multiple linear regression models **Covariates:** Age, yr for non-smokers and ever smokers **Dose-response Investigated?** No **Statistical Package:** SYSTAT 10.0 and SPSS 11.0	**Pollutant:** Respirable dust **Averaging Time:** 5-8 h **Mean (SD):** Drill and blast workers: 6.3 (2.8) Tunnel concrete workers: 6.1 (3.1) Shotcreting operators: 19 (11) TBM workers: 16 (6.6) Outdoor concrete workers: 1.4 (0.73) Foremen: 0.28 (0.48) Engineers: 0.09 (0.28) **Unit (i.e. µg/m^3):** mg·y/m^3 **Monitoring Stations**: 16 tunnel sites visited with sampling equipment **Copollutant (correlation):** Total dust: r = 0.99 α quartz: r = 0.48 NO_2: r = 0.75 CO: r = 0.61 Oil mist: r = 0.83 Oil vapor: r = 0.68 VOC: r = 0.89	**PM Increment:** NR-exposure respirable dust Effect Estimate (Lower CI, Upper CI): Lung function changes predicted by multiple linear regression models using one exposure variable adjusted for age and observation time by non-smokers and ever smokers Non-smokers: ß = -16.0 (-24- -6.8) SE = 4.5 Ever smokers: ß = -9.3 (-17- -1.6) SE = 4.0

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Bakke et al. (2004, 156246) **Period of Study:** Jan 1989-Jun 2002 **Location:** One of Norway's major construction companies	**Outcome:** Spirometric measurements **Age Groups:** All ages, mean = 39 yr **Study Design:** Cohort **N:** 651 male construction workers **Statistical Analyses:** Multiple linear regression models **Covariates:** Age, yr for non-smokers and ever smokers **Dose-response Investigated?** No **Statistical Package:** SYSTAT 10.0 and SPSS 11.0	**Pollutant:** Total dust **Averaging Time:** 5-8 h **Mean (SD):** Drill and blast workers: 18 (7.8) Tunnel concrete workers: 21 (11) Shotcreting operators: 73 (41) TBM workers: 48 (20) Outdoor concrete workers: 6.5 (3.4) Foremen: 0.78 (1.3) Engineers: 0.27 (0.78) **Unit (i.e. µg/m^3):** mg·y/m^3 **Monitoring Stations**: 16 tunnel sites visited with sampling equipment **Copollutant (correlation):** Respirable dust: r = 0.99 α quartz: r = 0.42 NO_2: r = 0.67 CO: r = 0.49 Oil mist: r = 0.81 Oil vapor: r = 0.64 VOC: r = 0.91	**PM Increment:** NR-exposure expirable dust Lung function changes predicted by multiple linear regression models using one exposure variable adjusted for age and observation time by non-smokers and ever smokers Non-smokers: ß = -4.0 (-6.5-1.4) SE = 1.3 Ever smokers: ß = -2.0 (-4.2-0.23) SE = 1.1
Reference: Bennett et al. (2007, 156268) **Period of Study:** 1992-2005 **Location:** Melbourne, Australia	**Outcome:** Respiratory symptoms (from questionnaire) **Age Groups:** All ages, mean = 37.2 yr **Study Design:** Cohort **N:** 1446 **Statistical Analyses:** Logistic regression models **Covariates:** Age, gender, use of ß2-agonists, use of inhaled corticosteroids, smoking, yr of data collection, and avg daily exposure to $PM_{2.5}$ in the 12 mo corresponding to the time frame of symptoms **Dose-response Investigated?** No **Statistical Package:** STATA, version 9	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** 6.8 **Range (Min, Max):** (1.8-73.3) **Monitoring Stations**: up to 3	**PM Increment:** NR **Effect Estimate [Lower CI, Upper CI]:** Respiratory symptoms in last 12 mo and exposure to ambient $PM_{2.5}$ over the same period Within-person (longitudinal) effects Wheeze: OR = 1.08 (0.79-1.48), p = 0.62 SOB on waking: OR = 1.34 (0.84-2.16), p = 0.22 Cough (AM): OR = 0.74 (0.47-1.15), p = 0.18 Phlegm (AM): OR = 1.55 (0.95-2.53), p = 0.08 Cough w/ phlegm (AM): OR = 1.28 (0.70-2.33), p = 0.42 Asthma attack: OR = 0.91 (0.55-1.49), p = 0.69 Between-person (cross-sectional) effects Wheeze: OR = 1.32 (0.82-2.10), p = 0.25 SOB on waking: OR = 1.29 (0.46-3.60), p = 0.63 Cough (AM): OR = 0.21 (0.07-0.62), p = 0.01 Phlegm (AM): OR = 0.49 (0.16-1.44), p = 0.19 Cough w/ phlegm (AM): OR = 0.28 (0.08-0.97), p = 0.05 Asthma attack: OR = 0.52 (0.17-1.59), p = 0.26

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: (Brauer et al., 2007, 090691) **Period of Study:** 1999-2000 **Location:** The Netherlands	**Outcome:** Allergen sensitivity (any, indoor, outdoor, food, total) IgE>100 IU/mL Asthma (probable, MD-diagnosed, ever MD-diagnosed) Bronchitis (MD-diagnosed, ever MD-diagnosed) Dry cough at night Itchy rash Itchy rash/eczema Ear/Nose/Throat (ENT) infection Eczema, MD-diagnosed Eczema, ever MD-diagnosed Flu/serious cold, MD-diagnosed Wheeze (ever, early, early frequent, persistent) **Age Groups:** Very young children (<4-yr-old) enrolled prenatally **Study Design:** Prospective birth cohort study **N:** ~4000 subjects **Statistical Analyses:** Multiple logistic regression **Dose-response Investigated?** No	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 12 mo **Mean (SD):** SD: NR 16.9 **Percentiles:** 25th: 14.8 50th(Median): 17.3 75th: 18.1 **Range (Min, Max):** (13.5, 25.2) **Monitoring Stations**: 40 **Copollutant (correlation):** Soot: r = 0.97 NO_2: r = 0.93	**PM Increment:** IQR 3.3 $\mu g/m^3$ Notes: Traffic-related pollution ($PM_{2.5}$, soot, NO_2) was associated with respiratory infections, asthma, and allergic sensitization in children during the first 4 yr of life. **Symptom At 4-Yr-Old** Wheeze 4-yr-old: 1.23 [1.00: 1.51] Early-life: 1.20 [0.99: 1.46] Asthma, MD-diagnosed 4-yr-old: 1.15 [0.82: 1.62] Early-life: 1.32 [0.96: 1.83] Dry cough at night 4-yr-old: 1.11 [0.94: 1.31] Early-life: 1.14 [0.98: 1.33] Bronchitis, MD-diagnosed 4-yr-old: 0.88 [0.66: 1.18] Early-life: 0.86 [0.66: 1.11] ENT infection 4-yr-old: 1.13 [0.98: 1.31] Early-life: 1.17 [1.02: 1.34] Flu/serious cold, MD-diagnosed 4-yr-old: 1.21 [1.02: 1.42] Early-life: 1.25 [1.07: 1.46] Itchy rash 4-yr-old: 0.96 [0.82: 1.11] Early-life: 0.98 [0.85: 1.14] Eczema, MD-diagnosed 4-yr-old: 1.00 [0.88: 1.21] Early-life: 0.98 [0.82: 1.17] **Allergen Sensitivity At 4-Yr-Old** Allergen, any: 1.55 [1.13: 2.11] Allergen, indoor: 1.03 [0.69: 1.55] Allergen, outdoor: 0.93 [0.54: 1.58] Allergen, food: 1.75 [1.23: 2.47] Allergen, total IgE>100 IU/mL: 0.84 [0.59: 1.18] **Cumulative Allergy/Asthma Symptoms At 4-Yr-Old** Wheeze, ever: 1.22 [1.06: 1.41] Asthma, ever MD-diagnosed: 1.32 [1.04: 1.69] Asthma, probable: 1.08 [0.90: 1.30] Wheeze, early: 1.16 [1.00: 1.34] Wheeze, persistent: 1.19 [0.96: 1.48] Wheeze, early frequent: 1.19 [0.96: 1.47] Bronchitis, ever MD-diagnosed: 0.96 [0.81: 1.13] Itchy rash/eczema: 0.99 [0.88: 1.13] Eczema, ever MD-diagnosed: 0.98 [0.85: 1.13]

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: (Brauer et al., 2007, 090691) **Period of Study:** 1999-2000 **Location:** The Netherlands	**Outcome:** Allergen sensitivity (any, indoor, outdoor, food, total) IgE>100 IU/mL Asthma (probable, MD-diagnosed, ever MD-diagnosed) Bronchitis (MD-diagnosed, ever MD-diagnosed) Dry cough at night Itchy rash Itchy rash/eczema Ear/Nose/Throat (ENT) infection Eczema, MD-diagnosed Eczema, ever MD-diagnosed Flu/serious cold, MD-diagnosed Wheeze (ever, early, early frequent, persistent) **Age Groups:** Very young children (<4-yr-old) enrolled prenatally **Study Design:** Prospective birth cohort study **N:** ~4000 subjects **Statistical Analyses:** Multiple logistic regression **Dose-response Investigated?** No	**Pollutant:** Soot (as $PM_{2.5}$ absorbance) **Averaging Time:** 12 mo **Mean (SD):** 1.71 **Percentiles:** 25th: 1.33 50th(Median): 1.78 75th: 1.91 **Range (Min, Max):** (0.77, 3.68) **Unit (i.e. µg/m^3):** 1E-5/m **Monitoring Stations**: 40 **Copollutant (correlation):** NO_2: r = 0.96 $PM_{2.5}$: r = 0.97	**PM Increment:** IQR 0.58 E-5/m Notes: Traffic-related pollution ($PM_{2.5}$, soot, NO_2) was associated with respiratory infections, asthma, and allergic sensitization in children during the first 4 yr of life. **Symptom At 4-Yr-Old** Wheeze 4-yr-old: 1.18 [0.98: 1.41] Early-life: 1.18 [1.00: 1.40] Asthma, MD-diagnosed 4-yr-old: 1.15 [0.85: 1.55] Early-life: 1.30 [0.98: 1.71] Dry cough at night 4-yr-old: 1.13 [0.97: 1.30] Early-life: 1.14 [1.00: 1.31] Bronchitis, MD-diagnosed 4-yr-old: 0.90 [0.69: 1.16] Early-life: 0.88 [0.69: 1.11] ENT infection 4-yr-old: 1.15 [1.01: 1.31] Early-life: 1.16 [1.03: 1.31] Flu/serious cold, MD-diagnosed 4-yr-old: 1.18 [1.02: 1.36] Early-life: 1.19 [1.04: 1.37] Itchy rash 4-yr-old: 0.94 [0.82: 1.08] Early-life: 0.97 [0.85: 1.10] Eczema, MD-diagnosed 4-yr-old: 0.99 [0.84: 1.17] Early-life: 0.97 [0.83: 1.14] **Allergen Sensitivity At 4-Yr-Old** Allergen, any: 1.45 [1.11: 1.91] Allergen, indoor: 1.02 [0.71: 1.46] Allergen, outdoor: 0.95 [0.59: 1.52] Allergen, food: 1.64 [1.21: 2.23] Allergen, total IgE>100 IU/mL: 0.80 [0.59: 1.09] **Cumulative Allergy/Asthma Symptoms At 4-Yr-Old** Wheeze, ever: 1.18 [1.04: 1.34] Asthma, ever MD-diagnosed: 1.26 [1.02: 1.56] Asthma, probable: 1.06 [0.90: 1.24] Wheeze, early: 1.11 [0.97: 1.26] Wheeze, persistent: 1.18 [0.98: 1.42] Wheeze, early frequent: 1.14 [0.95: 1.37] Bronchitis, ever MD-diagnosed: 0.95 [0.82: 1.10] Itchy rash/eczema: 0.99 [0.89: 1.11] Eczema, ever MD-diagnosed: 0.99 [0.87: 1.12]
Reference: Brauer et al. (2002, 035192) **Period of Study:** NR **Location:** The Netherlands	**Outcome:** Questionnaire derived wheezing, dry nighttime cough, ear, nose and throat infections, skin rash Physician diagnosed asthma, bronchitis, influenza, eczema **Age Groups:** age 2 **Study Design:** Prospective cohort **N:** 4146 children **Statistical Analyses:** Logistic regression **Covariates:** Maternal age, maternal smoking, mattress cover (allergen-free), maternal education, paternal education, gender, gas stove, gas water heater, any other siblings, ethnicity, breastfeeding, mold at home, pets, allergies in mother, allergies in father **Dose-response Investigated?** No	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 4 2-wk periods dispersed throughout 1 yr, adjusted for temporal trend **Mean (SD):** 16.9 **Percentiles:** 10th: 14.0 25th: 15.0 50th(Median): 17.3 75th: 18.2 90th: 19.1 **Range (Min, Max):** 13.5, 25.2 **Monitoring Stations:** 40 **Copollutant (correlation):** Soot: r = 0.99 NO_2: r = 0.97	**PM Increment:** 3.2 µg/m^3 **OR Estimate [Lower CI, Upper CI];** Unadjusted Wheeze 1.14 (0.99-1.30) Asthma 1.08 (0.84-1.37) Dry cough at night 1.10 (0.95-1.27) Bronchitis 1.00 (0.85-1.18) E, N, T infections 1.14 (0.99-1.33) Flu 1.15 (1.03-1.28) Itchy rash 1.07 (0.95-1.20) Eczema 1.02 (0.90-1.16) Adjusted Wheeze 1.14 (0.98-1.34) Asthma 1.12 (0.84-1.50) Dry cough at night 1.04 (0.88-1.23) Bronchitis 1.04 (0.85-1.26) E, N, T infections 1.20 (1.01-1.42) Flu 1.12 (1.00-1.27) Itchy rash 1.01 (0.88-1.16) Eczema 0.95 (0.83-1.10)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Brauer et al. (2002, 035192) **Period of Study:** NR **Location:** The Netherlands	**Outcome:** Questionnaire derived wheezing, dry nighttime cough, ear, nose and throat infections, skin rash Physician diagnosed asthma, bronchitis, influenza, eczema **Age Groups:** Age 2 **Study Design:** Prospective cohort **N:** 4146 children **Statistical Analyses:** Logistic regression **Covariates:** Maternal age, maternal smoking, mattress cover (allergen-free), maternal education, paternal education, gender, gas stove, gas water heater, any other siblings, ethnicity, breastfeeding, mold at home, pets, allergies in mother, allergies in father **Dose-response Investigated?** No	**Pollutant:** $PM_{2.5}$ "soot" **Averaging Time:** 4 2-wk periods dispersed throughout 1 yr, adjusted for temporal trend **Mean (SD):** 16.9 10-5/m Percentiles: 10th: 1.16 25th: 1.38 50th(Median): 1.78 75th: 1.92 90th: 2.19 **Range (Min, Max):** 0.77, 3.68 **Unit (i.e. µg/m^3):** 10-5/m **Monitoring Stations**: 40 **Copollutant (correlation):** $PM_{2.5}$ (r = 0.99) NO_2 (r = 0.96)	**PM Increment:** 0.54 x 10-5/m (equivalent to 0.8 µg/m^3 EC) **OR Estimate [Lower CI, Upper CI]** Unadjusted Wheeze 1.11 [0.99-1.24] Asthma 1.07 [0.87-1.31] Dry cough at night 1.08 [0.95-1.21] Bronchitis 0.98 [0.85-1.12] E, N, T infections 1.12 [0.99-1.27] Flu 1.13 [1.03-1.23] Itchy rash 1.07 [0.97-1.19] Eczema 1.01 [0.91-1.13] Adjusted Wheeze 1.11 [0.97-1.26] Asthma 1.12 [0.88-1.43] Dry cough at night 1.02 [0.88-1.17] Bronchitis 0.99 [0.84-1.17] E, N, T infections 1.15 [1.00-1.33] Flu 1.09 [0.98-1.21] Itchy rash 1.02 [0.91-1.15] Eczema 0.96 [0.85-1.08]
Reference: Brauer et al. (2006, 090757) **Period of Study:** 1997-2001 **Location:** Germany The Netherlands	**Outcome:** Otitis Media (parental report of doctor's diagnosis prior to age 2 yr) **Age Groups:** 0-2 yr **Study Design:** Prospective Cohort Study **N:** 4,379 children total The Netherlands: 3,714 Germany: 665 **Statistical Analyses:** Logistic regression **Covariates:** Sex, parental atopy, maternal education, siblings, maternal smoking during pregnancy, ETS exposure at home, use of gas for cooking, indoor moulds and dampness, number of siblings, breast-feeding, and presence of pets in the home **Season:** All **Dose-response Investigated?** No	**Pollutant:** $PM_{2.5}$ **PM Component:** EC (EC) **Averaging Time:** 8 wk (4 2-week periods dispersed throughout 1 yr, adjusted for temporal trends) **Mean:** The Netherlands: $PM_{2.5}$: 16.9 EC: 1.72 Germany: $PM_{2.5}$: 13.4 EC: 1.76 **Range (Min, Max):** The Netherlands: $PM_{2.5}$: 13.5, 25.2 EC: 0.77, 3.68 Germany: $PM_{2.5}$: 12.0, 21.9 EC: 1.40, 4.39 **Monitoring Stations**: 80 (40 for each cohort)	**PM Increment:** $PM_{2.5}$: 3 µg/m^3 (~ IQR) EC: ~0.5 µg/m^3 (~ IQR) OR Estimate [Lower CI, Upper CI] The Netherlands: $PM_{2.5}$: At age 1: 1.13 (0.98-1.32) At age 2: 1.13 (1.00-1.27) EC: At age 1: 1.11 (0.98-1.26) At age 2: 1.10 (1.00-1.22) Germany: $PM_{2.5}$: At age 1: 1.19 (0.73-1.92) At age 2: 1.24 (0.84-1.83) EC: At age 1: 1.12 (0.83-1.51) At age 2: 1.10 (0.86-1.41)
Reference: Burr et al. (2004, 087809) **Period of Study:** 3 wk in Jul and Jan 1997 and 2 wk in Nov 1996 and Apr 1997 **Location:** North Wales, England	**Outcome:** Self-report of symptoms only for wheeze, cough, phlegm, rhinitis, and itchy eyes. **Age Groups:** All **Study Design:** Repeated measures **N:** 386 persons in congested streets and 425 in the uncongested streets in 1996/1997. Of these, 165 and 283 completed the second phase of the study.	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Mean hourly concentrations **Mean (SD):** Congested Streets 1996-97 21.2 1998-99 16.2 Uncongested Streets 1996-97 6.7 1998-99 4.9 **Monitoring Stations**: 1 in congested street and 1 in uncongested	% change PM_{10} in congested streets: 23.6 % change PM_{10} in uncongested streets: 26.6 Uncongested street sampling site was 20 m from the congested street sampler. The opening of the by-pass produced a reduction in pollution in the congested streets. The health effects of these changed are likely to be greater for nasal and ocular symptoms than for lower respiratory symptoms. Uncertainty about the causality arises from low response rates and conflicting trends in respiratory and nasal symptoms.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Calderón-Garcidueñas et al. (2006, 091253) **Period of Study:** 1999-2000 **Location:** Southwest Mexico City & Tlaxcala, Mexico	**Outcome:** Hyperinflation, interstitial markings-measured by chest radiograph, and lung function-FVC, FEV_1, PEF, FEF25-75, measured using spirometry tests **Age Groups:** 5-13 yr **Study Design:** Cohort1999- **N:** 249 (total), 230 (Southwest Mexico City), 19 (Tlaxcala) **Statistical Analyses:** Bayes test, Spearman rank correlation, multiple regression **Covariates:** Age, sex **Dose-response Investigated?** No **Statistical Package:** SAS 8.2	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 1 yr **Mean (SD):** 21 2000-19 Tlaxacala: 1994-2000: <NAAQS std Mexico City **Monitoring Stations:** Southwest Mexico City-2 Tlxacala-periodic air monitoring data Co**pollutant:** O_3	**PM Increment:** NR **% Change:** % of children with FEV_1 <80% expected value: Mexico City (n = 77): 7.8% Tlaxacala (n = 19): 0% % children with hyperinflation: Mexico City: 65.6% Number with: No hyperinflation: 79 Mild: 72 Moderate: 56 Severe: 23 Tlaxacala: 5.3% Number with: No hyperinflation: 18 Mild: 1 Moderate: 0 Severe: 0 % children with interstitial markings: Mexico City: 52.6% Number with: No interstitial markings: 19 Mild: 0 Moderate: 0 Severe: 0 Tlaxacala: 0% Number with: No interstitial markings: 109 Mild: 112 Moderate: 9 Severe: 0
Reference: Cesaroni et al. (2008, 156326) **Period of Study:** Data on PM emissions collected in 2002 cross-sectional survey carried out in 1995 **Location:** Rome, Italy	**Outcome:** Self-reported chronic bronchitis or emphysema, asthma, and rhinitis **Age Groups:** 25-59 yr **Study Design:** Cross-sectional **N:** 9,488 subjects who had been residents in same place for at least 3 yr and who had participated in an extension of the ISAAC initiative in Italy in 1994 & 1995 **Statistical Analyses:** GEE with a logit link **Covariates:** Sex, age, smoking habits, education level, and variable to account for correlation of data for members of the same family Effect Modifiers: stratified analysis by smoking status (only presented for the traffic score variable) Also stratified by education level (data not shown) **Dose-response Investigated:** Wald test to calculate p for trend	**Pollutant:** PM emissions (estimated) Emissions estimated using a model/method based on factors such as vehicle park, driving conditions, emission factors, fuel consumption, fuel properties, road gradients, and climatic conditions **Mean:** 0.12 kg/km^2 SD: 0.081	**Odds Ratios for quartiles of PM emissions:** Chronic bronchitis or emphysema (n = 397): 1st: 1.00 2nd: 0.96 (0.71, 1.30) 3rd: 0.90 (0.66, 1.23) 4th: 1.05 (0.77, 1.42) p-trend = 0.871 Asthma (n = 472): 1st: 1.00 2nd: 1.10 (0.84, 1.44) 3rd: 0.94 (0.71, 1.24) 4th: 1.06 (0.80, 1.39) p-trend = 0.980 Rhinitis (n = 1227): 1st: 1.00 2nd: 1.41 (1.17, 1.69) 3rd: 1.11 (0.92, 1.34) 4th: 1.37 (1.14, 1.64) p-trend = 0.018

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Dales et al., (2008, 156378) **Period of Study:** **Location:** Windsor, ON	**Outcome:** Pulmonary function and inflammation **Age Groups:** Grades 4-6 **Study Design:** Cross-sectional prevalence design **Statistical Analyses:** Multivariate linear regression **Covariates:** Ethnic background, smokers at home, pets at home, acute respiratory illness, medication use	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual **Mean:** 15.4 5th: 14.2 95th: 17.2 **Copollutant:** SO_2 NO_2	**Increment:** Tertiles of exposure FEV_1: <15.19: 2.16 ± 0.01 15.19-15.96: 2.17 ± 0.02 >15.96: 2.18 ± 0.01 FVC: <15.19: 2.51 ± 0.02 15.19-15.96: 2.50 ± 0.02 >15.96: 2.52 ± 0.02 eNO: <15.19: 16.08 ± 0.70 15.19-15.96: 15.80 ± 0.76 >15.96: 16.79 ± 0.72
Reference: Gauderman et al. (2000, 012531) **Period of Study:** 1993-1997 **Location:** Southern California	**Outcome:** FVC, FEV_1, MMEF, FEF75 **Age Groups:** Fourth, seventh, or tenth graders **Study Design:** Cohort **N:** 3035 subjects **Statistical Analyses:** Linear regression **Covariates:** Height, weight, BMI, asthma, smoking, exercise, room temperature, barometric pressure **Dose-response Investigated?** Yes **Statistical Package:** SAS	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual avg of 2-wk avg $PM_{2.5}$ **Mean (SD):** $PM_{2.5}$ 25.9 **Copollutant (correlation):** 03: r = -0.32 $PM_{10-2.5}$: r = 0.76 NO_2: r = 0.74 Inorg. Acid: r = 0.79	**Increment:** 25.9 µg/m^3 **% Change (Lower CI, Upper CI)** $PM_{2.5}$-4th grade FVC -0.47 (-0.94, 0.01) FEV_1 -0.64 (-1.28, 0.01) MMEF -1.03 (-1.95 to -0.09) FEF75 -1.31 (-2.57 to -0.03) $PM_{2.5}$-7th grade FVC -0.42 (-0.89, 0.05) FEV_1 -0.32 (-0.88, 0.24) MMEF -0.29 (-1.99, 1.44) FEF75 -0.26 (-1.75, 1.25) $PM_{2.5}$-10th grade FVC 0.19 (-0.68, 1.07) FEV_1 -0.25 (-1.41, 0.93) MMEF -0.17 (-3.66, 3.46) FEF75 -0.79 (-4.27, 2.82)
Reference: Gauderman et al. (2002, 026013) **Period of Study:** 1996-2000 **Location:** Southern California	**Outcome:** Lung function development: FEV_1, maximal midexpiratory flow (MMEF) **Age Groups:** Fourth grade children (avg age = 9.9 yr) **Study Design:** Cohort study **N:** 1678 children, 12 communities **Statistical Analyses:** Mixed model linear regression **Covariates:** Height, BMI, doctor-diagnosed asthma and cigarette smoking in previous yr, respiratory illness and exercise on day of test, interaction of each of these variables with sex, barometric pressure, temperature at test time, indicator variables for field technician and spirometer **Dose-response Investigated?** Yes **Statistical Package:** SAS (10)	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual 24-h avg **Mean (SD):** The avg levels were presented in an online data supplement (Fig E1) **PM Component:** EC and OC. **Monitoring Stations**: 12 **Copollutant (correlation):** O_3: (10 AM to 6 PM) r = 0.14 O_3: r = -0.39 NO_2: r = 0.77 Acid vapor: r = 0.87 PM_{10}: r = 0.95 $PM_{10-2.5}$: r = 0.81 EC: r = 0.93 OC: r = 0.89	**PM Increment:** 22.2 µg/m^3 Association Estimate: Non-statistically significant negative correlation between $PM_{2.5}$ and $FEV_1$and FVC growth rates were observed. MMEF growth rates had a negative correlation with $PM_{2.5}$ (r = -0.43 p = 0.05). $PM_{2.5}$ was not significantly correlated to FEV_1 (r = -0.31 p = 0.25)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: (Gauderman et al., 2004, 056569) **Period of Study:** Air pollution data ascertainment: 1994-2000. Spirometry testing: spring 2001-spring 2003 **Location:** 12 Communities in Southern California	**Outcome:** Lung function FVC, FEV_1, MMEF (Maximal midexpiratory flow rate) **Age Groups:** Children, Avg age 10 yr **Study Design:** Prospective Cohort Study **N:** 12 Communities 2,034 children 24,972 child-mo **Statistical Analyses:** Linear regression of changes in sex-and-community specific lung growth function and PM Correlation between % with low attained FEV_1 and PM. **Covariates:** Random effect for communities **Dose-response Investigated?** No **Statistical Package:** SAS	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 2-wk measurements used to create annual avg Mean: Means are presented in figures only. **Range (Min, Max):** ~6, ~27 **Monitoring Stations**: 12 **Copollutant (correlation):** PM_{10}: r = 0.95 O_3: r = 0.18 NO_2: r = 0.79 EC: r = 0.91 OC: r = 0.91	**PM Increment:** Most to least polluted community Range: 22.8 µg/m^3 Difference in Lung Growth [Lower CI, Upper CI]; FVC -60.1 (-166.1 to 45.9) FEV_1 -79.7 (-153.0 to ¡6.4) MMEF -168.9 (-345.5 to 7.8) Correlation with % below 80% predicted Lung function (p-value) $PM_{2.5}$: 0.79 (0.002)
Reference: Gauderman et al. (2007, 090121) **Period of Study:** 1993-2004 **Location:** 12 Southern California Communities	**Outcome:** Pulmonary function tests FVC, FEV_1, MMEF/FEF25.75 **Age Groups:** Children (mean age 10 at recruitment, followed for 8 yr) **Study Design:** Cohort Study (Children's Health Study) **N:** 3677 children (1718 in cohort 1 recruited 1993 and 1959 in cohort 2 recruited 1996) 22686 pulmonary function tests. **Statistical Analyses:** Hierarchical mixed effects model with linear splines **Covariates:** Adjustments for height, height squared, BMI, BMI squared, present asthma status, exercise or respiratory illness on day of test, smoking in previous yr, field technician, traffic indicator (distance from freeway, distance from major roads), random effects for participant and community. **Dose-response Investigated?** No **Statistical Package:** SAS	**Pollutant:** $PM_{2.5}$ **Monitoring Stations**: 1 in each community	**PM Increment:** 22.8 µg/m^3 Pollutant effect reported as difference in 8 yr lung function growth from least to most polluted community. Negative difference indicate growth deficits associated with exposure. For $PM_{2.5}$ FEV growth deficit is -100
Reference: Gehring et al. (2002, 036250) **Period of Study:** 1995-2002 **Location:** Munich, Germany	**Outcome:** Wheezing, cough without infection, dry cough at night, obstructive, spastic or asthmoid bronchitis, respiratory infections, sneezing, runny/stuffed nose **Age Groups:** 0-2 yr **Study Design:** Prospective cohort **N:** 1756 infants **Statistical Analyses:** Logistic regression **Covariates:** Sex, parental atopy (yes/no), maternal education, siblings (y/n), environmental tobacco smoke at home (y/n), use of gas for cooking (y/n), home dampness (y/n), indoor moulds	**Pollutant:** $PM_{2.5}$ **Mean (SD):** $PM_{2.5}$ mass: 13.4 $PM_{2.5}$ absorb. 1.77 * 10-5/m Percentiles: $PM_{2.5}$ mass: 10th: 12.2 25th: 12.5 50th(Median): 13.1 75th: 14.0 90th: 14.9 $PM_{2.5}$ absorbance: 10th: 1.47 * 10-5 25th: 1.54 * 10-5	**PM Increment:** $PM_{2.5}$ mass: 1.5 µg/m^3 $PM_{2.5}$ absorb. 0.4 * 10-5/m (IQR) **RR Estimate [Lower CI, Upper CI]** **Wheeze ($PM_{2.5}$ mass)** Age of 1 yr: All: 0.91 (0.76-1.09) Males: 0.91 (0.72-1.16) Females: 0.94 (0.70-1.27) Age of 2 yr: All: 0.96 (0.83-1.12) Males: 0.93 (0.76-1.14) Females: 1.04 (0.83-1.30) **Cough W/O Infection** ($PM_{2.5}$ mass) Age of 1 yr: All: 1.34 (1.11-1.61) Males: 1.43 (1.14-1.80) Females: 1.19 (0.84-1.70) **Dry Cough At Night** ($PM_{2.5}$ mass) Age of 1 yr: All: 1.31 (1.07-1.60) Males: 1.39 (1.08-1.78) Females: 1.17 (0.81-1.68)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
	(y/n), keeping of dogs (y/n) and cats (y/n) study (GINI or LISA) **Dose-response Investigated?** No	50th(Median): 1.70 * 10-5 75th: 1.88 * 10-5 90th: 2.13 * 10-5 **Range (Min, Max):** $PM_{2.5}$ mass: 11.9, 21.9 $PM_{2.5}$ absorbance: 1.38 to 4.39 * 10-5 $PM_{2.5}$ mass: $PM_{2.5}$ absorbance: 1/m **PM Component:** $PM_{2.5}$ mass $PM_{2.5}$ absorbance (as a marker of diesel soot) **Monitoring Stations**: 40 **Copollutant (correlation):** NO_2: r = 0.99 $PM_{2.5}$ absorbance and NO_2: r = 0.95 $PM_{2.5}$ mass and $PM_{2.5}$ absorbance: r = 0.96	Age of 2 yr: All: 1.20 (1.02-1.42) Males: 1.25 (1.01-1.55) Females: 1.13 (0.86-1.48) **Bronchitis** ($PM_{2.5}$ mass) Age of 1 yr: All: 0.98 (0.80-1.20) Males: 0.97 (0.76-1.25) Females: 0.98 (0.68-1.41) Age of 2 yr: All: 0.92 (0.78-1.09) Males: 0.92 (0.74-1.14) Females: 0.91 (0.68-1.21) **Resp Infections** ($PM_{2.5}$ mass) Age of 1 yr: All: 1.04 (0.91-1.19) Males: 1.04 (0.87-1.25) Females: 1.06 (0.87-1.31) Age of 2 yr: All: 0.98 (0.80-1.20) Males: 0.99 (0.74-1.31): Females: 0.98 (0.73-1.31) **Sneezing/Runny Nose ($PM_{2.5}$ mass)** Age of 1 yr: All: 1.01 (0.85-1.20) Males: 0.97 (0.77-1.24) Females: 1.08 (0.84-1.41) Age of 2 yr: All: 0.96 (0.82-1.12) Males: 0.91 (0.73-1.12) Females: 1.04 (0.83-1.31) Wheeze ($PM_{2.5}$ absorbance) Age of 1 yr: All: 0.93 (0.78-1.12) Males: 0.91 (0.71-1.15) Females: 1.01 (0.74-1.37) Age of 2 yr: All: 0.98 (0.84-1.14) Males: 0.92 (0.75-1.13) Females: 1.07 (0.85-1.36) **Cough W/O Infection** ($PM_{2.5}$ absorbance) Age of 1 yr: All: 1.32 (1.10-1.59) Males: 1.38 (1.11-1.71) Females: 1.25 (0.87-1.78) **Dry Cough At Night** ($PM_{2.5}$ absorbance) Age of 1 yr: All: 1.27 (1.04-1.55) Males: 1.31 (1.04-1.67) Females: 1.16 (0.79-1.71) Age of 2 yr: All: 1.16 (0.98-1.37) Males: 1.17 (0.95-1.44) Females: 1.12 (0.84-1.48) **Bronchitis** ($PM_{2.5}$ absorbance) Age of 1 yr: All: 0.99 (0.81-1.22) Males: 1.00 (0.78-1.27) Females: 0.94 (0.63-1.39) Age of 2 yr: All: 0.94 (0.79-1.12) Males: 0.91 (0.72-1.13) Females: 0.95 (0.71-1.28) **Resp Infections ($PM_{2.5}$ absorbance)** Age of 1 yr: All: 1.03 (0.90-1.18) Males: 1.03 (0.86-1.23) Females: 1.05 (0.85-1.30) Age of 2 yr: All: 0.99 (0.80-1.22) Males: 0.96 (0.73-1.26) Females: 1.04 (0.75-1.43) **Sneezing/Runny Nose ($PM_{2.5}$ absorbance)** Age of 1 yr: All: 0.95 (0.79-1.14) Males: 0.90 (0.70-1.16) Females: 1.06 (0.80-1.39) Age of 2 yr: All: 0.92 (0.78-1.09) Males: 0.83 (0.66-1.05) Females: 1.06 (0.83-1.34))

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Goss et al. (2004, 055624) **Period of Study:** 1999-2000 **Location:** USA	**Outcome:** Cystic Fibrosis pulmonary exacerbations, FEV_1 **Age Groups:** Children and adults over the age of 6 **Study Design:** Ccohort **N:** 11484 patients **Statistical Analyses:** Logistic regression, t-tests, Mann-Whitney tests, Chi-squared tests, polytomous regression, multiple linear regression **Covariates:** Age, sex, lung function, weight, insurance status, pancreatic insufficiency, airway colonization, genotype, median household income by census tract, zipcode. **Dose-response Investigated?** No **Statistical Package:** STATA, SAS	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual mean of 24-h avg **Mean (SD):** 13.7(4.2) Percentiles: 25th: 11.8 50th(Median): 13.9 75th: 15.9 **Monitoring Stations**: 713	**PM Increment:** 10 µg/m^3 Odds Ratio Estimate [Lower CI, Upper CI]: Odds of having 2 or more pulmonary exacerbations as compared to 1 or less in 2000 1.21 (1.07 -1.33) Odds of having 1 pulmonary exacerbation as compared to no exacerbations in 2000 0.70 (0.59-0.98) Decrease in FEV_1 155ml(115-194) Decrease in FEV_1 in 2000 after adjusting for FEV_1 in 1999 24ml(7-40)
Reference: Hertz-Picciotto et al. (2005, 088678) **Period of Study:** May 1994-Mar 1999 **Location:** Teplice and Prachatice, Czech Republic	**Outcome:** Developmental immunotoxicity as assessed by neonatal immunophenotypes **Age Groups:** Not specified: every woman who delivered in the two aforementioned districts were asked to participate **Study Design:** Cohort study **N:** 1397 mother-infant pairs **Statistical Analyses:** Multiple linear regression with lymphocyte percentage as responding variable and pollutant exposure to 14day averaging period before the date of cord blood collection **Covariates:** Season, length of labor, parity, number of previous stillbirths, medication during delivery, working status of mother, maternal education, exposure to active and secondhand smoke, family history of allergy, self-reports of workplace exposure to dust during pregnancy, self-reported maternal chronic or severe respiratory diseases during pregnancy. Ambient temperature and season were controlled for. **Dose-response Investigated?** Yes **Statistical Package:** SUDAAN (version 8)	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h 14 day avg **Mean (SD):** Overall 24 h: 24.8 14-day avg: Teplice: 30.1 Prachatice 19.8 **PM Component:** PAHs **Monitoring Stations**: 2 stations: Teplice and Prachatice	**PM Increment:** 25 µg/m^3 Adjusted for 3-day temperature and season, $PM_{2.5}$ exposure during the 14 days before birth was associated with reduced T-lymphocyte fractions CD4+, CD3+ and an increase in B-lymphocyte fraction (CD19+). The associations were not quantitatively reported anywhere else in the paper other than in Fig 2 and Table 3

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: (Hertz-Picciotto et al., 2007, 135917) **Period of Study:** 1994-98 + follow-ups at up to 4.5 yr of age for child **Location:** Czech Republic districts of Teplice and Prachatice	**Outcome:** Lower respiratory illnesses, majority being acute laryngitis, tracheitis, bronchitis. ICD10 codes J04 and J20 **Age Groups:** Birth-4.5 yr of age. **Study Design:** Longitudinal follow up of a stratified random sample of mother-infant pairs from previous Pregnancy Outcome Study. Low birth weight and preterm births sampled at higher fractions. **N:** 1133 children **Statistical Analyses:** Generalized linear longitudinal models, GEE to adjust for within subject correlations, robust variance estimates were obtained. Model fit judged using Akaike Information criterion. **Covariates:** Age of child, breast feeding, environmental tobacco smoke, season, day of week, yr of birth, gender, birth weight, pregnancy data including age at delivery, length of gestation, maternal hypertension and diabetes, infant APGAR score, maternal work history, demographics, lifestyle, reproductive and medical histories, temperature, fuel type, other children in household **Dose-response Investigated?** No **Statistical Package:** SUDAAN version 8	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Used 3-, 7-, 14-, 30- and 45-day avg **Mean (SD):** Daily mean 22.3 (sd 16 for 3-day avg, 11 for 45-day avg)	**PM Increment:** 25 µg/m^3 **RR Estimate [Lower CI, Upper CI] lag:** Bronchitis, birth-23 mo of age Categorical model High 30-day avg $PM_{2.5}$ (greater than 50 µg/m^3) 2.26(1.81-2.82) Medium 30-day avg $PM_{2.5}$ (between 25 and 50 µg/m^3) 1.48(1.32-1.65) Continuous model 1.30(1.08-1.58) Bronchitis, 2-4.5 yr of age Categorical model High 30-day avg $PM_{2.5}$ (greater than 50 µg/m^3) 3.66(2.07-6.48) Medium 30-day avg $PM_{2.5}$ (between 25 and 50 µg/m^3) 1.60(1.41-1.82) Continuous model 1.23(0.94-1.62) **Notes:** Results of other averaging periods shown in plots.
Reference: (Hogervorst et al., 2006, 156559) **Period of Study:** NR **Location:** Maastricht, the Netherlands (six schools selected)	**Outcome:** Decreased lung function **Age Groups:** 8-13 yr old **Study Design:** Multivariate linear regression (enter method) analysis **N:** 342 children **Statistical Analyses:** ANOVA, Chi square **Covariates:** Independent variables: Age, height, gender, smoking at home by parents, pets, use of ventilation hoods during cooking, presence of unvented geysers, tapestry in the home, indoor/outdoor time, education level of parents. Dependent variables: lung function indices **Dose-response Investigated?** No	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily **Mean (SD):** 19.0 (3.2) **Monitoring Stations**: 6 **Copollutant:** PM_{10} TSP	**PM Increment:** 10 µg/m^3 **RR Estimate [Lower CI, Upper CI] lag:** FEV 3.62 [0.50,7.63] FVC 1.80 [-2.10, 5.80] FEF 5.93 [-2.34, 14.89]

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Islam et al. (2007, 090697) **Period of Study:** 1993-2001 **Location:** 12 communities in Southern California, U.S.	**Outcome:** New onset asthma **Age Groups:** 9-10 yr **Study Design:** Cohort **N:** 2057 **Statistical Analyses:** Cox proportional hazard model **Covariates:** Community, sex, race/ethnicity **Season:** All **Dose-response Investigated?** No **Statistical Package:** SAS V 9.1 **Lags Considered:** 0-2 yr	**Pollutant:** $PM_{2.5}$ **Range (Min, Max):** "Low" $PM_{2.5}$ Communities (5.7-8.5) "High" $PM_{2.5}$ Communities (13.7-29.5) **Monitoring Stations**: 12 **Copollutant:** NO_2, acid vapor, PM_{10} and elemental and OC correlated as a "non-O_3 package" of pollutants with a similar pattern relative to each other across the 12 communities.	**PM Increment:** NR **IR Estimate [Lower CI, Upper CI]** Low PM FVC ≤ 90: 19.4 (7.5, 50.5) FVC 90-110: 16.8 (7.0, 40.1) FVC >110: 7.9 (2.9, 21.9) FEV_1 ≤ 90: 23.7 (9.4, 59.4) FEV_1 90-110: 15.6 (6.5, 37.4) FEV_1 >110: 6.5 (2.3, 18.7) FEF25-75 ≤ 90: 21.1 (8.8, 50.5) FEF25-75 90-110: 11.9 (4.7, 30.0) FEF25-75 >110: 6.4 (2.3, 18.2) Overall: 14.2 (7.0, 28.7) High PM FVC ≤ 90: 14.2 (5.1, 39.6) FVC 90-110: 25.6 (11.1, 59.2) FVC >110: 16.7 (6.5, 42.9) FEV_1 ≤ 90: 20.8 (8.0, 54.0) FEV_1 90-110: 23.1 (10.0, 53.7) FEV_1 >110: 18.8 (7.5, 47.3) FEF25-75 ≤ 90: 23.8 (10.2, 55.6) FEF25-75 90-110: 23.9 (9.9, 57.7) FEF25-75 >110: 15.9 (6.3, 40.5) Overall: 18.4 (9.4, 35.9)
Reference: Karr et al. (2007, 090719) **Period of Study:** 1995-2000 **Location:** South Coast Air Basin of southern California	**Outcome:** Bronchioloitis **Study Design:** Case-control. Cases included subjects with a record of a single hospitalization with a discharge diagnosis of acute bronchiolitis.10 controls per case were matched on birth date and gestational age. **N:** 18,595 cases 169,472 controls **Statistical Analyses:** Conditional logistic regression to estimate relative risk of hospitalization for bronchiolitis. **Covariates:** Confounders included in the model were: gender, parity, chronic lung disease, cardiac and pulmonary anomalies, SES covariates Age, Gestational age, and season of birth were controlled for by matching **Dose-response Investigated?** Yes **Statistical Package:** STATA (Version 8)	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h (lifetime monthly avg from birth & 30 days preceding cases hospitalization) **Mean (SD):** 25 **Percentiles:** 25th: 19 50th(Median): 23 75th: 29 **Range (Min, Max):** 6 to 111 **Monitoring Stations:** 17	**PM Increment:** 10 µg/m^3 **RR Estimate [Lower CI, Upper CI]** Sub-chronic and chronic exposure: OR = 1.09 (1.04-1.14) Adjusted for adjusted: Sub-chronic OR = 1.10 (1.04, 1.16) Chronic OR = 1.09 (1.03-1.15) Adjusted for CO and NO_2: Sub-chronic OR = 1.14 (1.07, 1.21) Chronic OR = 1.12 (1.06, 1.20) Adjusted for O_3, CO, and NO_2: Chronic OR = 1.15 (1.08, 1.22) Sub-chronic OR = 1.13 (1.06, 1.21)
Reference: (Kim et al., 2004, 087383) **Period of Study:** Mar-Jun (spring) 2001 Sep-Nov (fall) 2001 **Location:** Alameda County, CA	**Outcome:** Asthma, bronchitis **Age Groups:** Children (grades 3-5) **Study Design:** Cross-sectional **N:** 1109 children, 871 (long term resident children), 462 (long term related females), 403 (long term related males) **Statistical Analyses:** 2-stage multiple logistic regression model **Covariates:** Respiratory illness before age of 2, household mold/moisture, pests, maternal history of asthma (for asthma) **Season:** spring and fall **Dose-response Investigated?** Yes **Statistical Package:** SAS 8.2	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 10 wk **Mean (SD):** Study Avg 12 **Monitoring Stations**: 10 **Copollutant (correlation):** r2 is approximately 0.9 for all copollutants-Black Carbon (BC), PM_{10}, NO_X, NO_2, NO (NO_X-NO_2)	**PM Increment:** 0.7 (IQR) **OR Estimate [Lower CI, Upper CI]:** Bronchitis All subjects: 1.02 [1.00, 1.08] LTR subjects: 1.03 [1.01, 1.08] LTR females: 1.04 [1.02, 1.05] LTR males: 1.02 [0.99, 1.05] Asthma All subjects: 1.00 [0.96, 1.12] LTR subjects: 1.01 [0.97, 1.06] LTR females: 1.06 [0.99, 1.15] LTR males: 0.99 [0.95, 1.04] Asthma excluding outlier school having a larger proportion of Hispanics All subjects: 1.04 [0.96, 1.12] LTR subjects: 1.03 [0.94, 1.13] LTR females: 1.03 [0.91, 1.17] LTR males: 1.03 [0.94, 1.18]

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Leonardi et al. (2000, 010272) **Period of Study:** 1996 **Location:** 17 cities of Central Europe (Bulgaria, Czech Republic, Hungary , Poland, Romania, Slovakia)	**Outcome:** Immune biomarkers **Age Groups:** 9-11 **Study Design:** Cross-sectional **N:** 366 school children **Statistical Analyses:** Linear regression **Covariates:** Age, gender, parental smoking, laboratory of analysis, recent respiratory illness **Dose-response Investigated?** No **Statistical Package:** STATA	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual $PM_{2.5}$ **Mean (SD):** $PM_{2.5}$: 46 (10) **Range (Min, Max):** $PM_{2.5}$: (29, 67) 5th, median, & 95th percentile $PM_{2.5}$: 29, 44, 67	**% Change (Lower CI, Upper CI) p-value** $PM_{2.5}$ Neutrophils -10 (-45, 46) >.20 Total lymphocytes 49 (11, 101); .008 B lymphocytes 63 (4, 155); .034 Total T lymphocytes 72 (32 123) <.001 CD4+ 80 (34 143) <.001 CD8+ 61 (17, 119); .003 CD4/CD8 16 (-17, 62) >.20 NK 63 (3, 158); .035 Total IgG 24 (2, 52); .034 Total IgM -9 (-32, 22) >.20 Total IgA -1 (-25, 32) >.20 Total IgE -4 (-61, 137) >.20
Reference: McConnell (1999, 007028) **Period of Study:** 1993 **Location:** Southern California	**Outcome:** Bronchitis, chronic cough, phlegm **Age Groups:** Children: 4th, 7th, & 10th graders **Study Design:** Cross-sectional **N:** 3676 people **Statistical Analyses:** Logistic regression **Covariates:** Age, sex, race, grade, health insurance **Dose-response Investigated?** Yes	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Yearly 2-wk avg **Mean (SD):** 15.3 **Range (Min, Max):** 6.7, 31.5 **Copollutant (correlation):** NO_2 r = 0.83 O_3 r = 0.50 Acid r = 0.71	**Child Respiratory symptoms OR Estimate (Lower CI, Upper CI)** **$PM_{2.5}$ Increment:** 15 µg/m^3 Children w/ asthma Bronchitis: 1.4 (0.9, 2.3) Phlegm: 2.6 (1.2, 5.4) Cough: 1.3 (0.7, 2.4) Children w/ wheeze, no asthma Bronchitis: 0.9 (0.6, 1.4) Phlegm: 1.0 (0.6, 1.8) Cough: 1.1 (0.6, 1.9) Children w/ no wheeze, no asthma Bronchitis: 0.5 (0.3, 1.0) Phlegm: 0.8 (0.4, 1.5) Cough: 0.9 (0.6, 1.3)
Reference: McConnell et al. (2003, 049490) **Period of Study:** 1993-1999 **Location:** 12 Southern CA communities	**Outcome:** Bronchitic symptoms **Age Groups:** 9-19 **Study Design:** Communities selected on basis of historic levels of criteria pollutants and low residential mobility. **N:** 475 children **Statistical Analyses:** 3 stage regression combined to give a logistic mixed effects model **Covariates:** Sex, ethnicity, allergies history, asthma history, SES, insurance status, current wheeze, current exposure to ETS, personal smoking status, participation in team sports, in utero tobacco exposure through maternal smoking, family history of asthma, amount of time routinely spent outside by child during 2-6 pm. **Dose-response Investigated?** No **Statistical Package:** SAS Glimmix macro	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 4-yr avg **Mean (SD):** 13.8(7.7) **Range (Min, Max):** 5.5-28.5 **Copollutant (correlation):** PM_{10}: r = 0.79 $PM_{10-2.5}$: r = 0.24 Inorganic acid: r = 0.76 Organic Acid: r = 0.58 EC: r = 0.83 OC: r = 0.84 NO_2: r = 0.54 O_3: r = 0.72	**PM Increment:** Between community range 23 µg/m^3 Between community unit 1 µg/m^3 Within community 1 µg/m^3 OR Estimate [Lower CI, Upper CI] Between community per range 1.81(1.14-2.88) Between Community per unit 1.03(1.01-1.05) Within community per unit 1.09(1.01-1.17)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: McConnell et al. (2003, 049490) **Period of Study:** 1993-1999 **Location:** 12 Southern CA communities	**Outcome:** Bronchitic symptoms **Age Groups:** 9-19 **Study Design:** Communities selected on basis of historic levels of criteria pollutants and low residential mobility. **N:** 475 children **Statistical Analyses:** 3 stage regression combined to give a logistic mixed effects model **Covariates:** Sex, ethnicity, allergies history, asthma history, SES, insurance status, current wheeze, current exposure to ETS, personal smoking status, participation in team sports, in utero tobacco exposure through maternal smoking, family history of asthma, amount of time routinely spent outside by child during 2-6 pm. **Dose-response Investigated?** No **Statistical Package:** SAS Glimmix macro	**Pollutant:** EC **Averaging Time:** 4-yr avg **Mean (SD):** 0.71(0.41) **Range (Min, Max):** 0.1-1.2 **Copollutant (correlation):** $PM_{2.5}$: r = 0.83 PM_{10}: r = 0.71 $PM_{10-2.5}$: r = 0.30 Inorganic acid: r = 0.82 Organic Acid: r = 0.66 OC: r = 0.88 NO_2: r = 0.54 O_3: r = 0.68	**PM Increment:** Between community range 1.1 µg/m^3 Between community unit 1 µg/m^3 Within community 1 µg/m^3 OR Estimate [Lower CI, Upper CI] Between community per range 1.64(1.06-2.54) Between Community per unit 1.55(1.05-2.30) Within community per unit 2.63(0.83-8.33)
Reference: McConnell et al. (2003, 049490) **Period of Study:** 1993-1999 **Location:** 12 Southern CA communities	**Outcome:** Bronchitic symptoms **Age Groups:** 9-19 **Study Design:** Communities selected on basis of historic levels of criteria pollutants and low residential mobility. **N:** 475 children **Statistical Analyses:** 3 stage regression combined to give a logistic mixed effects model **Covariates:** Sex, ethnicity, allergies history, asthma history, SES, insurance status, current wheeze, current exposure to ETS, personal smoking status, participation in team sports, in utero tobacco exposure through maternal smoking, family history of asthma, amount of time routinely spent outside by child during 2-6 pm. **Dose-response Investigated?** No **Statistical Package:** SAS Glimmix macro	**Pollutant:** OC **Averaging Time:** 4-yr avg **Mean (SD):** 4.5(2.7) **Range (Min, Max):** 1.4-11.6 **Copollutant (correlation):** $PM_{2.5}$: r = 0.84 PM_{10}: r = .70 $PM_{10-2.5}$: r = 0.27 Inorganic acid: r = 0.83 Organic Acid: r = 0.69 EC: r = 0.88 NO_2: r = 0.67 O_3: r = 0.81	**PM Increment:** Between community range 10.2 µg/m^3 Between community unit 1 µg/m^3 Within community 1 µg/m^3 OR Estimate [Lower CI, Upper CI] Between community per range 1.74(0.89-3.4) Between Community per unit 1.06(0.99-1.13) Within community per unit 1.41(1.12-1.78)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: McConnell, et al. (2006, 180226) **Period of Study:** 1996-1999 **Location:** 12 Southern California communities	**Outcome:** Prevalence of bronchitic symptoms (yrly). **Age Groups:** 10-15-yr-old **Study Design:** Longitudinal cohort **N:** 475 asthmatic children **Statistical Analyses:** Multilevel logistic mixed effects models. **Covariates:** Age, second-hand smoke Personal smoking history Sex, race. **Dose-response Investigated?** No **Statistical Package:** SAS	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 365 days **Percentiles:** Community by yr (n = 48 = 12 communities · 4 yr) 25th: NR 50th(Median): 3.4 75th: NR **Range (Min, Max):** Community by yr (n = 48 = 12 communities · 4 yr): (0.89, 8.7) **Monitoring Stations**: 12 **Copollutant:** O_3 NO_2 EC OC Acid vapor (acetic and formic acid)	**PM Increment:** 3.4 µg/m^3 **OR Estimate [Lower CI, Upper CI]** $PM_{2.5}$ Dog (n = 292): 1.56 [1.15: 2.12] No dog (n = 183): 1.03 [0.71: 1.49] $PM_{2.5}$*Dog interaction p-value: 0.06 Cat (n = 202): 1.30 [0.90: 1.88] No Cat (n = 273): 1.36 [0.99: 1.83] $PM_{2.5}$*Cat interaction p-value: 0.87 Neither pet (n = 112): 1.11 [0.71: 1.74] Cat only (n = 71): 0.85 [0.46: 1.57] Dog only (n = 161): 1.53 [1.04: 2.25] Both pets (n = 131): 1.58 [1.02: 2.46] Results suggest that dog ownership, a source of residential exposure to endotoxin, may worsen the severity of respiratory symptoms from exposure to air pollutants in asthmatic children. Although $PM_{2.5}$ was associated at a statistically significant level with ownership of both cats and dogs, it appears that dog ownership (with or without a cat) specifically worsens the association between $PM_{2.5}$ and respiratory symptoms in asthmatic children.
Reference: (Meng et al., 2007, 093275) **Period of Study:** Nov 2000 and Sep 2001 **Location:** Los Angeles and San Diego counties	**Outcome:** Poorly controlled asthma vs. controlled asthma ICD9NR **Age Groups:** 18-64, 65+ **Study Design:** Long-term exposure study comparison of cases and controls **N:** 1,609 adults (represented individuals age 18+ who reported ever having been diagnosed as having asthma by a physician and had their address successfully geocoded) **Statistical Analyses:** Logistic regression to evaluate associations between TD (traffic density) and annual avg air pollution concentrations and poorly controlled asthma. Used sample weights that adjusted for unequal probabilities of selection into the CHIS sample. **Covariates:** Age, sex, race/ethnicity, family federal poverty level, county, insurance status, delay in care for asthma, taking medications, smoking behavior, self-reported health status, employment, physical activity **Dose-response Investigated?** yes	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Copollutant (correlation):** O_3: r = -0.76 NO_2: r = 0.87 PM_{10}: r = 0.84 CO: r = 0.52 TD: r = 0.13	Results for $PM_{2.5}$ were nonsignificant and not reported quantitatively.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Millstein, J et al. (2004, 088629) **Period of Study:** Mar-Aug 1995, and Sep 1995-Feb 1996 Data were taken from the Children's Health Study **Location:** Alpine, Atascadero, Lake Arrowhead, Lake Elsinore, Lancaster, Lompoc, Long Beach, Mira Loma, Riverside, San Dimas, Santa Maria, and Upland, CA	**Outcome:** Wheezing & asthma medication use (ICD 9 NR) **Age Groups:** 4th grade students, mostly 9 yr at the time of the study **Study Design:** Cohort Study, stratified into 2 seasonal groups/ **N:** 2081 enrolled, 2034 provided parent-completed questionnaire. **Statistical Analyses:** Multilevel, mixed-effects logistic model. **Covariates:** Contagious respiratory disease, ambient airborne pollen and other allergens, temperature, sex, age race, allergies, pet cats, carpet in home, environmental tobacco smoke, heating fuel, heating system, water damage in home, education level of questionnaire signer, physician diagnosed asthma. **Season:** Mar-Aug, 1995, and Sep, 1995 to Feb, 1996 **Statistical Package:** GLIMMIX SAS 8.00 macro for generalized linear mixed models. **Lags Considered:** 14	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Integrated values for successive 2-wk periods **PM Component:** Nitric acid, formic acid, acetic acid **Monitoring Stations**: 1 central location in each community **Copollutant (correlation):** O_3: r = 0.09 NO_2: r = 0.28 PM_{10}: r = 0.33 $PM_{10-2.5}$: r = -0.08	**PM Increment:** IQR: 5.24 µg/m^3 **Odds Ratio [lower CI, Upper CI]** Annual $PM_{2.5}$: 1.04 [0.83, 1.29] Mar-Aug $PM_{2.5}$: 0.91 [0.64, 1.30] Sep-Feb $PM_{2.5}$: 1.18 [0.89, 1.58]
Reference: Morgenstern et al. (2007, 090747) **Period of Study:** Mar 1999-Jul 2000 **Location:** Munich, Germany	**Outcome:** Asthma, wheezing, spastic/obstructive bronchitis. Dry cough at night, respiratory infections, sneezing, runny/stuffed nose without a cold. **Age Groups:** at 1 yr & at 2 yr **Study Design:** Cohort **N:** 3577 children for the prediction models. Respiratory data available for 3129 children at 1 yr. **Statistical Analyses:** Pearson's correlation coefficient, prediction error expressed as root mean squared error (RMSE), multiple logistic regression with confounding factors, odds ratios **Covariates:** Sex, Parental atopy (genetic predisposition to allergies), environmental tobacco smoke at home, maternal education >or <12 yr, sibling, gas stove, home dampness, indoor mold, pets. Since it was not feasible to measure personal exposure to NO_2, $PM_{2.5}$, and $PM_{2.5}$ absorbance, exposure modeling was used. **Statistical Package:** SAS V.8.02	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual **Mean (SD):** 12.8 Percentiles: 25th: 12.5 50th(Median): 12.9 75th: 13.3 **Range (Min, Max):** 6.8, 15.3 **Monitoring Stations**: 40: traffic, n = 17 and background, n = 23. **Copollutant (correlation):** $PM_{2.5}$ absorbance r = 0.49 NO_2 r = 0.45	**PM Increment:** 1.04 µg/m^3 **Odds Ratio [Lower CI, Upper CI]** Adjusted OR for $PM_{2.5}$ and: sneezing, runny/stuffed nose during the first yr of life was 1.16 [1.01, 1.34] At age 1 yr For wheezing 1.01 [0.87, 1.18] For cough without infection 1.05 [0.88, 1.25] For dry cough at night1.08 [0.86, 1.27] For asthmatic, spastic, or obstructive bronchitis 1.04 [0.90, 1.29] For respiratory infection1.05 [0.88, 1.22] For sneezing, runny or stuffed nose 1.16 [1.01, 1.34] At age 2 yr For wheezing 1.10 [0.96, 1.25] For cough without infection NA, insufficient sample For dry cough at night 1.03 [0.86, 1.19] For asthmatic, spastic, or obstructive bronchitis 1.05 [0.92, 1.20] For respiratory infection 1.09 [0.94, 1.07] For sneezing, runny or stuffed nose 1.19 [1.04, 1.36]

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Morgenstern et al. (2007, 090747) **Period of Study:** May 1999-Jul 2000 **Location:** Munich, Germany	**Outcome:** Asthma, wheezing, spastic/obstructive bronchitis. Dry cough at night, respiratory infections, sneezing, runny/stuffed nose without a cold. **Age Groups:** at 1 yr & at 2 yr **Study Design:** Cohort **N:** 3577 children for the prediction models. Respiratory data were available for 3129 children at 1 yr. **Statistical Analyses:** Pearson's correlation coefficient, prediction error expressed as root mean squared error (RMSE), multiple logistic regression with confounding factors, odds ratios **Covariates:** Sex, Parental atopy (genetic predisposition to allergies), environmental tobacco smoke at home, maternal education >or <12 yr, sibling, gas stove, home dampness, indoor mold, pets. Since it was not feasible to measure personal exposure to NO_2, $PM_{2.5}$, and $PM_{2.5}$ absorbance, exposure modeling was used. **Statistical Package:** SAS V.8.02	**Pollutant:** $PM_{2.5}$ Absorbance ($PM_{2.5}$ ab) **Averaging Time:** Annual **Mean (SD):** 1.7 10 -5 m -1, **Percentiles:** 25th: 1.6 10 -5 m -1 50th(Median): 1.7 10 -5 m -1 75th: 1.8 10 -5 m -1 **Range (Min, Max):** 1.3, 3.2 10 -5 m -1 **Unit (i.e. μg/m^3):** 10 -5 m -1 **Monitoring Stations**: 40: traffic, n = 17 and background, n = 23.	**PM Increment:** 0.22 x 10 -5 **Odds Ratio [Lower CI, Upper CI]** **no lag** At age 1 yr For wheezing 0.97 [0.77, 1.23] For cough without infection 1.16 [0.87, 1.54] For dry cough at night1.09 [0.78, 1.51] For asthmatic, spastic, or obstructive bronchitis 1.14 [0.88, 1.48] For respiratory infections1.03 [0.86, 1.24] For sneezing, runny or stuffed nose 1.30 [1.03, 1.65] At age 2 yr For wheezing 1.09 [0.90, 1.33] For cough without infection NR insufficient data For dry cough at night1.18 [0.93, 1.50] For asthmatic, spastic, or obstructive bronchitis 0.85 [0.30, 2.34] For respiratory infections1.05 [0.79, 1.39] For sneezing, runny or stuffed nose 1.27 [1.04, 1.56]
Reference: Oftedal et al. (2008, 093202) **Period of Study:** 2001-2002 **Location:** Oslo, Norway	**Outcome:** Lung function (PEF, FEF25%, FEF50%, FEV_1, FVC) **Age Groups:** 9-10 yr **Study Design:** Cross-sectional **N:** 1847 children **Statistical Analyses:** Linear regression **Covariates:** Height, age, BMI, birth weight, temperature, maternal smoking, se **Dose-response Investigated?** Yes **Statistical Package:** SPSS, STATA, S-Plus **Lags Considered:** 1-3	**Pollutant:** $PM_{2.5}$ IQR: $PM_{2.5}$ in 1st yr of life: 6.2 $PM_{2.5}$ lifetime: 3.6	**PM Increment:** Per IQR **β (Lower CI, Upper CI)** $PM_{2.5}$ in 1st yr of life PEF -76.1 (-122.2 to -30.0) FEF25% -75.6 (-127.4 to -23.8) FEF 50% -62.4 (-107.4 to -17.4) FEV_1 -12.7 (-28.8, 3.4) FVC -2.9 (-20.5, 14.7) $PM_{2.5}$ lifetime exposure PEF -57.7 (-94.4 to -21.1) FEF25% -51.8 (-93.1 to -10.6) FEF 50% -48.4 (-84.2 to -12.6) FEV_1 -10.4 (-23.2, 2.4) FVC -3.9 (-17.9, 10.1)
Reference: (Parker et al., 2009, 192359) **Period of Study:** 1999-2005 **Location:** U.S.	**Outcome:** Respiratory allergy/hayfever **Study Design:** Cohort **Covariates:** Survey yr, age, family structure, usual source of care, health insurance, family income relative to federal poverty level, race/ethnicity **Statistical Analysis:** Logistic regression **Statistical Package:** SUDAAN **Age Groups:** 73,198 children aged 3-17 yr	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **Median:** 13.1 **IQR:** 10.9-15.2 **Copollutant (correlation):** Summer O_3: 0.10 SO_2: 0.21 NO_2: 0.53 $PM_{10-2.5}$: 0.02 PM_{10}: 0.51	**Increment:** 10 μg/m^3 **Odds Ratio (95% CI)** Single Pollutant Model, variable N Adjusted: 1.16 (1.04-1.30) Single Pollutant Model, constant N Adjusted: 1.23 (1.04-1.46) Multi-pollutant Model: 1.29 (1.07-1.56)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Sekine et al. (2004, 090762) **Period of Study:** 1987-1994 **Location:** Nine districts in the Tokyo, Japan metropolitan area: Chuo ward, Ohta ward, Shibuya ward, Itabashi ward, Hachioji City, Tachikawa City, Ome City, Machida City, Tanashi City	**Outcome:** Pulmonary function tests **Age Groups:** 30-59 yr **Study Design:** Cross-sectional and longitudinal **N:** 500 females **Statistical Analyses:** Multiple logistic regression analysis **Covariates:** Group (classification by air pollution level), pulmonary function at initial test, age and height at the time of the initial test, number of yr investigated, yr of residence in the area, type of heater, housing structure, and job status. **Dose-response Investigated?** No **Statistical Package:** SAS	**Pollutant:** Suspended PM (SPM) **Averaging Time:** Measured each month for three consecutive days (72 h) **Mean (SD):** 28.1-63.3 **Range (Min, Max):** 3.4-140.6 **Copollutant (correlation):** NO_2	Results of multiple logistic regression analysis for respiratory symptoms Persistent cough Group 3: OR = 1.00 Group 2: OR = 1.02 (0.70-1.48) Group 1: OR = 1.07 (0.67-1.70) Persistent phlegm Group 3: OR = 1.00 Group 2: OR = 1.51 (1.11-2.04) Group 1: OR = 1.78 (1.26-2.53) Asthma Group 3: OR = 1.00 Group 2: OR = 1.99 (0.82-4.83) Group 1: OR = 2.66 (0.98-7.19) Wheeze Group 3: OR = 1.00 Group 2: OR = 1.39 (0.95-2.01) Group 1: OR = 1.34 (0.85-2.11) Breathlessness Group 3: OR = 1.00 Group 2: OR = 0.84 (0.47-1.50) Group 1: OR = 2.70 (1.48-4.91)
Reference: Sharma et al. (2004, 156974) **Period of Study:** Nov 2002-Apr 2003 **Location:** 3 sections in Kanpur City, India 1) Indian Institute of Technology Kanpur (IITK) 2) Vikas Nagar (VN) 3) Juhilal Colony (JC)	**Outcome:** Lung function **Age Groups:** 20-55 yr **Study Design:** Cohort **N:** 91 people **Statistical Analyses:** Linear regression **Covariates:** NR **Season:** Fall, Winter, spring **Dose-response Investigated?** No **Statistical Package:** Microsoft Excel **Lags Considered:** 1 day lag & 5-day ma	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** IITK 158 (22) VN 85 (30) JC 59 (9) **PM Component:** Lead, Nickel, Cadmium, Chromium, Iron, Zinc Benzene soluble fraction (includes polycyclic aromatic hydrocarbons [PAHs]) **Copollutant (correlation):** ΔPEF = mean daily deviations in PEF $PM_{2.5}$-ΔPEF: -0.30 $PM_{2.5}$-PM_{10}: 0.67 $PM_{2.5}$-PM_{10} (1-day lag): 0.49 $PM_{2.5}$-$PM_{2.5}$ (1-day lag): 0.88	**PM Increment:** 1 μg/m^3 ΔPEF (difference or change in peak expiratory flow) -0.0297 L/min
Reference: (Singh et al., 2003, 052686) **Period of Study:** NR **Location:** Jaipur, India	**Outcome:** Lung function (peak expiratory flow variability) **Age Groups:** Medical school-aged students **Study Design:** Cross sectional **N:** 313 nonsmoker students **Statistical Analyses:** Amplitude % mean was used as the measure of PEF variability. Mean value of amplitude % mean of peak flow variability were compared for in the two groups by application of Student's t-test. The two groups were: living on campus and commuters. **Dose-response Investigated?** Yes	**Pollutant:** Respirable suspended PM (RSPM) **Averaging Time:** 8 h **Mean (SD):** Roadside: 1,666 Campus: 177 **Monitoring Stations**: 2	It appears that no associations between particulates and the outcome of interest were calculated and reported in this study

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: (Solomon et al., 2003, 087441) **Period of Study:** 1966-1997 **Location:** United Kingdom: Northern England, North-West Midlands, and Wales.	**Outcome:** Cardio-respiratory morbidity **Age Groups:** 45 yr and older **Study Design:** Cross-sectional **N:** 1,166 women **Statistical Analyses:** Prevalence ratios were reported for ischemic heart disease, asthma, productive cough, wheeze, and use of an inhaler for asthma or other breathing problems. **Covariates:** Smoked, passive smoking in childhood, tenancy, SES, worked in industry with respiratory hazards, childhood admission to hospital for chest problem, diabetes, BMI were all controlled for as potential confounders. **Dose-response Investigated?** yes **Statistical Package:** STATA	**Pollutant:** Black Smoke **Averaging Time:** Annual	RR Estimate [Lower CI, Upper CI] The findings provide no indication that prolonged residence in places that have had relatively high levels of particulate air pollution causes an important increase in cardio-respiratory morbidity. Prevalence ratios are based on high vs. low pollution with low as referent. Particulate pollution in place of residence: Rr = 1.0 (0.7-1.4) for ischemic heart disease; Rr = 0.7 (0.5-1.0) for asthma Rr = 1.0 (0.7 -1.5) for productive cough
Reference: Suglia et al. (2008, 157027) **Period of Study:** Mar 1986-Oct 1992 **Location:** Boston, MA	**Outcome:** Lung function **Age Groups:** 18-42 **Study Design:** Prospective cohort **N:** 272 women of childbearing age **Statistical Analyses:** Linear regression **Covariates:** Height, age, weight, race/ethnicity, yr, education **Dose-response Investigated?** yes-tertiles of exposure **Statistical Package:** SAS v. 9.0	**Pollutant:** Black Carbon (BC) **Averaging Time:** Annual **Mean (SD):** 0.62 (0.15)	**PM Increment:** 0.22 µg/m^3 (IQR) **Effect Estimate [Lower CI, Upper CI]** FEV_1: -1.08 (-2.5, 0.3) FVC: -0.62 (-1.9, 0.6) FEF25-75%: -2.97 (-5.8 to -0.2) Current Smokers: FEV_1: 0.62 (-2.1, 3.4) FVC: 0.64 (-2.0, 3.3) FEF25-75%: -2.63 (-3.7, 8.9) Former Smokers: FEV_1: -4.40 (-7.8 to -1.0) FVC: -3.11 (-6.1 to -0.2) FEF25-75%: -8.78 (-14.7 to -2.9) Nonsmokers: FEV_1: -0.98 (-2.9, 0.9) FVC: -0.32 (-2.0, 1.4) FEF25-75%: -4.39 (-8.1 to -0.6) Exposure-response relationship presented graphically in Fig 1: the highest BC exposure group had decreases in FEV_1, FVC, and FEF25-75% compared with the lowest tertile group, although these differences were not statistically significant.
Reference: (Sunyer et al., 2006, 089771) **Period of Study:** initial selection: 1991-1993, follow-up Jun 2000-Dec 2001 **Location:** 21 centers in 10 European countries	**Outcome:** Chronic bronchitis **Age Groups:** Mean age (range) Males- 42.62 (38.12-45.62) Females- 42.57 (39.92-45.69) **Study Design:** Hierarchical models **N:** 6924 **Statistical Analyses:** General additive models (GAM) **Covariates:** Smoking, age at end of education, occupational group, occupational exposures, respiratory infections during childhood, rhinitis, asthma, traffic intensity at household level. **Statistical Package:** STATA-8	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 18 mo **Mean (SD):** 3.7-44.9 **Copollutants:** NO_2, SO_2	**PM Increment:** NR **Odds ratio [Lower CI, Upper CI]** Chronic phlegm prevalence at follow up Males: 0.97 [0.70,1.35]

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Zhang et al. (2002, 034814) **Period of Study:** 1993-1996 **Location:** 4 Chinese cities (urban and suburban location in each city): Guangzhou, Wuhan, Lanzhou, Chongqing	**Outcome:** Interview-self reports of symptoms: Wheeze (ever wheezy when having a cold) Asthma (diagnosis by doctor) Bronchitis (diagnosis by doctor) Hospitalization due to respiratory disease (ever) Persistent cough (coughed for at least 1 month per yr with or apart from colds) Persistent phlegm (brought up phlegm or mucus from the chest for at least 1 month per yr with or apart from colds). **Age Groups:** Elementary school students age range: 5.4-16.2 **Study Design:** Cross-sectional **N:** 7,557 returned questionnaires 7,392 included in first stage of analysis **Statistical Analyses:** 2-stage regression approach: Calculated odds ratios and 95% CIs of respiratory outcomes and covariates Second stage consisted of variance-weighted linear regressions that examined associations between district-specific adjusted prevalence rates and district-specific ambient levels of each pollutant. **Covariates:** Age, gender, breast-fed, house type, number of rooms, sleeping in own or shared room, sleeping in own or shared bed, home coal use, ventilation device used, homes smokiness during cooking, eye irritation during cooking, parental smoking, mother's education level, mother's occupation, father's occupation, questionnaire respondent, yr of questionnaire administration, season of questionnaire administration, parental asthma prevalence.	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 2 yr **Mean (SD):** 92 (31) **Percentiles:** 25th: NR 50th(Median): NR 75th: NR IQR: 39 **Range (Min, Max):** Gives range (max.-min.): $PM_{2.5}$-98 **Monitoring Stations**: 2 types: municipal monitoring stations over a period of 4 yr (1993-1996) schoolyards of participating children over a period of 2 yr (1995-1996)	**PM Increment:** Interquartile range corresponded to 1 unit of change. **RR Estimate [Lower CI, Upper CI]** **lag:** No association between $PM_{2.5}$ and any type of respiratory morbidity. No between or within city association between $PM_{2.5}$ and any type of respiratory morbidity. When scaled to an increment of 50 $\mu g/m^3$ increase in $PM_{2.5}$, association (ORs) between respiratory outcome and $PM_{2.5}$ was: Wheeze: 1.06 Asthma: 1.29 Bronchitis: 1.68 Hospitalization: 1.08 Persistent cough: 1.24 Persistent phlegm: 3.09

[1]All units expressed in $\mu g/m^3$ unless otherwise specified.

Table E-25. Long-term exposure - respiratory morbidity outcomes - other PM size fractions.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: El-Zein et al. (2007, 093043) **Period of Study:** 2000-2004 **Location:** Beirut, Lebanon	ED Admissions **Outcome:** Acute respiratory symptoms: asthma, URTI, pneumonia, bronchitis **Age Groups:** <17 **Study Design:** Ecological (natural experiment comparing admissions before and after ban on diesel fuel) **N:** 5 hospitals, 7573 admissions Oct-Feb, 4303 admissions Oct-Dec **Statistical Analyses:** T-test, Poisson regression **Covariates:** Month of Year, temperature, humidity, orthogonalized rainfall **Season:** Oct-Dec (excluding flu season) and Oct-Feb **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** 1-2 yr before the ban compared to 1-2 yr after the ban	**Pollutant:** PM from diesel **Range (Min, Max):** NR **PM Component:** NR **Monitoring Stations:** 1 **Notes:** Did not look at specific exposure data looked at outcome with respect to a timeline that plotted admissions before and after a ban on diesel fuel. **Copollutant:** NR	**PM Increment:** NA β (p-value): **2-yr pre-ban vs. 2-yr post-ban** Oct to Feb All Resp: 0.128 (0.32) Asthma: -0.176 (0.16) Bronchitis: 0.505 (0.02) Pneumonia: 0.287 (0.17) URTI: -0.265 (0.41) Oct to Dec All Resp: -0.022 (0.87) Asthma: -0.21 (0.07) Bronchitis: 0.2 (0.35) Pneumonia: -0.065 (0.78) URTI: -0.628 (0.05) **2-yr pre-ban vs. 1-yr post-ban** Oct-Feb All Resp: -0.093 (0.45) Asthma: -0.208 (0.05) Bronchitis: 0.286 (0.32) Pneumonia: -0.07 (0.76) URTI: -0.715 (0.11) Oct to Dec All Resp: -0.147 (0.02) Asthma: -0.147 (0.00) Bronchitis: -0.011 (0.96) Pneumonia: -0.214 (0.15) URTI: -0.885 (0.06) **1-yr pre-ban vs. 1-yr post-ban** Oct-Feb All Resp: -0.165 (0.04) Asthma: -0.212 (0.09) Bronchitis: 0.059 (0.85) Pneumonia: -0.034 (0.84) URTI: -1.023 (0.00) Oct to Dec All Resp: -0.17 (0.00) Asthma: -0.131 (0.00) Bronchitis: -0.145 (0.001) Pneumonia: -0.168 (0.12) URTI: -1.036 (0.00)
Reference: Kasamatsu et al. (2006, 156627) **Period of Study:** 2001-2002 **Location:** Shenyang, China	**Outcome:** FVC, FEV_1, PEF, FEF75 **Age Groups:** School Children aged 8-10 **Study Design:** Children in three schools in three types of areas (commercial city area, residential city area, residential suburban area) invited to participate **N:** 322 children participated, 244 have complete data. **Statistical Analyses:** Genralized estimating equations **Covariates:** Age, height, **Dose-response Investigated?** No **Statistical Package:** SAS **Lags**: Considered: previous quarter.	**Pollutant:** PM_7 **Averaging Time:** Avg of 4 separate 2-7 consecutive day measurements within each designated measurement month of the quarter **Mean (SD):** School A 7/2001 86.4(14.2) 10/2001 114.1(35.1) 1/2002 118.2(28.2) 4/2002 182.7(102.1) School B 7/2001 90.1(8.3) 10/2001 161.5(45.7) 1/2002 118.8(28.2) 4/2002 152.0(31.3) School C 7/2001 78.1(16.9) 10/2001 131.2(29.6) 1/2002 142.2(37.6) 4/2002 173.6(121.5) **PM Component:** mainly pollutants associated with coal heating **Monitoring Stations**: 1 at each location	**PM Increment:** 63.0 $\mu g/m^3$ **Mean change of pulmonary function value [Lower CI, Upper CI] at lag 0** Boys FVC -0.095(-0.170,-0.019) FEV_1 -0.088(-0.158,-0.019) PEF -0.170(-0.365,0.032) FEF75 -0.063(-0.183,0.050) Girls FVC -0.082(-0.145,-0.019) FEV_1 -0.069(-0.126,-0.006) PEF 0.095(-0.095,0.290) FEF75 -0.032(-0.151,0.082) Mean change of pulmonary function value [Lower CI, Upper CI] at lag 1(previous quarter) Boys FVC -0.145(-0.189,-0.095) FEV_1 -0.095(-0.139,-0.057) PEF -0.082(-0.208,0.050) FEF75 0.013(-0.063,0.088) Girls FVC -0.126(-0.170,-0.088) FEV_1 -0.101(-0.139,-0.063) PEF -0.101(-0.227,0.025) FEF75 -0.057(-0.132,0.019)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Kasamatsu et al.(2006, 156627) **Period of Study:** 2001-2002 **Location:** Shenyang, China	**Outcome:** FVC, FEV_1, PEF, FEF75 **Age Groups:** School Children aged 8-10 **Study Design:** Children in three schools in three types of areas (commercial city area, residential city area, residential suburban area) invited to participate **N:** 322 children participated, 244 have complete data. **Statistical Analyses:** Genralized estimating equations **Covariates:** Age, height, **Dose-response Investigated?** no **Statistical Package:** SAS **Lags:** Considered: previous quarter.	**Pollutant:** $PM_{2.1}$ **Averaging Time:** Avg of 4 separate 2-7 consecutive day measurements within each designated measurement month of the quarter **Mean (SD):** School A 7/2001 47.6(6.4) 10/2001 54.2(20.5) 1/2002 68.9(15.8) 4/2002 115.8(76.7) School B 7/2001 45.6(6.5) 10/2001 74.4(27.1) 1/2002 63.3(17.9) 4/2002 96.3(27.6) School C 7/2001 42.5(9.5) 10/2001 59.7(13.1) 1/2002 76.4(22.1) 4/2002 123.0(100.9) **PM Component:** mainly pollutants associated with coal heating **Monitoring Stations**: 1 at each location	**PM Increment:** 42.1 µg/m^3 Mean change of pulmonary function value [Lower CI, Upper CI] at lag 0 Boys FVC -0.126(-0.181,-0.076) FEV_1 -0.122(-0.173,-0.076) PEF -0.164(-0.303,-0.025) FEF75 -0.046(-0.131,0.038) Girls FVC -0.110(-0.156,-0.067) FEV_1 -0.101(-0147,-0.059) PEF 0.008(-0.131,0.147) FEF75 -0.055(-0.139,0.030) Mean change of pulmonary function value [Lower CI, Upper CI] at lag 1(previous quarter) Boys FVC -0.099(-0.145,-0.053) FEV_1 -0.059(-0.106,-0.020) PEF -0.040(-0.158,0.086) FEF75 0.026(-0.046,0.092) Girls FVC -0.086(-0.125,-0.046) FEV_1 -0.066(-0.106,-0.026) PEF -0.079(-0.198,0.040) FEF75 -0.033(-0.106,0.040)

[1]All units expressed in µg/m^3 unless otherwise specified.

E.6. Long-Term Exposure and Cancer

Table E-26. Long-term exposure - cancer outcomes - PM_{10}.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: (Abbey et al., 1999, 047559) **Period of Study:** 1977-1992 **Location:** California	**Outcome (ICD9):** Lung Cancer Mortality (162) **Age Groups:** 27-95 at baseline **Study Design:** Cohort (AHSMOG) **N:** 6,338 nonsmoking CA Seventh-Day Adventists **Statistical Analyses:** Time-dependent, gender-specific, Cox proportional hazards regression models **Covariates:** Age, smoking, education, occupation, BMI	**Pollutant:** PM_{10} **Averaging Time:** Monthly estimates from 1966-1992 **Mean (SD):** 51.24 (16.63) **Percentiles:** IQR: 24.08 **Range (Min, Max):** 0, 83.9 **Correlations:** SO_4: r = 0.68) SO_2: r = 0.31 O_3: r = 0.77 NO_2: r = 0.56 **Lag:** 3 yr	**PM Increment:** 24.08 (IQR) RR, males: 3.36 [1.57, 7.19] RR, females: 1.33 [0.60, 2.96] PM_{10} **above 100µg/m^3 (days per yr)** IQR: 43 days/yr Males: 2.38 (1.42, 3.97) Females: 1.08 (0.55, 2.13)
Reference: Beeson et al. (1998, 048890) **Period of Study:** 1977-1992 **Location:** California	**Outcome (ICD9:** Lung Cancer Mortality (ICDO-1: 162, ICDO-2: C34.0-C34.9) **Age Groups:** 27-95 at baseline **Study Design:** Cohort (AHSMOG) **N:** 6,338 nonsmoking CA Seventh-Day Adventists (non-Hispanic white) **Statistical Analyses:** Time-dependent, gender-specific, Cox proportional hazards regression models **Covariates:** Smoking, Education, Age, Alcohol **Statistical Package:** SAS **Lags Considered:** 3 yr	**Pollutant:** PM_{10} **Averaging Time:** Averaged monthly estimates from 1966-1992 **Mean (SD):** 51 (16.52) **Percentiles:** IQR: 24 **Range (Min, Max):** 0, 84	**PM Increment:** 24 (IQR) RR, males: 5.21 [1.94, 13.99] RR, females: Positive, but not statistically significant
Reference: Binkova et al. (2007, 156273) **Period of Study:** Feb 2001 **Location:** Prague, Czech Republic	**Outcome:** Total DNA adducts (bulky aromatic PAH-DNA adducts and … **Age Groups:** 22-50 yr **Study Design:** Case Control **N:** 53 occupationally exposed policemen and 52 control policemen **Statistical Analyses:** Multivariate logistic regression, Mann-Whitney u-test **Covariates:** Smoking. Vitamin C, polymorphisms of XPD repair gene in exon 23 and 6 and GSTM 1 and XRCC1 genes **Season:** Winter	**Pollutant:** PM_{10} **Range (Min, Max):** 32-55 **Monitoring Stations:** 2 (and personal monitors)	No relationship between short term exposure to C-PAHs evaluated by personal monitors and DNA adduct level. Genetic damage was observed in city policemen working in winter outdoors in the Prague downtown area they had slightly elevated aromatic DNA adduct levels, which was statistically significant for a distinct DNA adduct spot that could originate from ambient exposure to B[α]P. **Total PAH-DNA adducts**: p = 0.065 Exposed: 0.92 ± 0.28 adducts/108 nucleotids Control: 0.82 ± 0.23 adducts/108 nucleotids **B[α]P-like adducts:** Exposed: 0.122 ± 0.36 adducts/108 nucleotids Control: 0.099 ± 0.035 adducts/108 nucleotids Multiple regression "like" B[α]P-DNA adduct for air pollution exposure group: B = 0.016, p = 0.01

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: (Liu et al., 2009, 190292) **Period of Study:** 1995-2005 **Location:** Taiwan	**Outcome:** Bladder Cancer Mortality (ICD-9 188) **Age Groups:** 50-69 **Study Design:** Case-crossover **Statistical Analysis:** Multiple Logistic Regression **Statistical Package:** NR **Covariates:** none **Dose-response Investigated?** No	**Pollutant:** PM_{10} **Averaging Time:** Annual mean of 24-h avg **Tertiles (median):** T1: ≤52.80 T2: 53.04-71.72 T3: 72.24-90.29 **Copollutant:** O_3, CO, NO_2, SO_2 **Copollutant (correlation):** NR **Monitoring Sattions:** 64	**Increment:** **Odds Ratio (Min CI, Max CI)** **Lag** T1 vs. T1: 1.00 (ref) T2 vs. T1: 1.08 (0.83-1.41) T3 vs. T1: 1.39 (1.06-1.83) P for trend = .020
Reference: (Pope et al., 2002, 024689) **Period of Study:** 1982-1998 **Location:** 50 U.S. states, District of Columbia, and Puerto Rico	**Outcome (ICD9):** Lung cancer mortality (162) **Age Groups:** Ages >30 yr **Study Design:** Longitudinal cohort (Cancer Prevention Study II) **N:** 1.2 million people **Statistical Analyses:** Cox proportional hazard, generalized additive **Covariates:** Age, sex, race, education, smoking status, marital status, occupational exposure, diet, body-mass index, alcohol consumption	**Pollutant:** PM_{10} **Mean (SD):** 1982-1998: 28.8(5.9)	Effect estimates: Effect estimates were recorded in Fig 5 and not presented quantitatively anywhere else
Reference: Sram et al, (2007, 188457) **Period of Study:** Jan and Mar of 2004 **Location:** Prague, Czech Republic	**Outcome:** Chromosomal aberrations **Study Design:** Panel **Covariates:** Urinary cotinine, plasma levels of vitamins A, E and C, folate, total cholesterol, HDL and LDL cholesterols, and triglycerides **Statistical Analysis:** Bivariate correlations, ANOVA, Mann-Whitney, Kruskal-Wallis and Spearman rank correlation **Statistical Package:** STATISTICA **Age Groups:** 61 city policemen, aged 34 ± 8 yr, spending 8+ h outdoors	**Pollutant:** PM_{10} **Averaging Time:** NR **Mean (SD) Unit:** Jan: 55.6 µg/m^3 Mar: 36.4 µg/m^3 **Copollutant:** $PM_{2.5}$	Results not given by PM increment.
Reference: Sram et al, (2007, 188457) **Period of Study:** Jan and Mar of 2004 **Location:** Prague, Czech Republic	**Outcome:** Chromosomal aberrations **Study Design:** Panel **Covariates:** Urinary cotinine, plasma levels of vitamins A, E and C, folate, total cholesterol, HDL and LDL cholesterols, and triglycerides **Statistical Analysis:** Bivariate correlations, ANOVA, Mann-Whitney, Kruskal-Wallis and Spearman rank correlation **Statistical Package:** STATISTICA **Age Groups:** 61 city policemen, aged 34 ± 8 yr, spending 8+ h outdoors	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **Mean (SD) Unit:** Jan: 44.4 µg/m^3 Mar: 24.8 µg/m^3 **Copollutant:** PM_{10}	Results not given by PM increment.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: (Tarantini et al., 2009, 192010)Period of Study: NR **Location:** Brescia, Italy	**Outcome:** DNA methylation content estimated by Alu, LINE-1 and iNOS analysis **Study Design:** Panel **Covariates:** age, BMI, smoking, number of cigarettes/day **Statistical Analysis:** Mixed effects models **Statistical Package:** NR **Age Groups:** 63 male workers between 27 and 55 yr, mean age 44.	**Pollutant:** PM_{10} **Averaging Time:** NR **Mean (SD) Unit:** NR **Individual Exposure Range:** 73.4-1220 µg/m^3 **Copollutant (correlation):** NR	**Difference in DNA Methylation before and after work exposure, mean (SE)** Alu (%5mC): 0.00 (0.08), p = 0.99 LINE-1 (%5mC): 0.02 (0.11), p = 0.89 iNOS (%5mC): -0.61 (0.26), p = 0.02
Reference: (Vineis et al., 2006, 192089) **Period of Study:** 1990-1999 **Location:** 10 European countries	**Outcome:** Lung cancer **Study Design:** Nested case-control **Covariates:** Age, sex, country, smoking status, time since recruitment, education, BMI, physical activity, intake of fruit, vegetables, meat, alcohol and energy **Statistical Analysis:** Conditional logistic regression models **Statistical Package:** NR **Age Groups:** 35-74 at recruitment	**Pollutant:** PM_{10} **Averaging Time:** NR **Mean by Country (µg/m^3):** France Ile-de-France 1990-1994: 22.3 1995-1999: 19.9 Northeast France 1990-1994: 30.2 1995-1999: 29.5 Italy Turin 1990-1994: 73.4 1995-1999: 61.1 Florence 1990-1994: 40.4 1995-1999: 33.3 United Kingdom Oxford 1990-1994: 29.0 1995-1999: 25.5 Cambridge 1990-1994: NR 1995-1999: 25.4 The Netherlands Utrecht 1990-1994: 42.8 1995-1999: 40.0 Bilthoven 1990-1994: 39.0 1995-1999: 37.2 Germany Heidelberg 1990-1994: NR 1995-1999: 27.0 Potsdam 1990-1994: 32.0 1995-1999: 28.9 **Range (Min, Max):** NR **Copollutant:** NO_2, O_3, SO_2	**Increment:** 10 µg/m^3 **Odds Ratios (Min CI, Max CI) for increase in lung cancer per increment increase in** PM_{10} 0.91 (0.70-1.18)
Reference: (Wei et al., 2009, 192361) **Period of Study:** Nov 2006-Jan 2007 **Location:** Peking, China	**Outcome:** Urinary 8-OHdG increase **Study Design:** Panel **Covariates:** NR **Statistical Analysis:** Analysis of variance model with autoregressive terms **Statistical Package:** SAS **Age Groups:** Two nonsmoking security guards, ages 18 and 20	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Median:** 154.87 µg/m^3 **IQR:** 166.29 **Copollutant (correlation):** NA	**Increment:** 166.29 µg/m^3 **8-OHdG Concentrations, pre and post-work shift, subjects avgd** Pre-work: 1.83 Post-work: 6.92 **Concentration Changes (95%CI) of 8-OHdG per IQR Increase** Pre-work: 0.256 (0.040, 0.472), p = 0.021 Post-work: 2.370 (0.907, 3.833), p = 0.002

[1]All units expressed in µg/m^3 unless otherwise specified.

Table E-27. Long-term exposure - cancer outcomes - $PM_{2.5}$ (including PM components/sources).

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Baccarelli et al, (2009, 188183) **Period of Study:** Jan 1999-Jun 2007 **Location:** Boston, Massachusetts	**Outcome:** DNA methylation of LINE-1 and Alu **Study Design:** Panel **Covariates:** age, BMI, smoking status, pack-yr, statin use, fasting blood glucose, diabetes mellitus, percent lymphocytes and neutrophils in differential blood count, day of the week, season, temperature **Statistical Analysis:** Mixed effects models **Statistical Package:** SAS **Age Groups:** 719 elderly individuals, mean age 73.3, range 55-100 yr	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **Mean (SD) Unit:** 4h: 12.2 (7.7) µg/m^3 1 day: 10.9 (6.3) µg/m^3 2 day: 10.6 (5.2) µg/m^3 3 day: 10.4 (4.8) µg/m^3 4 day: 10.3 (4.3) µg/m^3 5d: 10.2 (3.9) µg/m^3 6d: 10.3 (3.5) µg/m^3 7d: 10.3 (3.3) µg/m^3 **Copollutants:** Black carbon, Sulfate	**Increment:** SD for each lag **Correlation Coefficient (95% CI)** **Lag for LINE-1 Methylation** 4h: -0.07 (-0.13, -0.01), p = 0.03 1 day: -0.09 (-0.16, -0.02), p = 0.008 2 day: -0.10 (-0.17, -0.03), p = 0.003 3 day: -0.10 (-0.17, --0.04), p = 0.003 4 day: -0.10 (-0.16, -0.03), p = 0.004 5d: -0.10 (-0.16, -0.03), p = 0.004 6d: -0.11 (-0.17, -0.04), p = 0.001 7d: -0.13 (-0.19, -0.06), p < 0.001 **Correlation Coefficient (95% CI)** **Lag for Alu Methylation** 4h: 0.03 (-0.03, 0.09), p = 0.28 1 day: -0.01 (-0.07, 0.05), p = 0.74 2 day: -0.01 (-0.07, 0.05), p = 0.82 3 day: -0.01 (-0.07, 0.05), p = 0.78 4 day: -0.01 (-0.07, 0.05), p = 0.75 5d: -0.01 (-0.07, 0.05), p = 0.84 6d: -0.01 (-0.07, 0.05), p = 0.74 7d: -0.01 (-0.07, 0.05), p = 0.71 **Correlation Coefficient (95% CI)** **LINE-1 Methylation and ma of pollutant levels** 4h: -0.04 (-0.11, 0.03), p = 0.24 7d: -0.11 (-0.18, -0.05), p = 0.001
Reference: Binkova et al. (2007, 156273) **Period of Study:** Feb 2001 **Location:** Prague, Czech Republic	**Outcome:** Bulky aromatic PAH-DNA adducts **Age Groups:** 22-50 yr **Study Design:** Case Control **N:** 53 exposed policemen and 52 control policemen **Statistical Analyses:** Multivariate logistic regression, Mann-Whitney, Rank-Sum U-test **Covariates:** Smoking. Vitamin C, polymorphisms of XPD repair gene in exon 23 and 6 and GSTM 1 gene **Season:** Winter	**Pollutant:** $PM_{2.5}$ **Range (Min, Max):** 27-38 **c-PAHs: range** = 18-22 ng/m^3 **B[a]P: range** = 2.5-3.1 ng/m^3 **Monitoring Stations:** 2	Genetic damage was observed in city policemen working in winter outdoors in the Prague downtown area They had slightly elevated aromatic DNA adduct levels, which was more pronounced for a distinct DNA adduct spot that could originate from ambient exposure to B[α]P. **Total DNA-adduct level** Exposed: 0.92±0.28 adducts/108 nucleotides Control: 0.82±0.23 adducts/108 nucleotides p = 0.065 **"Like" B[α]P-derived DNA adducts** Exposed: 0.122±0.036 Control: 0.101±0.035 p < 0.01 **Multiple Regression (exposed vs. control)** B = 0.016, p = 0.011

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Brunekreef et al, (2009, 191947) **Period of Study:** 1987-1996 **Location:** The Netherlands	**Outcome:** Air pollution related lung cancer deaths (ICD-9 162) **Study Design:** Case-cohort **Covariates** Individual: Sex, age, Quetelet index, smoking status, passive smoking status, educational level, occupation, occupational exposure, marital status, alcohol use, intake of vegetables, fruits, energy, saturatured and monounsaturated fatty acids, trans fatty acids, total fiver, folic acid and fish Area-level: Percent of population with income below the 40th percentile and above the 80th percentile **Statistical Analysis:** Cox proportional hazards **Statistical Package:** Stata, SPSS, R **Age Groups:** 120,000 adults aged 55-69 yr at enrollment	**Pollutant:** $PM_{2.5}$, estimated from PM_{10} levelsf **Averaging Time:** 24 h **50th Percentile:** 28 µg/m^3 **Range (Min, Max):** 23-37 **Copollutant (correlation):** NO_2: 0.75 Black Smoke: 0.84 NO: 0.69 SO_2: 0.43	**Increment:** 10 µg/m^3 **Relative Risk (95% CI) for associations between $PM_{2.5}$ and lung cancer incidence** Case Cohort Unadjusted: 0.93 (0.71-1.22) Adjusted: 0.67 (0.41-1.10) Unadjusted Complete: 0.87 (0.60-1.25) Full Cohort Unadjusted: 0.96 (0.79-1.18) Adjusted: 0.81 (0.63-1.04) Unadjusted Complete: 0.92 (0.74-1.15)
Reference: Liu et al. (2008, 156708) **Period of Study:** 1995-2005 **Location:** Taiwan	**Outcome:** Brain cancer deaths ICD9: 191 **Age Groups**: 29 yr of age or younger **Study Design:** Matched case-control by sex, yr of birth and death **N:** 340 matched pairs **Statistical Analyses:** Conditional logistic regression **Covariates:** Age, gender, urbanization level of residence, nonpetrochemical air pollution exposure level	No direct measures of pollutants used an index to assign petrochemical air pollution exposure (each municipality was assigned an exposure by dividing the number of workers per municipality employed in the petrochemical industry by the municipalities total population). Study participants divided into tertiles based on this index.	People who lived in the group of municipalities with the highest levels of air pollutants arising from petrochemical sources were at a statistically significant increased risk for brain cancer development compared to the group living in municipalities with the lowest petrochemical air pollution exposure index. **Effect Measure:** OR (95%CI) Tertile 1: 1. ?0 Tertile 2: 1.54 (0.98-2.42) Tertile 3: 1.65 (1.00-2.73) P for trend <0.01
Reference: Nafstad et al. (2004, 087949) **Period of Study:** 1972-1998 **Location:** Oslo, Norway	**Outcome:** Lung cancer ICD7 162.1-162.9 **Age Groups:** 40-49 yr old men **Study Design:** Cohort **N:** 16,209 males **Statistical Analyses:** Cox regression models (proportional hazards) **Covariates:** Age at inclusion, smoking habits, education **Season:** all yr	PM values had small variations in exposure level, and strong correlations with another pollutant of interest (SO_2) and were not considered in analyses. **Copollutants:** SO_2 NO_X	No effect estimates for PM
Reference: (Pope and Burnett, 2007, 090928) **Period of Study:** 1982-1998 **Location:** 50 U.S. states, District of Columbia, and Puerto Rico	**Outcome:** Lung cancer mortality (162) **Age Groups:** >30 yr **Study Design:** Longitudinal cohort (Cancer Prevention II Study) **N:** 415,000 CPS II patients with information involving PM_{10} **Statistical Analyses:** Cox proportional hazard, incorporating a spatial random-effects component **Covariates:** Age, sex, race, education, ETS, smoking status, marital status, occupational exposure, diet, body-mass index, alcohol consumption	**Pollutant:** $PM_{2.5}$ **Mean (SD):** 1979-1983: 21.1(4.6) 1999-2000: 14.0(3.0) **Avg:** 17.7(3.7) **Averaging time:** 1982-1998	**PM Increment:** 10 µg/m^3 **RR Estimate [Lower CI, Upper CI]** **lag:** **Lung Cancer:** 1979-1983: 1.08[1.01, 1.16] 1999-2000: 1.13[1.04, 1.22] Avg: 1.14[1.04, 1.23] RR results were also presented in Fig 2-5. Authors found that $PM_{2.5}$ had the strongest association with increased risk of all-cause, cardiopulmonary, and lung cancer mortality.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Sram et al, (2007, 188457) **Period of Study:** Feb 2001 **Location:** Prague, Czech Republic	**Outcome:** Chromosomal aberrations **Study Design:** Panel **Covariates:** Urinary cotinine, plasma levels of vitamins A, E and C **Statistical Analysis:** Bivariate correlations, ANOVA, Mann-Whitney, Kruskal-Wallis and Spearman rank correlation **Statistical Package:** STATISTICA, SAS **Age Groups:** 53 city policemen, aged 22-50 yr, spending 8+ h outdoors	**Pollutant:** PM_{10} **Averaging Time:** NR **Range:** 32-55µg/m^3 **Copollutant:** $PM_{2.5}$	Results not given by PM increment.
Reference: Sram et al, (2007, 188457) **Period of Study:** Feb 2001 **Location:** Prague, Czech Republic	**Outcome:** Chromosomal aberrations **Study Design:** Panel **Covariates:** Urinary cotinine, plasma levels of vitamins A, E and C **Statistical Analysis:** Bivariate correlations, ANOVA, Mann-Whitney, Kruskal-Wallis and Spearman rank correlation **Statistical Package:** STATISTICA, SAS **Age Groups:** 53 city policemen, aged 22-50 yr, spending 8+ h outdoors	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **Range:** 27-38µg/m^3 **Copollutant:** PM_{10}	Results not given by PM increment.
Reference: Tovalin et al. (Tovalin et al., 2006, 091322) **Period of Study:** Apr-May 2002 **Location:** Mexico City and Puebla	**Outcome:** DNA damage (comet tail length) **Age Groups:** 18-60 **Study Design:** Panel Study **N:** 55 male workers **Statistical Analyses:** Mann-Whitney test, Chi-square, Spearman's correlation, logistic regression **Statistical Package:** SPSS and STATA	**Pollutant:** $PM_{2.5}$ Personal monitoring values observed in this study reported in Tovalin et al. 2003 **Median Personal Exposure to** $PM_{2.5}$**:** Mexico City Outdoor Worker: 133 µg/m^3 Indoor Worker: 86.6 µg/m^3 Puebla Outdoor Worker: 122 µg/m^3 Indoor Worker: 78.3 µg/m^3	OR for being a highly damaged worker: 1.02 (1.01-1.04), p = 0.03 Correlation between comet tail length and PM 2.5: 0.57, p = 0.000 OR for being a highly damaged worker: 1.03, p ≤ 0.07 **Comet Tail Length** Outdoor Worker: 46.80 µm Indoor Worker: 30.11 µm p < 0.01 **Percent Highly DNA Damaged Cells** Outdoor Worker: 68% Indoor Worker: 20%

[1]All units expressed in µg/m^3 unless otherwise specified.

Table E-28. Long-term exposure - cancer outcomes - other PM size fractions.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: (Pope et al., 2002, 024689) **Period of Study:** 1982-1998 **Location:** 50 U.S. states, District of Columbia, and Puerto Rico	**Outcome:** Lung cancer mortality (162) **Age Groups:** Ages >30 yr who were members of a household with at least 1 individual ≥45yrs. **Study Design:** Longitudinal cohort (Cancer Prevention Study II) **N:** 359,000 CPS II participants with information regarding PM15 and PM15-$PM_{2.5}$ **Statistical Analyses:** Cox proportional hazard, incorporating a spatial random-effects component **Covariates:** Age, sex, race, education, ETS, smoking status, marital status, occupational exposure, diet, body-mass index, alcohol consumption Smoking covariates adjusted for: Indicator: current smoker, former smoker, pipe or cigar smoker, started smoking before or after age 18 Continuous, current and former smokers: yr smoked, yr smoked squared, cigarettes per day, cigarettes per day squared, number of h per day exposed to passive cigarette smoke.	**Pollutant:** PM_{15} **Mean (SD):** 1979-1983: 40.3(7.7) **Pollutant:** PM15-2.5 **Mean (SD):** 1979-1983: 19.2(6.1) **Averaging Time:** 1979-1983	Relative risks effect estimates were recorded in Fig 5 and not presented quantitatively anywhere else.

[1]All units expressed in $\mu g/m^3$ unless otherwise specified.

E.7. Long-Term Exposure and Reproductive Effects

Table E-29. Long-term exposure - reproductive outcomes - PM_{10}.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Bell at al. (2007, 091059) **Period of Study:** 1999-2002 **Location:** Connecticut-Fairfield, Hartford, New Haven, New London, Windham, Massachusetts-Barnstable, Berkshire, Bristol, Essex, Hampden, Middlesex, Norfolk, Plymouth, Suffolk, Worcester	**Outcome:** Low birth weight **Age Groups:** Neonates **Study Design:** Cross-sectional **N:** 358,504 births **Statistical Analyses:** Multiple logistic and linear regressions **Covariates:** Child's sex, mother's education, tobacco use, mother's marital status, mother's race, time prenatal care began, mother's age, birth order, gestation length **Dose-response Investigated?** No **Statistical Package:** NR	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 22.3 (5.3) **Monitoring Stations:** NR **Copollutant:** NO_2, CO, SO_2 **Gestation exposure correlation:** $PM_{2.5}$: r = 0.77 NO_2: r = 0.55	**PM Increment:** 7.4 µg/m^3 (IQR) **Difference in birth weight [Lower CI, Upper CI]** **per IQR for the gestational period:** -8.2 [-11.1 to -5.3] **Difference in birth weight by race of mother [Lower CI, Upper CI]:** Black: -7.9 [-16.0, 0.2] White: -9.0 [-12.2 to -5.9] **Range among trimester models for change in birth weight per IQR increase (min, max)** **trimester:** -6.6 to -4.7 3rd **OR Estimate for birth weight <2500 g [Lower CI, Upper CI]** **per IQR for the gestational period:** 1.027 [0.991, 1.064] **Notes**: Analyses using first births alone yielded similar results. Two pollutant models for uncorrelated pollutants were analyzed but not presented quantitatively.
Reference: Brauer et al. (2008, 156292) **Period of Study:** 1999-2002 **Location:** Vancouver, BC	**Outcome:** Preterm birth, SGA, LBW **Age Groups: Study Design:** Cross-sectional **N:** 70,249 births **Statistical Analyses:** Logistic regression **Covariates:** Sex, parity, month and yr of birth, maternal age and smoking, neighborhood level income and education **Statistical Package:** SAS	**Pollutant:** PM_{10} **Averaging Time:** 24-h **Mean (SD):** 12.7 **Range (Min, Max):** 5.6, 35.4 **Monitoring Stations:** 19 **Copollutant:** NO NO_2 CO SO_2 O_3	**PM Increment:** 1 µg/m^3 **Effect Estimate [Lower CI, Upper CI]** **pollutant assessed for entire pregnancy period:** SGA: 1.02 (0.99, 1.05) LBW: 1.01 (0.95, 1.08) Preterm (<30 wk): 1.13 (0.95, 1.35)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Chen et al. (2002, 024945) **Period of Study:** 1991-1999 **Location:** Washoe County, Nevada	**Outcome:** Birth weight **Age Groups:** Sngle births with gestational age between 37-44 wk and maternal all ages **Study Design:** Cross-sectional **N:** 33,859 single births **Statistical Analyses:** multiple linear and logistic regression **Covariates:** infant sex, maternal residential city, education, medical risk factors, active tobacco use, drug use, alcohol use, prenatal care, mother's age, race and ethnicity of mothers and weight gain of mothers **Dose-response Investigated?** No **Statistical Package:** SPSS 10.0	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 31.53 (22.32) **Percentiles: 25th:** 16.80 **50th(Median):** 26.30 **75th:** 39.35 **Range (Min, Max):** (0.97-157.32) **Monitoring Stations:** 4 **Copollutant:** CO O_3	**PM Increment:** 10 µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** Using continuous pollutant variables Model 1-PM_{10} 1 trimester Crude model: ß = -0.186 (0.225) Adjusted model: ß = -0.082 (0.221) 2 trimester Crude model: ß = 0.045 (0.223) Adjusted model: ß = -0.020 (0.221) 3 trimester Crude model: ß = -0.509 (0.231) Adjusted model: ß = -0.395 (0.227) Whole Crude model: ß = -0.823 (0.459) Adjusted model: ß = -0.726 (0.483) Model 2 CO and PM_{10} 3 trimester Crude model: ß = -1.044 (0.457) Adjusted model: ß = -1.078 (0.445) O_3 and PM_{10} 3 trimester Crude model: ß = -1.035 (0.385) Adjusted model: ß = -0.966 (0.378) Model 3 PM_{10}, O_3, and CO 3 trimester Crude model: ß = -1.070 (0.458) Adjusted model: ß = -1.102 (0.446) Whole Crude model: ß = -1.413 (0.733) Adjusted model: ß = -1.332 (0.738) Using categorical pollutant variables-3 trimester Model 1-PM_{10} Adjusted model: ß = -10.243 (5.235) Model 2 PM_{10} and CO Adjusted model: ß = -11.883 (6.108) PM_{10} and O_3 Adjusted model: ß = -9.144 (5.860) Model 3 PM_{10}, CO, and O_3 Adjusted model: ß = -10.937 (6.222) Using logistic regression (ref value = <19.72 µg/m^3 Exposure to PM_{10} at 3 trimester at >44.74 µg/m^3: OR = 1.105 (0.714-1.709) Between 19.72-44.74 µg/m^3: OR = 1.050 (0.811-1.360) **Notes:** Crude model: model with air-pollutant variables controlled with gestational age only. Adjusted model: model with air-pollutant variables controlled with confounding variables including gestational age, infant sex, maternal residential city, education, medical risk factors, active tobacco use, drug use, alcohol use, the trimester begins prenatal visits, total prenatal visits, mother's age, race and ethnicity of mother, and weight gain of mother.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Dales et al. (2004, 087342) **Period of Study:** Jan 1984-Dec 1999 **Location:** Canada (12 cities)	**Outcome:** SIDS (a sudden, unexplained death of a child <1 yr of age for which a clinical investigation and autopsy fail to reveal a cause of death) **Age Groups:** Infants <1 yr **Study Design:** Time-series **N:** Total population of 12 cities: 10,310,309 1556 cases of SIDS over study period **Statistical Analyses:** Random-effects regression model for count data (a linear association between air pollution and the incidence of SIDS was assumed on the logarithmic scale) **Covariates:** Weather factors (daily mean temp, daily mean relative humidity, maximum change in barometric pressure, all measured on the day of death), length of time-period adjustment, seasonal indicator variables, and size-fractionated PM **Season:** Used piece-wise constant functions in time that varied by 3, 6, or 12 mo **Dose-response Investigated?** No **Statistical Package:** NR	**Pollutant:** PM_{10} **Averaging Time:** 24-hs (PM measures every 6 days gaseous pollutants every day) **Mean (IQR):** PM_{10}: 23.43 (15.56) **Range (Min, Max):** IQR presented above **Monitoring Stations:** When data were available from more than 1 monitoring site, they were avgd **Copollutant:** $PM_{2.5}$ PM_{10} CO NO_2 O_3 SO_2	**Notes:** The abstract reports no association between increased daily rates of SIDS and fine particles measured every sixth day. However, no effect estimates presented for PM (only gaseous pollutants adjusted for PM).

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Dugandzic et al. (2006, 088681) **Period of Study:** Jan 1988-Dec 2000 **Location:** Nova Scotia, Canada	**Outcome:** Low birth weight (LBW) (<2500 grams) **Age Groups:** Babies born ≥ 37 wk (full term) **Study Design:** Cross-sectional **N:** 74,284 births **Statistical Analyses:** Logistic regression **Covariates:** Maternal age, parity, prior fetal death, prior neonatal death, prior low birth weight infant, smoking during pregnancy, neighborhood family income, infant gender, gestational age, weight change, yr of birth **Season:** All **Dose-response Investigated?** Yes **Statistical Package:** SAS	**Pollutant:** PM_{10} **Averaging Time:** 24-h **Mean (SD):** **Percentiles: 25th:** 14 **50th(Median):** 16 **75th:** 19 **Range (Min, Max):** Max: 53 **Monitoring Stations:** 18 **Copollutant:** SO_2, O_3 **Notes:** Only 3 stations monitored more than 1 pollutant. Daily data were available for gaseous pollutants while particulate levels were measured every sixth day.	**PM Increment:** 1) IQR (5 μg/m^3) 2) Quartiles (first quartile is the reference) **Exposure period: first trimester** Unadjusted model 2nd quartile: 1.24 (0.95, 1.62) 3rd quartile: 1.25 (0.96, 1.62) 4th quartile: 1.28 (1.00, 1.65) Per IQR: 1.09 (1.00, 1.18) Adjusted model 2nd quartile: 1.24 (0.94, 1.64) 3rd quartile: 1.24 (0.95, 1.64) 4th quartile: 1.33 (1.02, 1.74) Per IQR: 1.09 (1.00, 1.19) Adjusted for Birth Year model 2nd quartile: 1.14 (0.86, 1.52) 3rd quartile: 1.08 (0.82, 1.44) 4th quartile: 1.11 (0.84, 1.48) Per IQR: 1.03 (0.94, 1.14) **Exposure period: second trimester** Unadjusted model 2nd quartile: 0.98 (0.76, 1.28) 3rd quartile: 1.09 (0.84, 1.40) 4th quartile: 1.00 (0.77, 1.28) Per IQR: 1.00 (0.91, 1.09) Adjusted model 2nd quartile: 1.02 (0.77, 1.34) 3rd quartile: 1.16 (0.89, 1.51) 4th quartile: 1.09 (0.83, 1.42) Per IQR: 1.02 (0.93, 1.12) Adjusted for Birth Year model 2nd quartile: 0.99 (0.75, 1.31) 3rd quartile: 1.10 (0.84, 1.45) 4th quartile: 1.01 (0.76, 1.34) Per IQR: 1.00 (0.90, 1.10) **Exposure period: third trimester** Unadjusted model 2nd quartile: 0.93 (0.72, 1.20) 3rd quartile: 1.07 (0.83, 1.37) 4th quartile: 0.92 (0.71, 1.18) Per IQR: 0.95 (0.87, 1.05) Adjusted model 2nd quartile: 0.96 (0.73, 1.26) 3rd quartile: 1.14 (0.88, 1.48) 4th quartile: 1.03 (0.79, 1.35) Per IQR: 0.99 (0.89, 1.09) Adjusted for Birth Year model 2nd quartile: 0.92 (0.70, 1.21) 3rd quartile: 1.04 (0.80, 1.36) 4th quartile: 0.92 (0.69, 1.22) Per IQR: 0.94 (0.85, 1.05)
Reference: Gilboa, et al. (2005, 087892) **Period of Study:** Jan 1996-Dec 2000 **Location:** Seven Counties in Texas, USA: (Bexar, Dallas, El Paso, Harris, Hidalgo, Tarrant, Travis)	**Outcome:** Birth defects **Age Groups:** Newborn babies **Study Design:** Case-control **N:** 5,338 newborn babies 4574 controls **Statistical Analyses:** Logistic regression **Covariates:** Alcohol consumption during pregnancy, attendant of delivery (i.e., the person who delivered the baby (physician/nursemaid-wife vs. other)), gravidity, marital status, maternal age, maternal education, maternal illness, maternal race/ethnicity, parity, place of delivery, plurality, prenatal care, season of conception, and tobacco use during pregnancy Control frequency matched to cases by vital status, yr and maternal county of residence	**Pollutant:** PM_{10} **Averaging Time:** NR **Percentiles: 25th:** <19.5 **50th(Median):** 19.5-<23.8 **75th:** 23.8-<29.0 **100th:** ≥ 29.0 **Monitoring Stations:** The Environmental Protection Agency provided raw data or hourly (for gases) or daily (for PM) air pollution concentrations for the seven study counties **Copollutant:** CO, NO_2, O_3, SO_2	**PM Increment:** calculated as quartiles of avg concentration during wk 3-8 of pregnancy **Isolated Cardiac Defects** **Aortic artery and valve defects:** 25th: 0.40 (0.15, 1.03) 50th: 0.45 (0.18, 1.13) 75th: 0.68 (0.28, 1.65) **Atrial Sepal defects:** 25th: 1.41 (0.86, 2.31) 50th: 2.13 (1.34, 3.37) 75th: 2.27 (1.43, 3.60) **Pulmonary artery and valve defects:** 25th: 1.14 (0.62, 2.10) 50th: 0.79 (0.41, 1.55) 75th: 0.68 (0.33, 1.40) **Ventricular Sepal defects:** 25th: 0.83 (0.61, 1.11) 50th: 1.12 (0.85, 1.48) 75th: 0.98 (0.73, 1.32) **Multiple Cardiac Defects** **Conotruncal defects:** 25th: 1.13 (0.79, 1.62) 50th: 1.20 (0.84, 1.72) 75th: 1.26 (0.86, 1.84)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
	Season: Covariate in model **Dose-response Investigated?** Yes **Statistical Package:** SAS v 8.2		**Endocardial cushion and mitral valve defects:** 25th: 0.82 (0.54, 1.25) 50th: 0.66 (0.42, 1.05) 75th: 0.63 (0.38, 1.03) **Isolated Oral Clefts** **Cleft lip with or without palate:** 25th: 1.29 (0.90, 1.85) 50th: 1.45 (1.01, 2.07) 75th: 1.37 (0.94,2.00) **Cleft palate:** 25th: 0.99 (0.55, 1.78) 50th: 1.14 (0.64, 2.03) 75th: 1.11 (0.60, 2.06) **Individual Birth Defects** **Aortic valve stenosis:** 25th: 0.91 (0.53, 1.57) 50th: 0.86 (0.50, 1.50) 75th: 1.12 (0.63, 1.99) **Atrial Sepal defects:** 25th: 1.10 (0.89, 1.35) 50th: 1.28 (1.04, 1.57) 75th: 1.26 (1.03, 1.55) **Coarctation of the aorta:** 25th: 0.78 (0.53, 1.15) 50th: 0.68 (0.45, 1.02) 75th: 0.75 (0.48, 1.15) **Endocardial cushion defects:** 25th: 0.87 (0.49, 1.55) 50th: 1.12 (0.64, 1.96) 75th: 0.89 (0.47, 1.65) **Ostium secundum:** 25th: 1.15 (0.85, 1.55) 50th: 1.13 (0.83, 1.53) 75th: 1.06 (0.77, 1.48) **Pulmonary artery atresia without ventricular Sepal defects:** 25th: 1.93 (1.08, 3.45) 50th: 2.01 (1.11, 3.64) 75th: 0.86 (0.41, 1.83) **Pulmonary valve stenosis:** 25th: 1.16 (0.88, 1.55) 50th: 1.25 (0.94, 1.66) 75th: 1.27 (0.94, 1.71) **Tetralogy of Fallot:** 25th: 1.21 (0.72, 2.01) 50th: 1.40 (0.84, 2.33) 75th: 1.45 0.85, 2.48) **Ventricular Sepal defects:** 25th: 1.06 (0.90, 1.24) 50th: 1.10 (0.94, 1.29) 75th: 1.08 (0.92, 1.27)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Gouveia et al. (2004, 055613) **Period of Study:** 1997 **Location:** São Paulo, Brazil	**Outcome:** Birth weight **Age Groups:** Singleton full term live births within 1000 g to 5500 g **Study Design:** Cross sectional study **N:** 179,460 live births **Statistical Analyses:** GAM and Logistic regression models **Covariates:** Maternal age, length of gestation, season, infant gender, maternal education, number of antenatal care visits, parity, and the type of delivery **Season:** All seasons **Dose-response Investigated?** Yes **Statistical Package:** S-Plus 2000	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 60.3 (25.2) **Range (Min, Max):** (25.5-153.0) **Monitoring Stations:** maximum of 12 sites **Copollutant (correlation):** CO: r = 0.9 SO_2 NO_2 O_3	**PM Increment:** 10 µg/m^3 **Mean [Lower CI, Upper CI]:** Changes in birth weight (in g) First trimester = -13.7 (-27.0, -0.4) Second trimester = -4.4 (-18.9, 10.1) Third trimester = 14.6 (0.0, 29.2) **RR Estimate [Lower CI, Upper CI]:** (RR estimates are adjusted odds ratios for low birth weight according to quartiles of air pollution in each trimester of pregnancy.) 1st quartile First trimester = 1 (REF) Second trimester = 1 (REF) Third trimester = 1 (REF) 2nd quartile First trimester = 1.105 (0.994, 1.229) Second trimester = 1.003 (0.904, 1.113) Third trimester = 1.004 (0.914, 1.104) 3rd quartile First trimester = 1.049 (0.903, 1.219) Second trimester = 1.074 (0.920, 1.254) Third trimester = 1.003 (0.861, 1.169) 4th quartile First trimester = 1.144 (0.878, 1.491) Second trimester = 1.252 (1.028, 1.525) Third trimester = 0.970 (0.780, 1.205) Multiple linear regression coefficients (SE) obtained from single, dual, and three pollutant models Single pollutant model = -1.37 (0.68) Two pollutant (PM_{10} and CO) = -0.51 (0.87) Two pollutant (PM_{10} and SO_2) = -0.94 (0.75) Three pollutant = -0.47 (0.88)
Reference: Ha et al. (2003, 042552) **Period of Study:** Jan 1995-Dec 1999 **Location:** Seoul, South Korea	**Outcome:** Post-neonate total and respiratory mortality **Age Groups:** 1 month-1 yr 2 yr-65 yr, >65 yr **Study Design:** Time-series **N:** 1045 post-neonate deaths, 67,597 2-65 yr old deaths, 100,316 >65 yr old deaths **Statistical Analyses:** Generalized additive model **Covariates:** Seasonality, temperature, relative humidity, day of the week **Dose-response Investigated?** No **Statistical Package:** S Plus **Lags Considered:** 0, 1, 2, 3, 4, 5, 6, 7, ma from 1-5 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 69.2 (31.6) **Percentiles: 25th:** 44.8 50th(Median): 64.2 75th: 87.7 **Range (Min, Max):** 10.5 µg/m^3, 245.4 µg/m^3 **Monitoring Stations:** 27 **Copollutant (correlation):** NO_2: r = 0.73 SO_2: r = 0.62 O_3: r = -0.02 CO: r = 0.63	**PM Increment:** 42.9 µg/m^3 **RR Estimate [Lower CI, Upper CI] lag:** Total Mortality: 1 month-1 yr (post-neonates): 1.142 [1.096, 1.190] lag 0 2 yr-65 yr: 1.008 [1.006, 1.010] lag 0 >65 yr (elderly): 1.023 [1.023, 1.024] lag 0 Respiratory Mortality: 1 month-1 yr (post-neonates): 2.018 [1.784, 2.283] lag 0 2 yr-65 yr: 1.066 [1.044, 1.090] lag 0 >65 yr (elderly): 1.063 [1.055, 1.072] lag 0

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Hansen, et al. (2006, 089818) **Period of Study:** Jul 2000-Jun 2003 **Location:** Brisbane, Australia	**Outcome:** Pre-term birth (<37 wk) **Age Groups:** Newborn babies **Study Design:** Cross-sectional **N:** 1583 live pre-terms births 28,200 singleton live births **Statistical Analyses:** Multiple logistic regression models **Covariates:** Neonate gender, mother's age, parity, indigenous status, number of antenatal visits, marital status, number of previous abortions/miscarriages, type of delivery, and index of SES **Season:** all **Dose-response Investigated?** Yes **Statistical Package:** SAS version 8.2	**Pollutant:** PM_{10} **Averaging Time:** recorded hourly, avgd daily **Mean (SD):** 19.6 (9.4) **Range (Min, Max):** 4.9, 171.7 **Monitoring Stations:** 5 **Copollutant (correlation):** Fine PM or bsp, 0.1 to <2.5 µg in diameter (0.58 to 0.76) O_3 (0.54 to 0.83) NO_2 (0.54 to 0.75) PM_{10} (0.80 to 0.93) **Note:** Correlations presented are for the individual pollutant across monitoring stations (not correlations between PM_{10} and the pollutant.)	**PM Increment:** Trimester One 4.5 µg/m^3 Last 90 days prior to birth 5.7 µg/m^3 **Odds Ratio [Lower CI, Upper CI]:** Trimester 1 1.15 [1.06, 1.25] Last 90 days prior to birth 1.04 [0.92, 1.16]
Reference: Hansen et al. (2007, 090703) **Period of Study:** Jul 2000-Jun 2003 **Location:** Brisbane, Australia	**Outcome:** Birth weight and Small for Gestational Age (SGA <10th percentile for age and gender) Head circumference (HC) and crown-heel length (CHL) among subsample **Study Design:** Cross-sectional **N:** 26,617 births (birth weight analysis) and 21,432 (HC and CHL analyses) **Statistical Analyses:** Logistic (SGA) and linear (birth weight, HC, CHL) regressions **Covariates:** Gender, gestational age (with a quadratic term), maternal age, parity, number of previous abortions/miscarriages, marital status, indigenous status, number of antenatal visits, type of delivery, an index of SES, and season of birth **Season:** Assessed as a covariate **Dose-response Investigated?** Yes, assessed exposures as quartiles **Statistical Package:** SAS v8.2	**Pollutant:** PM_{10} **Averaging Time:** Trimester and monthly avg were used in analyses (calculated as the mean of daily values Hourly data was use to calculate daily means City-wide avg used) **Mean (SD):** 19.6 (9.4) **Percentiles:** 25th: 14.6 50th: 18.1 75th: 22.7 **Range (Min, Max):** (4.9, 171.7) **Monitoring Stations:** 5 **Copollutant (correlation):** By trimesters: PM_{10} T1: PM_{10} T2: r = 0.12 PM_{10} T3: r = -0.55 O_3 T1: r = 0.77 O_3 T2: r = 0.28 O_3 T3: r = -0.61 NO_2 T1: r = 0.32 NO_2 T2: r = -0.65 NO_2 T3: r = -0.17 visibility reducing particles (bsp) T1: r = 0.82 visibility reducing particles (bsp) T2: r = -.15 visibility reducing particles (bsp) T3: r = -0.50 PM_{10} T1: r = 0.12 PM_{10} T2: PM_{10} T3: r = 0.04 O_3 T1: r = -0.11 O_3 T2: r = 0.80 O_3 T3: r = 0.18 NO_2 T1: r = 0.77 NO_2 T2: r = 0.25 NO_2 T3: r = -0.72 visibility reducing particles (bsp) T1: r = 0.23 visibility reducing particles (bsp) T2: r = 0.80 visibility reducing particles (bsp) T3: r = -0.24 PM_{10} T1: r = -0.55 PM_{10} T2: r = 0.04 PM_{10} T3:	**PM Increment:** IQR (8.1 µg/m^3) **Effect Estimate [Lower CI, Upper CI]:** **Change (β) in mean birth weight (g) associated with trimester-specific exposures** Trimester 1: Continuous exposure: -3.2 (-11.9, 5.5) Quartiles of exposure: 1: Ref 2: -4.7 (-19.7, 10.2) 3: 4.2 (-12.9, 21.3) 4: -0.2 (-19.2, 18.8) p-trend: 0.864 Trimester 2: Continuous exposure: 0.4 (-9.4, 10.2) Quartiles of exposure: 1: Ref 2: 12.7 (-2.3, 27.6) 3: 7.6 (-10.6, 25.7) 4: 1.0 (-18.7, 20.7) p-trend: 0.922 Trimester 3: Continuous exposure: 3.6 (-6.9, 14.0) Quartiles of exposure: 1: Ref 2: 2.9 (-12.8, 18.7) 3: 18.5 (0.0, 36.9) 4: 4.3 (-15.8, 24.4) p-trend: 0.524 **ORs for SGA associated with trimester-specific exposures** Trimester 1: Continuous exposure: 1.04 (0.96, 1.12) Quartiles of exposure: 1: Ref 2: 1.23 (1.07, 1.42) 3: 1.12 (0.95, 1.31) 4: 1.12 (0.94, 1.34) p-trend: 0.361 Trimester 2: Continuous exposure: 0.95 (0.88, 1.04) Quartiles of exposure: 1: Ref 2: 0.96 (0.83, 1.11) 3: 1.06 (0.89, 1.25) 4: 0.98 (0.81, 1.18) p-trend: 0.962 3: -0.02 (-0.08, 0.04) 4: -0.02 (-0.08, 0.05) p-trend: 0.605 Trimester 2: Continuous exposure: -0.01 (-0.04, 0.02)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
		O_3 T1: r = -0.56 O_3 T2: r = -0.18 O_3 T3: r = 0.81 NO_2 T1: r = -0.20 NO_2 T2: r = 0.75 NO_2 T3: r = 0.22 visibility reducing particles (bsp) T1: r = -0.62 visibility reducing particles (bsp) T2: r = 0.19 visibility reducing particles (bsp) T3: r = 0.79	Quartiles of exposure: 1: Ref Trimester 3: Continuous exposure: 0.93 (0.85, 1.03) Quartiles of exposure: 1: Ref 2: 0.90 (0.78, 1.04) 3: 0.81 (0.68, 0.96) 4: 0.86 (0.71, 1.04) p-trend: 0.098 **Change (β) in mean head circumference (HC cm) associated with trimester-specific exposures** Trimester 1: Continuous exposure: -0.01 (-0.04, 0.02) Quartiles of exposure: 1: Ref 2: -0.02 (-0.07, 0.04) 2: 0.03 (-0.02, 0.08) 3: 0.00 (-0.06, 0.06) 4: -0.01 (-0.08, 0.05) p-trend: 0.538 Trimester 3: Continuous exposure: 0.02 (-0.02, 0.05) Quartiles of exposure: 1: Ref 2: 0.02 (-0.04, 0.07) 3: 0.07 (0.01, 0.13) 4: 0.04 (-0.03, 0.11) p-trend: 0.171 **Change (β) in mean crown-heel length (CHL cm) associated with trimester-specific exposures** Trimester 1: Continuous exposure: 0.00 (-0.05, 0.05) Quartiles of exposure: 1: Ref 2: 0.02 (-0.07, 0.11) 3: 0.01 (-0.10, 0.11) 4: 0.04 (-0.07, 0.16) p-trend: 0.511 Trimester 2: Continuous exposure: 0.07 (0.01, 0.13) Quartiles of exposure: 1: Ref 2: 0.10 (0.01, 0.18) 3: 0.11 (0.00, 0.21) 4: 0.13 (0.01, 0.24) p-trend: 0.049 Trimester 3: Continuous exposure: -0.01 (-0.07, 0.05) Quartiles of exposure: 1: Ref 2: -0.02 (-0.11, 0.07) 3: 0.10 (-0.01, 0.21) 4: -0.01 (-0.13, 0.10) p-trend: 0.883

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: (Hansen et al., 2009, 192362) **Period of Study:** Jan 1997-Dec 2004 **Location:** Brisbane, Australia	**Outcome:** Birth defects- artery and valve, atrial and ventricular Sepal, conotruncal, endocardial cushion and mitral valve, cleft lip and palate **Study Design:** Case-control **Covariates:** Mother's age, marital status, indigenous status, previous pregnancies, last menstrual period, area-level socioeconomic status, distance to a pollution monitor **Statistical Analysis:** Conditional logistic regression **Statistical Package:** R **Age Groups:** Neonates	**Pollutant:** PM_{10} **Averaging Time:** daily **Mean (SD) Unit:** 18.0 µg/m^3 **Range (Min, Max):** (4.4, 151.7) **Copollutant (correlation):** NR	**Increment:** 4µg/m^3 **Odds Ratios (95% CI) for risk of defect** Aortic Artery and Valve Defects All Births, Matched: 1.10 (0.76-1.56) Births ≤ 12km to Monitor: 1.83 (1.16-2.98) Births ≤ 6km to Monitor: 1.43 (0.73-2.90) All Births, Unmatched: 1.09 (0.84-1.39) Atrial Sepal Defects All Births, Matched: 1.06 (0.86-1.30) Births ≤ 12km to Monitor: 1.07 (0.84-1.37) Births ≤ 6km to Monitor: 0.88 (0.60-1.27) All Births, Unmatched: 1.14 (0.98-1.33) Pulmonary Artery and Valve Defects All Births, Matched: 0.90 (0.61-1.29) Births ≤ 12km to Monitor: 0.69 (0.43-1.08) Births ≤ 6km to Monitor: 1.46 (0.76-2.73) All Births, Unmatched: 0.99 (0.78-1.24) Ventricular Sepal Defects All Births, Matched: 0.87 (0.73-1.04) Births ≤ 12km to Monitor: 0.85 (0.69-1.03) Births ≤ 6km to Monitor: 0.90 (0.68-1.18) All Births, Unmatched: 1.15 (1.02-1.30) Conotruncal Defects All Births, Matched: 0.80 (0.54-1.19) Births ≤ 12km to Monitor: 0.94 (0.55-1.49) Births ≤ 6km to Monitor: 0.66 (0.27-1.45) All Births, Unmatched: 0.97 (0.74-1.24) Endocardial Cushion and Mitral Valve Defects All Births, Matched: 1.29 (0.82-2.04) Births ≤ 12km to Monitor: 1.28 (0.75-2.19) Births ≤ 6km to Monitor: 0.90 (0.44-1.86) All Births, Unmatched: 0.94 (0.68-1.26) Cleft Lip All Births, Matched: 1.05 (0.72-1.51) Births ≤ 12km to Monitor: 1.16 (0.72-1.82) Births ≤ 6km to Monitor: 1.03 (0.56-1.82) All Births, Unmatched: 1.01 (0.79-1.27) Cleft Palate All Births, Matched: 0.69 (0.50-0.93) Births ≤ 12km to Monitor: 0.53 (0.29-0.87) Births ≤ 6km to Monitor: 0.71 (0.49-1.00) All Births, Unmatched: 0.89 (0.72-1.10) Cleft Lip with or without Cleft Palate All Births, Matched: 1.05 (0.84-1.30) Births ≤ 12km to Monitor: 1.03 (0.79-1.34) Births ≤ 6km to Monitor: 0.83 (0.58-1.19) All Births, Unmatched: 1.04 (0.89-1.21)\

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Jalaludin et al. (2007, 156601) **Period of Study:** 1998-2000 **Location:** Sydney, Australia	**Outcome:** Gestational age (categorized: preterm birth: <37 wk term birth: ≥ 37 wk but <42 wk) **Age Groups:** Infants **Study Design:** Cross-sectional **N:** 123,840 singleton births of >20 wk gestation **Statistical Analyses:** Logistic regression **Covariates:** Sex of child, maternal age, maternal smoking during pregnancy, gestational age at first antenatal visit, whether mother identifies as being Aboriginal or Torres Strait Islander, whether first pregnancy, season of conception, SES, (temperature and relative humidity were not significant in single variable models and therefore, were not included) **Season:** Examined as covariate and effect modifier **Dose-response Investigated?** No **Statistical Package:** SAS v8	**Pollutant:** PM_{10} **Averaging Time:** 24 h avg used to calculate the mean concentration over the first trimester, the 3 mo preceding birth, the first month after the estimated date of conception, and the month prior to delivery **Mean (SD):** (24 h avg) All yr: 16.3 (6.38) Summer: 18.2 (7.20) Fall: 17.0 (6.23) Winter: 14.5 (5.57) Spring: 15.7 (5.82) **Monitoring Stations:** 14 stations within the Sydney metropolitan area (levels avgd to provide 1 estimate for the entire study area) **Copollutant (correlation):** PM_{10} $PM_{2.5}$ (r = 0.83) CO (r = 0.28) NO_2 (r = 0.48) O_3 (r = 0.50) SO_2 (r = 0.42) **Notes:** Correlations between monitoring stations measuring PM_{10} ranged from 0.67 to 0.91	**PM Increment:** 1 µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** ORs (air pollutant concentration during the 1st trimester and preterm birth by season) Fall: 1.462 (1.267, 1.688) Winter: 1.343 (1.190, 1.516) Spring: 1.119 (0.973, 1.288) Summer: 0.913 (0.889, 0.937) ORs (air pollutant concentrations during different exposure periods and preterm birth for all of Sydney and among only those residing within 5 km of a monitoring station) 1 month preceding birth Sydney: 0.991 (0.979, 1.003) 5km: 1.008 (0.993, 1.022) 3 mo preceding birth Sydney: 0.989 (0.975, 1.004) 5km: 1.012 (0.995, 1.030) 1st month of gestation Sydney: 0.983 (0.973, 0.993) 5km: 0.957 (0.914, 1.002) 1st trimester Sydney: 0.987 (0.973, 1.001) 5km: 1.009 (0.978, 1.041) **Notes:** Authors note that effect of PM_{10} on preterm birth for infants conceived during the fall did not remain in 2 pollutant models (ORs between 0.77 and 1.04)
Reference: Kaiser et al. (2004, 076674) **Period of Study:** 1995-1997 **Location:** 25 U.S. counties (23 metropolitan areas): Jackson, AL Fresno, CA Los Angeles, CA Sacramento, CA San Diego, CA San Francisco, CA Denver, CO Hartford, CT Cook, IL Baltimore, MD Wayne, MI St. Louis, MO Bronx, NY Kings, NY New York, NY Philadelphia, PA El Paso, TX Harris, TX Dallas, TX Oklahoma, OK Tulsa, OK Providence, RI Salt Lake City, UT King, WA Milwaukee, WI	**Outcome:** Postneonatal death: All cause, SIDS (798.0) Respiratory disease (460-519) **Age Groups:** Infants between 1-12 mo **Study Design:** Attributable risk assessment **N:** 700,000 infants (# deaths NR) **Statistical Analyses:** Risk assessment methods described in: Kunzli et al. Public-health impact of outdoor and traffic-related air pollution: a European assessment. Lancet 2000, 356: 795-801. **Covariates:** Maternal education, maternal ethnicity, parental marital status, maternal smoking during pregnancy, infant's month and yr of birth, avg temperature in the first 2 mo of life **Season:** All adjusted for month/yr of birth **Dose-response Investigated?** NR **Statistical Package:** NR **Lags Considered:** Annual, county-level mean	**Pollutant:** PM_{10} **Averaging Time:** "annual mean levels" in each county **Mean (SD):** 28.4 **Range (Min, Max):** County range: 18.0, 44.8 **Monitoring Stations:** NR **Notes:** 14 out of 25 counties had PM_{10} levels >25 µg/m^3	**PM Increment:** Analysis 1: 16.4 µg/m^3 (difference between reference level of 12 µg/m^3 and observed mean level of 28.4 µg/m^3) Analysis 2: 13 µg/m^3 (difference between reference level of 12 µg/m^3 and 25 µg/m^3) **AR Estimate [Lower CI, Upper CI]:** Analysis 1: All cause 6% [3, 11] SIDS 16% [9, 23] Respiratory 24% [7, 44] Attributable # deaths per 100,000 infants: All cause 14.7 [7.3, 25.6] SIDS 11.7 [6.8, 16.6] Respiratory 2.3 [0.7, 4.1] Analysis 2: All cause 5% [2, 8] SIDS 12% [7, 18] Respiratory 19% [6, 34] Attributable # deaths per 100,000 infants: All cause 10.9 [5.5, 19.1] SIDS 9.0 [5.3, 12.8] Respiratory 1.8 [0.5, 3.2] **Notes: -**Authors did not extrapolate attributable cases below 12 µg/m^3 (i.e., reference level was set at 12 µg/m^3) -Attributable risks are based on the RRs reported by Woodruff et al, 1997 for a 10 µg/m^3 increase: All cause 1.04 [1.02-1.07] SIDS 1.12 [1.07, 1.17] Respiratory 1.20 [1.06, 1.36]
Reference: (Kim et al., 2007, 156642) **Period of Study:** May 2001-May 2004	**Outcome (ICD9 and ICD10):** LBW (low birth weight, less than 2500 g at later than gestational week 37), premature delivery (birth before the completion of	**Pollutant:** PM_{10} **Averaging Time:** Used hourly exposure levels to calculate avg	**PM increment:** 10 µg/m^3 **Preterm:** 1st Trimester Odds Ratios:

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Location: Seoul, Korea	the 37th week), stillbirth (intrauterine fetal death), IUGR (birth weight lower than the 10th percentile for the given gestational age), and congenital anomaly (a defect in the infant's body structure) **Age Groups:** Infants **Study Design:** Cross-sectional (women visiting the clinic for prenatal care were recruited with follow-up until discharge after delivery) **N:** 1514 observations (births) **Statistical Analyses:** Multiple logistic and linear regression (in addition, for birth weight, used generalized additive model to account for long-term trends and nonlinear relationships between the response variable and the predictors, and to produce smoothed plots of the relationship between PM and birth weight) **Covariates:** Adjustment 1: infant sex, infant order, maternal age and education, paternal education, season of birth Adjustment 2: adjustment 1 factors plus alcohol, maternal BMI, maternal weight prior to delivery (collected information on smoking, ETS, parity, past history of illnesses, history of illnesses during pregnancy but did not use in analyses due to small numbers or non-significance) **Season:** Adjusted for season of delivery **Dose-response Investigated?** Yes **Statistical Package:** SAS 8.01, S-Plus 2000	exposure levels at each trimester, each month of pregnancy, and 6 wk before delivery from the nearest monitoring station (based on home address of mother) Also created categories within each pregnancy period (<25th percentile [referent], 25th to 50th percentile, and >50th percentile) **Mean (SD):** Range of PM means across pregnancy periods: 88.7-89.7 **Monitoring Stations:** 27 stations	Crude: 0.95 (0.90, 1.01) Adj 1: 0.93 (0.87, 1.00) Adj 2: 0.93 (0.85, 1.01) 2nd Trimester Odds Ratios: Crude: 0.99 (0.94, 1.06) Adj 1: 0.98 (0.92, 1.04) Adj 2: 1.00 (0.93, 1.07) 3rd Trimester Odds Ratios: Crude: 1.02 (0.98, 1.06) Adj 1: 1.05 (1.00, 1.10) Adj 2: 1.05 (0.99, 1.11) **LBW**: 1st Trimester Odds Ratios: Crude: 1.02 (0.93, 1.12) Adj 1: 1.03 (0.93, 1.14) Adj 2: 1.07 (0.96, 1.19) 2nd Trimester Odds Ratios: Crude: 1.03 (0.94, 1.14) Adj 1: 1.04 (0.93, 1.17) Adj 2: 1.07 (0.94, 1.22) 3rd Trimester Odds Ratios: Crude: 1.04 (0.97, 1.11) Adj 1: 1.05 (0.97, 1.14) Adj 2: 1.05 (0.96, 1.16) **IUGR**: 1st Trimester Odds Ratios: Crude: 1.07 (0.97, 1.19) Adj 1: 1.07 (0.95, 1.21) Adj 2: 1.14 (0.99, 1.31) 2nd Trimester Odds Ratios: Crude: 0.97 (0.85, 1.12) Adj 1: 0.97 (0.82, 1.13) Adj 2: 0.93 (0.77, 1.13) 3rd Trimester Odds Ratios: Crude: 0.82 (0.68, 0.99) Adj 1: 0.88 (0.72, 1.08) Adj 2: 0.85 (0.67, 1.08) **Birth defect**: 1st Trimester Odds Ratios: Crude: 1.08 (0.98, 1.20) Adj 1: 1.12 (1.00, 1.25) Adj 2: 1.08 (0.95, 1.22) 2nd Trimester Odds Ratios: Crude: 1.09 (0.99, 1.21) Adj 1: 1.11 (0.98, 1.26) Adj 2: 1.16 (1.00, 1.34) 3rd Trimester Odds Ratios: Crude: 1.00 (0.90, 1.11) Adj 1: 0.97 (0.86, 1.08) Adj 2: 0.97 (0.87, 1.10) **Stillbirth**: 1st Trimester Odds Ratios: Crude: 0.83 (0.76, 0.90) Adj 1: 0.93 (0.85, 1.02) Adj 2: 0.95 (0.85, 1.02) 2nd Trimester Odds Ratios: Crude: 0.99 (0.93, 1.05) Adj 1: 1.03 (0.95, 1.11) Adj 2: 1.07 (0.98, 1.17) 3rd Trimester Odds Ratios: Crude: 1.14 (1.10, 1.18) Adj 1: 1.09 (1.04, 1.15) Adj 2: 1.08 (1.02, 1.14) **LBW (categorical PM exposure):** 1st Trimester ORs: <25th: 1.0 25th-50th: 0.5 (0.1, 3.2) >50th: 1.0 (0.3, 3.8) 3rd Trimester ORs: <25th: 1.0 25th-50th: 1.3 (0.2, 10.4) >50th: 3.0 (0.5, 18.5) 6 wk before birth ORs: <25th: 1.0 25th-50th: 3.2 (0.3, 33.7) >50th: 5.2 (0.6, 47.6) **Changes in Birth Weight (95%CI) per 10 µg/m^3 increase in PM concentration:**

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			1st trimester: 7.8 (1.2, 14.5) 2nd trimester: -0.3 (-7.3, 6.8) 3rd trimester: -2.1 (-7.5, 3.4) 1st month: 4.4 (-1.0, 9.8) 2nd month: 6.4 (0.6, 12.2) 3rd month: 4.3 (-1.5, 10.2) 4th month: 3.0 (-3.7, 9.6) 5th month: -3.9 (-10.5, 2.7) 6th month: 0.1 (-5.7, 5.8) 7th month: 0.1 (-5.1, 5.3) 8th month: 0.0 (-4.5, 4.5) 9th month: 1.8 (-2.3, 5.9) Last 6 wk: -4.8 (-9.9, 0.4)
Reference: Lee et al. (2003, 043202) **Period of Study:** Jan 1996-Dec 1998 **Location:** Seoul, South Korea	**Outcome:** Low birth weight (LBW), <2500 g **Age Groups:** Child-bearing age women and their newborn children-delivered at 37-44 gestational wk **Study Design:** Cross-section **N:** 388,905 full-term single births **Statistical Analyses:** Generalized additive model, LOESS, Akaike's criterion, **Covariates:** Infant sex, birth order, maternal age, parental education level, time trend and gestational age. **Season:** All **Dose-response Investigated?** Yes **Statistical Package:** NR	**Pollutant:** PM_{10} **Averaging Time:** Arithmetic avg of hourly measurements at 20 stations **Mean (SD):** 71.1 (30.1) **Percentiles:** **25th:** 47.4 **50th(Median):** 67.6 **75th:** 89.3 **Range (Min, Max):** 18.4, 236.9 **Monitoring Stations:** 20 **Copollutant (correlation):** 1st trimester: PM_{10}-CO: 0.47 PM_{10}-SO_2: 0.78 PM_{10}-NO_2: 0.66 2nd trimester: PM_{10}-CO: 0.68 PM_{10}-SO_2: 0.82 PM_{10}-NO_2: 0.81 3rd trimester: PM_{10}-CO: 0.69 PM_{10}-SO_2: 0.85 PM_{10}-NO_2: 0.80	**PM Increment:** IQR, 41.9 **RR Estimate [Lower CI, Upper CI]:** 1st trimester: 1.03 [1.00, 1.07] 2nd trimester: 1.04 [1.00, 1.08] 3rd trimester: 1.00 [0.95, 1.04] All trimesters: 1.06 [1.01, 1.10] Low exposure in last 5 mo using IQR during last 5 mo: 0.94 [0.85, 1.05] Low exposure in first 5 mo using IQR during first 5 mo: 1.04 [1.01, 1.08] **Notes:** Birth weight was decreased by 19.6 g for an IQR increase in the 2nd trimester. The OR for LBW increased for female children, fourth or higher order child, mother <20 yr of age, and low parental education level.
Reference: Leem et al. (2006, 089828) **Period of Study:** 2001-2002 **Location:** Incheon, Korea	**Outcome (ICD9 and ICD10): Age Groups:** Pre-term delivery **Study Design:** Cross-sectional **N:** Cases: 2,082 Controls: 50,031 **Statistical Analyses:** Log-binomial regression (corrected for overdispersion Used the log link function) **Covariates:** Maternal age, parity, sex, season of birth, and education level of each parent **Season:** Controlled as a covariate **Dose-response Investigated?** Yes, assessed quartiles of exposure **Statistical Package:** NR	**Pollutant:** PM_{10} **Averaging Time:** Trimesters (daily hourly data used to calculate) **Range (Min, Max):** Reported ranges within quartiles by trimester: 1st Trimester: 4: 64.57-106.39 3: 53.84-64.56 2: 45.95-53.83 1: 26.99-45.94 3rd Trimester: 4: 65.63-95.91 3: 56.07-65.62 2: 47.07-56.06 1: 33.12-47.06 **Monitoring Stations:** 27 monitoring stations Pollutant levels for each area were predicted from the levels recorded at the monitors using ordinary block kriging **Copollutant (correlation):** SO_2 (r = 0.13) NO_2 (r = 0.37) CO (r = 0.27)	**Effect Estimate [Lower CI, Upper CI]:** **Crude and Adjusted RR for preterm delivery and exposure during the 1st trimester** Crude Quartiles of exposure: 4: 1.07 (0.95, 1.21) 3: 1.02 (0.90, 1.15) 2: 1.06 (0.94, 1.20) 1: 1.00 Adjusted Quartiles of exposure: 4: 1.27 (1.04, 1.56) 3: 1.13 (0.94, 1.37) 2: 1.14 (0.97, 1.34) 1: 1.00 p-trend: 0.39 **Crude and Adjusted RR for preterm delivery and exposure during the 3rd trimester** Crude Quartiles of exposure: 4: 1.06 (0.94, 1.20) 3: 1.06 (0.94, 1.19) 2: 1.05 (0.93, 1.18) 1: 1.00 Adjusted Quartiles of exposure: 4: 1.09 (0.91, 1.30) 3: 1.04 (0.90, 1.21) 2: 1.05 (0.91, 1.20) 1: 1.00 p-trend: 0.33

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Lin et al. (2004, 095787) **Period of Study:** Jan 1998-Dec 2000 **Location:** São Paulo, Brazil	**Outcome:** Neonatal death **Age Groups:** Neonates (infants 0-28 days after birth) **Study Design:** Time series **N:** 1096 days, 6697 deaths **Statistical Analyses:** Poisson regression (GAM) **Covariates:** Non-parametric LOESS smoothers to control for: time (long term trend), temperature, humidity, and day of week Also controlled for holidays with linear term **Season:** All **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** Lag 0, "ma from 2 to 7 days" **Notes:** No explicit control for season apart from temperature	**Pollutant:** PM_{10} **Averaging Time:** Daily values **Mean (SD):** 48.62 (21.18) **Range (Min, Max):** 13.9, 157.3 **Monitoring Stations:** NR (indicated more than 1) **Copollutant (correlation):** CO r = 0.71 NO_2 r = 0.76 SO_2 r = 0.80 O_3 r = 0.36	**PM Increment:** 1 µg/m^3 **Log relative rate (standard error) lag** Single pollutant model 0.0017 (0.0008) lag 0 This translates to a 4.0% [95% CI: 0.3, 7.9] increase in neonatal mortality for a 23.3 µg/m^3 increase in PM_{10} Two-pollutant model 0.0000 (0.0011) lag 0 **Notes:** -In two-pollutant model with PM_{10} and SO_2 (which are highly correlated), effect of PM disappeared and effect of SO_2 remained constant - Results from pollutant ma from 2-7 days not reported, authors indicate effects only found for lag 0 (same day levels) - Confidence intervals reported in abstract are incompatible with βs/standard errors and plotted results in text: abstract indicates a 4% increase in mortality with 95% CI: 2-6 for a 23.3 µg/m^3 increase in PM_{10}
Reference: (Lin et al., 2004, 089827) **Period of Study:** 1995-1997 **Location:** Taipei and Kaoshiung, Taiwan	**Outcome:** Low birth weight (<2500 grams) **Age Groups:** Newborns **Study Design:** Cross-sectional **N:** 92,288 infants **Statistical Analyses:** Logistic regression **Covariates:** Gender, birth order, gestational weeks, season of birth, maternal age, maternal education, copollutants **Season:** All **Dose-response Investigated?** Yes **Statistical Package:** NR **Lags Considered:** The 9-month pregnancy period for each infant, and each trimester	**Pollutant:** PM_{10} **Averaging Time:** NR, "daily measurements" **Mean (SD):** Reported by monitoring station: Taipei: 1. 48.78 2. 46.29 3. 48.79 4. 50.80 5. 52.54 Kaohsiung 1. 69.99 2. 63.39 3. 64.89 4. 75.79 5. 77.27 **Monitoring Stations:** 10 (5 in each city) **Notes:** All pregnant women/infants included in study lived within 3 km of an air quality monitoring station Pollution assigned based on nearest air quality station to the maternal residence **Co-pollutant:** CO, SO_2, O_3, NO_2	**PM Increment:** Tertiles Entire pregnancy T1: <46.4 ppb T2: 46.4-63.1 ppb T3: >63.1 ppb First trimester T1: <45.8 ppb T2: 45.8-67.6 ppb T3: >67.6 ppb Second trimester T1: <44.6 ppb T2: 44.6-64.2 ppb T3: >64.2 ppb Third trimester T1: <43.7 ppb T2: 43.7-63.7 ppb T3: >63.7 ppb **RR Estimate [Lower CI, Upper CI]** Entire pregnancy T1: 1.00 T2: 0.96 [0.83, 1.11] T3: 0.87 [0.71, 1.05] First trimester T1: 1.00 T2: 0.96 [0.84, 1.09] T3: 0.97 [0.80, 1.17] Second trimester T1: 1.00 T2: 1.03 [0.90, 1.17] T3: 1.00 [0.83, 1.21] Third trimester T1: 1.00 T2: 1.02 [0.90, 1.16] T3: 0.97 [0.81, 1.17] **Notes:** RR for births in Kaoshiung vs. Taipei: 1.13 [1.03, 1.24]
Reference: Lipfert et al. (2000, 004103) **Period of Study:** 1990 **Location:** U.S.	**Outcome:** Infant mortality Including respiratory mortality (traditional definition, ICD9 460-519), expanded definition (adds ICD9 769 and 770) **Age Groups:** Infants **Study Design:** Cross-sectional **N:** 2,413,762 infants in 180 counties	**Pollutant:** PM_{10} **Averaging Time:** Yearly avg used **Mean (SD):** 33.1 (9.17) (based on 180 counties) **Range (Min, Max):** (16.9, 59) **Monitoring Stations:** NR **Copollutant (correlation):**	**PM Increment:** NR (present regression coefficients) **Effect Estimate [Lower CI, Upper CI]:** Presented regression coefficients (standard errors) (3 PM exposures regressed jointly) bold = p <0.05 Cause of death: All Birth weight: All PM_{10}: 0.0114 (0.0015)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
	(Ns differ for various models) **Statistical Analyses:** Logistic regression **Covariates:** Mother's smoking, education, marital status, and race Month of birth And county avg heating degree days **Dose-response Investigated?** NR **Statistical Package:** NR	PM_{10} SO_4^{2-} (r = 0.10) $NSPM_{10}$-non-sulfate portion of PM_{10} (r = 0.91) CO (r = 0.27) SO_2 (r = 0.04) **Notes:** TSP-based sulfate was adjusted for compatibility with the PM_{10}-based data	SO_4^{2-}: -0.0002 (0.0061) $NSPM_{10}$: 0.0115 (0.0014) Cause of death: All Birth weight: LBW PM_{10}: 0.0088 (0.0019) SO_4^{2-}: 0.0265 (0.0080) $NSPM_{10}$: 0.0086 (0.0020) Cause of death: All Birth weight: normal PM_{10}: 0.0092 (0.0024) SO_4^{2-}: -0.0488 (0.0098) $NSPM_{10}$: 0.0096 (0.0024) Cause of death: All neonatal Birth weight: All PM_{10}: 0.0126 (0.0018) SO_4^{2-}: 0.0267 (0.0076) $NSPM_{10}$: 0.0126 (0.0018) Cause of death: All neonatal Birth weight: LBW PM_{10}: 0.0086 (0.0022) SO_4^{2-}: 0.0388 (0.0088) $NSPM_{10}$: 0.0093 (0.0022) Cause of death: All neonatal Birth wt: normal PM_{10}: 0.0123 (0.0041) SO_4^{2-}: -0.0334 (0.0169) $NSPM_{10}$: 0.0125 (0.0040) Cause of death: All post neonatal Birth wt: All PM_{10}: 0.0091 (0.0024) SO_4^{2-}: -0.0474 (0.0100) $NSPM_{10}$: 0.0096 (0.0024) Cause of death: All post neonatal Birth wt: LBW PM_{10}: 0.0096 (0.0043) SO_4^{2-}: -0.0247 (0.0173) $NSPM_{10}$: 0.0101 (0.0042) Cause of death: All post neonatal Birth wt: normal PM_{10}: 0.0074 (0.0030) SO_4^{2-}: -0.0569 (0.0121) $NSPM_{10}$: 0.0080 (0.0029) Cause of death: SIDS Birth weight: All PM_{10}: 0.0138 (0.0038) SO_4^{2-}: -0.1078 (0.0151) $NSPM_{10}$: 0.0149 (0.0037) Cause of death: SIDS Birth weight: LBW PM_{10}: 0.0115 (0.0088) SO_4^{2-}: -0.1378 (0.0337) $NSPM_{10}$: 0.0146 (0.0085) Cause of death: SIDS Birth weight: normal PM_{10}: 0.0137 (0.0042) SO_4^{2-}: -0.0995 (0.0168) $NSPM_{10}$: 0.0147 (0.0041) Cause of death: All respiratory (ICD9: 460-519, 769, 770) Birth weight: All PM_{10}: 0.0168 (0.0034) SO_4^{2-}: 0.0706 (0.0146) $NSPM_{10}$: 0.0166 (0.0034) Cause of death: All respiratory (ICD9: 460-519, 769, 770) Birth weight: LBW PM_{10}: 0.0144 (0.0038) SO_4^{2-}: 0.0821 (0.0158) $NSPM_{10}$: 0.0139 (0.0038) Cause of death: All respiratory (ICD9: 460-519, 769, 770) Birth weight: normal PM_{10}: 0.0177 (0.0091) SO_4^{2-}: 0.0001 (0.0392) $NSPM_{10}$: 0.0118 (0.0090) Cause of death: Respiratory disease (ICD9: 460-519) Birth weight: All

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			PM_{10}: 0.0133 (0.0089) SO_4^{2-}: 0.0093 (0.0384) $NSPM_{10}$: 0.0134 (0.0089) Cause of death: Respiratory disease (ICD9: 460-519) Birth weight: LBW PM_{10}: 0.0092 (0.0137) SO_4^{2-}: 0.0434 (0.0580) $NSPM_{10}$: 0.0089 (0.0138) Cause of death: Respiratory disease (ICD9: 460-519) Birth weight: normal PM_{10}: 0.0126 (0.0120) SO_4^{2-}: -0.0177 (0.0509) $NSPM_{10}$: 0.0128 (0.0119) Associations with SIDS by smoking status Smoking status: Yes Birth weight: Normal PM_{10}: 0.0202 (0.0073) SO_4^{2-}: -0.0722 (0.0284) $NSPM_{10}$: 0.0206 (0.0071) Smoking status: No Birth weight: Normal PM_{10}: 0.0104 (0.0051) SO_4^{2-}: -0.114 (0.021) $NSPM_{10}$: 0.0117 (0.005) Smoking status: Yes Birth weight: LBW PM_{10}: 0.0322 (0.0130) SO_4^{2-}: -0.0958 (0.0483) $NSPM_{10}$: 0.0345 (0.0125) Smoking status: No Birth weight: LBW PM_{10}: -0.0044 (0.012) SO_4^{2-}: -0.0172 (0.047) $NSPM_{10}$: -0.0007 (0.012) Mean risks (95%CI) between post neonatal SIDS among normal birth weight babies pollutants regressed one at a time PM_{10}: 1.20 (1.02, 1.42) SO_4^{2-}: 0.43 (0.37, 0.51) $NSPM_{10}$: 1.33 (1.18, 1.50)
Reference: Maisonet et al. (2001, 016624) **Period of Study:** 1994-1996 **Location:** Northeastern U.S. (6 cities: Boston, Hartford, Philadelphia, Pittsburgh, Springfield, Washington DC)	**Outcome:** Low birth weight (LBW): infants with a birth weight <2,500 g and having a gestational age between 37 and 44 wk **Age Groups:** Term live births (singleton) **Study Design:** Cross-sectional **N:** 89,557 infants **Statistical Analyses:** Logistic regression (LBW) and linear regression (for reductions in birth weight) **Covariates:** Gestational age, gender, birth order, maternal age, race/ethnicity, yr of education, marital status, adequacy of prenatal care, previous induced or spontaneous abortions, weight gain during pregnancy, maternal prenatal smoking, and alcohol consumption Season **Season:** Yes, as covariate **Dose-response Investigated?** Yes, categorical exposure variables assessed **Statistical Package:** STATA	**Pollutant:** PM_{10} **Averaging Time:** Trimester avg calculated using 24-h measurements taken every 6 days **Range (Min, Max):** Ranges for categories of exposure: 1st Trimester <25th: <24.821 25 to <50th: 24.821, 30.996 50 to <75th: 30.997, 36.142 75 to <95th: 36.143, 46.547 ≥ 95th: ≥ 46.548 2nd Trimester <25th: <24.702 25 to <50th: 24.702, 30.294 50 to <75th: 30.295, 35.410 75 to <95th: 35.411, 43.928 ≥ 95th: ≥ 43.929 3rd Trimester <25th: <24.702 25 to <50th: 24.702, 30.162 50 to <75th: 30.163, 35.642 75 to <95th: 35.643, 43.588 ≥ 95th: ≥ 43.589 **Monitoring Stations:** 3-4 per city **Copollutants:** CO, SO_2	**PM Increment:** 10 $\mu g/m^3$ for analyses assessing exposures continuously **Effect Estimate [Lower CI, Upper CI]:** ORs for term LBW by trimester 1st Trimester Crude <25th: 1.00 25 to <50th: 1.02 (0.90, 1.14) 50 to <75th: 0.90 (0.65, 1.24) 75 to <95th: 0.87 (0.58, 1.30) ≥ 95th: 0.89 (0.60, 1.33) Continuous: 0.93 (0.77, 1.13) 1st Trimester Adjusted <25th: 1.00 25 to <50th: 1.02 (0.94, 1.11) 50 to <75th: 0.90 (0.78, 1.03) 75 to <95th: 0.85 (0.73, 1.00) ≥ 95th: 0.83 (0.70, 0.97) Continuous: 0.93 (0.85, 1.00) 2nd Trimester Crude <25th: 1.00 25 to <50th: 1.01 (0.93, 1.10) 50 to <75th: 0.90 (0.66, 1.21) 75 to <95th: 0.92 (0.62, 1.34) ≥ 95th: 0.90 (0.61, 1.33) Continuous: 0.95 (0.78, 1.16) 2nd Trimester Adjusted <25th: 1.00 25 to <50th: 1.06 (0.97, 1.15) 50 to <75th: 0.95 (0.85, 1.07) 75 to <95th: 0.91 (0.79, 1.05) ≥ 95th: 0.77 (0.63, 0.95) Continuous: 0.93 (0.85, 1.02) 3rd Trimester Crude <25th: 1.00

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			25 to <50th: 0.94 (0.85, 1.05) 50 to <75th: 0.86 (0.58, 1.25) 75 to <95th: 0.86 (0.57, 1.29) ≥ 95th: 0.92 (0.61, 1.38) Continuous: 0.95 (0.75, 1.20) 3rd Trimester Adjusted <25th: 1.00 25 to <50th: 0.98 (0.87, 1.10) 50 to <75th: 0.92 (0.76, 1.11) 75 to <95th: 0.88 (0.75, 1.04) ≥ 95th: 0.91 (0.77, 1.07) Continuous: 0.96 (0.88, 1.06) Adjusted ORs by race/ethnicity Whites: 1st Trimester <25th: 1.00 25 to <50th: 1.13 (0.96, 1.33) 50 to <75th: 1.00 (0.92, 1.08) 75 to <95th: 1.00 (0.91, 1.09) ≥ 95th: 0.92 (0.81, 1.04) Continuous: 0.94 (0.90, 0.98) 2nd Trimester <25th: 1.00 25 to <50th: 0.88 (0.77, 1.02) 50 to <75th: 0.95 (0.89, 1.02) 75 to <95th: 0.95 (0.84, 1.07) ≥ 95th: 0.89 (0.64, 1.26) Continuous: 0.96 (0.89, 1.04) 3rd Trimester <25th: 1.00 25 to <50th: 0.84 (0.64, 1.11) 50 to <75th: 0.91 (0.83, 1.01) 75 to <95th: 0.80 (0.71, 0.90) ≥ 95th: 1.03 (0.86, 1.24) Continuous: 0.95 (0.90, 1.00) African Americans: 1st Trimester <25th: 1.00 25 to <50th: 1.01 (0.98, 1.05) 50 to <75th: 0.88 (0.79, 0.98) 75 to <95th: 0.83 (0.70, 0.97) ≥ 95th: 0.81 (0.67, 0.99) Continuous: 0.93 (0.85, 1.01) 2nd Trimester <25th: 1.00 25 to <50th: 1.10 (0.93, 1.30) 50 to <75th: 0.95 (0.80, 1.12) 75 to <95th: 0.88 (0.69, 1.11) ≥ 95th: 0.75 (0.54, 1.03) Continuous: 0.92 (0.80, 1.05) 3rd Trimester <25th: 1.00 25 to <50th: 1.08 (0.92, 1.27) 50 to <75th: 0.89 (0.70, 1.12) 75 to <95th: 0.94 (0.75, 1.18) ≥ 95th: 0.83 (0.71, 0.97) Continuous: 0.99 (0.87, 1.11) Hispanics: 1st Trimester <25th: 1.00 25 to <50th: 0.83 (0.64, 1.06) 50 to <75th: 0.86 (0.70, 1.05) 75 to <95th: 0.79 (0.68, 0.93) ≥ 95th: 1.36 (1.06, 1.75) Continuous: 0.96 (0.84, 1.09) 2nd Trimester <25th: 1.00 25 to <50th: 1.16 (0.84, 1.61) 50 to <75th: 0.86 (0.63, 1.19) 75 to <95th: 0.98 (0.71, 1.34) ≥ 95th: 0.68 (0.38, 1.21) Continuous: 0.92 (0.81, 1.05) 3rd Trimester <25th: 1.00 25 to <50th: 0.77 (0.55, 1.07) 50 to <75th: 1.12 (0.76, 1.66) 75 to <95th: 0.93 (0.65, 1.31) ≥ 95th: 0.90 (0.55, 1.47)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Continuous: 0.96 (0.80, 1.15)
Reference: Mannes et al.(2005, 087895) **Period of Study:** Jan 1998-Dec 2000 **Location:** Metropolitan Sydney, Australia	**Outcome:** Risk of SGA and birth weight **Age Groups:** All singleton births >20 wk and ≥ 400 grams birth weight and maternal all ages **Study Design:** Cross-sectional **N:** 138,056 singleton births **Statistical Analyses:** Logistic and linear regression models **Covariates:** Sex of child, maternal age, gestational age, maternal smoking, gestational age at first antenatal visit, maternal indigenous status, whether first pregnancy, season of birth, socioeconomic status **Season:** All seasons Included as covariate **Dose-response Investigated?** No **Statistical Package:** SAS v8.02	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 16.8 (7.1) **25th:** 12.3 **50th(Median):** 15.7 **75th:** 19.9 **Range (Min, Max):** (3.8-104.0) **Monitoring Stations:** up to 14 **Copollutants (correlations):** CO: r = 0.26 NO_2: r = 0.47 O_3: r = 0.52 $PM_{2.5}$: r = 0.81	**PM Increment:** 1 µg/m^3 Risk of SGA All births One month before birth: OR = 1.01 (1.00-1.03) Third trimester: OR = 1.00 (0.99-1.013) Second trimester: OR = 1.01 (1.00-1.04) First trimester: OR = 1.00 (0.98-1.02) 5 km births One month before birth: OR = 1.00 (0.99-1.02) Third trimester: OR = 1.01 (0.99-1.02) Second trimester: OR = 1.02 (1.01-1.03) First trimester: OR = 1.01 (0.99-1.02) Change in birth weight All births One month before birth: ß = -1.21 (-2.31- -0.11) Third trimester: ß = -0.95 (-2.30-0.40) Second trimester: ß = -2.05 (-3.36- -0.74) First trimester: ß = -0.14 (-1.37- 1.09) 5 km births One month before birth: ß = -2.98 (-4.25- -1.71) Third trimester: ß = -3.84 (-5.35- -2.33) Second trimester: ß = -4.28 (-5.79- -2.77) First trimester: ß = -2.57 (-4.04- -1.10) Key second trimester findings Single pollutant model: ß = -4.28 (-5.79- -2.77) 2 pollutant (PM_{10} and CO): ß = -3.72 (-6.29- -1.15) 2 pollutant (PM_{10} and NO_2): ß = -2.65 (-4.32- -0.98) 2 pollutant (PM_{10} and O_3): ß = -5.47 (-7.06- -3.88) 4 pollutant (PM_{10}, NO_2, CO and O_3): ß = -3.27 (-7.05-0.51) Controlling for exposures in other pregnancy periods: ß = -3.03 (-4.85- -1.21)
Reference: Pereira et al. (1998, 007264) **Period of Study:** Jan 1991-Dec 1992 **Location:** Sao Paulo, Brazil **Notes:** Paper does not focus on PM as a pollutant of interest.	**Outcome:** Intrauterine mortality (fetuses over 28 wk of pregnancy) **Study Design:** Time-series **N:** 730 days with PM measures **Statistical Analyses:** Poisson regression **Covariates:** Season, day of the week and weather (temperature and relative humidity) **Season:** Assessed by including 24 indicator variables for month and yr **Dose-response Investigated?** No **Statistical Package:** NR **Lags Considered:** Paper focuses on other pollutants (lags for PM not reported)	**Pollutant:** PM_{10} **Averaging Time:** 24 h mean **Mean (SD):** 65.04 (27.28) **Range (Min, Max):** (14.80, 192.80) **Monitoring Stations:** 13 (avgd to provide city-wide pollutant level) **Copollutants (correlation):** NO_2 (r = 0.45) SO_2 (r = 0.74) CO (r = 0.41) O_3 (r = 0.25)	**PM Increment:** NR (reported only regression coefficients for PM) **Effect Estimate [Lower CI, Upper CI]:** Regression coefficients (standard errors) for pollutants when considered separately and simultaneously in the completed model: Separately: 0.0008 (0.0006) Simultaneously: -0.0005 (0.0010)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ritz et al. (2000, 012068) **Period of Study:** 1989-1993 **Location:** Southern California	**Outcome:** Preterm birth (treated dichotomously as birth at <37 wk gestation Also analyzed continuously) **Age Groups:** Infants (born vaginally between 26-44 wk of gestation) **Study Design:** Cross-sectional **N:** 97,158 births **Statistical Analyses:** Logistic and linear regression **Covariates:** Maternal age, race, education, parity, interval since the previous live birth, access to prenatal care, infant sex, previous low weight or preterm births, smoking (reported as "pregnancy complications") To examine effect modification, authors conducted stratified analysis by region, birth and conception seasons, maternal age, race, education, and infant gender **Season:** Some models included season of birth or conception Also assessed as effect modifier in stratified analyses **Dose-response Investigated?** Examined adequacy of linear or log-linear relation using indicator terms for pollutant-avg quartiles Results presented in Fig 2 (dose-response demonstrated for last 6 wk exposure period) **Statistical Package:** NR	**Pollutant:** PM_{10} **Averaging Time:** 24-h avg at 6 day intervals avgd pollutant measures for 1, 2, 4, 6, 8, 12, and 26 wk before birth and the whole pregnancy period **Mean (SD):** 6 wk before birth: 47.5 (15.0) 1st month of pregnancy: 49.3 (16.9) **Range (Min, Max):** 6 wk before birth: 12.3-152.3 1st month of pregnancy: 9.5-178.8 **Monitoring Stations:** 17 stations (PM measured at only 8 stations) **Copollutants (correlations):** 6 wk before birth: CO (r = 0.43) NO_2 (r = 0.74) O_3 (r = 0.20) 1st month of pregnancy: CO (r = 0.37) NO_2 (r = 0.71) O_3 (r = 0.23) **Notes:** Avgd pollutant measures taken at the air monitoring station closest to the residence	**PM Increment:** 50 $\mu g/m^3$ **Effect Estimate [Lower CI, Upper CI]:** **All 8 stations** 6 wk before birth Crude: 1.20 (1.09, 1.33) 2 exposure periods: 1.18 (1.07, 1.31) Other risk factors: 1.15 (1.04, 1.26) Other RFs plus season: 1.15 (1.03, 1.29) Multipollutant model: 1.19 (1.01, 1.40) 1st month of pregnancy Crude: 1.16 (1.06, 1.26) 2 exposure periods: 1.13 (1.04, 1.24) Other risk factors: 1.09 (1.00, 1.19) Other RFs plus season: 1.09 (0.99, 1.20) Multipollutant model: 1.12 (0.97, 1.29) **Coastal stations only** 6 wk before birth Crude: 1.22 (1.00, 1.49) 2 exposure periods: 1.28 (1.04, 1.56) Other risk factors: 1.13 (0.93, 1.38) Other RFs plus season: 1.18 (0.92, 1.51) Multipollutant model: 1.42 (097, 2.01) 1st month of pregnancy Crude: 1.28 (1.06, 1.54) 2 exposure periods: 1.32 (1.09, 1.59) Other risk factors: 1.17 (0.97, 1.40) Other RFs plus season: 0.99 (0.79, 1.24) Multipollutant model: 1.09 (0.83, 1.41) **Inland stations only** 6 wk before birth Crude: 1.27 (1.12, 1.44) 2 exposure periods: 1.27 (1.11, 1.44) Other risk factors: 1.19 (1.05, 1.35) Other RFs plus season: 1.27 (1.10, 1.48) Multipollutant model: 1.18 (0.97, 1.43) 1st month of pregnancy Crude: 1.16 (1.04, 1.29) 2 exposure periods: 1.16 (1.04, 1.29) Other risk factors: 1.09 (0.98, 1.21) Other RFs plus season: 1.09 (0.97, 1.24) Multipollutant model: 1.11 (0.93, 1.33) **Crude estimates for last 6 wk exposure by season** Fall: 1.08 (0.88, 1.31) Summer: 1.06 (0.87, 1.29) Winter: 1.33 (1.07, 1.65) Spring: 1.81 (1.41, 2.31) **Reduction in mean gestation length for each increase in PM_{10} during last 6 wk before birth (linear regression analysis)** Crude: 0.66 (± 0.24) days Adj: 0.90 (± 0.27) days **Notes:** Effect estimates remain stable when excluding SGA or LBW children or when restricting preterm births to SGA or LBW children only (results not presented)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ritz, et al. (2002, 023227) **Period of Study:** 1987-1993 **Location:** Southern California (Jul 1990-Jul 1993 for Los Angeles, 1989 for Riverside, 1988-1989 for San Bernardino, and 1987-1989 for Orange counties	**Outcome:** 1) Aortic defects 2) Defects of the atrium and atrium Sepum 3) Endocardial and mitral valve defects 4) Pulmonary artery and valve defects 5) Conotruncal defects including tetralogy of Fallot, transposition of great vessels, truncus arteriosus communis, double outlet right ventricle, and aorticopulmonary window and 6) Ventricular Sepal defects not included in the conotruncal category. **Age Groups:** All live born infants and fetal deaths diagnosed between 20 wk of gestation and 1 yr after birth **Study Design:** Case-control **N:** 10,649 infants and fetuses **Statistical Analyses:** Hierarchical (two-level) regression model, polytomous logistic regression, linear model **Covariates:** Gender, no prenatal care, multiple births, no siblings, maternal race, maternal age, maternal education, born before 1990, season of conception, **Season:** All **Dose-response Investigated?** Yes, for O_3 and CO, study found a clear dose-response pattern for aortic Sepum and valve and ventricular Sepal defects and possibly for conotruncal and pulmonary artery and valve defects **Statistical Package:** SAS	**Pollutant:** PM_{10} **Averaging Time:** 24 h (every 6 days) **PM Component:** vehicle emissions **Monitoring Stations:** 11 (for PM_{10}) **Copollutants (correlations):** CO: r = 0.32 NO_2(NR) O_3 (NR)	**Notes:** The authors did not observe consistently increased risks and dose-response patterns for PM_{10} after controlling for the effects of CO and O_3 on these cardiac defects. (Quantitative results not shown).

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ritz et al. (2006, 089819) **Period of Study:** 1989-2000 **Location:** 389 South Coast Air Basin (SoCAB) zip codes	**Outcome:** Total infant deaths during the first yr of life as well as all respiratory causes of death (ICD-9 codes 460-519, 769, 770.4, 770.7, 770.8, and 770.9 and ICD-10 codes J00-J98, P22.0, P22.9, P27.1, P27.9, P28.0, P28.4, P28.5, and P28.9) and sudden infant death syndrome (SIDS) (ICD-9 code 798.0 and ICD-10 code R95). **Age Groups:** Infants 0-1 yr **Study Design:** Case-control **N:** 2,975,059 births and 19,664 infant deaths Cases, n = 13,146 Controls, n = 151,015 **Statistical Analyses:** Conditional logistic regression analysis **Covariates:** Risk factors available on birth and/or death certificates (maternal age, race/ethnicity, and education, level of prenatal care, infant gender, parity, birth country, and death season) **Season:** Death season (spring, summer, fall, winter) **Dose-response Investigated?** Yes **Statistical Package:** NR	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** **2** wk before death: 46.2 1 month before death: 46.3 2 mo before death: 46.3 6 mo before death: 46.3 **Range (Min, Max):** **2** wk before death: (21.0-83.5) 1 month before death: (25.0-77.2) 2 mo before death: (27.6-74.2) 6 mo before death: (31.3-69.5) **Monitoring Stations:** maximum of 31 **Copollutants (correlation):** **2** wk before death CO: r = 0.33 NO_2: r = 0.48 O_3: r = 0.12 1 month before death CO: r = 0.33 NO_2: r = 0.48 O_3: r = 0.12 2 mo before death CO: r = 0.32 NO_2: r = 0.48 O_3: r = 0.12 6 mo before death CO: r = 0.29 NO_2: r = 0.44 O_3: r = 0.16	**PM Increment:** 10 $\mu g/m^3$ **Effect Estimate [Lower CI, Upper CI]:** **All-cause death** **2 mo before death** Single-pollutant model: <25th = 1.04 (1.01-1.06) 25th-75th = 0.96 (0.89-1.04) >75th = 1.14 (1.03-1.27) Multiple-pollutant model: <25th = 1.02 (0.99-1.05) 25th-75th = 0.92 (0.84-1.00) >75th = 1.07 (0.95-1.20) **SIDS** **2 mo before death:** Single-pollutant model: <25th = 1.03 (0.99-1.08) 25th-75th = 0.94 (0.81-1.08) >75th = 1.13 (0.93-1.36) Multiple-pollutant model: <25th = 1.01 (0.95-1.07) 25th-75th = 0.90 (0.76-1.06) >75th = 0.99 (0.80-1.24) **Respiratory death** **2 wk before death** **Postneonatal deaths (28 days to 1 y)** Single-pollutant model: <25th = 1.05 (1.01-1.10) 25th-75th = 1.13 (1.01-1.10) >75th = 1.46 (1.13-1.88) Multiple-pollutant model: <25th = 1.04 (0.98-1.09) 25th-75th = 1.09 (0.86-1.38) >75th = 1.40 (1.03-1.89) **Postneonatal deaths (28 days to 3 mo)** Single-pollutant model: <25th = 1.01 (0.95-1.08) 25th-75th = 1.16 (0.82-1.63) >75th = 1.44 (0.96-2.17) Multiple-pollutant model: <25th = 1.00 (0.92-1.09) 25th-75th = 0.97 (0.67-1.42) >75th = 1.23 (0.76-2.00) **Post neonatal deaths (4-12 mo)** Single-pollutant model: <25th = 1.12 (1.02-1.23) 25th-75th = 1.08 (0.81-1.44) >75th = 1.41 (1.02-1.96) Multiple-pollutant model: <25th = 1.07 (1.00-1.15) 25th-75th = 1.02 (0.75-1.40) >75th = 1.36 (0.92-2.01)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Rogers et al. (2006, 091232) **Period of Study:** 1986-1988 **Location:** Georgia, USA	**Outcome**: VLBW Term, AGA, Preterm AGA, Preterm, SGA **Age Groups:** Newborns and their mothers (<19 to ≥ 35-yr-old) **Study Design:** Case-control **N:** 325 infants (69 preterm SGA 59 preterm AGA 197 term AGA) and their mothers **Statistical Analyses:** Logistic regression **Covariates:** Maternal age, maternal race, maternal education, active and passive smoking, birth season, prepregnancy weight, pregnancy weight gain, maternal toxemia, anemia, asthma **Dose-response Investigated?** Yes, used **Statistical Package**: SUDAAN Cochran-Armitage test for trend to determine whether the observed proportions of cases and controls differed in a linear manner across exposure categories.	**Pollutant:** PM_{10} **Averaging Time:** annual Preterm SGA: **50th(Median)**: 3.38 Preterm AGA: **50th(Median)**: 7.84 Term AGA: **50th(Median)**: 3.23 **Monitoring Stations**: NR **Percent Mothers Residing In County With Industrial Point Source** Preterm SGA: 60.9% Preterm AGA: 79.7% Term AGA: 60.4% **Percent Mothers Residing In** PM_{10} **Quartile** (based on environmental transport model) Preterm SGA 1st quartile (<1.48): 31.9% 2nd quartile (1.48-3.74): 18.8% 3rd quartile (3.75-15.07): 26.1% 4th quartile (>15.07): 23.2% Preterm AGA 1st quartile (<1.48): 16.9% 2nd quartile (1.48-3.74): 22.1% 3rd quartile (3.75-15.07): 28.8% 4th quartile (>15.07): 32.2% Term AGA 1st quartile (<1.48): 24.7% 2nd quartile (1.48-3.74): 28.4% 3rd quartile (3.75-15.07): 27.9% 4th quartile (>15.07): 19.3%	**PM Increment:** Quartile **Notes:** Statistically significant increases in the odds of VLBW and preterm AGA births are associated with living in a county with a PM_{10} point source. Preterm AGA births are also associated with living in an area with very high (4th quartile) estimated PM_{10} exposure. Delivery of VLBW vs. Term AGA infant County with point source 2.54 [1.46, 4.22] PM_{10} quartile 1st quartile: reference 2nd quartile: 0.81 [0.42, 1.55] 3rd quartile: 0.85 [0.45, 1.16] 4th quartile: 1.94 [0.98, 3.83] Delivery of Preterm AGA vs. Term AGA infant County with point source 4.31 [1.88: 9.87] PM_{10} quartile 1st quartile: reference 2nd quartile: 1.56 [0.56: 4.35] 3rd quartile: 1.19 [0.44: 3.23] 4th quartile: 3.68 [1.44: 9.44] Delivery of Preterm AGA vs. Preterm SGA infant County with point source 2.07 [0.83: 5.16] PM_{10} quartile 1st quartile: reference 2nd quartile: 1.96 [0.59: 6.43] 3rd quartile: 2.10 [0.66: 6.73] 4th quartile: 2.58 [0.78: 8.51]

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Romieu et al. (2004, 093074) **Period of Study:** 1997-2001 **Location:** Ciudad Juarez, Mexico	**Outcome:** Respiratory-related infant mortality ICD9 (460-519) ICD10 (J00-J99) **Age Groups:** 1 month to 1 yr **Study Design:** Case crossover **N:** 216 respiratory-related deaths N = 412 other causes and N = 628 total deaths **Statistical Analyses:** The acute effects of air pollution was modeled on both total and respiratory-related mortality as a function of the pollution levels on the same day and preceding days and over 2- and 3-day avg before the date of death. Case-crossover with semi-symmetric bidirectional referent selection was the approach used. Data were stratified by day of the week and calendar month. Data were analyzed with conditional logistic regression. Second and third polynomial distributed lag models were used to study lag structure. BIC was used to determine lag length. **Covariate**: Temperature, season **Dose-response Investigated?** Yes **Statistical Package:** STATA 7.0 **Lags Considered:** 1-15 days	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 1997: 33.04 (20.67) µg/m^3 1998: 35.25 (17.32) µg/m^3 1999: 45.92 (28.69) µg/m^3 2000: 43.38 (23.77) µg/m^3 2001: 39.46 (29.43) µg/m^3 **Monitoring Stations:** 5 stations in Ciudad Juarez 2 stations in El Paso (close to U.S.-Mexico border) **Copollutant (correlation):** O_3: r = 0.01 **Notes:** Ciudad Juarez monitors measured PM_{10} every 6 days while El Paso monitors measured on a daily basis.	**PM Increment:** 20 µg/m^3 **RR Estimate [Lower CI, Upper CI] lag:** **Total mortality:** OR = 1.02 (0.94-1.11) lag 1 OR = 1.03 (0.95-1.12) lag 2 OR = 1.03 (0.94-1.13 ac2 OR = 1.04 (0.95-1.15) ac3 **Respiratory mortality** OR = 0.95 (0.83-1.09) lag 1 OR = 1.04 (0.91-1.19) lag 2 OR = 0.98 (0.81-1.19) ac2 OR = 0.97 (0.74-1.26) ac3 **Higher SES** OR = 0.82 (0.59, 1.14) lag 1 OR = 1.08 (0.84, 1.40) lag 2 OR = 0.89 (0.58, 1.35) ac2 OR = 0.97 (0.52, 1.82) ac3 **Medium SES** OR = 0.99 (0.79, 1.27) lag 1 OR = 1.11 (0.86, 1.43) lag 2 OR = 1.03 (0.73, 1.45) ac2 OR = 1.17 (0.72, 1.90) ac3 **Lower SES** OR = 1.61 (0.97-2.66) lag 1 OR = 1.07 (0.65, 1.75) lag 2 OR = 2.56 (1.06-6.17) ac2 OR = 1.76 (0.59, 5.23) ac3 **Notes:** ac2 and ac3 represent cumulative PM_{10} ambient levels over 2 or 3 days before death.
Reference: Sagiv et al. (2005, 087468) **Period of Study:** Jan 1997-Dec 2001 **Location:** Allegheny county, Beaver county, Lackawanna county, Philadelphia county, Pennsylvania, U.S.A.	**Outcome:** Preterm birth (<36 wk) **Age Groups:** Babies born between 20 and 44 wk **Study Design:** Time series **N:** 3704 observation days, 187,997 births **Statistical Analyses:** Poisson regression Multivariable mixed-effects model with a random intercept for each county to incorporate count-level information. **Covariates:** Temperature, dew point temperature, mean 6-week level of copollutants (CO, NO_2, and SO_2), long-term preterm birth trends **Season:** All **Dose-response Investigated?** Yes **Statistical Package:** NR **Lags Considered:** 1, 2, 3, 4, 5, 6, 7	**Pollutant:** PM_{10} **Averaging Time:** Daily used to calculate 6-week period **Mean (SD):** 6-week period 27.1 (8.3) Daily 25.3 (14.6) **Percentiles:** 6-week period **50th (Median):** 26.0 Daily **50th (Median):** 21.6 **Range (Min, Max):** 6-week period: 8.7, 68.9 Daily: 2.0, 156.3 **Monitoring Stations:** NR **Copollutant (correlation):** Daily PM_{10}-daily SO_2: r = 0.46 Also considered CO, NO_2 and O_3 as copollutants.	**PM Increment:** 1) 50 µg/m^3 2) Quartiles (first quartile is the reference) **Exposure period: 6 wk before birth** Per 50 µg/m^3: 1.07 (0.98, 1.18) 2nd quartile: 1.00 (0.95, 1.05) 3rd quartile: 1.04 (0.99, 1.09) 4th quartile: 1.03 (0.98, 1.08) **Exposure period: 1-day acute time windows** Per 50 µg/m^3: 2-day lag: 1.10 (1.00, 1.21) 5-day lag: 1.07 (0.98, 1.18) **Notes:** Within the article, authors provide a Fig 1 displaying a graph of the relative risk (RR) and 95% confidence i ntervals (CI) for 1- to 7-day lags. While the authors report the 2- and 5-day lag RRs and 95% CIs in the text, the others are not specifically reported. However, the Fig shows the approximate RRs per 50 µg/m^3 as indicated below: 1-day lag: 1.05 3-day lag: 1.05 4-day lag: 1.00 6-day lag: 0.97 7-day lag: 1.03

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: (Salam et al., 2005, 087885) **Period of Study:** 1975-1987 **Location:** Southern California	**Outcome:** Birth weight Low birth weight (LBW <2500 g) Intrauterine growth retardation (IUGR) **Age Groups:** Children born full-term (between 37 and 44 wk) **Study Design:** Cohort study **N:** 3901 children **Statistical Analyses:** Linear mixed-effects Logistic regression **Covariates:** Maternal age, months since last live birth, parity, maternal smoking during pregnancy, SES, marital status at childbirth, gestational diabetes, child's sex, child's race/ethnicity, child's grade in school (4th, 7th, and 10th), Julian day of birth **Season:** All **Dose-response Investigated?** Yes **Statistical Package:** SAS	**Pollutant:** PM_{10} **Averaging Time:** Monthly **Mean (SD):** Entire pregnancy: 45.8 (12.9) First trimester: 46.6 (15.9) Second trimester: 45.4 (14.8) Third trimester: 45.4 (15.5) **Monitoring Stations:** 1 or 3 (See notes) **Copollutant (correlation):** Entire pregnancy PM_{10}-O_3[10-6]: r = 0.54 PM_{10}-O_3[24 h): r = 0.20 PM_{10}-NO_2: r = 0.55 PM_{10}-CO: r = 0.41 First trimester PM_{10}-O_3[10-6]: r = 0.54 PM_{10}-O_3[24 h]: r = 0.34 PM_{10}-NO_2: r = 0.48 PM_{10}-CO: r = 0.29 Second trimester PM_{10}-O_3[10-6): r = 0.50 PM_{10}-O_3(24 h): r = 0.27 PM_{10}-NO_2: r = 0.53 PM_{10}-CO: r = 0.35 Third trimester PM_{10}-O_3[10-6]: r = 0.52 PM_{10}-O_3[24 h]: r = 0.31 PM_{10}-NO_2: r = 0.52 PM_{10}-CO: r = 0.37 **Notes:** Exposure estimates were calculated by spatially interpolated monthly avg which were based off of three monitoring stations located within 50 km of the ZIP code region of maternal birth residences.	**PM Increment:** IQR (interquartile range) **Outcome: birth weight (g)** Single-pollutant model Entire pregnancy 18 µg/m^3: -19.9 (-43.6, 3.8) First trimester 20 µg/m^3: -3.0 (-22.7, 16.7) Second trimester 19 µg/m^3: -15.7 (-36.1, 4.7) Third trimester 20 µg/m^3: -21.7 (-42.2 to -1.1) Multipollutant model (Included O_3 (24 h) in model Third trimester exposure) 20 µg/m^3: -10.8 (-31.8, 10.2) **Outcome: IUGR (ORs)** Single-pollutant model Entire pregnancy 18 µg/m^3: 1.1 (0.9, 1.3) First trimester 20 µg/m^3: 1.0 (0.9, 1.2) Second trimester 19 µg/m^3: 1.0 (0.9, 1.2) Third trimester 20 µg/m^3: 1.1 (0.9, 1.3) **Outcome: LBW** Single-pollutant model Entire pregnancy 18 µg/m^3: 1.3 (0.8, 2.2) First trimester 20 µg/m^3: 1.0 (0.7, 1.5) Second trimester 19 µg/m^3: 1.2 (0.8, 1.7) Third trimester 20 µg/m^3: 1.3 (0.9, 1.9) **Notes:** Numbers reported for birth weight outcome are the effects on birth weight outcome (the change in birth weight in grams) across the IQR (which vary depending on air pollutant and duration of exposure measurement).
Reference: (Sokol et al., 2006, 098539) **Period of Study:** Jan 1996-Dec 1998 **Location:** Los Angeles, California	**Outcome:** Semen Quality **Study Design:** Panel **Statistical Analysis:** Univariate and Multivariate Regression **Statistical Package:** SAS **Age Groups:** Males ranging 19-35 in age	**Pollutant:** PM_{10} **Averaging Time:** 0-9d, 10-14d and 70-90d **Mean (SD) Unit:** 35.74 ± 13.83 µg/m^3 **Copollutant (correlation):** O_3, NO_2, CO	PM_{10} specific results are given in Fig 3-. PM_{10} was not significantly correlated with sperm quality.
Reference: (Suh et al., 2007, 157028) **Period of Study:** 2001-2004 **Location:** Seoul, Korea	**Outcome:** Birth weight **Age Groups:** Prenatal follow-up for newborns **Study Design:** based prospective cohort study **N:** 199 pregnant mothers **Statistical Analyses:** ANCOVA, generalized linear models **Covariates:** infant's sex, maternal age, maternal and paternal education, parity, presence of illness during pregnancy, delivery month, gestational age (squared) **Dose-response Investigated?** Yes **Statistical Package**: SAS	**Pollutant:** PM_{10} **Averaging Time:** 24-h **Mean (SD):** 1st trimester: 76.41 (28.80) 2nd trimester: 77.84 (31.63) 3rd trimester: 95.61 (26.15) **Percentiles:** 1st trimester **25th:** 55.28 **50th(Median):** 71.09 **75th:** 92.38 2nd trimester **25th:** 48.65 **50th(Median):** 72.36 **75th:** 108.00 3rd trimester **25th:** 77.10 **50th(Median):** 96.35 **75th:** 116.68 **Range (Min, Max):** 1st trimester (21.00, 151.65) 2nd trimester (31.45, 139.13)	**PM Increment:** Trimester ≥ 90th percentile compared to <90thpercentile Least-square (ANCOVA) mean (SE) **All Genotypes** 1st trimester <90th , N(%): 158 (90.3%): 3253 (37) ≥ 90th percentile, N(%): 17 (9.7%): 2841 (145) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.009 Adjusted, with CO: 0.041 Adjusted, with NO_2: 0.092 Adjusted, with SO_2: 0.012 2nd trimester <90th percentile, N(%): 153 (89.5%): 3253 (39) ≥ 90th percentile, N(%): 18 (10.5%): 3026 (157) P-Value for mean birth weight for ≥ 90th

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
		3rd trimester (23.45, 172.75) **Monitoring Stations**: 27 **Copollutant:** CO SO_2 NO_2	percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.177 Adjusted, with CO: 0.203 Adjusted, with NO_2: 0.151 Adjusted, with SO_2: 0.151 3rd trimester <90th percentile, N(%): 162 (90.5%): 3226 (38) ≥ 90th percentile, N(%): 17 (9.5%): 3122 (140) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.487 Adjusted, with CO: 0.748 Adjusted, with NO_2: 0.420 Adjusted, with SO_2: 0.466 **Genotype** MspI TT 1st trimester <90th percentile, N(%): 60 (34.3%): 3350 (64) ≥ 90th percentile, N(%): 5 (2.9%): 3001 (229) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.147 Adjusted, with CO: 0.186 Adjusted, with NO_2: 0.430 Adjusted, with SO_2: 0.155 2nd trimester <90th percentile, N(%): 59 (34.5%): 3335 (66) ≥ 90th percentile, N(%): 6 (3.5%): 3281 (249) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.833 Adjusted, with CO: 0.833 Adjusted, with NO_2: 0.778 Adjusted, with SO_2: 0.806 3rd trimester <90th percentile, N(%): 61 (34.1%): 3327 (65) ≥ 90th percentile, N(%): 6 (3.4%): 3227 (300) p-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.749 Adjusted, with CO: 0.980 Adjusted, with NO_2: 0.635 Adjusted, with SO_2: 0.687 **Genotype** MspI TC/CC 1st trimester <90th percentile, N(%): 98 (56.0%): 3193 (48) ≥ 90th percentile, N(%): 12 (6.9%): 2799 (169) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.033 Adjusted, with CO: 0.073 Adjusted, with NO_2: 0.150 Adjusted, with SO_2: 0.036 2nd trimester <90th percentile, N(%): 94 (55.0%): 3200 (52) ≥ 90th percentile, N(%): 12 (7.0%): 2933 (176) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.161 Adjusted, with CO: 0.172

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Adjusted, with NO_2: 0.152 Adjusted, with SO_2: 0.158 3rd trimester <90th percentile, N(%): 101 (56.4%): 3165 (49) ≥ 90th percentile, N(%): 11 (6.2%): 3087 (147) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.626 Adjusted, with CO: 0.978 Adjusted, with NO_2: 0.551 Adjusted, with SO_2: 0.614 **Genotype** NcoI IleIle 1st trimester <90th percentile, N(%): 87 (49.7%): 3244 (52) ≥ 90th percentile, N(%): 7 (4.0%): 2983 (232) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.289 Adjusted, with CO: 0.344 Adjusted, with NO_2: 0.641 Adjusted, with SO_2: 0.293 2nd trimester <90th percentile, N(%): 82 (48.0%): 3243 (55) ≥ 90th percentile, N(%): 11 (6.4%): 3185 (207) p-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.790 Adjusted, with CO: 0.783 Adjusted, with NO_2: 0.707 Adjusted, with SO_2: 0.733 3rd trimester <90th percentile, N(%): 90 (50.3%): 3239 (53) ≥ 90th percentile, N(%): 9 (5.0%): 2944 (198) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.161 Adjusted, with CO: 0.279 Adjusted, with NO_2: 0.134 Adjusted, with SO_2: 0.150 **Genotype** NcoI IleVal/ValVal 1st trimester <90th percentile, N(%): 71 (40.6%): 3262 (56) ≥ 90th percentile, N(%): 10 (5.7%): 2773 (171) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.009 Adjusted, with CO: 0.031 Adjusted, with NO_2: 0.058 Adjusted, with SO_2: 0.010 2nd trimester <90th percentile, N(%): 71 (41.5%): 3264 (61) ≥ 90th percentile, N(%): 7 (4.1%): 2862 (208) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.076 Adjusted, with CO: 0.093 Adjusted, with NO_2: 0.063 Adjusted, with SO_2: 0.061 3rd trimester <90th percentile, N(%): 72 (40.2%): 3207

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			(58) ≥ 90th percentile, N(%): 8 (4.5%): 3262 (180) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.777 Adjusted, with CO: 0.607 Adjusted, with NO_2: 0.843 Adjusted, with SO_2: 0.791
Reference: Tsai et al. (2006, 090709) **Period of Study:** 1994-2000 **Location:** Kaohsiung, Taiwan	**Outcome:** Post neonatal mortality **Age Groups:** Infants more than 27 days and less than 1 yr **Study Design:** Case-crossover study **N:** 207 deaths **Statistical Analyses:** Conditional logistic regression **Covariates:** Temperature, humidity **Dose-response Investigated?** No **Statistical Package:** SAS, version 8.2	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 81.45 µg/m^3 **Percentiles: 25th:** 44.50 **50th(Median):** 79.20 **75th:** 111.50 **Range (Min, Max):** (20.50-232.00) **Monitoring Stations:** 6 **Copollutant:** SO_2 NO_2 CO O_3	**PM Increment:** 67.00 µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** OR = 1.040 (0.340-3.177) **Note:** Air pollution levels at the dates of infant death were compared with air pollution levels 1 week before and 1 week after death A cumulative lag up to 2 previous days was used to assign exposure.
Reference: Wilhelm and Ritz (2005, 088668) **Period of Study:** 1994-2000 **Location:** Los Angeles County, California, U.S.	**Outcome:** Term low birth weight (LBW) (<2500 g at ≥ 37 completed wk gestation), Vaginal birth <37 completed wk gestation **Age Groups:** LBW: ≥ 37 completed wk Preterm births: <37 completed wk **Study Design:** Cross-sectional **N:** For LBW: 136,134 For preterm birth: 106,483 **Statistical Analyses:** Logistic regression **Covariates:** Maternal age, maternal race, maternal education, parity, interval since previous live birth, level of prenatal care, infant sex, previous LBW or preterm infant, birth season, other pollutants (CO, NO_2, O_3, PM_{10}), gestational age (in birth weight analysis) **Dose-response Investigated?** Yes **Statistical Package:** NR	**Pollutant:** PM_{10} **Averaging Time:** 24 h (every 6 days) Entire pregnancy Trimesters of pregnancy Months of pregnancy 6 wk before birth **Mean (SD):** First trimester: 42.2 Third trimester: 41.5 6 wk before birth: 39.1 **Range (Min, Max):** First trimester: 26.3, 77.4 Third trimester: 25.7, 74.6 6 wk before birth: 13.0, 103.7 **Monitoring Stations:** Zip-code-level analysis: 8 Address-level analysis: 6 **Copollutant (correlation):** **First trimester:** PM_{10}-CO: r = 0.12 PM_{10}-NO_2: r = 0.29 PM_{10}-O_3: r = -0.01 PM_{10}-$PM_{2.5}$: r = 0.43 **Third trimester:** PM_{10}-CO: r = 0.32 PM_{10}-NO_2: r = 0.45 PM_{10}-O_3: r = -0.08 PM_{10}-$PM_{2.5}$: r = 0.52 **6 wk before birth:** PM_{10}-CO: r = 0.36 PM_{10}-NO_2: r = 0.49 PM_{10}-O_3: r = -0.16 PM_{10}-$PM_{2.5}$: r = 0.60	**PM Increment:** 1) 10 µg/m^3 2) 3 levels: a) <25 percentile (reference) b) 25%-75 percentile c) ≥ 75 percentile **Incidence of LBW (third trimester exposure)** <32.8 µg/m^3: 2.0 (1.8, 2.2) 32.8 to <43.4 µg/m^3: 2.0 (1.9, 2.1) ≥ 43.4 µg/m^3: 2.2 (2.0, 2.4) **Incidence of preterm birth (first trimester exposure)** <32.9 µg/m^3: 8.7 (8.3, 9.2) 32.9 to <43.9 µg/m^3: 8.8 (8.5, 9.1) ≥ 43.9 µg/m^3: 8.6 (8.1, 9.0) **Incidence of preterm birth (6 wk before birth exposure)** <31.8 µg/m^3: 8.8 (8.4, 9.3) 31.8 to <44.1 µg/m^3: 8.6 (8.3, 8.9) ≥ 44.1 µg/m^3: 8.8 (8.4, 9.2) **Outcome: LBW** **Exposure Period: Third trimester** **Address-level analysis:** Single-pollutant model: Distance ≤ 1 mile Per 10 µg/m^3: 1.22 (1.05, 1.41) 33.4 to <44.7 µg/m^3: 1.08 (0.76, 1.52) ≥ 44.7 µg/m^3: 1.48 (1.00, 2.19) Multipollutant model: Distance ≤ 1 mile Per 10 µg/m^3: 1.36 (1.12, 1.65) 33.4 to <44.7 µg/m^3: 1.16 (0.77, 1.74) ≥ 44.7 µg/m^3: 1.58 (0.95, 2.62) Single-pollutant model: 1 <distance ≤ 2 mile Per 10 µg/m^3: 0.98 (0.90, 1.06) 33.4 to <44.7 µg/m^3: 0.95 (0.80, 1.13) ≥ 44.7 µg/m^3: 0.96 (0.78, 1.18) Multipollutant model: 1 <distance ≤ 2 mile Per 10 µg/m^3: 1.02 (0.92, 1.14) 33.4 to <44.7 µg/m^3: 0.93 (0.77, 1.12) ≥ 44.7 µg/m^3: 1.02 (0.79, 1.32) Single-pollutant model:

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			2 <distance ≤ 4 mile Per 10 µg/m^3: 1.03 (0.99, 1.08) 33.9 to <45.0 µg/m^3: 1.04 (0.96, 1.14) ≥ 45.0 µg/m^3: 1.08 (0.97, 1.20) Multipollutant model: 2 <distance ≤ 4 mile Per 10 µg/m^3: 1.04 (0.98, 1.09) 33.9 to <45.0 µg/m^3: 1.02 (0.92, 1.12) ≥ 45.0 µg/m^3: 1.06 (0.93, 1.21) **Zip-code-level analysis** Single-pollutant model: Per 10 µg/m^3: 1.03 (0.97, 1.09) 33.2 to <43.6 µg/m^3: 0.98 (0.86, 1.11) ≥ 43.6 µg/m^3: 1.03 (0.88, 1.21) Multipollutant model: Per 10 µg/m^3: 1.07 (0.99, 1.15) 33.2 to <43.6 µg/m^3: 0.97 (0.85, 1.12) ≥ 43.6 µg/m^3: 1.09 (0.90, 1.31) **Outcome: LBW** **Exposure Period: Entire pregnancy period** **Address-level analysis:** Multipollutant model: Per 10 µg/m^3: 1.24 (0.91, 1.70) **Outcome: Preterm Birth** **Exposure Period: First trimester of pregnancy** **Address-level analysis**: Single-pollutant model: Distance ≤ 1 mile Per 10 µg/m^3: 1.00 (0.93, 1.09) 33.3 to <45.1 µg/m^3: 1.07 (0.90, 1.26) ≥ 45.1 µg/m^3: 1.12 (0.91, 1.38) Multipollutant model: Distance ≤ 1 mile Per 10 µg/m^3: 1.00 (0.90, 1.12) 33.3 to <45.1 µg/m^3: 1.12 (0.92, 1.36) ≥ 45.1 µg/m^3: 1.17 (0.90, 1.50) Single-pollutant model: 1 <distance ≤ 2 mile Per 10 µg/m^3: 1.01 (0.97, 1.05) 33.7 to <45.3 µg/m^3: 1.03 (0.95, 1.12) ≥ 45.3 µg/m^3: 1.07 (0.97, 1.19) Multipollutant model: 1 <distance ≤ 2 mile Per 10 µg/m^3: 1.04 (0.99, 1.10) 33.7 to <45.3 µg/m^3: 1.07 (0.98, 1.17) ≥ 45.3 µg/m^3: 1.13 (1.00, 1.27) Single-pollutant model: 2 <distance ≤ 4 mile Per 10 µg/m^3: 1.01 (0.99, 1.03) 34.1 to <45.5 µg/m^3: 1.03 (0.99, 1.08) ≥ 45.5 µg/m^3: 1.02 (0.96, 1.07) Multipollutant model: 2 <distance ≤ 4 mile Per 10 µg/m^3: 0.99 (0.97, 1.02) 34.1 to <45.5 µg/m^3: 0.99 (0.95, 1.04) ≥ 45.5 µg/m^3: 0.94 (0.89, 1.01) **Zip-code-level analysis** Single-pollutant model: Per 10 µg/m^3: 0.99 (0.96, 1.01) 33.3 to <44.2 µg/m^3: 1.01 (0.95, 1.08) ≥ 44.2 µg/m^3: 0.98 (0.90, 1.05) Multipollutant model: Per 10 µg/m^3: 0.99 (0.96, 1.03) 33.3 to <44.2 µg/m^3: 1.03 (0.97, 1.11) ≥ 44.2 µg/m^3: 1.01 (0.92, 1.11) **Outcome: Preterm birth** **Exposure Period: 6 wk before birth** **Address-level analysis:** Single-pollutant model: Distance ≤ 1 mile Per 10 µg/m^3: 1.02 (0.95, 1.10)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			32.5 to <44.8 µg/m^3: 1.09 (0.92, 1.29) ≥ 44.8 µg/m^3: 1.12 (0.92, 1.37) Multipollutant model: Distance ≤ 1 mile Per 10 µg/m^3: 1.06 (0.97, 1.16) 32.5 to <44.8 µg/m^3: 1.09 (0.90, 1.31) ≥ 44.8 µg/m^3: 1.17 (0.91, 1.49) Single-pollutant model: 1 <distance ≤ 2 mile Per 10 µg/m^3: 1.00 (0.96, 1.03) 32.3 to <45.3 µg/m^3: 0.99 (0.91, 1.07) ≥ 45.3 µg/m^3: 0.99 (0.89, 1.10) Multipollutant model: 1 <distance ≤ 2 mile Per 10 µg/m^3: 1.01 (0.97, 1.06) 32.3 to <45.3 µg/m^3: 1.00 (0.92, 1.10) ≥ 45.3 µg/m^3: 1.02 (0.91, 1.16) Single-pollutant model: 2 <distance ≤ 4 mile Per 10 µg/m^3: 0.99 (0.98, 1.01) 33.1 to <45.3 µg/m^3: 1.00 (0.96, 1.05) ≥ 45.3 µg/m^3: 0.98 (0.93, 1.03) Multipollutant model: 2 <distance ≤ 4 mile Per 10 µg/m^3: 1.00 (0.98, 1.02) 33.1 to <45.3 µg/m^3: 1.01 (0.96, 1.05) ≥ 45.3 µg/m^3: 0.98 (0.92, 1.04) **Zip-code-level analysis** Single-pollutant model: Per 10 µg/m^3: 1.02 (0.99, 1.04) 32.1 to <44.3 µg/m^3: 1.01 (0.95, 1.07) ≥ 44.3 µg/m^3: 1.04 (0.96, 1.12) Multipollutant model: Per 10 µg/m^3: 1.02 (0.99, 1.06) 32.1 to <44.3 µg/m^3: 1.02 (0.95, 1.09) ≥ 44.3 µg/m^3: 1.04 (0.95, 1.14) **Notes:** multipollutant model adds CO,NO_2, and O_3 in addition to the main pollutant of interest, PM_{10}.
Reference: Woodruff et al. (1997, 084271) **Period of Study:** 1989-1991 **Location:** 86 Metropolitan Statistical Areas in the U.S. (counties with populations less than 100,000 were excluded)	**Outcome:** Postneonatal mortality (death of an infant between 1 month and 1 yr of age) 1) All post neonatal deaths 2) Normal birth weight (NBW, ≥ 2500 g) SIDS deaths 3) NBW respiratory deaths 4) Low birth weight (LBW) respiratory death Respiratory deaths: ICD9 codes 460-519 SIDS: ICD9 code 798.0 **Age Groups:** Infants (1 month-1yr of age) **Study Design:** Cross-sectional **N:** 3,788,079 infants **Statistical Analyses:** Logistic regression **Covariates:** Maternal education, maternal race, parental marital status, maternal smoking during pregnancy Avg temperature during the first 2 mo of life Infant's month and yr of birth Assessed race as an effect modifier (p-val for interaction terms >0.2) **Dose-response Investigated?** Yes **Statistical Package:** NR	**Pollutant:** PM_{10} **Averaging Time:** Mean of 1st 2 mo of life analyzed as tertiles of exposure and as continuous exposure **Mean (SD):** 31.4 (7.8) **Range (Min, Max):** Overall: 11.9-68.8 Low category: <28.0 Medium category: 28.1-40.0 High category: >40.0 **Monitoring Stations:** NR	**PM Increment:** 10 µg/m^3 (for continuous exposure analysis) **Adjusted ORs for cause-specific post neonatal mortality by pollution category (tertiles)** All causes Low: Ref Medium: 1.05 (1.01, 1.09) High: 1.10 (1.04, 1.16) SIDS, NBW: Low: Ref Medium: 1.09 (1.01, 1.17) High: 1.26 (1.14, 1.39) Respiratory death, NBW: Low: Ref Medium: 1.08 (0.87, 1.33) High: 1.40 (1.05, 1.85) Respiratory death, LBW: Low: Ref Medium: 0.93 (0.73, 1.18) High: 1.18 (0.86, 1.61) All other causes: Low: Ref Medium: 1.03 (0.97, 1.08) High: 0.97 (0.90, 1.04) **Adjusted ORs for a continuous 10 µg/m^3 change in exposure** All causes: 1.04 (1.02, 1.07) SIDS, NBW: 1.12 (1.07, 1.17) Respiratory death NBW: 1.20 (1.06, 1.36) Respiratory death LBW: 1.05 (0.91, 1.22) All other causes: 1.00 (0.99, 1.00)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Woodruff et al. (2008, 098386) **Period of Study:** 1999-2002 **Location:** U.S. counties with >250,000 residents (96 counties)	**Outcome:** Postneonatal deaths Respiratory mortality (ICD10: J000-99, plus bronchopulmonary dysplasia [BPD] P27.1) SIDS (ICD10: R95) Ill-defined causes (R99); All other deaths evaluated as a control category **Age Groups:** Infants aged >28 days and <1 yr **Study Design:** Cross-sectional **N:** 3,583,495 births (6,639 post neonatal deaths) **Statistical Analyses:** Logistic GEE (exchangeable correlation structure) **Covariates:** Maternal race/ethnicity, marital status, age, education, primiparity, county-level poverty and per capita income levels, yr and month of birth dummy variables to account for time trend and seasonal effects, and region of the country Sensitivity analyses performed among only those mothers with smoking information (adjustment for smoking had no effect on the estimates) **Season:** Adjusted for yr and month of birth dummy variables to account for time trend and seasonal effects **Dose-response Investigated?** Evaluated the appropriateness of a linear form from analysis based on quartiles of exposure and concluded that linear form was appropriate (data not shown) **Statistical Package:** SAS	**Pollutant:** PM_{10} **Averaging Time:** Measured continuously for 24 h once every 6 days exposure assigned by calculating avg concentration of pollutant during first 2 mo of life **Median and IQR (25th-75th percentile):** Survivors: 28.9 (23.3-34.4) All causes of death: 29.1 (23.9-34.5) Respiratory: 29.8 (24.3-36.5) SIDS: 28.6 (23.5-33.8) SIDS + ill-defined: 28.8 (23.9-33.9) Other causes: 29.2 (23.9-34.5) **Percentiles:** see above **PM Component:** Not assessed, but controlled for region of the country to account for PM composition variation **Monitoring Stations:** NR **Copollutant (correlation):** PM_{10} $PM_{2.5}$ (r = 0.34) CO (r = 0.18) SO_2 (r = 0.00) O_3 (r = 0.20) **Notes:** Monthly avg calculated if there were at least 3 available measures for PM Assigned exposures using the avg concentration of the county of residence	**PM Increment:** IQR (11 µg/m^3) **Effect Estimate [Lower CI, Upper CI]:** Adjusted ORs for single pollutant models All causes: 1.04 (0.99, 1.10) Respiratory: 1.18 (1.06, 1.31) SIDS: 1.02 (0.89, 1.16) Ill-defined + SIDS: 1.06 (0.97, 1.16) Other causes: 1.02 (0.96, 1.07) Adjusted ORs for multipollutant models (including CO, O_3, SO_2) Respiratory: 1.16 (1.04, 1.30) SIDS: 1.02 (0.90, 1.16) OR for deaths coded as BPD per increase in IQR: 1.19 (0.85, 1.65) OR for respiratory post neonatal death stratified by birth weight NBW only: 1.19 (1.05, 1.36) LBW only: 1.12 (0.95, 1.31) OR for respiratory deaths removing region of U.S. as a confounding variable: 1.30 (1.04, 1.61) OR for respiratory deaths assessing exposure as quartiles Highest vs. Lowest quartile: 1.31 (1.00, 1.71) OR for respiratory deaths among only those deaths that occurred during the first 90 days (most closely matched exposure metric of the avg over the first 2 mo of life): 1.25 (1.06, 1.47)
Reference: (Suh et al., 2007, 157028) **Period of Study:** 2001-2004 **Location:** Seoul, Korea	**Outcome:** Birth weight **Age Groups:** Prenatal follow-up for newborns **Study Design:** Based prospective cohort study **N:** 199 pregnant mothers **Statistical Analyses:** ANCOVA, generalized linear models **Covariates:** Infant's sex, maternal age, maternal and paternal education, parity, presence of illness during pregnancy, delivery month, gestational age (squared) **Dose-response Investigated?** Yes **Statistical Package**: SAS	**Pollutant:** PM_{10} **Averaging Time:** 24-h **Mean (SD):** 1st trimester: 76.41 (28.80) 2nd trimester: 77.84 (31.63) 3rd trimester: 95.61 (26.15) **Percentiles:** 1st trimester **25th:** 55.28 **50th(Median):** 71.09 **75th:** 92.38 2nd trimester **25th:** 48.65 **50th(Median):** 72.36 **75th:** 108.00 3rd trimester **25th:** 77.10 **50th(Median):** 96.35 **75th:** 116.68 **Range (Min, Max):** 1st trimester (21.00, 151.65) 2nd trimester (31.45, 139.13) 3rd trimester (23.45, 172.75) **Monitoring Stations**: 27 **Copollutant:** CO SO_2	**PM Increment:** Trimester ≥ 90th percentile compared to <90th percentile Least-square (ANCOVA) mean (SE) **All Genotypes** 1st trimester <90th percentile, N(%): 158 (90.3%): 3253 (37) ≥ 90th percentile, N(%): 17 (9.7%): 2841 (145) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.009 Adjusted, with CO: 0.041 Adjusted, with NO_2: 0.092 Adjusted, with SO_2: 0.012 2nd trimester <90th percentile, N(%): 153 (89.5%): 3253 (39) ≥ 90th percentile, N(%): 18 (10.5%): 3026 (157) p-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.177 Adjusted, with CO: 0.203 Adjusted, with NO_2: 0.151 Adjusted, with SO_2: 0.151 3rd trimester <90th percentile, N(%):

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
		NO_2	162 (90.5%): 3226 (38) ≥ 90th percentile, N(%): 17 (9.5%): 3122 (140) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.487 Adjusted, with CO: 0.748 Adjusted, with NO_2: 0.420 Adjusted, with SO_2: 0.466 **Genotype** MspI TT 1st trimester <90th percentile, N(%): 60 (34.3%): 3350 (64) ≥ 90th percentile, N(%): 5 (2.9%): 3001 (229) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.147 Adjusted, with CO: 0.186 Adjusted, with NO_2: 0.430 Adjusted, with SO_2: 0.155 2nd trimester <90th percentile, N(%): 59 (34.5%): 3335 (66) ≥ 90th percentile, N(%): 6 (3.5%): 3281 (249) p-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.833 Adjusted, with CO: 0.833 Adjusted, with NO_2: 0.778 Adjusted, with SO_2: 0.806 3rd trimester <90th percentile, N(%): 61 (34.1%): 3327 (65) ≥ 90th percentile, N(%): 6 (3.4%): 3227 (300) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.749 Adjusted, with CO: 0.980 Adjusted, with NO_2: 0.635 Adjusted, with SO_2: 0.687 **Genotype** MspI TC/CC 1st trimester <90th percentile, N(%): 98 (56.0%): 3193 (48) ≥ 90th percentile, N(%): 12 (6.9%): 2799 (169) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.033 Adjusted, with CO: 0.073 Adjusted, with NO_2: 0.150 Adjusted, with SO_2: 0.036 2nd trimester <90th percentile, N(%): 94 (55.0%): 3200 (52) ≥ 90th percentile, N(%): 12 (7.0%): 2933 (176) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.161 Adjusted, with CO: 0.172 Adjusted, with NO_2: 0.152 Adjusted, with SO_2: 0.158 3rd trimester <90th percentile, N(%): 101 (56.4%): 3165 (49) ≥ 90th percentile, N(%): 11 (6.2%): 3087 (147) P-Value for mean birth weight for

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.626 Adjusted, with CO: 0.978 Adjusted, with NO_2: 0.551 Adjusted, with SO_2: 0.614 **Genotype** NcoI IleIle 1st trimester <90th percentile, N(%): 87 (49.7%): 3244 (52) ≥ 90th percentile, N(%): 7 (4.0%): 2983 (232) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.289 Adjusted, with CO: 0.344 Adjusted, with NO_2: 0.641 Adjusted, with SO_2: 0.293 2nd trimester <90th percentile, N(%): 82 (48.0%): 3243 (55) ≥ 90th percentile, N(%): 11 (6.4%): 3185 (207) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.790 Adjusted, with CO: 0.783 Adjusted, with NO_2: 0.707 Adjusted, with SO_2: 0.733 3rd trimester <90th percentile, N(%): 90 (50.3%): 3239 (53) ≥ 90th percentile, N(%): 9 (5.0%): 2944 (198) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.161 Adjusted, with CO: 0.279 Adjusted, with NO_2: 0.134 Adjusted, with SO_2: 0.150 **Genotype** NcoI IleVal/ValVal 1st trimester <90th percentile, N(%): 71 (40.6%): 3262 (56) ≥ 90th percentile, N(%): 10 (5.7%): 2773 (171) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.009 Adjusted, with CO: 0.031 Adjusted, with NO_2: 0.058 Adjusted, with SO_2: 0.010 2nd trimester <90th percentile, N(%): 71 (41.5%): 3264 (61) ≥ 90th percentile, N(%): 7 (4.1%): 2862 (208) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.076 Adjusted, with CO: 0.093 Adjusted, with NO_2: 0.063 Adjusted, with SO_2: 0.061 3rd trimester <90th percentile, N(%): 72 (40.2%): 3207 (58) ≥ 90th percentile, N(%): 8 (4.5%): 3262 (180) P-Value for mean birth weight for ≥ 90th percentile PM_{10} vs. for <90th percentile PM_{10} Adjusted: 0.777 Adjusted, with CO: 0.607

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Adjusted, with NO_2: 0.843 Adjusted, with SO_2: 0.791
Reference: Tsai et al. (2006, 098312) **Period of Study:** 1994-2000 **Location:** Kaohsiung, Taiwan	**Outcome:** Post neonatal mortality **Age Groups:** Infants more than 27 days and less than 1 yr **Study Design:** Case-crossover study **N:** 207 deaths **Statistical Analyses:** Conditional logistic regression **Covariates:** Temperature, humidity **Dose-response Investigated?** No **Statistical Package:** SAS, version 8.2	**Pollutant:** PM_{10} **Averaging Time:** 24 h **Mean (SD):** 81.45 µg/m^3 **Percentiles: 25th:** 44.50 **50th(Median):** 79.20 **75th:** 111.50 **Range (Min, Max):** (20.50-232.00) **Monitoring Stations:** 6 **Copollutant:** SO_2 NO_2 CO O_3	**PM Increment:** 67.00 µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** OR = 1.040 (0.340-3.177) **Note:** Air pollution levels at the dates of infant death were compared with air pollution levels 1 week before and 1 week after death A cumulative lag up to 2 previous days was used to assign exposure.
Reference: Wilhelm and Ritz (2005, 088668) **Period of Study:** 1994-2000 **Location:** Los Angeles County, California, U.S.	**Outcome:** Term low birth weight (LBW) (<2500 g at ≥ 37 completed wk gestation), Vaginal birth <37 completed wk gestation **Age Groups:** LBW: ≥ 37 completed wk Preterm births: <37 completed wk **Study Design:** Cross-sectional **N:** For LBW: 136,134 For preterm birth: 106,483 **Statistical Analyses:** Logistic regression **Covariates:** Maternal age, maternal race, maternal education, parity, interval since previous live birth, level of prenatal care, infant sex, previous LBW or preterm infant, birth season, other pollutants (CO, NO_2, O_3, PM_{10}), gestational age (in birth weight analysis) **Dose-response Investigated?** Yes **Statistical Package:** NR	**Pollutant:** PM_{10} **Averaging Time:** 24 h (every 6 days) Entire pregnancy Trimesters of pregnancy Months of pregnancy 6 wk before birth **Mean (SD):** First trimester: 42.2 Third trimester: 41.5 6 wk before birth: 39.1 **Range (Min, Max):** First trimester: 26.3, 77.4 Third trimester: 25.7, 74.6 6 wk before birth: 13.0, 103.7 **Monitoring Stations:** Zip-code-level analysis: 8 Address-level analysis: 6 **Copollutant (correlation):** First trimester: PM_{10}-CO: r = 0.12 PM_{10}-NO_2: r = 0.29 PM_{10}-O_3: r = -0.01 PM_{10}-$PM_{2.5}$: r = 0.43 Third trimester: PM_{10}-CO: r = 0.32 PM_{10}-NO_2: r = 0.45 PM_{10}-O_3: r = -0.08 PM_{10}-$PM_{2.5}$: r = 0.52 6 wk before birth: PM_{10}-CO: r = 0.36 PM_{10}-NO_2: r = 0.49 PM_{10}-O_3: r = -0.16 PM_{10}-$PM_{2.5}$: r = 0.60	**PM Increment:** 1) 10 µg/m^3 2) 3 levels: a) <25 percentile (reference) b) 25%-75 percentile c) ≥ 75 percentile **Incidence of LBW (third trimester exposure)** <32.8 µg/m^3: 2.0 (1.8, 2.2) 32.8 to <43.4 µg/m^3: 2.0 (1.9, 2.1) ≥ 43.4 µg/m^3: 2.2 (2.0, 2.4) **Incidence of preterm birth (first trimester exposure)** <32.9 µg/m^3: 8.7 (8.3, 9.2) 32.9 to <43.9 µg/m^3: 8.8 (8.5, 9.1) ≥ 43.9 µg/m^3: 8.6 (8.1, 9.0) **Incidence of preterm birth (6 wk before birth exposure)** <31.8 µg/m^3: 8.8 (8.4, 9.3) 31.8 to <44.1 µg/m^3: 8.6 (8.3, 8.9) ≥ 44.1 µg/m^3: 8.8 (8.4, 9.2) **Outcome: LBW** **Exposure Period: Third trimester** **Address-level analysis:** Single-pollutant model: Distance ≤ 1 mile Per 10 µg/m^3: 1.22 (1.05, 1.41) 33.4 to <44.7 µg/m^3: 1.08 (0.76, 1.52) ≥ 44.7 µg/m^3: 1.48 (1.00, 2.19) Multipollutant model: Distance ≤ 1 mile Per 10 µg/m^3: 1.36 (1.12, 1.65) 33.4 to <44.7 µg/m^3: 1.16 (0.77, 1.74) ≥ 44.7 µg/m^3: 1.58 (0.95, 2.62) Single-pollutant model: 1 <distance ≤ 2 mile Per 10 µg/m^3: 0.98 (0.90, 1.06) 33.4 to <44.7 µg/m^3: 0.95 (0.80, 1.13) ≥ 44.7 µg/m^3: 0.96 (0.78, 1.18) Multipollutant model: 1 <distance ≤ 2 mile Per 10 µg/m^3: 1.02 (0.92, 1.14) 33.4 to <44.7 µg/m^3: 0.93 (0.77, 1.12) ≥ 44.7 µg/m^3: 1.02 (0.79, 1.32) Single-pollutant model: 2 <distance ≤ 4 mile Per 10 µg/m^3: 1.03 (0.99, 1.08) 33.9 to <45.0 µg/m^3: 1.04 (0.96, 1.14) ≥ 45.0 µg/m^3: 1.08 (0.97, 1.20) Multipollutant model: 2 <distance ≤ 4 mile Per 10 µg/m^3: 1.04 (0.98, 1.09) 33.9 to <45.0 µg/m^3: 1.02 (0.92, 1.12) ≥ 45.0 µg/m^3: 1.06 (0.93, 1.21) **Zip-code-level analysis** Single-pollutant model:

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Per 10 µg/m^3: 1.03 (0.97, 1.09) 33.2 to <43.6 µg/m^3: 0.98 (0.86, 1.11) ≥ 43.6 µg/m^3: 1.03 (0.88, 1.21) Multipollutant model: Per 10 µg/m^3: 1.07 (0.99, 1.15) 33.2 to <43.6 µg/m^3: 0.97 (0.85, 1.12) ≥ 43.6 µg/m^3: 1.09 (0.90, 1.31) **Outcome: LBW** **Exposure Period: Entire pregnancy period** **Address-level analysis:** Multipollutant model: Per 10 µg/m^3: 1.24 (0.91, 1.70) **Outcome: Preterm Birth** **Exposure Period: First trimester of pregnancy** **Address-level analysis**: Single-pollutant model: Distance ≤ 1 mile Per 10 µg/m^3: 1.00 (0.93, 1.09) 33.3 to <45.1 µg/m^3: 1.07 (0.90, 1.26) ≥ 45.1 µg/m^3: 1.12 (0.91, 1.38) Multipollutant model: Distance ≤ 1 mile Per 10 µg/m^3: 1.00 (0.90, 1.12) 33.3 to <45.1 µg/m^3: 1.12 (0.92, 1.36) ≥ 45.1 µg/m^3: 1.17 (0.90, 1.50) Single-pollutant model: 1 <distance ≤ 2 mile Per 10 µg/m^3: 1.01 (0.97, 1.05) 33.7 to <45.3 µg/m^3: 1.03 (0.95, 1.12) ≥ 45.3 µg/m^3: 1.07 (0.97, 1.19) Multipollutant model: 1 <distance ≤ 2 mile Per 10 µg/m^3: 1.04 (0.99, 1.10) 33.7 to <45.3 µg/m^3: 1.07 (0.98, 1.17) ≥ 45.3 µg/m^3: 1.13 (1.00, 1.27) Single-pollutant model: 2 <distance ≤ 4 mile Per 10 µg/m^3: 1.01 (0.99, 1.03) 34.1 to <45.5 µg/m^3: 1.03 (0.99, 1.08) ≥ 45.5 µg/m^3: 1.02 (0.96, 1.07) Multipollutant model: 2 <distance ≤ 4 mile Per 10 µg/m^3: 0.99 (0.97, 1.02) 34.1 to <45.5 µg/m^3: 0.99 (0.95, 1.04) ≥ 45.5 µg/m^3: 0.94 (0.89, 1.01) **Zip-code-level analysis** Single-pollutant model: Per 10 µg/m^3: 0.99 (0.96, 1.01) 33.3 to <44.2 µg/m^3: 1.01 (0.95, 1.08) ≥ 44.2 µg/m^3: 0.98 (0.90, 1.05) Multipollutant model: Per 10 µg/m^3: 0.99 (0.96, 1.03) 33.3 to <44.2 µg/m^3: 1.03 (0.97, 1.11) ≥ 44.2 µg/m^3: 1.01 (0.92, 1.11) **Outcome: Preterm birth** **Exposure Period: 6 wk before birth** **Address-level analysis:** Single-pollutant model: Distance ≤ 1 mile Per 10 µg/m^3: 1.02 (0.95, 1.10) 32.5 to <44.8 µg/m^3: 1.09 (0.92, 1.29) ≥ 44.8 µg/m^3: 1.12 (0.92, 1.37) Multipollutant model: Distance ≤ 1 mile Per 10 µg/m^3: 1.06 (0.97, 1.16) 32.5 to <44.8 µg/m^3: 1.09 (0.90, 1.31) ≥ 44.8 µg/m^3: 1.17 (0.91, 1.49) Single-pollutant model: 1 <distance ≤ 2 mile Per 10 µg/m^3: 1.00 (0.96, 1.03) 32.3 to <45.3 µg/m^3: 0.99 (0.91, 1.07) ≥ 45.3 µg/m^3: 0.99 (0.89, 1.10) Multipollutant model:

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			1 <distance ≤ 2 mile Per 10 µg/m^3: 1.01 (0.97, 1.06) 32.3 to <45.3 µg/m^3: 1.00 (0.92, 1.10) ≥ 45.3 µg/m^3: 1.02 (0.91, 1.16) Single-pollutant model: 2 <distance ≤ 4 mile Per 10 µg/m^3: 0.99 (0.98, 1.01) 33.1 to <45.3 µg/m^3: 1.00 (0.96, 1.05) ≥ 45.3 µg/m^3: 0.98 (0.93, 1.03) Multipollutant model: 2 <distance ≤ 4 mile Per 10 µg/m^3: 1.00 (0.98, 1.02) 33.1 to <45.3 µg/m^3: 1.01 (0.96, 1.05) ≥ 45.3 µg/m^3: 0.98 (0.92, 1.04) **Zip-code-level analysis** Single-pollutant model: Per 10 µg/m^3: 1.02 (0.99, 1.04) 32.1 to <44.3 µg/m^3: 1.01 (0.95, 1.07) ≥ 44.3 µg/m^3: 1.04 (0.96, 1.12) Multipollutant model: Per 10 µg/m^3: 1.02 (0.99, 1.06) 32.1 to <44.3 µg/m^3: 1.02 (0.95, 1.09) ≥ 44.3 µg/m^3: 1.04 (0.95, 1.14) **Notes:** multipollutant model adds CO,NO_2, and O_3 in addition to the main pollutant of interest, PM_{10}.
Reference: Woodruff et al. (1997, 084271) **Period of Study:** 1989-1991 **Location:** 86 Metropolitan Statistical Areas in the U.S. (counties with populations less than 100,000 were excluded)	**Outcome:** Postneonatal mortality (death of an infant between 1 month and 1 yr of age 1) All post neonatal deaths 2) Normal birth weight (NBW, ≥ 2500 g) SIDS deaths 3) NBW respiratory deaths 4) Low birth weight (LBW) respiratory death Respiratory deaths: ICD9 codes 460-519 SIDS: ICD9 code 798.0 **Age Groups:** Infants (1 month-1yr of age) **Study Design:** Cross-sectional **N:** 3,788,079 infants **Statistical Analyses:** Logistic regression **Covariates:** Maternal education, maternal race, parental marital status, maternal smoking during pregnancy Avg temperature during the first 2 mo of life Infant's month and yr of birth Assessed race as an effect modifier (p-val for interaction terms >0.2) **Dose-response Investigated?** Yes **Statistical Package:** NR	**Pollutant:** PM_{10} **Averaging Time:** Mean of 1st 2 mo of life analyzed as tertiles of exposure and as continuous exposure **Mean (SD):** 31.4 (7.8) **Range (Min, Max):** Overall: 11.9-68.8 Low category: <28.0 Medium category: 28.1-40.0 High category: >40.0 **Monitoring Stations:** NR	**PM Increment:** 10 µg/m^3 (for continuous exposure analysis) **Adjusted ORs for cause-specific post neonatal mortality by pollution category (tertiles)** All causes Low: Ref Medium: 1.05 (1.01, 1.09) High: 1.10 (1.04, 1.16) SIDS, NBW: Low: Ref Medium: 1.09 (1.01, 1.17) High: 1.26 (1.14, 1.39) Respiratory death, NBW: Low: Ref Medium: 1.08 (0.87, 1.33) High: 1.40 (1.05, 1.85) Respiratory death, LBW: Low: Ref Medium: 0.93 (0.73, 1.18) High: 1.18 (0.86, 1.61) All other causes: Low: Ref Medium: 1.03 (0.97, 1.08) High: 0.97 (0.90, 1.04) **Adjusted ORs for a continuous 10 µg/m^3 change in exposure** All causes: 1.04 (1.02, 1.07) SIDS, NBW: 1.12 (1.07, 1.17) Respiratory death, NBW: 1.20 (1.06, 1.36) Respiratory death, LBW: 1.05 (0.91, 1.22) All other causes: 1.00 (0.99, 1.00)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Woodruff et al. (2008, 098386) **Period of Study:** 1999-2002 **Location:** U.S. counties with >250,000 residents (96 counties)	**Outcome:** Postneonatal deaths Respiratory mortality (ICD10: J000-99, plus bronchopulmonary dysplasia [BPD] P27.1) SIDS (ICD10: R95) Ill-defined causes (R99); All other deaths evaluated as a control category **Age Groups:** Infants aged >28 days and <1 yr **Study Design:** Cross-sectional **N:** 3,583,495 births (6,639 post neonatal deaths) **Statistical Analyses:** Logistic GEE (exchangeable correlation structure) **Covariates:** Maternal race/ethnicity, marital status, age, education, primiparity, county-level poverty and per capita income levels, yr and month of birth dummy variables to account for time trend and seasonal effects, and region of the country Sensitivity analyses performed among only those mothers with smoking information (adjustment for smoking had no effect on the estimates) **Season:** Adjusted for yr and month of birth dummy variables to account for time trend and seasonal effects **Dose-response Investigated?** Evaluated the appropriateness of a linear form from analysis based on quartiles of exposure and concluded that linear form was appropriate (data not shown) **Statistical Package:** SAS	**Pollutant:** PM_{10} **Averaging Time:** Measured continuously for 24 h once every 6 days exposure assigned by calculating avg concentration of pollutant during first 2 mo of life **Median and IQR (25th-75th percentile):** Survivors: 28.9 (23.3-34.4) All causes of death: 29.1 (23.9-34.5) Respiratory: 29.8 (24.3-36.5) SIDS: 28.6 (23.5-33.8) SIDS + ill-defined: 28.8 (23.9-33.9) Other causes: 29.2 (23.9-34.5) **Percentiles:** see above **PM Component:** Not assessed, but controlled for region of the country to account for PM composition variation **Monitoring Stations:** NR **Copollutant (correlation):** PM_{10} $PM_{2.5}$ (r = 0.34) CO (r = 0.18) SO_2 (r = 0.00) O_3 (r = 0.20) **Notes:** Monthly avg calculated if there were at least 3 available measures for PM Assigned exposures using the avg concentration of the county of residence	**PM Increment:** IQR (11 µg/m^3) **Effect Estimate [Lower CI, Upper CI]:** Adjusted ORs for single pollutant models All causes: 1.04 (0.99, 1.10) Respiratory: 1.18 (1.06, 1.31) SIDS: 1.02 (0.89, 1.16) Ill-defined + SIDS: 1.06 (0.97, 1.16) Other causes: 1.02 (0.96, 1.07) Adjusted ORs for multipollutant models (including CO, O_3, SO_2) Respiratory: 1.16 (1.04, 1.30) SIDS: 1.02 (0.90, 1.16) OR for deaths coded as BPD per increase in IQR: 1.19 (0.85, 1.65) OR for respiratory post neonatal death stratified by birth weight NBW only: 1.19 (1.05, 1.36) LBW only: 1.12 (0.95, 1.31) OR for respiratory deaths removing region of U.S. as a confounding variable: 1.30 (1.04, 1.61) OR for respiratory deaths assessing exposure as quartiles Highest vs. Lowest quartile: 1.31 (1.00, 1.71) OR for respiratory deaths among only those deaths that occurred during the first 90 days (most closely matched exposure metric of the avg over the first 2 mo of life): 1.25 (1.06, 1.47)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Jedrychowski, et al., (2007, 156607) **Period of Study:** Jan 2001-Feb 2004 **Location:** Krakow, Poland	**Outcome:** Birth weight (grams), birth length (cm) **Age Groups:** Pregnant women 18-35 yr **Study Design:** Prospective cohort **N:** 493 women **Statistical Analyses:** Linear regression **Covariates:** Environmental tobacco smoke (# cigarettes smoked daily in presence of pregnant woman), season of birth, size of mother, parity, gestational age, gender of child, vitamin A intake **Season:** All **Dose-response Investigated?** Yes **Statistical Package:** NR **Lags Considered:** Two consecutive days in the second trimester	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 48 h period **Percentiles: 50th(Median):** 35.3 **Range (Min, Max):** 10.3, 294.9 **Monitoring Stations:** No stations, personal monitoring **Notes:** PM measured during a 2 day period in the second trimester by Personal Environmental Monitoring Sampler (PEMS)	**PM Increment:** in 1 µg/m^3 and tertiles T1: <27.0 µg/m^3 T2: 27.0-46.2 µg/m^3 T3: ≥ 46.2 µg/m^3 **Mean [Lower CI, Upper CI]:** Birth weight (g) For ln unit PM: β = -172.39 (p = 0.02) Tertiles: T1: ref T2: β = -16.510 [-94.630, 61.610] T3: β = -109.956 [-196.649 to -23.263] In low Vitamin A group (<1,378 µg) T1: ref T2: β = -68.354 [-165.643, 28.935] T3: β = -185.070 [-293.393 to -76.747] In high Vitamin A group (>1,378 µg) T1: ref T2: β = 64.262 [-70.464, 198.988] T3: β = 38.593 [-109.853, 187.039] Birth length (cm) For ln unit PM: β = -1.39 (p = 0.00) Tertiles: T1: ref T2: β = -0.288 [-0.790, 0.214] T3: β = -0.810 [-1.367 to -0.253] In low Vitamin A group (<1,378 µg) T1: ref T2: β = -0.514 [-1.114, 0.086] T3: β = -1.100 [-1.768 to -0.432] In high Vitamin A group (>1,378 µg) T1: ref T2: β = 0.039 [-0.896, 0.974] T3: β = -0.301 [-1.326, 0.724]
Reference: (Lipfert et al., 2000, 004103) **Period of Study:** 1990 **Location:** U.S.	**Outcome (ICD9 and ICD10):** Infant mortality Including respiratory mortality (traditional definition, ICD9 460-519), expanded definition (adds ICD9 769 and 770) **Age Groups:** Infants **Study Design:** Cross-sectional **N:** 2,413,762 infants in 180 counties (Ns differ for various models) **Statistical Analyses:** Logistic regression **Covariates:** Mother's smoking, education, marital status, and race Month of birth And county avg heating degree days **Dose-response Investigated?** NR **Statistical Package:** NR	**Pollutant:** SO_4^{2-}/ $NSPM_{10}$ (regressed jointly) **Averaging Time:** Yearly avg used **Mean (SD):** 33.1 (9.17) (based on 180 counties) **Range (Min, Max):** (16.9, 59) **Monitoring Stations:** NR **Copollutant:** PM_{10} $NSPM_{10}$ CO SO_2 **Notes:** TSP-based sulfate was adjusted for compatibility with the PM_{10}-based data	**PM Increment:** NR (present regression coefficients) **Effect Estimate [Lower CI, Upper CI]:** Presented regression coefficients (standard errors) (3 PM exposures regressed jointly) bold = p <0.05 Cause of death: All Birth weight: All SO_4^{2-}: -0.0002 (0.0061) $NSPM_{10}$: 0.0115 (0.0014) Cause of death: All Birth weight: LBW SO_4^{2-}: 0.0265 (0.0080) $NSPM_{10}$: 0.0086 (0.0020) Cause of death: All Birth weight: normal SO_4^{2-}: -0.0488 (0.0098) $NSPM_{10}$: 0.0096 (0.0024) Cause of death: All neonatal Birth weight: All SO_4^{2-}: 0.0267 (0.0076) $NSPM_{10}$: 0.0126 (0.0018) Cause of death: All neonatal Birth weight: LBW SO_4^{2-}: 0.0388 (0.0088) $NSPM_{10}$: 0.0093 (0.0022) Cause of death: All neonatal Birth wt: normal SO_4^{2-}: -0.0334 (0.0169) $NSPM_{10}$: 0.0125 (0.0040) Cause of death: All post neonatal Birth wt: All PM_{10}: 0.0091 (0.0024) SO_4^{2-}: -0.0474 (0.0100) $NSPM_{10}$: 0.0096 (0.0024) Cause of death: All post neonatal Birth wt: LBW SO_4^{2-}: -0.0247 (0.0173) $NSPM_{10}$: 0.0101 (0.0042) Cause of death: All post neonatal Birth wt: normal SO_4^{2-}: -0.0569 (0.0121)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			$NSPM_{10}$: 0.0080 (0.0029) Cause of death: SIDS Birth weight: All SO_4^{2-}: -0.1078 (0.0151) $NSPM_{10}$: 0.0149 (0.0037) Cause of death: SIDS Birth weight: LBW SO_4^{2-}: -0.1378 (0.0337) $NSPM_{10}$: 0.0146 (0.0085) Cause of death: SIDS Birth weight: normal PM_{10}: 0.0137 (0.0042) SO_4^{2-}: -0.0995 (0.0168) $NSPM_{10}$: 0.0147 (0.0041) Cause of death: All respiratory (ICD9: 460-519, 769, 770) Birth weight: All SO_4^{2-}: 0.0706 (0.0146) $NSPM_{10}$: 0.0166 (0.0034) Cause of death: All respiratory (ICD9: 460-519, 769, 770) Birth weight: LBW SO_4^{2-}: 0.0821 (0.0158) $NSPM_{10}$: 0.0139 (0.0038) Cause of death: All respiratory (ICD9: 460-519, 769, 770) Birth weight: normal PM_{10}: 0.0177 (0.0091) SO_4^{2-}: 0.0001 (0.0392) $NSPM_{10}$: 0.0118 (0.0090) Cause of death: Respiratory disease (ICD9: 460-519) Birth weight: All PM_{10}: 0.0133 (0.0089) SO_4^{2-}: 0.0093 (0.0384) $NSPM_{10}$: 0.0134 (0.0089) Cause of death: Respiratory disease (ICD9: 460-519) Birth weight: LBW PM_{10}: 0.0092 (0.0137) SO_4^{2-}: 0.0434 (0.0580) $NSPM_{10}$: 0.0089 (0.0138) Cause of death: Respiratory disease (ICD9: 460-519) Birth weight: normal SO_4^{2-}: -0.0177 (0.0509) $NSPM_{10}$: 0.0128 (0.0119) Associations with SIDS by smoking status Smoking status: Yes Birth weight: Normal SO_4^{2-}: -0.0722 (0.0284) $NSPM_{10}$: 0.0206 (0.0071) Smoking status: No Birth weight: Normal SO_4^{2-}: -0.114 (0.021) $NSPM_{10}$: 0.0117 (0.005) Smoking status: Yes Birth weight: LBW SO_4^{2-}: -0.0958 (0.0483) $NSPM_{10}$: 0.0345 (0.0125) Smoking status: No Birth weight: LBW SO_4^{2-}: -0.0172 (0.047) $NSPM_{10}$: -0.0007 (0.012) Mean risks (95%CI) between post neonatal SIDS among normal birth weight babies pollutants regressed one at a time SO_4^{2-}: 0.43 (0.37, 0.51) $NSPM_{10}$: 1.33 (1.18, 1.50)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: (Liu et al., 2007, 090429) **Period of Study:** 1985-2000 **Location:** 3 Canadian cities: Calgary, Edmonton, and Montreal	**Outcome:** Intrauterine growth restriction (IUGR) **Age Groups:** Singleton term live births (37-42 wks gestation) **Study Design:** Retrospective cohort **N:** 386,202 singleton live births **Statistical Analyses:** Multiple logistic regression **Covariates:** Maternal age, parity, infant gender, season, and city of residence at time period of birth **Season:** All seasons **Dose-response Investigated?** No **Statistical Package:** NR	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h (6-day schedule) **Mean (SD):** 12.2 **Percentiles: 25th:** 6.3 **50th(Median):** 9.7 **75th:** 15 **PM Component:** metals and organic matter such as polycyclic aromatic hydrocarbons **Monitoring Stations:** Calgary (4), Edmonton (2), and Montreal (8) **Copollutant (correlation):** SO_2: r = 0.44, p < 0.0001 NO_2: r = 0.41, p < 0.0001 CO: r = 0.31, p < 0.0001 O_3: r = -0.14, p < 0.0001	**PM Increment:** 10 µg/m^3 **Effect Estimate** **Single-pollutant model [Lower CI, Upper CI]:** 1st trimester OR = 1.07 (1.03-1.10) 2nd trimester OR = 1.06 (1.03-1.10) 3rd trimester OR = 1.06 (1.03-1.10) **Effect Estimate** **multi-pollutant model [Lower CI, Upper CI]:** 1st trimester OR= 1.03 (0.99-1.06) 2nd trimester OR= 1.01 (0.98-1.05) 3rd trimester OR= 1.03 (0.99-1.06) **Note:** ORs and CIs estimated from Fig. 6 and 7
Reference: Loomis et al. (1999, 087288) **Period of Study:** Jan 1993-Jul 1995 **Location:** Mexico City (southwestern section)	**Outcome (ICD9 and ICD10):** Infant mortality (daily counts of deaths) All ICD9 codes, excluding accidents, poisoning, and violence (ICD9 ≥800) **Age Groups:** Children <1 yr of age **Study Design:** Time-series **N:** 942 deaths (days were the unit of observation) **Statistical Analyses:** Poisson regression (generalized additive model) **Covariates:** Final models controlled for mean temp of 3 days before death and nonparametrically smoothed periodic cycles **Season:** Yes (considered) **Dose-response Investigated?** Loess smoother **Statistical Package:** NR **Lags Considered:** 0-5 (also considered lags with avg exposure levels during "windows" of 2 to 4 days)	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h **Mean (SD):** 27.4 (10.5) **Percentiles:** Lower quartile: 20 Median: 26 Upper quartile: 34 **Range (Min, Max):** 4, 85 **Monitoring Stations:** 1 **Copollutant:** O_3 NO_2 NO NO_X SO_2 **Notes:** Pearson correlation coefficients ranging from 0.52 to 0.71	**PM Increment:** 10 µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** %Change in infant mortality Lags 0-5 (single day) presented in Fig 1: Lag0,1,2: No association (results not presented) Lag3: 4.8 (0.97, 8.61) Lag4: 4.2 (0.37, 7.93) %Change in mortality when avg exposure levels during "windows" of 2 to 4 days were considered 2 Days: No lag: -1.36 (-5.51, 2.8) Lag1: -0.95 (-5.10, 3.20) Lag2: 2.78 (-1.33, 6.89) Lag3: 4.93 (0.86, 9.01) 3 Days: No lag: -0.81 (-5.29, 3.67) Lag1: 1.99 (-2.46, 6.45) Lag2: 4.54 (0.12, 8.96) Lag3: 6.87 (2.48, 11.26) 4 Days: No lag: 1.95 (-2.76, 6.66) Lag1: 3.74 (-0.95, 8.42) Lag2: 5.87 (1.21, 10.53) Multipollutant models (3-day mean w/ 3-day lag) 1 pollutant model: 6.87 (2.48, 11.26) 2 pollutant models: w/ O_3: 6.24 (1.35, 11.14) w/ NO_2: 5.91 (-0.76, 12.59) 3 Pollutant model (w/ O_3 and NO_2): 6.30 (-0.54, 13.15)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Mannes et al. (2005, 087895) **Period of Study:** Jan 1998-Dec 2000 **Location:** metropolitan Sydney, Australia	**Outcome:** Risk of small for gestational age (SGA) and birth weight **Age Groups:** All singleton births >20 wk and ≥ 400 grams birth weight and maternal all ages **Study Design:** Cross-sectional **N:** 138,056 singleton births **Statistical Analyses:** Logistic and linear regression models **Covariates:** Sex of child, maternal age, gestational age, maternal smoking, gestational age at first antenatal visit, maternal indigenous status, whether first pregnancy, season of birth, and socioeconomic status (SES) **Season:** All seasons included as covariate. **Dose-response Investigated?** No **Statistical Package:** SAS System for Windows v8.02	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD):** 9.4 (5.1) **Percentiles: 25th:** 6.5 **50th(Median):** 8.4 **75th:** 11.2 **Range (Min, Max):** (2.4- 82.1) **Monitoring Stations:** up to 14 **Copollutant (correlation):** CO: r = 0.53 NO_2: r = 0.66 O_3: r = 0.36 PM_{10}: r = 0.81	**PM Increment:** 1 µg/m^3 Risk of SGA All births 1 month before birth: OR = 1.01 (0.99-1.03) Third trimester: OR = 0.99 (0.97-1.02) Second trimester: OR = 1.03 (1.01-1.05) First trimester: OR = 0.99 (0.97-1.01) 5 km births 1 month before birth: OR = 1.01 (0.97-1.04) Third trimester: OR = 1.00 (0.95-1.05) Second trimester: OR = 1.00 (0.96-1.05) First trimester: OR = 0.99 (0.94-1.04) Change in birth weight All births 1 month before birth: ß = -2.48 (-4.58- -0.38) Third trimester: ß = -0.98 (-3.74-1.78) Second trimester: ß = -4.10 (-6.79- -1.41) First trimester: ß = 0.36 (-2.29- 3.01) 5 km births 1 month before birth: ß = -2.70 (-6.80- 1.40) Third trimester: ß = -2.83 (-9.00-3.34) Second trimester: ß = 1.54 (-4.59-7.67) First trimester: ß = 1.89 (-1.99-5.77)
Reference: Parker et al. (2005, 087462) **Period of Study:** 1999-2000 **Location:** California	**Outcome:** Small for gestational age (SGA) and birth weight **Age Groups:** Infants delivered at 40 wk gestation maternal all ages **Study Design:** Cross-sectional **N:** 18,247 singleton births **Statistical Analyses:** Linear and logistic regression models **Covariates:** Maternal race, maternal Hispanic origin, marital status, parity, maternal education, and maternal age **Season:** Season of delivery (covariate) **Dose-response Investigated?** Yes **Statistical Package:** STATA	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR (measurement taken every 6 days) **Mean (SD):** 15.42 (5.08) **PM Component:** metals, polycyclic aromatic hydrocarbons **Monitoring Stations:** 40 **Copollutant (correlation):** $PM_{2.5}$-CO: r = 0.6 **Notes:** Mean calculated for 9-month exposure. The following means (SDs) are calculated for trimester: First: 15.70 (6.26) Second: 15.40 (6.53) Third: 14.29 (6.35) PM categorized into quartiles: Q1: <11.9 Q2: 11.9-13.9 Q3: 13.9-18.4 Q4: >18.4	**PM Increment:** <11.9 µg/m^3| Referent **PM Increment:** 11.9-13.9 µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** First Trimester Birth weight: ß = -5.7 (-27.9-16.5) SGA: OR = 1.02 (0.84-1.23) Second Trimester Birth weight: ß = 11.3 (-12.2-34.9) SGA: OR = 0.89 (0.73-1.09) Third Trimester Birth weight: ß = 8.3 (-13.1-29.8) SGA: OR = 1.00 (0.83-1.19) **PM Increment:** 13.9-18.4 µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** First Trimester Birth weight: ß = -2.5 (-24.5-19.5) SGA: OR = 1.12 (0.93-1.34) Second Trimester Birth weight: ß = -17.2 (-39.4-4.9) SGA: OR = 1.05 (0.88-1.26) Third Trimester Birth weight: ß = -8.1 (-30.2-13.9) SGA: OR = 0.98 (0.82-1.18) **PM Increment:** >18.4 µg/m^3 **Effect Estimate [Lower CI, Upper CI]:** First Trimester Birth weight: ß = -35.8 (-58.4--13.3) SGA: OR = 1.26 (1.04-1.51) Second Trimester Birth weight: ß = -46.6 (-68.6- -24.6) SGA: OR = 1.24 (1.04-1.49) Third Trimester Birth weight: ß = -31.6 (-52.0- -11.1) SGA: OR = 1.21 (1.02-1.43)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Parker and Woodruff (2008, 156846) **Period of Study:** 2001-2003 **Location:** U.S.	**Outcome:** Low birth weight **Study Design:** Cohort **N:** 785,965 Singleton births delivered at 40 wk gestation **Statistical Analyses:** GEE regression models linear and logistic regression **Covariates:** Race/ethnicity, parity, maternal age **Season:** Season of delivery **Statistical Package:** SUDAAN	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 9 mo **Mean (SD):** 14.5 25th: 12.1 75th: 17.6 **Copollutant (correlation):** SO_2, NO_2 CO O_3	**PM Increment:** 10 µg/m^3 **Change in Birth weight (9 month exposure):** Unadjusted: 19.4 (9.8, 29.0) Adjusted for maternal factors: 18.4 (9.2, 27.7) **Stratified by region:** Industrial Midwest: -15.3 (-43.4, 12.9) Northeast: -9.8 (-11.9, 26.6) Northwest: 27.5 (5.5, 49.4) Southern CA: 5.5 (-9.6, 20.5) Southeast: 7.3 (-11.9, 26.6) Southwest: 72.3 (34.0, 110.5) Upper Midwest: -0.7 (-62.0, 60.6) **Multipollutant models:** $PM_{2.5}$ +$PM_{10-2.5}$: 14.2 (4.3, 24.1) $PM_{2.5}$ +$PM_{10-2.5}$+SO_2+CO+NO_2+O_3: 28.6 (14.2, 43.0)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Rich et al. (2009, 180122) **Period of Study:** 1999-2003 **Location:** New Jersey, United States	**Outcome:** Small for gestational age **Study Design:** Retrospective Cohort **Covariates:** Month and calendar yr of birth, apparent temperature, pregnancy complications **Statistical Analysis:** Polytomous logistic regression **Statistical Package:** SAS **Age Groups:** Gestational age 37-42 wks	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD) Unit:** *All values are for first trimester, other trimesters are available in paper Reference Births: 13.8 (2.5) SGA Births: 13.9 (2.5) VSGA Births: 13.9 (2.4) **Range (Min, Max):** 2.0, 29.0 **Copollutant (correlation):** *All values are for first trimester, other trimesters are available in paper NO_2: 0.01 SO_2: 0.17 CO: 0.25	*All values are for first trimester, other trimesters are available in paper **Increment:** 4 µg/m^3 **Percent Change in Risk (95% CI)** SGA: 4.5 (0.5-8.7) VSGA: 2.6 (-4.4-10.0) **Percent Change in Risk (95% CI) for single and two-pollutant models** Single, SGA: 4.6 (-0.3-9.8) Single, VSGA: 4.5 (-4.0-13.4) Two ($PM_{2.5}$ & NO_2), SGA: 4.5 (-0.4-9.7) Two ($PM_{2.5}$ & NO_2), VSGA: 3.2 (-5.2-12.4) **Percent Change in Risk (95% CI) by pregnancy complication in third trimester** SGA Any Complication No: 4.7 (0.6-9.0) Yes: 2.2 (-6.1-11.3) Placental Abruption No: 4.0 (0.3-7.9) Yes: 11.7 (-21.7-59.5) Placental Praevia No: 3.9 (0.2-7.8) Yes: 23.2 (-20.9-91.9) Pre-eclampsia No: 4.2 (0.4-8.2) Yes: 2.7 (-13.8-22.3) Gestational Hypertension No: 4.3 (0.4-8.4) Yes: 3.9 (-7.8-17.1) Premature Rupture of the Membrane No: 3.7 (-0.1-7.7) Yes: 14.6 (-3.3-35.9) Gestational Diabetes No: 4.6 (0.8-8.6) Yes: -9.3 (-24.7-9.3) VSGA Any Complication No: 1.5 (-6.1-9.7) Yes: 12.6 (0.1-26.7) Placental Abruption No: 4.1 (-2.6-11.2) Yes: 7.6 (-29.8-64.9) Placental Praevia No: 4.1 (-2.5-11.2) Yes: 3.2 (-43.0-86.9) Pre-eclampsia No: 4.4 (-2.6-11.9) Yes: 3.9 (-15.7-28.1) Gestational Hypertension No: 3.2 (-4.0-10.9) Yes: 12.9 (-3.3-31.9) Premature Rupture of the Membrane No: 3.3 (-3.5-10.5) Yes: 21.9 (-3.6-54.2) Gestational Diabetes No: 4.3 (-2.5-11.5) Yes: 1.4 (-27.0-40.9)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Ritz et al. (2007, 096146) **Period of Study:** Jan 2003-Dec 2003 **Location:** Los Angeles, California	**Outcome:** Preterm births (infants delivered before 37 wk) **Age Groups:** Births **Study Design:** Case-control nested within a birth cohort (cases and controls matched on zip code and birth month) Phase 1: cross-sectional including all birth cohort Phase 2: nested case-control of survey respondents **N:** Phase 1: Birth cohort consisted of 58,316 eligible births. Phase II: 2,543 **Statistical Analyses:** Logistic regression **Covariates:** Birth certificate information: maternal age, race/ethnicity, parity, education, season of birth survey information: maternal smoking, alcohol consumption, living with a smoker, and marital status during pregnancy income (imputed) occupation and pregnancy weight gain considered but not included in final models **Season:** Yes **Dose-response Investigated?** Yes, examined categories of exposure **Statistical Package:** NR	**Pollutant:** $PM_{2.5}$ **Averaging Time:** daily or every 3rd day used to calculate the entire pregnancy, the first trimester, and the last 6 wk before delivery Only reported first trimester exposures for PM **Range (Min, Max):** NR Ranges for 3 categories reported: Low (ref): ≤ 18.63 Mid: 18.64-21.36 High: >21.36 **Monitoring Stations:** Each zip code was linked to the nearest monitoring station (number not reported) **Copollutant (correlation):** CO NO_2 O_3 **Notes:** Daily or every 3rd day measurements used for mean calculations	**PM Increment:** Reported analyses using exposure categories **Effect Estimate [Lower CI, Upper CI]:** Birth cohort (phase I) Crude: Low: 1.0 Mid: 0.96 (0.90, 1.03) High: 1.05 (0.99, 1.12) Adj for birth cert Covariates: Low: 1.0 Mid: 1.01 (0.93, 1.09) High: 1.10 (1.01, 1.20) Survey respondents (phase II) Crude: Low: 1.0' Mid: 1.11 (0.90, 1.36) High: 1.27 (1.06, 1.53) Adj for birth cert Covariates: Low: 1.0 Mid: 1.14 (0.90, 1.46) High: 1.27 (0.99, 1.64) Adj for all Covariates: Low: 1.0 Mid: 1.15 (0.90, 1.47) High: 1.29 (1.00, 1.67) Two-phase model: * Low: 1.0 Mid: 0.98 (0.84, 1.15) High: 1.07 (0.85, 1.35) *Method to reduce potential selection bias and increase statistical efficiency
Reference: Slama et al. (2007, 093216) **Period of Study:** Jan 1998-Jan 1999 **Location:** Munich, Germany	**Outcome:** Birth weight offspring at term **Study Design:** Cohort study **N:** 1016 births **Statistical Analyses:** Poisson model **Covariates:** Maternal passive smoking, maternal age, gestational duration, sex of child, parity, maternal education, maternal size, prepregnancy weight, other pollutants ($PM_{2.5}$, $PM_{2.5}$ absorbance, NO_2), season of conception **Dose-response Investigated?** Yes **Statistical Package:** STATA	**Pollutant:** $PM_{2.5}$ (estimated based on larger PM size fractions) **Averaging Time:** Entire pregnancy period and trimesters **Mean (SD):** 14.4 **Percentiles: 25th:** 13.5 **50th(Median):** 14.4 **75th:** 15.4 **Monitoring Stations:** Spatial component: 40 Temporal component: 1 **Copollutant (correlation):** p.a. = pregnancy avg trim. = trimester $PM_{2.5}$ (p.a.)-$PM_{2.5}$ (1st trim.): 0.85 $PM_{2.5}$ (p.a.)-$PM_{2.5}$ (2nd trim.): 0.77 $PM_{2.5}$ (p.a.)-$PM_{2.5}$ (3rd trim.): 0.87 $PM_{2.5}$ (p.a.)-NO_2 (p.a.): 0.45 $PM_{2.5}$ (p.a.)-NO_2 (1st trim.): 0.18 $PM_{2.5}$ (p.a.)-NO_2 (2nd trim.): 0.32 $PM_{2.5}$ (p.a.)-NO_2 (3rd trim.): 0.37 $PM_{2.5}$ (1st trim.)-$PM_{2.5}$ (2nd trim.): 0.40 $PM_{2.5}$ (1st trim.)-$PM_{2.5}$ (3rd trim.): 0.68 $PM_{2.5}$ (1st trim.)-NO_2 (p.a.): 0.48 $PM_{2.5}$ (1st trim.)-NO_2 (1st trim.): 0.15 $PM_{2.5}$ (1st trim.)-NO_2 (2nd trim.): 0.41 $PM_{2.5}$ (1st trim.)-NO_2 (3rd trim.): 0.39 $PM_{2.5}$ (2nd trim.)-$PM_{2.5}$ (3rd trim.): 0.51 $PM_{2.5}$ (2nd trim.)-NO_2 (p.a.): 0.23 $PM_{2.5}$ (2nd trim.)-NO_2 (1st trim.): -0.03 $PM_{2.5}$ (2nd trim.)-NO_2 (2nd trim.): 0.17 $PM_{2.5}$ (2nd trim.)-NO_2 (3rd trim.): 0.30	**PM Increment:** 1) 1 μg/m^3 2) Quartiles: a) 1st (reference) (7.2-13.5 μg/m^3) b) 2nd (13.5-14.4 μg/m^3) c) 3rd (14.4-15.4 μg/m^3) day) 4th (15.41-17.5 μg/m^3) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over the whole pregnancy** **Single-pollutant models** Unadjusted models 2nd quartile: 1.07 (0.65, 1.73); 3rd quartile: 1.38 (0.91, 2.09) 4th quartile: 1.45 (0.92, 2.25) Per 1 μg/m^3: 1.06 (0.95, 1.19) Adjusted models 2nd quartile: 1.08 (0.63, 1.82); 3rd quartile: 1.34 (0.86, 2.13) 4th quartile: 1.73 (1.15, 2.69); Per 1 μg/m^3: 1.13 (1.00, 1.29) **Multipollutant models** Adjusted models 2nd quartile: 1.01 (0.57, 1.85) 3rd quartile: 1.12 (0.64, 1.87) 4th quartile: 1.36 (0.72, 2.45); Per 1 μg/m^3: 1.07 (0.91, 1.26) **Single-pollutant models** (restricted analysis to $PM_{2.5}$ absorbance below the median) Per 1 μg/m^3: 1.15 (0.89, 1.52) **Prevalence ratios (PRs) of birth weight <3000 g** **Multipollutant models (simultaneous**

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
		$PM_{2.5}$ (3rd trim.)-NO_2 (p.a.): 0.39 $PM_{2.5}$ (3rd trim.)-NO_2 (1st trim.): 0.33 $PM_{2.5}$ (3rd trim.)-NO_2 (2nd trim.): 0.21 $PM_{2.5}$ (3rd trim.)-NO_2 (3rd trim.): 0.23 $PM_{2.5}$ (p.a.)- $PM_{2.5}$ absorbance (p.a.): 0.69 $PM_{2.5}$ (p.a.)- $PM_{2.5}$ abs (1st trim.): 0.33 $PM_{2.5}$ (p.a.)- $PM_{2.5}$ abs (2nd trim.): 0.48 $PM_{2.5}$ (p.a.)- $PM_{2.5}$ abs (3rd trim.): 0.52 $PM_{2.5}$ (1st trim.)- $PM_{2.5}$ abs (p.a.): 0.68 $PM_{2.5}$ (1st trim.)- $PM_{2.5}$ abs (1st trim.): 0.27 $PM_{2.5}$ (1st trim.)- $PM_{2.5}$ abs (2nd trim.): 0.53 $PM_{2.5}$ (1st trim.)- $PM_{2.5}$ abs (3rd trim.): 0.51 $PM_{2.5}$ (2nd trim.)- $PM_{2.5}$ abs(p.a.): 0.41 $PM_{2.5}$ (2nd trim.)- $PM_{2.5}$ abs (1st trim.): 0.08 $PM_{2.5}$ (2nd trim.)- $PM_{2.5}$ abs (2nd trim.): 0.29 $PM_{2.5}$ (2nd trim.)- $PM_{2.5}$ abs (3rd trim.): 0.41 $PM_{2.5}$ (3rd trim.)- $PM_{2.5}$ abs (p.a.): 0.62 $PM_{2.5}$ (3rd trim.)- $PM_{2.5}$ abs (1st trim.): 0.48 $PM_{2.5}$ (3rd trim.)- $PM_{2.5}$ abs (2nd trim.): 0.36 $PM_{2.5}$ (3rd trim.)- $PM_{2.5}$ abs (3rd trim.): 0.37	**Adjustment of 3rd trimester $PM_{2.5}$ and whole pregnancy $PM_{2.5}$)** $PM_{2.5}$ (whole pregnancy) Per 1 µg/m^3: 0.96 (0.75, 1.19) $PM_{2.5}$ (3rd trimester) Per 1 µg/m^3: 1.17 (0.98, 1.40) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over the whole pregnancy (adjustment for season of conception)** 4th quartile: 1.68 (1.05, 2.75); Per 1 µg/m^3: 1.12 (0.97, 1.28) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over first trimester of pregnancy** Each trimester separately 2nd quartile: 1.14 (0.74, 1.96); 3rd quartile: 1.28 (0.84, 2.10) 4th quartile: 1.65 (1.02, 2.60) Per 1 µg/m^3: 1.10 (0.99, 1.20) All trimesters adjusted simultaneously 2nd quartile: 0.97 (0.60, 1.73); 3rd quartile: 0.98 (0.57, 1.75) 4th quartile: 1.22 (0.71, 2.18) Per 1 µg/m^3: 1.03 (0.90, 1.17) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over second trimester of pregnancy** Each trimester separately 2nd quartile: 0.83 (0.52, 1.32); 3rd quartile: 1.08 (0.71, 1.60) 4th quartile: 0.94 (0.61, 1.47) Per 1 µg/m^3: 1.01 (0.92, 1.12) All trimesters adjusted simultaneously 2nd quartile: 0.75 (0.46, 1.24) 3rd quartile: 0.86 (0.56, 1.30); 4th quartile: 0.75 (0.48, 1.23) Per 1 µg/m^3: 0.94 (0.84, 1.06) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over third trimester of pregnancy** Each trimester separately 2nd quartile: 1.30 (0.80, 2.17) 3rd quartile: 1.44 (0.85, 2.27) 4th quartile: 1.90 (1.20, 2.82) Per 1 µg/m^3: 1.14 (1.02, 1.24) All trimesters adjusted simultaneously 2nd quartile: 1.34 (0.79, 2.30) 3rd quartile: 1.48 (0.86, 2.58) 4th quartile: 1.91 (1.00, 3.20) Per 1 µg/m^3: 1.14 (0.99, 1.29) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over third trimester of pregnancy (adjustment for season of conception)** All trimesters adjusted simultaneously Per 1 µg/m^3: 1.25 (1.04, 1.50) **Sensitivity analysis**(bootstrapped PR) 2nd quartile: 0.98 (0.63, 1.61); 3rd quartile: 1.22 (0.82, 2.02) 4th quartile: 1.57 (1.02, 2.57) Per 1 µg/m^3: 1.11 (0.98, 1.27) **Estimated increments in prevalence of birth weight of <3000 g during exposure 9 mo after birth** Per 1 µg/m^3: 7% (-7%, 22%)
Reference: (Slama et al., 2007, 093216) **Period of Study:** Jan 1998-Jan 1999	**Outcome:** Birth weight offspring at term **Study Design:** Cohort study	**Pollutant:** $PM_{2.5}$ absorbance (estimated) **Averaging Time:** Entire pregnancy period and trimesters	**PM Increment:** 1) 0.5 * 10-5/m 2) Quartiles: a) 1st (reference) (1.29-1.61) b) 2nd (1.61-1.72)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Location: Munich, Germany	**N:** 1016 births **Statistical Analyses:** Poisson model **Covariates:** Maternal passive smoking, maternal age, gestational duration, sex of child, parity, maternal education, maternal size, prepregnancy weight, other pollutants ($PM_{2.5}$, $PM_{2.5}$ absorbance, NO_2), season of conception **Dose-response Investigated?** Yes **Statistical Package:** STATA	**Mean (SD):** 1.76 * **Percentiles: 25th:** 1.61* **50th(Median):** 1.72* **75th:** 1.89 * **Unit (i.e. µg/m^3):** 10-5/m **Monitoring Stations:** Spatial component: 40 Temporal component: 1 **Copollutant (correlation):** p.a. = pregnancy avg trim. = trimester abs = absorbance $PM_{2.5}$ abs (p.a.)-$PM_{2.5}$ abs (1st trim.): 0.54 $PM_{2.5}$ abs (p.a.)-$PM_{2.5}$ abs (2nd trim.): 0.84 $PM_{2.5}$ abs (p.a.)-$PM_{2.5}$ abs (3rd trim.): 0.55 $PM_{2.5}$ abs (p.a.)-$PM_{2.5}$ (p.a.): 0.69 $PM_{2.5}$ abs (p.a.)-$PM_{2.5}$ (1st trim.): 0.68 $PM_{2.5}$ abs (p.a.)-$PM_{2.5}$ (2nd trim.): 0.41 $PM_{2.5}$ abs (p.a.)-$PM_{2.5}$ (3rd trim.): 0.62 $PM_{2.5}$ abs (p.a.)-NO_2 (p.a.): 0.67 $PM_{2.5}$ abs (p.a.)-NO_2 (1st trim.): 0.34 $PM_{2.5}$ abs (p.a.)-NO_2 (2nd trim.): 0.63 $PM_{2.5}$ abs (p.a.)-NO_2 (3rd trim.): 0.36 $PM_{2.5}$ abs (1st trim.)-$PM_{2.5}$ abs (2nd trim.): 0.32 $PM_{2.5}$ abs (1st trim.)-$PM_{2.5}$ abs (3rd trim.): -0.26 $PM_{2.5}$ abs (1st trim.)-$PM_{2.5}$ (p.a.): 0.33 $PM_{2.5}$ abs (1st trim.)-$PM_{2.5}$ (1st trim.): 0.27 $PM_{2.5}$ abs (1st trim.)-$PM_{2.5}$ (2nd trim.): 0.08 $PM_{2.5}$ abs (1st trim.)-$PM_{2.5}$ (3rd trim.): 0.48 $PM_{2.5}$ abs (1st trim.)-NO_2 (p.a.): 0.29 $PM_{2.5}$ abs (1st trim.)-NO_2 (1st trim.): 0.84 $PM_{2.5}$ abs (1st trim.)-NO_2 (2nd trim.): 0.16 $PM_{2.5}$ abs (1st trim.)-NO_2 (3rd trim.): -0.39 $PM_{2.5}$ abs (2nd trim.)-$PM_{2.5}$ abs (3rd trim.): 0.31 $PM_{2.5}$ abs (2nd trim.)-$PM_{2.5}$ (p.a.): 0.48 $PM_{2.5}$ abs (2nd trim.)-$PM_{2.5}$ (1st trim.): 0.53 $PM_{2.5}$ abs (2nd trim.)-$PM_{2.5}$ (2nd trim.): 0.29 $PM_{2.5}$ abs (2nd trim.)-$PM_{2.5}$ (3rd trim.): 0.36 $PM_{2.5}$ abs (2nd trim.)-NO_2 (p.a.): 0.61 $PM_{2.5}$ abs (2nd trim.)-NO_2 (1st trim.): 0.19 $PM_{2.5}$ abs (2nd trim.)-NO_2 (2nd trim.): 0.85 $PM_{2.5}$ abs (2nd trim.)-NO_2 (3rd trim.): 0.17 $PM_{2.5}$ abs (3rd trim.)-$PM_{2.5}$ (p.a.): 0.52 $PM_{2.5}$ abs (3rd trim.)-$PM_{2.5}$ (1st trim.): 0.51 $PM_{2.5}$ abs (3rd trim.)-$PM_{2.5}$ (2nd trim.): 0.41 $PM_{2.5}$ abs (3rd trim.)-$PM_{2.5}$ (3rd trim.): 0.37 $PM_{2.5}$ abs (3rd trim.)-NO_2 (p.a.): 0.40 $PM_{2.5}$ abs (3rd trim.)-NO_2 (1st trim.):-0.34 $PM_{2.5}$ abs (3rd trim.)-NO_2 (2nd trim.): 0.21 $PM_{2.5}$ abs (3rd trim.)-NO_2 (3rd trim.): 0.88	c) 3rd (1.72-1.89) day) 4th (1.89-3.10) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over the whole pregnancy** **Single-pollutant models** Unadjusted models 2nd quartile: 1.19 (0.74, 1.99) 3rd quartile: 1.56 (0.98, 2.50); 4th quartile: 1.52 (0.96, 2.46) Per 0.5 * 10-5/m: 1.25 (0.90, 1.70) Adjusted models 2nd quartile: 1.21 (0.73, 1.97) 3rd quartile: 1.63 (0.98, 2.57); 4th quartile: 1.78 (1.10, 2.70) Per 0.5 * 10-5/m: 1.45 (1.06, 1.87) **Multipollutant models** Adjusted models 2nd quartile: 1.19 (0.70, 2.01) 3rd quartile: 1.55 (0.80, 2.80); 4th quartile: 1.46 (0.67, 2.90) Per 0.5 * 10-5/m: 1.33 (0.76, 2.38) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over the whole pregnancy (adjustment for season of conception)** 4th quartile: 1.72 (1.08, 2.73) Per 0.5 * 10-5/m: 1.38 (0.96, 1.86) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over the whole pregnancy** **Single-pollutant models** (Restricted analysis to $PM_{2.5}$ below the median) Per 0.5 * 10-5/m: 1.67 (0.66, 3.73) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over first trimester of pregnancy** Each trimester separately 2nd quartile: 1.15 (0.73, 1.80) 3rd quartile: 1.01 (0.61, 1.53); 4th quartile: 1.04 (0.70, 1.57) Per 0.5 * 10-5/m: 1.03 (0.82, 1.28) All trimesters adjusted simultaneously 2nd quartile: 0.90 (0.52, 1.58) 3rd quartile: 0.82 (0.45, 1.31); 4th quartile: 0.88 (0.53, 1.42) Per 0.5 * 10-5/m: 1.02 (0.77, 1.29) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over second trimester of pregnancy** Each trimester separately 2nd quartile: 1.33 (0.85, 2.22) 3rd quartile: 1.76 (1.07, 2.91); 4th quartile: 1.83 (1.11, 2.81) Per 0.5 * 10-5/m: 1.27 (1.04, 1.54) All trimesters adjusted simultaneously 2nd quartile: 1.30 (0.77, 2.16) 3rd quartile: 1.63 (0.93, 2.73); 4th quartile: 1.99 (1.12, 3.33) Per 0.5 * 10-5/m: 1.21 (0.93, 1.54) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over third trimester of pregnancy** Each trimester separately 2nd quartile: 1.30 (0.85, 2.09) 3rd quartile: 0.92 (0.55, 1.50); 4th quartile: 1.50 (1.00, 2.27) Per 0.5 * 10-5/m: 1.20 (0.98, 1.44) All trimesters adjusted simultaneously 2nd quartile: 0.99 (0.64, 1.62) 3rd quartile: 0.71 (0.40, 1.20);

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			4th quartile: 1.14 (0.68, 1.91) Per 0.5 * 10-5/m: 1.15 (0.92, 1.42) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over first trimester of pregnancy (adjustment for season of conception)** All trimesters adjusted simultaneously 4th quartile: 0.73 (0.38, 1.38) Per 0.5 * 10-5/m: 0.93 (0.41, 1.32) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over second trimester of pregnancy (adjustment for season of conception)** All trimesters adjusted simultaneously 4th quartile: 2.45 (1.22, 4.77) Per 0.5 * 10-5/m: 1.14 (0.70, 1.64) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over third trimester of pregnancy (adjustment for season of conception)** All trimesters adjusted simultaneously 4th quartile: 1.19 (0.60, 2.48) Per 0.5 * 10-5/m: 1.29 (0.90, 1.75) **Sensitivity analysis** (bootstrapped PR) 2nd quartile: 1.19 (0.76, 1.91) 3rd quartile: 1.52 (0.99, 2.34); 4th quartile: 1.62 (1.06, 2.55) Per 0.5 * 10-5/m: 1.35 (1.01, 1.83) **Estimated increments in prevalence of birth weight <3000 g during exposure 9 mo after birth** Per 0.5 * 10-5/m: 18% (-16%, 57%)
Reference: Wilhelm et al. (2005, 088668) **Period of Study:** 1994-2000 **Location:** Los Angeles County, California, U.S.	**Outcome:** Term low birth weight (LBW) (<2500 g at ≥ 37 completed wk gestation) Vaginal birth <37 completed wk gestation **Age Groups:** LBW: ≥ 37 completed wk Preterm births: <37 completed wk **Study Design:** Cross-sectional study **N:** For LBW: 136,134 For preterm birth: 106,483 **Statistical Analyses:** Logistic regression **Covariates:** Maternal age, maternal race, maternal education, parity, interval since previous live birth, level of prenatal care, infant sex, previous LBW or preterm infant, birth season, other pollutants (not specified in birth weight analyses, also adjusted for gestational age) **Dose-response Investigated?** Yes **Statistical Package:** NR	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h (every 3 days) Entire pregnancy Trimesters of pregnancy Months of pregnancy 6 wk before birth **Mean (SD):** First trimester: 21.9 Third trimester: 21.0 6 wk before birth: 21.0 **Range (Min, Max):** First trimester: 11.8-38.9 Third trimester: 11.8-.38.9 6 wk before birth: 9.9-48.5 **Monitoring Stations:** Zip-code-level analysis: 9 Address-level analysis: 8 **Copollutant (correlation):** First trimester $PM_{2.5}$-CO: 0.57 $PM_{2.5}$-NO_2: 0.73 $PM_{2.5}$-O_3: -0.55 $PM_{2.5}$-PM_{10}: 0.43 Third trimester: $PM_{2.5}$-CO: 0.67 $PM_{2.5}$-NO_2: 0.78 $PM_{2.5}$-O_3: -0.60 $PM_{2.5}$-PM_{10}: 0.52 6 wk before birth: $PM_{2.5}$-CO: 0.63 $PM_{2.5}$-NO_2: 0.74 $PM_{2.5}$-O_3: -0.60 $PM_{2.5}$-PM_{10}: 0.60	**PM Increment:** 1) 10 µg/m^3 2) 3 levels: a) <25 percentile (reference) b) 25%-75 percentile c) ≥ 75 percentile **Incidence of LBW (third trimester exposure)** <17.1 µg/m^3: 2.4 (2.0, 2.8) 17.1 to <24.0 µg/m^3: 2.2 (2.0, 2.5) ≥ 24.0 µg/m^3: 2.1 (1.7, 2.4) **Incidence of preterm birth (first trimester exposure)** <18.0 µg/m^3: 10.6 (9.6, 11.7) 18.0 to <25.4 µg/m^3: 8.8 (8.1, 9.5) ≥ 25.4 µg/m^3: 9.0 (8.1, 10.0) **Incidence of preterm birth (6 wk before birth exposure)** <16.5 µg/m^3: 8.2 (7.4, 9.1) 16.5 to <24.7 µg/m^3: 8.8 (8.2, 9.4) ≥ 24.7 µg/m^3: 9.6 (8.7, 10.5) **Outcome: Preterm birth** **Exposure Period: First trimester of pregnancy** **Address-level analysis:** Single-pollutant model: Distance ≤ 1 mile Per 10 µg/m^3: 0.85 (0.70, 1.02) 18.1 to <25.2 µg/m^3: 0.91 (0.72, 1.16) ≥ 25.2 µg/m^3: 0.83 (0.60, 1.14) Single-pollutant model: 1 <distance ≤ 2 mile Per 10 µg/m^3: 0.85 (0.74, 0.99) 18.3 to <25.2 µg/m^3: 0.81 (0.69, 0.94)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			≥ 25.2 µg/m^3: 0.79 (0.65, 0.97) Multipollutant model1 <distance ≤ 2 mile Per 10 µg/m^3: 1.18 (0.84, 1.65) Single-pollutant model: 2 <distance ≤ 4 mile Per 10 µg/m^3: 0.83 (0.78, 0.88) 18.5 to <24.9 µg/m^3: 0.79 (0.74, 0.85) ≥ 24.9 µg/m^3: 0.76 (0.70, 0.84) **Zip-code-level analysis:** Single-pollutant model: Per 10 µg/m^3: 0.73 (0.67, 0.80) 18.0 to <25.4 µg/m^3: 0.70 (0.61, 0.80) ≥ 25.4 µg/m^3: 0.64 (0.53, 0.76) **Outcome: Preterm birth** **Exposure Period: 6 wk before birth** **Address-level analysis:** Single-pollutant model: Distance ≤ 1 mile Per 10 µg/m^3: 1.09 (0.91, 1.30) 16.8 to <24.1 µg/m^3: 1.21 (0.97, 1.51) ≥ 24.1 µg/m^3: 1.25 (0.93, 1.68) Single-pollutant model: 1 <distance ≤ 2 mile Per 10 µg/m^3: 1.08 (0.97, 1.21) 17.2 to <24.5 µg/m^3: 0.94 (0.82, 1.08) ≥ 24.5 µg/m^3: 1.04 (0.87, 1.24) Single-pollutant model: 2 <distance ≤ 4 mile Per 10 µg/m^3: 1.05 (0.99, 1.10) 17.3 to <24.6 µg/m^3: 1.06 (1.00, 1.13) ≥ 24.6 µg/m^3: 1.08 (0.99, 1.17) **Zip-code-level analysis** Single-pollutant model: Per 10 µg/m^3: 1.10 (1.00, 1.21) 16.5 to <24.7 µg/m^3: 1.06 (0.94, 1.20) ≥ 24.7 µg/m^3: 1.19 (1.02, 1.40) **(See Notes)** Multipollutant model Per 10 µg/m^3: 1.12 (0.90, 1.40) ≥ 24.6 µg/m^3: 1.12 (0.82, 1.52) **Notes:** In the table, the 75 percentile is noted as 24.7 µg/m^3. However, the text notes the 75 percentile as 24.3 µg/m^3.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Woodruff et al. (2006, 088758) **Period of Study:** 1999-2000 **Location:** California	**Outcome (ICD10):** SIDS (R95) Respiratory mortality (J00-J99) Bronchopulmonary dysplasia (P27.1) External accidents (V01-Y98) Ill-defined and unspecified causes of mortality (R99) **Age Groups:** >28 days old **Study Design:** Matched case-control (matched on date of birth and birth weight) **N:** 3877 infants **Statistical Analyses:** Conditional logistic regression **Covariates:** Maternal race, education, parity, age, marital status **Dose-response Investigated?** Yes **Statistical Package:** STATA	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 hrs (every 6 days) (time period between birth and post neonatal death for the infant who died and the same period for its four matched surviving infants) **Percentiles:** Infants who died of all causes (cases) **25th:** 13.4 **50th(Median):** 19.2 **75th:** 23.6 Matched controls **25th:** 13.5 **50th(Median):** 18.4 **75th:** 22.7 **Monitoring Stations:** 73 (from 39 counties)	**PM Increment:** 10 µg/m^3 **RR Estimate [Lower CI, Upper CI] lag:** All-cause mortality: Unadjusted: 1.15 (1.00, 1.32) Adjusted: 1.07 (0.93, 1.24) Cause-specific mortality: Respiratory (all): Unadjusted: 2.15 (1.15, 4.02) Adjusted: 2.13 (1.12, 4.05) Respiratory (excluding deaths due to BPD): Adjusted: 1.42 (0.66, 3.03) Respiratory (BPD alone): Unadjusted: 6.00 (1.40, 27.76) Respiratory (low birth weight infants only): Unadjusted: 3.09 (1.14, 8.40) Respiratory (normal birth weight infants only): Unadjusted: 1.66 (0.74, 3.70) Respiratory (with matched $PM_{2.5}$ avgd over all monitors in county) Adjusted: 2.28 (0.94, 5.52) Respiratory (averaging all $PM_{2.5}$ measurements in county over the 2-yr study period): Adjusted: 2.26 (0.83, 6.21) SIDS: Unadjusted: 0.86 (0.61, 1.22) Adjusted: 0.82 (0.55, 1.23) SIDS (includes ICD10 code R99: ill-defined and unspecified causes of mortality): Adjusted: 1.03 (0.79, 1.35) External causes: Unadjusted: 0.91 (0.56, 1.47) Adjusted: 0.83 (0.50, 1.39) Compare against the lowest quartile, estimates for respiratory-specific mortality were provided: 2nd quartile: 1.28 (0.47, 3.51) 3rd quartile: 1.75 (0.65, 4.72) 4th quartile: 2.35 (0.85, 6.54)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Woodruff et al. (2008, 098386) **Period of Study:** 1999-2002 **Location:** U.S. counties with >250,000 residents (96 counties)	**Outcome (ICD10):** Postneonatal deaths: Respiratory mortality (J000-99, plus bronchopulmonary dysplasia [BPD] P27.1) SIDS (R95) Ill-defined causes (R99) All other deaths evaluated as a control category **Age Groups:** Infants aged >28 days and <1 yr **Study Design:** Cross-sectional **N:** 3,583,495 births (6,639 post neonatal deaths) **Statistical Analyses:** Logistic GEE (exchangeable correlation structure) **Covariates:** maternal race/ethnicity, marital status, age, education, primiparity, county-level poverty and per capita income levels, yr and month of birth dummy variables to account for time trend and seasonal effects, and region of the country sensitivity analyses performed among only those mothers with smoking information (adjustment for smoking had no effect on the estimates) **Season:** Adjusted for yr and month of birth dummy variables to account for time trend and seasonal effects **Dose-response Investigated?** Evaluated the appropriateness of a linear form from analysis based on quartiles of exposure and concluded that linear form was appropriate (data not shown) **Statistical Package:** SAS	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Measured continuously for 24 h once every 6 days exposure assigned by calculating avg concentration of pollutant during first 2 mo of life **Median and IQR (25th-75th percentile):** Survivors: 14.8 (11.7-18.7) All causes of death: 14.9 (12.0-18.6) Respiratory: 14.8 (11.5-18.5) SIDS: 14.5 (12.0-17.5) SIDS + ill-defined: 14.8 (12.1-18.5) Other causes: 14.9 (12.0-18.6) **Percentiles:** See above **PM Component:** Not assessed, but controlled for region of the country to account for PM composition variation **Monitoring Stations:** NR **Copollutant (correlation):** PM_{10} (r = 0.34) $PM_{2.5}$ CO (r = 0.35) SO_2 (r = 0.21) O_3 (r = -0.10) **Notes:** Monthly avg calculated if there were at least 3 available measures for PM Assigned exposures using the avg concentration of the county of residence	**PM Increment:** IQR (7 $\mu g/m^3$) **Effect Estimate [Lower CI, Upper CI]:** Adjusted ORs for single pollutant models All causes: 1.04 (0.98, 1.11) Respiratory: 1.11 (0.96, 1.29) SIDS: 1.01 (0.86, 1.20) Ill-defined + SIDS: 1.06 (0.97, 1.17) Other causes: 1.03 (0.96, 1.12) Adjusted ORs for multipollutant models (including CO, O_3, SO_2) Respiratory: 1.05 (0.89, 1.24) SIDS: 1.04 (0.87, 1.23) OR for respiratory deaths assessing exposure as quartiles Highest vs. Lowest quartile: 1.39 (1.04, 1.85)

[1]All units expressed in $\mu g/m^3$ unless otherwise specified.

E.8. Long-Term Exposure and Mortality

Table E-30. Long-term exposure-mortality - PM_{10}.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: (Breitner et al., 2009, 188439) **Period of Study:** Oct 1991-Mar 2002 **Location:** Efurt, Germany	**Outcome:** Mortality, excluding infants and ICD-9 ≥ 800 **Study Design:** Time-series **Covariates:** Seasonal and weekday variations, influenza epidemics, air temperature, relative humidity **Statistical Analysis:** Semiparametric Poisson regression, polynomial distributed lag (PDL) **Statistical Package:** R **Age Groups:** All	**Pollutant:** PM_{10} **Averaging Time:** Daily **Mean (SD) Unit:** 1 (10/1/1991-8/31/1995): 50.6 ± 32.2 µg/m^3 2 (9/1/1995-2/28/1998): 41.1 ± 28.4 µg/m^3 3 (3/1/1998-3/31/2002): 24.3 ± 15.4 µg/m^3 Total: 38.0 ±28.3 µg/m^3 **Range (Min, Max):** NR **Copollutant:** NO_2, CO, UFP	**Increment:** IQR **Relative Risk (95% CI) Lag** New City Limits 6-day IQR: 17.2 PDL: 0.997 (0.972-1.022) Mean of lags 0-5: 0.995 (0.971-1.019) Old City Limits 6-day IQR: 17.2 PDL: 1.004 (0.978-1.031) Mean of lags 0-5: 1.001 (0.976-1.027) New City Limits 15-day IQR: 14.5 PDL: 1.008 (0.982-1.036) Mean of lags 0-14: 1.006 (0.981-1.032) Old City Limits 15-day IQR: 14.5 PDL: 1.019 (0.991-1.048) Mean of lags 0-14: 1.017 (0.990-1.044) Multiday Ma, 6-day Overall IQR: 24.2 Overall RR (95% CI): 0.998 (0.976-1.021) Period 1: 0.996 (0.969-1.024) Period 2: 1.013 (0.972-1.056) Period 3: 0.949 (0.897-1.004) Multiday Ma, 15-day Overall IQR: 22.3 Overall RR (95% CI): 1.020 (0.993-1.093) Period 1: 1.017 (0.984-1.051) Period 2: 1.012 (0.973-1.071) Period 3: 0.978 (0.911-1.051)
Reference: (Slama et al., 2007, 093216) **Period of Study:** Jan 1998-Jan 1999 **Location:** Munich, Germany	**Outcome:** Birth weight offspring at term **Study Design:** Cohort study **N:** 1016 births **Statistical Analyses:** Poisson model **Covariates:** Maternal passive smoking, maternal age, gestational duration, sex of child, parity, maternal education, maternal size, prepregnancy weight, other pollutants ($PM_{2.5}$, $PM_{2.5}$ absorbance, NO_2), season of conception **Dose-response Investigated?** Yes **Statistical Package:** STATA	**Pollutant:** $PM_{2.5}$ (estimated based on larger PM size fractions) **Averaging Time:** Entire pregnancy period and trimesters **Mean (SD):** 14.4 **Percentiles: 25th:** 13.5 **50th(Median):** 14.4 **75th:** 15.4 **Monitoring Stations:** Spatial component: 40 Temporal component: 1 **Copollutant (correlation):** p.a. = pregnancy avg trim. = trimester $PM_{2.5}$ (p.a.)-$PM_{2.5}$ (1st trim.): 0.85 $PM_{2.5}$ (p.a.)-$PM_{2.5}$ (2nd trim.): 0.77 $PM_{2.5}$ (p.a.)-$PM_{2.5}$ (3rd trim.): 0.87 $PM_{2.5}$ (p.a.)-NO_2 (p.a.): 0.45 $PM_{2.5}$ (p.a.)-NO_2 (1st trim.): 0.18 $PM_{2.5}$ (p.a.)-NO_2 (2nd trim.): 0.32	**PM Increment:** 1) 1 µg/m^3 2) Quartiles: a) 1st (reference) (7.2-13.5 µg/m^3) b) 2nd (13.5-14.4 µg/m^3) c) 3rd (14.4-15.4 µg/m^3) day) 4th (15.41-17.5 µg/m^3) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over the whole pregnancy** **Single-pollutant models** Unadjusted models 2nd quartile: 1.07 (0.65, 1.73); 3rd quartile: 1.38 (0.91, 2.09) 4th quartile: 1.45 (0.92, 2.25) Per 1 µg/m^3: 1.06 (0.95, 1.19) Adjusted models 2nd quartile: 1.08 (0.63, 1.82); 3rd quartile: 1.34 (0.86, 2.13) 4th quartile: 1.73 (1.15, 2.69); Per 1 µg/m^3: 1.13 (1.00, 1.29) **Multipollutant models** Adjusted models 2nd quartile: 1.01 (0.57, 1.85) 3rd quartile: 1.12 (0.64, 1.87) 4th quartile: 1.36 (0.72, 2.45); Per 1 µg/m^3: 1.07 (0.91, 1.26) **Single-pollutant models** (restricted

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
		$PM_{2.5}$ (p.a.)-NO_2 (3rd trim.): 0.37 $PM_{2.5}$ (1st trim.)-$PM_{2.5}$ (2nd trim.): 0.40 $PM_{2.5}$ (1st trim.)-$PM_{2.5}$ (3rd trim.): 0.68 $PM_{2.5}$ (1st trim.)-NO_2 (p.a.): 0.48 $PM_{2.5}$ (1st trim.)-NO_2 (1st trim.): 0.15 $PM_{2.5}$ (1st trim.)-NO_2 (2nd trim.): 0.41 $PM_{2.5}$ (1st trim.)-NO_2 (3rd trim.): 0.39 $PM_{2.5}$ (2nd trim.)-$PM_{2.5}$ (3rd trim.): 0.51 $PM_{2.5}$ (2nd trim.)-NO_2 (p.a.): 0.23 $PM_{2.5}$ (2nd trim.)-NO_2 (1st trim.): -0.03 $PM_{2.5}$ (2nd trim.)-NO_2 (2nd trim.): 0.17 $PM_{2.5}$ (2nd trim.)-NO_2 (3rd trim.): 0.30 $PM_{2.5}$ (3rd trim.)-NO_2 (p.a.): 0.39 $PM_{2.5}$ (3rd trim.)-NO_2 (1st trim.): 0.33 $PM_{2.5}$ (3rd trim.)-NO_2 (2nd trim.): 0.21 $PM_{2.5}$ (3rd trim.)-NO_2 (3rd trim.): 0.23 $PM_{2.5}$ (p.a.)- $PM_{2.5}$ absorbance (p.a.): 0.69 $PM_{2.5}$ (p.a.)- $PM_{2.5}$ abs (1st trim.): 0.33 $PM_{2.5}$ (p.a.)- $PM_{2.5}$ abs (2nd trim.): 0.48 $PM_{2.5}$ (p.a.)- $PM_{2.5}$ abs (3rd trim.): 0.52 $PM_{2.5}$ (1st trim.)- $PM_{2.5}$ abs (p.a.): 0.68 $PM_{2.5}$ (1st trim.)- $PM_{2.5}$ abs (1st trim.): 0.27 $PM_{2.5}$ (1st trim.)- $PM_{2.5}$ abs (2nd trim.): 0.53 $PM_{2.5}$ (1st trim.)- $PM_{2.5}$ abs (3rd trim.): 0.51 $PM_{2.5}$ (2nd trim.)- $PM_{2.5}$ abs(p.a.): 0.41 $PM_{2.5}$ (2nd trim.)- $PM_{2.5}$ abs (1st trim.): 0.08 $PM_{2.5}$ (2nd trim.)- $PM_{2.5}$ abs (2nd trim.): 0.29 $PM_{2.5}$ (2nd trim.)- $PM_{2.5}$ abs (3rd trim.): 0.41 $PM_{2.5}$ (3rd trim.)- $PM_{2.5}$ abs (p.a.): 0.62 $PM_{2.5}$ (3rd trim.)- $PM_{2.5}$ abs (1st trim.): 0.48 $PM_{2.5}$ (3rd trim.)- $PM_{2.5}$ abs (2nd trim.): 0.36 $PM_{2.5}$ (3rd trim.)- $PM_{2.5}$ abs (3rd trim.): 0.37	Analysis to $PM_{2.5}$ absorbance below the median) Per 1 µg/m^3: 1.15 (0.89, 1.52) **Prevalence ratios (PRs) of birth weight <3000 g** **Multipollutant models (simultaneous adjustment of 3rd trimester** $PM_{2.5}$ **and whole pregnancy** $PM_{2.5}$**)** $PM_{2.5}$ (whole pregnancy) Per 1 µg/m^3: 0.96 (0.75, 1.19) $PM_{2.5}$ (3rd trimester) Per 1 µg/m^3: 1.17 (0.98, 1.40) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over the whole pregnancy (adjustment for season of conception)** 4th quartile: 1.68 (1.05, 2.75); Per 1 µg/m^3: 1.12 (0.97, 1.28) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over first trimester of pregnancy** Each trimester separately 2nd quartile: 1.14 (0.74, 1.96); 3rd quartile: 1.28 (0.84, 2.10) 4th quartile: 1.65 (1.02, 2.60) Per 1 µg/m^3: 1.10 (0.99, 1.20) All trimesters adjusted simultaneously 2nd quartile: 0.97 (0.60, 1.73); 3rd quartile: 0.98 (0.57, 1.75) 4th quartile: 1.22 (0.71, 2.18) Per 1 µg/m^3: 1.03 (0.90, 1.17) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over second trimester of pregnancy** Each trimester separately 2nd quartile: 0.83 (0.52, 1.32); 3rd quartile: 1.08 (0.71, 1.60) 4th quartile: 0.94 (0.61, 1.47) Per 1 µg/m^3: 1.01 (0.92, 1.12) All trimesters adjusted simultaneously 2nd quartile: 0.75 (0.46, 1.24) 3rd quartile: 0.86 (0.56, 1.30); 4th quartile: 0.75 (0.48, 1.23) Per 1 µg/m^3: 0.94 (0.84, 1.06) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over third trimester of pregnancy** Each trimester separately 2nd quartile: 1.30 (0.80, 2.17) 3rd quartile: 1.44 (0.85, 2.27) 4th quartile: 1.90 (1.20, 2.82) Per 1 µg/m^3: 1.14 (1.02, 1.24) All trimesters adjusted simultaneously 2nd quartile: 1.34 (0.79, 2.30) 3rd quartile: 1.48 (0.86, 2.58) 4th quartile: 1.91 (1.00, 3.20) Per 1 µg/m^3: 1.14 (0.99, 1.29) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over third trimester of pregnancy (adjustment for season of conception)** All trimesters adjusted simultaneously Per 1 µg/m^3: 1.25 (1.04, 1.50) **Sensitivity analysis**(bootstrapped PR) 2nd quartile: 0.98 (0.63, 1.61); 3rd quartile: 1.22 (0.82, 2.02) 4th quartile: 1.57 (1.02, 2.57) Per 1 µg/m^3: 1.11 (0.98, 1.27) **Estimated increments in prevalence of birth weight of <3000 g during exposure 9 mo after birth**

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Per 1 µg/m^3: 7% (-7%, 22%)
Reference: (Slama et al., 2007, 093216) **Period of Study:** Jan 1998-Jan 1999 **Location:** Munich, Germany	**Outcome:** Birth weight offspring at term **Study Design:** Cohort study **N:** 1016 births **Statistical Analyses:** Poisson model **Covariates:** Maternal passive smoking, maternal age, gestational duration, sex of child, parity, maternal education, maternal size, prepregnancy weight, other pollutants ($PM_{2.5}$, $PM_{2.5}$ absorbance, NO_2), season of conception **Dose-response Investigated?** Yes **Statistical Package:** STATA	**Pollutant:** $PM_{2.5}$ absorbance (estimated) **Averaging Time:** Entire pregnancy period and trimesters **Mean (SD):** 1.76 * **Percentiles: 25th:** 1.61* **50th(Median):** 1.72* **75th:** 1.89 * **Unit (i.e. µg/m^3):** 10-5/m **Monitoring Stations:** Spatial component: 40 Temporal component: 1 **Copollutant (correlation):** p.a. = pregnancy avg trim. = trimester abs = absorbance $PM_{2.5}$ abs (p.a.)-$PM_{2.5}$ abs (1st trim.): 0.54 $PM_{2.5}$ abs (p.a.)-$PM_{2.5}$ abs (2nd trim.): 0.84 $PM_{2.5}$ abs (p.a.)-$PM_{2.5}$ abs (3rd trim.): 0.55 $PM_{2.5}$ abs (p.a.)-$PM_{2.5}$ (p.a.): 0.69 $PM_{2.5}$ abs (p.a.)-$PM_{2.5}$ (1st trim.): 0.68 $PM_{2.5}$ abs (p.a.)-$PM_{2.5}$ (2nd trim.): 0.41 $PM_{2.5}$ abs (p.a.)-$PM_{2.5}$ (3rd trim.): 0.62 $PM_{2.5}$ abs (p.a.)-NO_2 (p.a.): 0.67 $PM_{2.5}$ abs (p.a.)-NO_2 (1st trim.): 0.34 $PM_{2.5}$ abs (p.a.)-NO_2 (2nd trim.): 0.63 $PM_{2.5}$ abs (p.a.)-NO_2 (3rd trim.): 0.36 $PM_{2.5}$ abs (1st trim.)-$PM_{2.5}$ abs (2nd trim.): 0.32 $PM_{2.5}$ abs (1st trim.)-$PM_{2.5}$ abs (3rd trim.): -0.26 $PM_{2.5}$ abs (1st trim.)-$PM_{2.5}$ (p.a.): 0.33 $PM_{2.5}$ abs (1st trim.)-$PM_{2.5}$ (1st trim.): 0.27 $PM_{2.5}$ abs (1st trim.)-$PM_{2.5}$ (2nd trim.): 0.08 $PM_{2.5}$ abs (1st trim.)-$PM_{2.5}$ (3rd trim.): 0.48 $PM_{2.5}$ abs (1st trim.)-NO_2 (p.a.): 0.29 $PM_{2.5}$ abs (1st trim.)-NO_2 (1st trim.): 0.84 $PM_{2.5}$ abs (1st trim.)-NO_2 (2nd trim.): 0.16 $PM_{2.5}$ abs (1st trim.)-NO_2 (3rd trim.): -0.39 $PM_{2.5}$ abs (2nd trim.)-$PM_{2.5}$ abs (3rd trim.): 0.31 $PM_{2.5}$ abs (2nd trim.)-$PM_{2.5}$ (p.a.): 0.48 $PM_{2.5}$ abs (2nd trim.)-$PM_{2.5}$ (1st trim.): 0.53 $PM_{2.5}$ abs (2nd trim.)-$PM_{2.5}$ (2nd trim.): 0.29 $PM_{2.5}$ abs (2nd trim.)-$PM_{2.5}$ (3rd trim.): 0.36 $PM_{2.5}$ abs (2nd trim.)-NO_2 (p.a.): 0.61 $PM_{2.5}$ abs (2nd trim.)-NO_2 (1st trim.): 0.19 $PM_{2.5}$ abs (2nd trim.)-NO_2 (2nd trim.): 0.85 $PM_{2.5}$ abs (2nd trim.)-NO_2 (3rd trim.): 0.17 $PM_{2.5}$ abs (3rd trim.)-$PM_{2.5}$ (p.a.): 0.52 $PM_{2.5}$ abs (3rd trim.)-$PM_{2.5}$ (1st trim.): 0.51 $PM_{2.5}$ abs (3rd trim.)-$PM_{2.5}$ (2nd trim.): 0.41 $PM_{2.5}$ abs (3rd trim.)-$PM_{2.5}$ (3rd trim.): 0.37 $PM_{2.5}$ abs (3rd trim.)-NO_2 (p.a.): 0.40 $PM_{2.5}$ abs (3rd trim.)-NO_2 (1st trim.): -	**PM Increment:** 1) 0.5 * 10-5/m 2) Quartiles: a) 1st (reference) (1.29-1.61) b) 2nd (1.61-1.72) c) 3rd (1.72-1.89) day) 4th (1.89-3.10) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over the whole pregnancy** **Single-pollutant models** Unadjusted models 2nd quartile: 1.19 (0.74, 1.99) 3rd quartile: 1.56 (0.98, 2.50); 4th quartile: 1.52 (0.96, 2.46) Per 0.5 * 10-5/m: 1.25 (0.90, 1.70) Adjusted models 2nd quartile: 1.21 (0.73, 1.97) 3rd quartile: 1.63 (0.98, 2.57); 4th quartile: 1.78 (1.10, 2.70) Per 0.5 * 10-5/m: 1.45 (1.06, 1.87) **Multipollutant models** Adjusted models 2nd quartile: 1.19 (0.70, 2.01) 3rd quartile: 1.55 (0.80, 2.80); 4th quartile: 1.46 (0.67, 2.90) Per 0.5 * 10-5/m: 1.33 (0.76, 2.38) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over the whole pregnancy (adjustment for season of conception)** 4th quartile: 1.72 (1.08, 2.73) Per 0.5 * 10-5/m: 1.38 (0.96, 1.86) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over the whole pregnancy** **Single-pollutant models** (Restricted analysis to $PM_{2.5}$ below the median) Per 0.5 * 10-5/m: 1.67 (0.66, 3.73) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over first trimester of pregnancy** Each trimester separately 2nd quartile: 1.15 (0.73, 1.80) 3rd quartile: 1.01 (0.61, 1.53); 4th quartile: 1.04 (0.70, 1.57) Per 0.5 * 10-5/m: 1.03 (0.82, 1.28) All trimesters adjusted simultaneously 2nd quartile: 0.90 (0.52, 1.58) 3rd quartile: 0.82 (0.45, 1.31); 4th quartile: 0.88 (0.53, 1.42) Per 0.5 * 10-5/m: 1.02 (0.77, 1.29) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over second trimester of pregnancy** Each trimester separately 2nd quartile: 1.33 (0.85, 2.22) 3rd quartile: 1.76 (1.07, 2.91); 4th quartile: 1.83 (1.11, 2.81) Per 0.5 * 10-5/m: 1.27 (1.04, 1.54) All trimesters adjusted simultaneously 2nd quartile: 1.30 (0.77, 2.16) 3rd quartile: 1.63 (0.93, 2.73); 4th quartile: 1.99 (1.12, 3.33) Per 0.5 * 10-5/m: 1.21 (0.93, 1.54) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over third trimester of pregnancy** Each trimester separately 2nd quartile: 1.30 (0.85, 2.09) 3rd quartile: 0.92 (0.55, 1.50);

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
		0.34 $PM_{2.5}$ abs (3rd trim.)-NO_2 (2nd trim.): 0.21 $PM_{2.5}$ abs (3rd trim.)-NO_2 (3rd trim.): 0.88	4th quartile: 1.50 (1.00, 2.27) Per 0.5 * 10-5/m: 1.20 (0.98, 1.44) All trimesters adjusted simultaneously 2nd quartile: 0.99 (0.64, 1.62) 3rd quartile: 0.71 (0.40, 1.20); 4th quartile: 1.14 (0.68, 1.91) Per 0.5 * 10-5/m: 1.15 (0.92, 1.42) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over first trimester of pregnancy (adjustment for season of conception)** All trimesters adjusted simultaneously 4th quartile: 0.73 (0.38, 1.38) Per 0.5 * 10-5/m: 0.93 (0.41, 1.32) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over second trimester of pregnancy (adjustment for season of conception)** All trimesters adjusted simultaneously 4th quartile: 2.45 (1.22, 4.77) Per 0.5 * 10-5/m: 1.14 (0.70, 1.64) **Prevalence ratios (PRs) of birth weight <3000 g during exposure over third trimester of pregnancy (adjustment for season of conception)** All trimesters adjusted simultaneously 4th quartile: 1.19 (0.60, 2.48) Per 0.5 * 10-5/m: 1.29 (0.90, 1.75) **Sensitivity analysis** (bootstrapped PR) 2nd quartile: 1.19 (0.76, 1.91) 3rd quartile: 1.52 (0.99, 2.34); 4th quartile: 1.62 (1.06, 2.55) Per 0.5 * 10-5/m: 1.35 (1.01, 1.83) **Estimated increments in prevalence of birth weight <3000 g during exposure 9 mo after birth** Per 0.5 * 10-5/m: 18% (-16%, 57%)
Reference: Wilhelm et al. (2005, 088668) **Period of Study:** 1994-2000 **Location:** Los Angeles County, California, U.S.	**Outcome:** Term low birth weight (LBW) (<2500 g at ≥ 37 completed wk gestation) Vaginal birth <37 completed wk gestation **Age Groups:** LBW: ≥ 37 completed wk Preterm births: <37 completed wk **Study Design:** Cross-sectional study **N:** For LBW: 136,134 For preterm birth: 106,483 **Statistical Analyses:** Logistic regression **Covariates:** Maternal age, maternal race, maternal education, parity, interval since previous live birth, level of prenatal care, infant sex, previous LBW or preterm infant, birth season, other pollutants (not specified in birth weight analyses, also adjusted for gestational age) **Dose-response Investigated?** Yes **Statistical Package:** NR	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h (every 3 days) Entire pregnancy Trimesters of pregnancy Months of pregnancy 6 wk before birth **Mean (SD):** First trimester: 21.9 Third trimester: 21.0 6 wk before birth: 21.0 **Range (Min, Max):** First trimester: 11.8-38.9 Third trimester: 11.8-.38.9 6 wk before birth: 9.9-48.5 **Monitoring Stations:** Zip-code-level analysis: 9 Address-level analysis: 8 **Copollutant (correlation):** First trimester $PM_{2.5}$-CO: 0.57 $PM_{2.5}$-NO_2: 0.73 $PM_{2.5}$-O_3: -0.55 $PM_{2.5}$-PM_{10}: 0.43 Third trimester: $PM_{2.5}$-CO: 0.67 $PM_{2.5}$-NO_2: 0.78 $PM_{2.5}$-O_3: -0.60 $PM_{2.5}$-PM_{10}: 0.52 6 wk before birth:	**PM Increment:** 1) 10 µg/m^3 2) 3 levels: a) <25 percentile (reference) b) 25%-75 percentile c) ≥ 75 percentile **Incidence of LBW (third trimester exposure)** <17.1 µg/m^3: 2.4 (2.0, 2.8) 17.1 to <24.0 µg/m^3: 2.2 (2.0, 2.5) ≥ 24.0 µg/m^3: 2.1 (1.7, 2.4) **Incidence of preterm birth (first trimester exposure)** <18.0 µg/m^3: 10.6 (9.6, 11.7) 18.0 to <25.4 µg/m^3: 8.8 (8.1, 9.5) ≥ 25.4 µg/m^3: 9.0 (8.1, 10.0) **Incidence of preterm birth (6 wk before birth exposure)** <16.5 µg/m^3: 8.2 (7.4, 9.1) 16.5 to <24.7 µg/m^3: 8.8 (8.2, 9.4) ≥ 24.7 µg/m^3: 9.6 (8.7, 10.5) **Outcome: Preterm birth** **Exposure Period: First trimester of pregnancy** **Address-level analysis:** Single-pollutant model: Distance ≤ 1 mile Per 10 µg/m^3: 0.85 (0.70, 1.02) 18.1 to <25.2 µg/m^3:

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
		$PM_{2.5}$-CO: 0.63 $PM_{2.5}$-NO_2: 0.74 $PM_{2.5}$-O_3: -0.60 $PM_{2.5}$-PM_{10}: 0.60	0.91 (0.72, 1.16) ≥ 25.2 µg/m^3: 0.83 (0.60, 1.14) Single-pollutant model: 1 <distance ≤ 2 mile Per 10 µg/m^3: 0.85 (0.74, 0.99) 18.3 to <25.2 µg/m^3: 0.81 (0.69, 0.94) ≥ 25.2 µg/m^3: 0.79 (0.65, 0.97) Multipollutant model1 <distance ≤ 2 mile Per 10 µg/m^3: 1.18 (0.84, 1.65) Single-pollutant model: 2 <distance ≤ 4 mile Per 10 µg/m^3: 0.83 (0.78, 0.88) 18.5 to <24.9 µg/m^3: 0.79 (0.74, 0.85) ≥ 24.9 µg/m^3: 0.76 (0.70, 0.84) **Zip-code-level analysis:** Single-pollutant model: Per 10 µg/m^3: 0.73 (0.67, 0.80) 18.0 to <25.4 µg/m^3: 0.70 (0.61, 0.80) ≥ 25.4 µg/m^3: 0.64 (0.53, 0.76) **Outcome: Preterm birth** **Exposure Period: 6 wk before birth** **Address-level analysis:** Single-pollutant model: Distance ≤ 1 mile Per 10 µg/m^3: 1.09 (0.91, 1.30) 16.8 to <24.1 µg/m^3: 1.21 (0.97, 1.51) ≥ 24.1 µg/m^3: 1.25 (0.93, 1.68) Single-pollutant model: 1 <distance ≤ 2 mile Per 10 µg/m^3: 1.08 (0.97, 1.21) 17.2 to <24.5 µg/m^3: 0.94 (0.82, 1.08) ≥ 24.5 µg/m^3: 1.04 (0.87, 1.24) Single-pollutant model: 2 <distance ≤ 4 mile Per 10 µg/m^3: 1.05 (0.99, 1.10) 17.3 to <24.6 µg/m^3: 1.06 (1.00, 1.13) ≥ 24.6 µg/m^3: 1.08 (0.99, 1.17) **Zip-code-level analysis** Single-pollutant model: Per 10 µg/m^3: 1.10 (1.00, 1.21) 16.5 to <24.7 µg/m^3: 1.06 (0.94, 1.20) ≥ 24.7 µg/m^3: 1.19 (1.02, 1.40) **(See Notes)** Multipollutant model Per 10 µg/m^3: 1.12 (0.90, 1.40) ≥ 24.6 µg/m^3: 1.12 (0.82, 1.52) **Notes:** In the table, the 75 percentile is noted as 24.7 µg/m^3. However, the text notes the 75 percentile as 24.3 µg/m^3.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Woodruff et al. (2006, 088758) **Period of Study:** 1999-2000 **Location:** California	**Outcome (ICD10):** SIDS (R95) Respiratory mortality (J00-J99) Bronchopulmonary dysplasia (P27.1) External accidents (V01-Y98) Ill-defined and unspecified causes of mortality (R99) **Age Groups:** >28 days old **Study Design:** Matched case-control (matched on date of birth and birth weight) **N:** 3877 infants **Statistical Analyses:** Conditional logistic regression **Covariates:** Maternal race, education, parity, age, marital status **Dose-response Investigated?** Yes **Statistical Package:** STATA	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h (every 6 days) (time period between birth and post neonatal death for the infant who died and the same period for its four matched surviving infants) **Percentiles:** Infants who died of all causes (cases) **25th:** 13.4 **50th(Median):** 19.2 **75th:** 23.6 Matched controls **25th:** 13.5 **50th(Median):** 18.4 **75th:** 22.7 **Monitoring Stations:** 73 (from 39 counties)	**PM Increment:** 10 $\mu g/m^3$ **RR Estimate [Lower CI, Upper CI] lag:** All-cause mortality: Unadjusted: 1.15 (1.00, 1.32) Adjusted: 1.07 (0.93, 1.24) Cause-specific mortality: Respiratory (all): Unadjusted: 2.15 (1.15, 4.02) Adjusted: 2.13 (1.12, 4.05) Respiratory (excluding deaths due to BPD): Adjusted: 1.42 (0.66, 3.03) Respiratory (BPD alone): Unadjusted: 6.00 (1.40, 27.76) Respiratory (low birth weight infants only): Unadjusted: 3.09 (1.14, 8.40) Respiratory (normal birth weight infants only): Unadjusted: 1.66 (0.74, 3.70) Respiratory (with matched $PM_{2.5}$ avgd over all monitors in county) Adjusted: 2.28 (0.94, 5.52) Respiratory (averaging all $PM_{2.5}$ measurements in county over the 2-yr study period): Adjusted: 2.26 (0.83, 6.21) SIDS: Unadjusted: 0.86 (0.61, 1.22) Adjusted: 0.82 (0.55, 1.23) SIDS (includes ICD10 code R99: ill-defined and unspecified causes of mortality): Adjusted: 1.03 (0.79, 1.35) External causes: Unadjusted: 0.91 (0.56, 1.47) Adjusted: 0.83 (0.50, 1.39) Compare against the lowest quartile, estimates for respiratory-specific mortality were provided: 2nd quartile: 1.28 (0.47, 3.51) 3rd quartile: 1.75 (0.65, 4.72) 4th quartile: 2.35 (0.85, 6.54)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Woodruff et al. (2008, 098386) **Period of Study:** 1999-2002 **Location:** U.S. counties with >250,000 residents (96 counties)	**Outcome (ICD10):** Postneonatal deaths: Respiratory mortality (J000-99, plus bronchopulmonary dysplasia [BPD] P27.1) SIDS (R95) Ill-defined causes (R99) All other deaths evaluated as a control category **Age Groups:** Infants aged >28 days and <1 yr **Study Design:** Cross-sectional **N:** 3,583,495 births (6,639 post neonatal deaths) **Statistical Analyses:** Logistic GEE (exchangeable correlation structure) **Covariates:** Maternal race/ethnicity, marital status, age, education, primiparity, county-level poverty and per capita income levels, yr and month of birth dummy variables to account for time trend and seasonal effects, and region of the country sensitivity analyses performed among only those mothers with smoking information (adjustment for smoking had no effect on the estimates) **Season:** Adjusted for yr and month of birth dummy variables to account for time trend and seasonal effects **Dose-response Investigated?** Evaluated the appropriateness of a linear form from analysis based on quartiles of exposure and concluded that linear form was appropriate (data not shown) **Statistical Package:** SAS	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Measured continuously for 24 h once every 6 days Exposure assigned by calculating avg concentration of pollutant during first 2 mo of life **Median and IQR (25th-75th percentile):** Survivors: 14.8 (11.7-18.7) All causes of death: 14.9 (12.0-18.6) Respiratory: 14.8 (11.5-18.5) SIDS: 14.5 (12.0-17.5) SIDS + ill-defined: 14.8 (12.1-18.5) Other causes: 14.9 (12.0-18.6) **Percentiles:** See above **PM Component:** Not assessed, but controlled for region of the country to account for PM composition variation **Monitoring Stations:** NR **Copollutant (correlation):** PM_{10} (r = 0.34) $PM_{2.5}$ CO (r = 0.35) SO_2 (r = 0.21) O_3 (r = -0.10) **Notes:** Monthly avg calculated if there were at least 3 available measures for PM Assigned exposures using the avg concentration of the county of residence	**PM Increment:** IQR (7 µg/m^3) **Effect Estimate [Lower CI, Upper CI]:** Adjusted ORs for single pollutant models All causes: 1.04 (0.98, 1.11) Respiratory: 1.11 (0.96, 1.29) SIDS: 1.01 (0.86, 1.20) Ill-defined + SIDS: 1.06 (0.97, 1.17) Other causes: 1.03 (0.96, 1.12) Adjusted ORs for multipollutant models (including CO, O_3, SO_2) Respiratory: 1.05 (0.89, 1.24) SIDS: 1.04 (0.87, 1.23) OR for respiratory deaths assessing exposure as quartiles Highest vs. Lowest quartile: 1.39 (1.04, 1.85)

[1]All units expressed in µg/m^3 unless otherwise specified.

E.9. Long-Term Exposure and Mortality

Table E-31. Long-term exposure-mortality - PM_{10}.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: (Breitner et al., 2009, 188439) **Period of Study:** Oct 1991-Mar 2002 **Location:** Efurt, Germany	**Outcome:** Mortality, excluding infants and ICD-9 ≥ 800 **Study Design:** Time-series **Covariates:** Seasonal and weekday variations, influenza epidemics, air temperature, relative humidity **Statistical Analysis:** Semiparametric Poisson regression, polynomial distributed lag (PDL) **Statistical Package:** R **Age Groups:** All	**Pollutant:** PM_{10} **Averaging Time:** Daily **Mean (SD) Unit:** 1 (10/1/1991-8/31/1995): 50.6 ± 32.2 µg/m^3 2 (9/1/1995-2/28/1998): 41.1 ± 28.4 µg/m^3 3 (3/1/1998-3/31/2002): 24.3 ± 15.4 µg/m^3 Total: 38.0 ±28.3 µg/m^3 **Range (Min, Max):** NR **Copollutant:** NO_2, CO, UFP	**Increment:** IQR **Relative Risk (95% CI) lag** New City Limits 6-day IQR: 17.2 PDL: 0.997 (0.972-1.022) Mean of lags 0-5: 0.995 (0.971-1.019) Old City Limits 6-day IQR: 17.2 PDL: 1.004 (0.978-1.031) Mean of lags 0-5: 1.001 (0.976-1.027) New City Limits 15-day IQR: 14.5 PDL: 1.008 (0.982-1.036) Mean of lags 0-14: 1.006 (0.981-1.032) Old City Limits 15-day IQR: 14.5 PDL: 1.019 (0.991-1.048) Mean of lags 0-14: 1.017 (0.990-1.044) Multiday Ma, 6-day Overall IQR: 24.2 Overall RR (95% CI): 0.998 (0.976-1.021) Period 1: 0.996 (0.969-1.024) Period 2: 1.013 (0.972-1.056) Period 3: 0.949 (0.897-1.004) Multiday Ma, 15-day Overall IQR: 22.3 Overall RR (95% CI): 1.020 (0.993-1.093) Period 1: 1.017 (0.984-1.051) Period 2: 1.012 (0.973-1.071) Period 3: 0.978 (0.911-1.051)

[1]All units expressed in µg/m^3 unless otherwise specified.

Table E-32. Long-term exposure-mortality - $PM_{10-2.5}$.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: (Chen et al., 2005, 087942) **Period of Study:** 1973-1998 **Location:** San Francisco, San Diego, Los Angeles, CA	**Outcome:** Mortality: CHD **Study Design:** Cohort **Statistical Analyses:** Cox proportion hazards model **Age Groups:** >25	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** 25 yr **Mean (SD):** 25.4 **Range (Min, Max):** NR **Copollutant:** NO_2 O_3 SO_2	**Increment:** 10 µg/m^3 **Relative Risk (Lower CI, Upper CI) lag:** Males $PM_{10-2.5}$: 0.93 (0.68, 1.29) 0-1 $PM_{10-2.5}$+NO_2: 0.86 (0.62, 1.20) 0-1 $PM_{10-2.5}$+SO_2: 0.90 (0.64,1.27) 0-1 $PM_{10-2.5}$+O_3: 1.01 (0.67,1.51) 0-1 Females $PM_{10-2.5}$: 1.20 (0.95, 1.53) 0-1 $PM_{10-2.5}$+NO_2: 1.19 (0.92, 1.54) 0-1 $PM_{10-2.5}$+SO_2: 1.31 (1.03,1.68) 0-1 $PM_{10-2.5}$+O_3: 1.47 (1.10,1.96) 0-1
Reference: Goss et al. (2004, 055624) **Period of Study:** 1999-2000 **Location:** United States	**Outcome:** Mortality **Study Design:** Cohort Study (Cystic Fibrosis Cohort) **Statistical Analyses:** Logistic Regression **Age Groups:** >6 yr	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual avg **Mean (SD) unit:** $PM_{2.5}$: 13.7 (4.2) **IQR:** $PM_{2.5}$: 11.8-15.9 **Copollutant:** O_3 NO_2 SO_2 CO	**Increment:** 10 µg/m^3 $PM_{2.5}$: 1.32 (0.91-1.93)
Reference: Lipert et al**. (2009, 190271)** **Period of Study:** 1989-1996 **Location:** Various parts of the Untied States	**Outcome:** Mortality **Study Design:** Retrospective Cohort **Statistical Analyses:** Cox proportional hazards regression **Age Groups:** Male U.S. veterans between ages of 39 and 63 (Avg. age: 51)	**Pollutant:** $PM_{10-2.5}$ **Mean (SD):** 16.0 (5.1)	**Increment:** 12 1.07 (1.01, 1.13)
Reference: McDonnell et al. (2000, 010319) **Period of Study:** 1973-1977 **Location:** California	**Outcome:** Mortality **Study Design:** Cohort (AHSMOG airport cohort) **Statistical Analyses:** Cox regression models **Age Groups:** Males, 27 yr+	**Pollutant:** $PM_{10-2.5}$ **Averaging Time:** Monthly avg **Mean (SD):** $PM_{10-2.5}$: 27.3 (8.6) **IQR:** 9.7 **Copollutant:** O_3: 0.70 SO_2: 0.31 NO_2: 0.23 SO_4: 0.47	**Increment:** IQR All Cause: 1.05 (0.92-1.20) Resp: 1.19 (0.88, 1.62) Lung Cancer: 1.25 (0.63-2.49)

[1]All units expressed in µg/m^3 unless otherwise specified.

Table E-33. Long-term exposure-mortality - $PM_{2.5}$ (including PM components/sources).

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Abrahamowicz et al. (2003, 086292) **Period of Study:** 1982-1989 **Location:** 151 Cities	**Outcome:** Mortality: All-causes **Study Design:** Case-cohort study **Statistical Analyses:** Cox proportion-hazards model flexible regression spline generalization **Age Groups:** >18	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual **Mean (SD):** 18.2 **Range (Min, Max):** (9.0, 33.5) **Copollutant:** Sulfates	**Relative Risk (Min CI, Max CI)** **Estimated from graph (Fig 1):** log HR for a 24.5 µg/m^3 increase in $PM_{2.5}$ over time Yr 0: 0.5 (-1.1, 1.6) 2: 0.6 (0.2, 0.9) 4: 0.6 (0.3, 0.8) 6: 0.8 (0.3, 1.1) 8: -1.0 (-1.5, 1.0)
Reference: Abrahamowicz et al. (2003, 086292) **Period of Study:** 1982-1989 **Location:** 151 Cities	**Outcome:** Mortality: All-causes **Study Design:** Case-cohort study **Statistical Analyses:** Cox proportion-hazards model flexible regression spline generalization **Age Groups:** >18	**Pollutant:** Sulfates **Averaging Time:** Annual **Mean (SD):** 18.2 **Range (Min, Max):** (9.0, 33.5) **Copollutant:** $PM_{2.5}$	**Relative Risk (Min CI, Max CI)** **Estimated from graph (Fig 1):** Log HR for a 19.9 µg/m^3 increase in Sulfates over time Yr 0: 0.1 (-0.2, 0.7) 2: 0.1 (-0.2, 0.4) 4: 0.0 (-0.4, 0.3) 6: 0.3 (-0.1, 0.5) 8: 0.4 (-0.4, 1.6)
Reference: Ballester et al. (2008, 189977) **Period of Study:** 2001-2002 **Location:** Europe	**Outcome:** Mortality- All-causes **Study Design:** Health Impact Assessment **Statistical Analyses:** Aphesis Network **Age Groups:** >30	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual **Mean (SD):** NR **Range (Min, Max):** NR	**Potential Reduction in the total burden of mortality (min CI, max CI) for four different decreases in annual $PM_{2.5}$ using a conservative estimate** Reduction to 25 µg/m^3 - 0.4 (0.1, 0.8) Reduction to 20 µg/m^3 - 0.8 (0.2, 1.6) Reduction to 15 µg/m^3 - 1.6 (0.4, 3.1) Reduction to 10 µg/m^3 - 3.0 (0.8, 5.8)
Reference: Beelen et al. (2008, 156263) **Period of Study:** 1987-1996 **Location:** Netherlands	**Outcome:** Mortality: Total (nonaccidental) (<800) Cardio-respiratory (390-448, 490-496, 487, 480-486, 507) Pulmonary (460-519) Cardiovascular (400-440) Lung Cancer (162) Other-causes **Study Design:** Case-cohort study and prospective cohort **Statistical Analyses:** Cox proportion-hazards model **Age Groups:** 55-69	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual **Mean (SD):** 28.3 (2.1) µg/m^3 **Range (Min, Max):** (23.0, 36.8) **Copollutant (correlation):** NO_2: (>0.8) BS: (>0.8) SO_2: (>0.6)	**Increment:** 11 µg/m^3 **Relative Risk (Min CI, Max CI)** **RR for the association between exposures to $PM_{2.5}$ and cause specific mortality** Natural Cause: Full cohort: 1.06 (0.97, 1.16) Case cohort: 0.86 (0.66, 1.13) Cardiovascular: Full cohort: 1.04 (0.90, 1.21) Case cohort: 0.83 (0.60, 1.15) Respiratory: Full cohort: 1.07 (0.75, 1.52) Case cohort: 1.02 (0.56, 1.88) Lung Cancer: Full cohort: 1.06 (0.82, 1.38) Case cohort: 0.87 (0.52, 1.47) Other cause: F Ull cohort: 1.08 (0.96, 1.23) Case cohort: 0.85 (0.65, 1.12) **RR for the association between exposures to BS and cause specific mortality** Natural Cause: Full cohort: 1.05 (1.00, 1.11) Case cohort: 0.97 (0.83, 1.13) Cardiovascular: Full cohort: 1.04 (0.95, 1.13) Case cohort: 0.98 (0.81, 1.18) Respiratory: Full cohort: 1.22 (0.99, 1.50) Case cohort: 1.29 (0.91, 1.83) Lung Cancer: Full cohort: 1.03 (0.88, 1.20) Case cohort: 1.03 (0.77, 1.38) Other cause: Full cohort: 1.04 (0.97, 1.12) Case cohort: 0.91 (0.78, 1.07)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Breitner et al. (2009, 188439) **Period of Study:** Oct 1991-Mar 2002 **Location:** Efurt, Germany	**Outcome:** Mortality, excluding infants and ICD-9 ≥ 800 **Study Design:** Time-series **Covariates:** Seasonal and weekday variations, influenza epidemics, air temperature, relative humidity **Statistical Analysis:** Semiparametric Poisson regression, polynomial distributed lag (PDL) **Statistical Package:** R **Age Groups:** All	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily **Mean (SD) Unit:** 1 (10/1/1991-8/31/1995): 50.6 ± 32.2 µg/m^3 2 (9/1/1995-2/28/1998): 41.1 ± 28.4 µg/m^3 3 (3/1/1998-3/31/2002): 24.3 ± 15.4 µg/m^3 Total: 38.0 ±28.3 µg/m^3 **Range (Min, Max):** NR **Copollutant:** NO_2, CO, UFP	**Increment:** IQR **Relative Risk (95% CI) lag** New City Limits 6-day IQR: 13.3 PDL: 1.009 (0.984-1.035) Mean of lags 0-5: 1.004 (0.981-1.027) Old City Limits 6-day IQR: 13.3 PDL: 1.017 (0.990-1.044) Mean of lags 0-5: 1.010 (0.986-1.035) New City Limits 15-day IQR: 11.5 PDL: 1.019 (0.988-1.050) Mean of lags 0-14: 1.017 (0.992-1.042) Old City Limits 15-day IQR: 11.5 PDL: 1.030 (0.997-1.063) Mean of lags 0-14: 1.025 (0.999-1.052) Multiday Ma, 6-day Overall IQR: 13.3 Overall RR (95% CI): 1.004 (0.981-1.027) Period 1: NR Period 2: 1.017 (0.990-1.044) Period 3: 0.974 (0.937-1.013) Multiday Ma, 15-day Overall IQR: 11.5 Overall RR (95% CI): 1.017 (0.992-1.042) Period 1: NR Period 2: 1.016 (0.988-1.045) Period 3: 1.016 (0.971-1.063)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Brunekreef et al. (2009, 191947) **Period of Study:** 1987-1996 **Location:** The Netherlands	**Outcome:** All cause mortality (ICD-9 400-440, 460-519, > 800) **Study Design:** Case-cohort **Covariates:** Individual: sex, age, Quetelet index, smoking status, passive smoking status, educational level, occupation, occupational exposure, marital status, alcohol use, intake of vegetables, fruits, energy, saturated and monounsaturated fatty acids, trans fatty acids, total fiver, folic acid and fish Area-level: Percent of population with income below the 40th percentile and above the 80th percentile **Statistical Analysis:** Cox proportional hazards **Statistical Package:** Stata, SPSS, R **Age Groups:** 120,000 adults aged 55-69 yr at enrollment	**Pollutant:** $PM_{2.5}$, estimated from PM_{10} levelsf **Averaging Time:** 24 h **50th Percentile:** 28 µg/m^3 **Range (Min, Max):** 23-37 **Copollutant (correlation):** NO_2: 0.75 BS: 0.84 NO: 0.69 SO_2: 0.43	**Increment:** 10 µg/m^3 **Relative Risk (95 % CI) for $PM_{2.5}$ concentrations and cause specific mortality** Case Cohort Natural Cause: 0.86 (0.66-1.13) Cardiovascular: 0.83 (0.60-1.15) Respiratory: 1.02 (0.56-1.88) Lung Cancer: 0.87 (0.52-1.47) Noncardiopulmonary, non-lung cancer: 0.85 (0.65-1.23) Full Cohort Natural Cause: 1.06 (0.97-1.16) Cardiovascular: 1.04 (0.90-1.21) Respiratory: 1.07 (0.75-1.52) Lung Cancer: 1.06 (0.82-1.38) Noncardiopulmonary, non-lung cancer: 1.08 (0.72-1.19) **Relative Risk (95%CI) for $PM_{2.5}$ concentrations and cause specific mortality in full cohort analysis by confounder model** Natural Cause Mortality Unadjusted: 1.11 (1.04-1.20) Smoking: 1.04 (0.96-1.13) Smoking, area-level income: 1.06 (0.97-1.16) Cardiovascular Mortality Unadjusted: 1.09 (0.97-1.23) Smoking: 1.02 (0.90-1.16) Smoking, area-level income: 1.04 (0.90-1.21) Respiratory Mortality Unadjusted: 1.23 (0.92-1.65) Smoking: 1.10 (0.81-1.50) Smoking, area-level income: 1.07 (0.75-1.52) Lung Cancer Mortality Unadjusted: 1.17 (0.95-1.46) Smoking: 1.06 (0.85-1.33) Smoking, area-level income: 1.06 (0.82-1.38) Noncardiopulmonary, Non-Lung Cancer Mortality Unadjusted: 1.10 (1.00-1.22) Smoking: 1.05 (0.94-1.16) Smoking, area-level income: 1.08 (0.96-1.22)
Reference: Chen et al. (2005, 087942) **Period of Study:** 1973-1998 **Location:** San Francisco, San Diego, Los Angeles, CA	**Outcome:** Mortality: CHD **Study Design:** Cohort **Statistical Analyses:** Cox proportion hazards model **Age Groups:** >25	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 25 yr **Mean (SD):** 29.0 **Range (Min, Max):** NR **Copollutant:** NO_2, O_3, SO_2	**Increment:** 10 µg/m^3 **Relative Risk (Lower CI, Upper CI) lag:** Males $PM_{2.5}$: 0.89 (0.69, 1.17) 0-1 $PM_{2.5}$+NO_2: 0.82 (0.61, 1.10); 0-1 $PM_{2.5}$+SO_2: 0.86 (0.65,1.14) 0-1 $PM_{2.5}$+O_3: 0.92 (0.65,1.29) 0-1 Females $PM_{2.5}$: 1.19 (0.96, 1.47) 0-1 $PM_{2.5}$+NO_2: 1.18 (0.95, 1.47); 0-1 $PM_{2.5}$+SO_2: 1.36 (1.05,1.74) 0-1 $PM_{2.5}$+O_3: 1.61 (1.17,2.22) 0-1

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Eftim et al. (2008, 099104) **Period of Study:** 2000-2002 **Location:** USA, Same cities as six cities and ACS cohorts	**Outcome (ICD-9):** All nonaccidental causes (<800) **Study Design:** Cross-sectional **Statistical Analyses:** Log-linear regression, Poisson **Age Groups:** >65	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual avg **Mean (SD): |** ACS: 13.6 (2.8) SCS: 14.1 (3.1) **Range (Min, Max):** ACS: (6.0, 25.1); SCS: (9.6, 19.1)	**Increment:** 10 µg/m^3 **% Increase in Mortality for overall exposure period and individual yr (95%CI Min, 95%CI Max):** ACS (adjusted for age, sex) Overall: 10.8 (8.6, 13.0) 2000: 10.9 (7.3, 14.6) 2001: 9.1 (5.3, 12.7) 2002: 10.1 (6.0, 14.3) SCS (adjusted for age, sex) Overall: 20.8 (14.8, 27.1) 2000: 17.8 (9.8, 26.4) 2001: 16.5 (7.4, 25.0) 2002: 33.5 (19.2, 49.3)
Reference: Enstrom et al. (2005, 087356) **Period of Study:** 1973-2002 **Location:** 25 California Colonies 11 California Colonies (EPA IPN study)	**Outcome:** Mortality: Cardiovascular-respiratory (390-448) (480-486, 487, 490-496, 507) **Study Design:** Retrospective cohort **Statistical Analyses:** Cox proportional hazards regression model, SAS PHREG **Age Groups:** 35 or older	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual **Mean (SD):** 23.4 **Range (Min, Max):** (13.1 µg/m^3, 36.1)	**Relative Risk (Lower CI, Upper CI)** **RR from causes for both sexes by county from 1973-2002** Alameda: 0.962 (0.926,0.999) Butte: 0.999 (0.910,1.096) Contra Costa: 0.999 (0.943,1.058) Fresno: 0.935 (0.872,1.002) Humboldt: 0.992 (0.900,1.092) Kern: 0.944 (0.872,1.023) Marin: 0.939 (0.867,1.016) Napa: 0.949 (0.868,1.038) Orange: 0.990 (0.948,1.034) Riverside: 0.959 (0.906,1.015) Sacramento: 0.998 (0.944,1.055) San Bernardino: 0.992 (0.938,1.049) San Diego: 0.992 (0.954, 1.033) San Francisco: 0.963 (0.914,1.014) San Joaquin: 0.925 (0.816,1.049) San Mateo: 0.949 (0.899, 1.003) Santa Barbara: 0.968 (0.878,1.068) Santa Clara: 0.955 (0.910,1.003) Santa Cruz: 0.890 (0.793,0.999) Solano: 0.901 (0.815,0.995) Sonoma: 0.968 (0.884,1.060) Stanislaus: 0.984 (0.904,1.072) Tulare: 1.047 (0.979,1.119) Ventura: 0.967 (0.872,1.072) **RR from all causes for 11 counties for both sexes (EPA IPN study)** Santa Barbara: 0.968 (0.878,1.068) Contra Costa: 0.999 (0.943,1.058) Alameda: 0.962 (0.926,0.999) Butte: 0.999 (0.910,1.096) San Francisco: 0.963 (0.914,1.014) Santa Clara: 0.955 (0.910,1.003) Fresno: 0.935 (0.872,1.002) San Diego: 0.992 (0.954,1.033) Kern: 0.944 (0.872,1.023) Riverside: 0.959 (0.906,1.015)
Reference: Filleul et al. (2005, 087357) **Period of Study:** 1974-1976 **Location:** 7 cities in France	**Outcome:** Nonaccidental causes (<800), cardiopulmonary disease (401-440 and 460-519), lung cancer (162) **Age Groups:** 25-59 yr **Study Design:** Cohort **N:** 14,284 people **Statistical Analyses:** Cox proportional hazard, regression **Covariates:** Sex, smoking habits, educational level, body-mass index (BMI), occupational exposure **Statistical Package:** Proc Phreg SAS	**Pollutant:** Total suspended particles (TSP) **Averaging Time:** NR **Mean (SD):** NR **Range (Min, Max):** (45, 243) **PM Component:** NR **Monitoring Stations:** 1 station **Copollutant (correlation):** BS r = 0.87 SO_2 r = 0.17 NO r = 0.84 NO_2 r = 0.60	**Increment:** 10 µg/m^3 Adjusted mortality rate ratios: 24 areas: All nonaccidental causes: 1.00[0.99, 1.01] Lung cancer: 0.97[0.94, 1.01] Cardiopulmonary disease: 1.01[0.99, 1.03] 18 areas: All nonaccidental causes: 1.05[1.02, 1.08] Lung cancer: 1.00[0.92, 1.10] Cardiopulmonary disease: 1.06[1.01, 1.12]

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Fuentes et al. (2006, 097647) **Period of Study:** Jun 2000 **Location:** Conterminous U.S.	**Outcome:** Mortality: **Study Design:** Time-series **Statistical Analyses:** Generalized Poisson Regression **Age Groups:** 0-14, 15-64, >65 **Covariates:** Temperature, pressure, dew point, wind speed, elevation, age, ethnicity	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Monthly **Mean (SD):** 6.60 (0.76) **Copollutant:** PM_{10}, O_3	**Increment:** 10 µg/m^3 $PM_{2.5}$: 1.066 (1.064, 1.069) PM_{10}: 1.030 (1.028, 1.032)
Reference: Janes et al. (2007, 090927) **Period of Study:** 2000-2002 **Location:** 113 U.S. counties	**Outcome:** Mortality: **Study Design:** Time-series **Statistical Analyses:** Cox proportional hazards model **Age Groups:** 65-74 75-84 85+	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual avg **Mean (SD):** NR **Range (Min, Max):** NR	**Increment:** 1 µg/m^3 **% Increase (Lower CI, Upper CI) lag:** Overall % Increase by age-sex stratum Age Category 65-74: Male: 1.48 (0.93,2.03) Female: 0.83 (0.24,1.43) 75-84: Male: 0.85 (0.34,1.35) Female: 0.77 (0.28,1.27) 85+: Male: 0.70 (0.03,1.38) Female: 0.59 (0.05,1.12) National Trend % Increase by age-sex stratum Age Category 65-74: Male: 3.55 (2.77,4.34) Female: 1.97 (1.12,2.83) 75-84: Male: 2.48 (1.83,3.14) Female: 2.29 (1.66,2.93) 85+: Male: 1.38 (0.52,2.26) Female: 1.65 (1.01,2.29) Local Trend % Increase by age-sex stratum Age Category 65-74: Male: 0.04 (-0.58,0.67) Female: -0.03 (-0.71,0.66) 75-84: Male: -0.34 (-0.87,0.19) Female: -0.31 (-0.82, 0.21) 85+: Male: <0.01 (-0.71,0.73) Female: -0.22 (-0.74,0.31) *Local trends are county specific deviations from national trends
Reference: Jerrett et al. (2003, 087380) **Period of Study:** 1982 **Location:** 151 cities from ACS	**Outcome:** Mortality **Study Design:** Multilevel, individual-ecologic analysis **Statistical Analysis:** Cox proportional hazards model **Covariates:** Smoking, education, occupational exposures, BMI, marital status, alcohol consumption, gender	**Pollutant:** Sulfates **Mean (SD):** 10.6 **Range (Min, Max):** 3.6,23.5	**Increment:** 19.9 (Range) All Cause: SO_4: 1.17 (1.07, 1.27) SO_4 + CO: 1.16 (1.10, 1.23) SO_4 + NO_2: 1.16 (1.08, 1.24) SO_4 + O_3: 1.17 (1.11, 1.24) SO_4 + SO_2: 1.05 (0.98, 1.12) CPD: SO_4: 1.25 (1.16, 1.35) SO_4 + CO: 1.28 (1.18, 1.39) SO_4 + NO_2: 1.29 (1.17, 1.42) SO_4 + O_3: 1.27 (1.17, 1.38) SO_4 + SO_2: 1.13 (1.03, 1.24) Lung Cancer: SO_4: 1.31 (1.09, 1.58) SO_4 + CO: 1.26 (1.03, 1.53) SO_4 + NO_2: 1.31 (1.05, 1.65) SO_4 + O_3: 1.30 (1.07, 1.59) SO_4 + SO_2: 1.37 (1.08, 1.73)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Jerrett et al. (2005, 087600) **Period of Study:** 1982-2000 **Location:** Los Angeles, California	**Outcome:** Mortality: Non- accidental (<800) IHD (410-414) Cardiopulmonary (400-440, 460-519) Lung Cancer (162) Other Cancers (140-149,160, 161, 163-239) Other causes **Study Design:** Retrospective Cohort **Statistical Analyses:** Cox regression hazards model kriging, radial basis function multiquadric interpolator **Age Groups:** All ages	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual avg **Mean (SD):** NR **Range (Min, Max):** NR **Copollutant:** O_3	**Increment:** 10 µg/m^3 **Relative Risk (Lower CI, Upper CI)** All Causes - $PM_{2.5}$ Only: 1.24 (1.11,1.37) 44 Ind. Covariates together+$PM_{2.5}$: 1.17 (1.03,1.32) 44 Ind. Covariates together+ $PM_{2.5}$+O_3: 1.20 (1.07,1.34) 44 Ind. Covariates together+intersection within freeways within 500 m+ $PM_{2.5}$+O_3: 1.17 (1.05,1.31) IHD - $PM_{2.5}$ Only: 1.49 (1.20,1.85) 44 Ind. Covariates together+$PM_{2.5}$: 1.39 (1.12,1.73) 44 Ind. Covariates together+$PM_{2.5}$+O_3: 1.45 (1.15,1.82) 44 Ind. Covariates together+intersection within freeways within 500 m+ $PM_{2.5}$+O_3: 1.38 (1.11,1.72) Cardiopulmonary - $PM_{2.5}$ Only: 1.20 (1.04,1.39) 44 Ind. Covariates together+ $PM_{2.5}$+O_3: 1.19 (1.02,1.38) 44 Ind. Covariates together+intersection within freeways within 500 m+ $PM_{2.5}$+O_3: 1.13 (0.97,1.31) Lung Cancer - $PM_{2.5}$ Only: 1.60 (1.09,2.33) 44 Ind. Covariates together+$PM_{2.5}$: 1.44 (0.98,2.11) 44 Ind. Covariates together+intersection within freeways within 500 m+ $PM_{2.5}$+O_3: 1.46 (0.99,2.16) Other Cancers - $PM_{2.5}$ Only: 1.09 (0.85,1.40) 44 Ind. Covariates together+ $PM_{2.5}$+O_3: 1.08 (0.83,1.39) 44 Ind. Covariates together+intersection within freeways within 500 m+ $PM_{2.5}$+O_3: 1.08 (0.83,1.39) All Other Causes - $PM_{2.5}$ Only: 1.11 (0.74,1.67) 44 Ind. Covariates together+ $PM_{2.5}$+O_3: 0.95 (0.64,1.39) 44 Ind. Covariates together+intersection within freeways within 500 m+ $PM_{2.5}$+O_3: 1.02 (0.71,1.48)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Laden et al. (2006, 087605) **Period of Study:** 1974-1998 Period 1: 1974-1989 Period 2: 1990-1998 **Location:** Nine U.S. Cities Watertown, MA Kingston, TN Harriman, TN St. Louis, MO Steubenville, OH Portage, WI |Wyocena, WI Pardeeville, WI Topeka, KS	**Outcome:** Total mortality Nonaccidental (<800) Cardiovascular (400-440) Respiratory (485-496) Lung Cancer (162) Other **Study Design:** Prospective Cohort **Statistical Analyses:** Cox proportional hazards regression **Age Groups:** 25-74	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual avg **Mean (SD):** Period 1 Portage: 11.4 Topeka: 12.4 Watertown: 15.4 Harriman: 20.9 St Louis: 19.2 Steubenville: 29.0 Period 2 Portage: 10.2 Topeka: 13.1 Watertown: 12.1 Harriman: 18.1 St. Louis: 13.4 Steubenville: 22.0	**Increment:** 10 µg/m^3 **Relative Risk (Lower CI, Upper CI) lag:** **Period 1:** Portage: 1.00 Topeka: 1.06 (0.86, 1.31) Watertown: 1.06 (0.87, 1.28) Harriman: 1.19 (0.98, 1.44) St Louis: 1.15 (0.96, 1.38) Steubenville: 1.31 (1.10, 1.57) **Period 2:** Portage: NR Topeka: 1.01 (0.83, 1.22) Watertown: 0.82 (0.67, 1.00) Harriman: 1.10 (0.91, 1.33) St Louis: 0.96 (0.80, 1.15) Steubenville: 1.06 (0.89, 1.27) **Complete Period:** Portage: 1.00 Topeka: 1.03 (0.89, 1.19) Watertown: 0.95 (0.83, 1.08) Harriman: 1.15 (1.01, 1.32) St. Louis: 1.05 (0.93, 1.20) Steubenville: 1.18 (1.04, 1.34) **RR for complete follow up avg $PM_{2.5}$** Total Mortality: 1.16 (1.07, 1.26) Cardiovascular: 1.28 (1.13, 1.44) Respiratory: 1.08 (0.79, 1.49) Lung Cancer: 1.27 (0.96, 1.69) Other: 1.02 (0.90, 1.17) **RR for Period 1 avg $PM_{2.5}$** Total Mortality: 1.18 (1.09, 1.27) Cardiovascular: 1.28 (1.14, 1.43) Respiratory: 1.21 (0.89, 1.66) Lung Cancer: 1.20 (0.91, 1.58) Other: 1.05 (0.93, 1.19) **Decrease in avg $PM_{2.5}$ over the 2 periods** Total Mortality: 0.73 (0.57, 0.95) Cardiovascular: 0.69 (0.46, 1.01) Respiratory: 0.43 (0.16, 1.13) Lung Cancer: 1.06 (0.43, 2.62) Other: 0.85 (0.56, 1.27)
Reference: Lipfert et al. (2006, 088756) **Period of Study:** 1989-1996 **Location:** Various parts of the Untied States	**Outcome:** Mortality **Study Design:** Retrospective Cohort **Statistical Analyses:** Cox proportional hazards regression **Age Groups:** Male U.S. veterans between ages of 39 and 63 (Avg. age: 51)	**Pollutant:** Sulfate **Mean (SD) from 1976-81:** 10.7 (3.6)	**Increment:** 8 1.045 (0.944, 1.157)
Reference: Lipfert et al. (2006, 088756) **Period of Study:** 1989-1996 **Location:** Various parts of the Untied States	**Outcome:** Mortality **Study Design:** Retrospective Cohort **Statistical Analyses:** Cox proportional hazards regression **Age Groups:** Male U.S. veterans between ages of 39 and 63 (Avg age 51)	**Pollutant:** $PM_{2.5}$ **Mean (SD):** 14.3 (3.2)	**Increment:** 8 1.118 (1.038, 1.203)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Lipfert et al. (2006, 088218) **Period of Study:** 1997-2002 **Location:** Various parts of the Untied States	**Outcome:** Mortality: Non- accidental (<800) **Study Design:** Retrospective cohort **Statistical Analyses:** Cox proportional hazards regression AIC **Age Groups:** Male U.S. veterans between ages of 39 and 63 (Avg. age: 51)	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual avg **Mean (SD):** 15.02 (4.80) µg/m^3 (2000-2003) **Range (Min, Max):** (3.29, 24.96) **Copollutant (correlation):** As: r = 0.443 Cr: r = 0.379 Cu: r = 0.530 Fe: r = 0.379; Pb: r = 0.489 Mn: r = 0.389; Ni: r = 0.140 Se: r = 0.312; V: r = 0.197 Zn: r = 0.420; OC: r = 0.620 EC: r = 0.544; | SO_4: r = 0.827 NO_3: r = 0.649 NO_2: r = 0.641 Peak CO: r = 0.040 Peak O_3: r = 0.222 Peak SO_2: r = 0.714	**Increment:** 10 µg/m^3 **% Increase per 10 µg/m^3 increase in $PM_{2.5}$** **Single-Pollutant Model** As: -5.23% Cr: -2.11% Cu: 2.12% Fe: 2.81% Pb: -2.40% Mn: -1.20% Ni: 3.75% Se: -0.30% V: 5.08% Zn: 1.52% OC: -0.02% EC: 9.16% SO_4: 3.04% NO_3: 6.60% NO_2: 6.92% Peak CO: -0.61% Peak O_3: 4.95% Peak SO_2: -4.20% **Multiple Pollutants model- Pollutant with traffic density** NO_3: 3.42% SO_4: -2.73% EC: 6.27% Ni: 2.51% V: 3.27% **Pollutant with NO_3** EC: 5.93% Ni: 2.31% V: 3.11% **Pollutant with Peak O_3** **Traffic density: 2.40%** EC: 10.79% Fe: 5.94% NO_3: 7.57% $PM_{2.5}$: 8.97% V: 4.93% Ni: 3.65% SO_4: 6.75% Cu: 1.55% OC: 0.21%

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Krewski et al. (2009, 191193) **Period of Study:** 1979-2000 **Location:** 48 contiguous states U.S.	**Outcome:** Death **Study Design:** Cohort **Covariates:** Demographic, socioeconomic and ecologic characteristics **Statistical Analysis:** Cox proportional-hazards model **Statistical Package:** NR **Age Groups:** Adults of at least 30 yr	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **Mean Unit:** 1979-1983: 21.20 µg/m^3 1999-2000: 14.02 µg/m^3 **Range (Min, Max):** 1979-1983: 10.77-30.01 1999-2000: 5.80-22.20 **Copollutant:** SO_4^{2-}, SO_2, PM_{15}, TSP, O_3, NO_2, CO	**Increment:** 10 µg/m^3 **Hazard Ratio (95% CI)** **MSA & DIFF** Increment Change: 10.78 (1.043-1.115) Change 5-15 µg/m^3: 1.128 (1.077-1.183) Change 10-20 µg/m^3: 1.079 (1.048-1.112) **HR (95% CI)** **Los Angeles** Parsimonious ecologic covariates: 1.126 (1.014-1.251) **HR (95% CI)** **15-yr time window** Group A: 0.98 (0.92-1.06) Group B: 1.01 (0.99-1.02) **HR (95% CI)** **Third follow-up, 7 Ecologic Variables** 1979-1983: 1.044 (1.028-1.060) 1999-2000: 1.057 (1.036-1.079) **HR (95% CI)** **Nationwide analysis, 1999-2000** Standard Cox: 1.03 (1.01-1.05) Random Effects Cox: 1.06 (1.04-1.08) **Increment:** 1.5 µg/m^3 **HR (95% CI)** **28 County, 3-yr model** All 7 ecologic covariates: 0.977 (0.932-1.025)
Reference: Krewski et al. (2009, 191193) **Period of Study:** 1979-2000 **Location:** 48 contiguous states U.S.	**Outcome:** Death from cardiopulmonary disease **Study Design:** Cohort **Covariates:** Demographic, socioeconomic and ecologic characteristics **Statistical Analysis:** Cox proportional-hazards model **Statistical Package:** NR **Age Groups:** Adults of at least 30 yr	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **Mean Unit:** 1979-1983: 21.20 µg/m^3 1999-2000: 14.02 µg/m^3 **Range (Min, Max):** 1979-1983: 10.77-30.01 1999-2000: 5.80-22.20 **Copollutant:** SO_4^{2-}, SO_2, PM_{15}, TSP, O_3, NO_2, CO	**Increment:** 10 µg/m^3 **Hazard Ratio (95% CI)** **MSA & DIFF** Increment Change: 1.078 (1.077-1.182) Change 5-15 µg/m^3: 1.208 (1.132-1.290) Change 10-20 µg/m^3: 1.127 (1.081-1.174) **HR (95% CI)** **Los Angeles** Parsimonious ecologic covariates: 1.086 (0.939-1.285) **HR (95% CI)** **15-yr time window** Group A: 1.00 (0.90-1.11) Group B: 1.05 (1.03-1.07) **HR (95% CI)** **Third follow-up, 7 Ecologic Variables** 1979-1983: 1.094 (1.070-1.118) 1999-2000: 1.138 (1.106-1.172) **HR (95% CI)** **Nationwide analysis, 1999-2000** Standard Cox: 1.09 (1.06-1.12) Random Effects Cox: 1.13 (1.10-1.16) **Increment:** 1.5 µg/m^3 **HR (95% CI)** **28 County, 3-yr model** All 7 ecologic covariates: 0 .940 (0.875-1.011)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Krewski et al. (2009, 191193) **Period of Study:** 1979-2000 **Location:** 48 contiguous states U.S.	**Outcome:** Death from ischemic heart disease **Study Design:** Cohort **Covariates:** Demographic, socioeconomic and ecologic characteristics **Statistical Analysis:** Cox proportional-hazards model **Statistical Package:** NR **Age Groups:** Adults of at least 30 yr	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **Mean Unit:** 1979-1983: 21.20 µg/m^3 1999-2000: 14.02 µg/m^3 **Range (Min, Max):** 1979-1983: 10.77-30.01 1999-2000: 5.80-22.20 **Copollutant:** SO_4^{2-}, SO_2, PM_{15}, TSP, O_3, NO_2, CO	**Increment:** 10 µg/m^3 **Hazard Ratio (95% CI)** **MSA & DIFF** Increment Change: 1.196 (1.177-1.407) Change 5-15 µg/m^3: 1.484 (1.311-1.680) Change 10-20 µg/m^3: 1.283 (1.186-1.387) **HR (95% CI)** **Los Angeles** Parsimonious ecologic covariates: 1.263 (10.22-1.563) **HR (95% CI)** **Third follow-up, 7 Ecologic Variables** 1979-1983: 1.184 (1.146-1.222) 1999-2000: 1.242 (1.191-1.295) **HR (95% CI)** **Nationwide analysis, 1999-2000** Standard Cox: 1.15 (1.11-1.20) Random Effects Cox: 1.24 (1.19-1.29) **Increment:** 1.5 µg/m^3 **HR (95% CI)** **28 County, 3 yr model** All 7 ecologic covariates: 1.072 (0.980-1.172)
Reference: Krewski et al. (2009, 191193) **Period of Study:** 1979-2000 **Location:** 48 contiguous states U.S.	**Outcome:** Death from lung cancer **Study Design:** Cohort **Covariates:** Demographic, socioeconomic and ecologic characteristics **Statistical Analysis:** Cox proportional-hazards model **Statistical Package:** NR **Age Groups:** Adults of at least 30 yr	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **Mean Unit:** 1979-1983: 21.20 µg/m^3 1999-2000: 14.02 µg/m^3 **Range (Min, Max):** 1979-1983: 10.77-30.01 1999-2000: 5.80-22.20 **Copollutant:** SO_4^{2-}, SO_2, PM_{15}, TSP, O_3, NO_2, CO	**Increment:** 10 µg/m^3 **Hazard Ratio (95% CI)** **MSA & DIFF** Increment Change: 1.142 (1.057-1.234) Change 5-15 µg/m^3: 1.236 (1.114-1.372) Change 10-20 µg/m^3: 1.143 (1.071-1.221) **HR (95% CI)** **Los Angeles** Parsimonious ecologic covariates: 1.311 (0.897-1.915) **HR (95% CI)** **15-yr time window** Group A: 1.08 (0.87-1.35) Group B: 1.07 (1.02-1.13) **HR (95% CI)** **Third follow-up, 7 Ecologic Variables** 1979-1983: 1.092 (1.033-1.154) 1999-2000: 1.138 (1.057-1.225) **HR (95% CI)** **Nationwide analysis, 1999-2000** Standard Cox: 1.11 (1.04-1.18) Random Effects Cox: 1.14 (1.06-1.23) **Increment:** 1.5 µg/m^3 **HR (95% CI)** **28 County, 3-yr model** All 7 ecologic covariates: 0.985 (0.832-1.166)
Reference: Krewski et al. (2009, 191193) **Period of Study:** 1979-2000 **Location:** 48 contiguous states U.S.	**Outcome:** Death from diabetes **Study Design:** Cohort **Covariates:** Demographic, socioeconomic and ecologic characteristics **Statistical Analysis:** Cox proportional-hazards model **Statistical Package:** NR **Age Groups:** Adults of at least 30 yr	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **Mean Unit:** 1979-1983: 21.20 µg/m^3 1999-2000: 14.02 µg/m^3 **Range (Min, Max):** 1979-1983: 10.77-30.01 1999-2000: 5.80-22.20 **Copollutant:** SO_4^{2-}, SO_2, PM_{15}, TSP, O_3, NO_2, CO	**Increment:** 1.5 µg/m^3 **HR (95% CI)** **28 County, 3 yr model** All 7 ecologic covariates: 1.083 (0.723-1.621)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Krewski et al. (2009, 191193) **Period of Study:** 1979-2000 **Location:** 48 contiguous states U.S.	**Outcome:** Death from endocrine disease **Study Design:** Cohort **Covariates:** Demographic, socioeconomic and ecologic characteristics **Statistical Analysis:** Cox proportional-hazards model **Statistical Package:** NR **Age Groups:** Adults of at least 30 yr	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **Mean Unit:** 1979-1983: 21.20 µg/m^3 1999-2000: 14.02 µg/m^3 **Range (Min, Max):** 1979-1983: 10.77-30.01 1999-2000: 5.80-22.20 **Copollutant:** SO_4^{2-}, SO_2, PM_{15}, TSP, O_3, NO_2, CO	**Increment:** 1.5 µg/m^3 **HR (95% CI)** **28 County, 3-yr model** All 7 ecologic covariates: 1.143 (0.835-1.564)
Reference: Krewski et al. (2009, 191193) **Period of Study:** 1979-2000 **Location:** 48 contiguous states U.S.	**Outcome:** Death from digestive cancer **Study Design:** Cohort **Covariates:** Demographic, socioeconomic and ecologic characteristics **Statistical Analysis:** Cox proportional-hazards model **Statistical Package:** NR **Age Groups:** Adults of at least 30 yr	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **Mean Unit:** 1979-1983: 21.20 µg/m^3 1999-2000: 14.02 µg/m^3 **Range (Min, Max):** 1979-1983: 10.77-30.01 1999-2000: 5.80-22.20 **Copollutant:** SO_4^{2-}, SO_2, PM_{15}, TSP, O_3, NO_2, CO	**Increment:** 10 µg/m^3 **HR (95% CI)** **Los Angeles** Parsimonious ecologic covariates: 1.199 (0.817-1.758)
Reference: Krewski et al. (2009, 191193) **Period of Study:** 1979-2000 **Location:** 48 contiguous states U.S.	**Outcome:** Death cancers other than lung and digestive **Study Design:** Cohort **Covariates:** Demographic, socioeconomic and ecologic characteristics **Statistical Analysis:** Cox proportional-hazards model **Statistical Package:** NR **Age Groups:** Adults of at least 30 yr	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **Mean Unit:** 1979-1983: 21.20 µg/m^3 1999-2000: 14.02 µg/m^3 **Range (Min, Max):** 1979-1983: 10.77-30.01 1999-2000: 5.80-22.20 **Copollutant:** SO_4^{2-}, SO_2, PM_{15}, TSP, O_3, NO_2, CO	**Increment:** 10 µg/m^3 **HR (95% CI)** **Los Angeles** Parsimonious ecologic covariates: 1.012 (0.788-1.299)
Reference: Krewski et al. (2009, 191193) **Period of Study:** 1979-2000 **Location:** 48 contiguous states U.S.	**Outcome:** Deaths from causes other than CPD, IHD and lung cancer **Study Design:** Cohort **Covariates:** Demographic, socioeconomic and ecologic characteristics **Statistical Analysis:** Cox proportional-hazards model **Statistical Package:** NR **Age Groups:** Adults of at least 30 yr	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **Mean Unit:** 1979-1983: 21.20 µg/m^3 1999-2000: 14.02 µg/m^3 **Range (Min, Max):** 1979-1983: 10.77-30.01 1999-2000: 5.80-22.20 **Copollutant:** SO_4^{2-}, SO_2, PM_{15}, TSP, O_3, NO_2, CO	**Increment:** 10 µg/m^3 **Hazard Ratio (95% CI)** **MSA & DIFF** Increment Change: 1.010 (0.968-1.055) Change 5-15 µg/m^3: 1.026 (0.970-1.085) Change 10-20 µg/m^3: 1.016 (0.981-1.053) **HR (95% CI)** **Third follow-up, 7 Ecologic Variables** 1979-1983: 0.983 (0.960-1.007) 1999-2000: 0.953 (0.923-0.984)
Reference: McDonnell et al. (2000, 010319) **Period of Study:** 1973-1977 **Location:** California	**Outcome:** Mortality **Study Design:** Cohort (AHSMOG airport cohort) **Statistical Analyses:** Cox regression models **Age Groups:** Males, 27 yr+	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Monthly avg **Mean (SD):** 31.9 (10.7) **IQR:** 24.3 **Copollutants (correlation):** O_3: 0.68 SO_2: 0.18 NO_2: -0.08; SO_4: 0.33	**Increment:** IQR All Cause: 1.22 (0.95-1.58) Resp: 1.64 (0.93-2.90) Lung Cancer: 2.23 (0.56-8.94)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Miller et al. (2007, 090130) **Period of Study:** 1994-1998 **Location:** 36 U.S. Metropolitan Areas	**Outcome:** CVD Mortality **Study Design:** Prospective Cohort (WHI) **Statistical Analyses:** Cox proportional hazards regression **Age Groups:** Postmenopausal women ages 50-79	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual avg (2000) **Mean (SD):** 13.4 **IQR:** 11.6, 18.3 **Range:** 3.4, 28.3	**Increment:** 10 µg/m^3 CVD Death: 1.76 (1.25, 2.47) CHD Death: 2.21 (1.17, 4.16) CV Death: 1.83 (1.11, 3.00)
Reference: Naess et al. (2007, 090736) **Period of Study:** 1992-1998 **Location:** Oslo, Norway	**Outcome:** Mortality: Nonaccidental (<800) Lung cancer (162) COPD (490-496) Cardiovascular (390-459) **Study Design:** Prospective Cohort **Statistical Analyses:** Cox proportional hazards regression model **Age Groups:** 51-70, 71-90	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 4-yr avg **Mean (SD):** $PM_{2.5}$: 15 **Range (Min, Max):** $PM_{2.5}$: (7, 22) **Copollutant (correlation):** NO_2: r = 0.95	**Relative Risk (CI min, CI max)** **RR for deaths from all causes** Men (ages 51-70) $PM_{2.5}$ exposure (in µg/m^3) 6.56-11.45: 1.00 11.46-14.25: 0.96 (0.89, 1.04) 14.26-18.43: 1.12 (1.03, 1.22) 18.44-22.34: 1.48 (1.36, 1.60) Men (ages 71-90) $PM_{2.5}$ exposure (in µg/m^3) 6.56-11.45: 1.00 11.46-14.25: 0.99 (0.93, 1.06) 14.26-18.43: 1.10 (1.03, 1.17) 18.44-22.34: 1.19 (1.12, 1.27) Women (ages 51-70) $PM_{2.5}$ exposure (in µg/m^3) 6.56-11.45: 1.00 11.46-14.25: 0.96 (0.87, 1.07) 14.26-18.43: 1.08 (0.98, 1.20) 18.44-22.34: 1.44 (1.30, 1.59) Women (ages 71-90) $PM_{2.5}$ exposure (in µg/m^3) 6.56-11.45: 1.00 11.46-14.25: 1.03 (0.97, 1.09) 14.26-18.43: 1.07 (1.01, 1.12) 18.44-22.34: 1.11 (1.05, 1.16) **Increment:** 10 µg/m^3 RR for death from CVD and lung cancer Men (ages 51-70) CVD- $PM_{2.5}$: 1.11 (1.06, 1.16) COPD- $PM_{2.5}$: 1.32 (1.17, 1.49) Lung Cancer- $PM_{2.5}$: 1.07 (0.98, 1.17) Women (ages 51-70) CVD: $PM_{2.5}$: 1.16 (1.09, 1.24) COPD: $PM_{2.5}$: 1.18 (1.03, 1.34) Lung Cancer: $PM_{2.5}$: 1.23 (1.10, 1.37) Men (ages 71-90) CVD: $PM_{2.5}$: 1.06 (1.03, 1.09) COPD: PM_{10}: 1.13 (1.04, 1.24) $PM_{2.5}$: 1.14 (1.04, 1.24) Lung Cancer: $PM_{2.5}$: 1.08 (0.98, 1.19) Women (ages 71-90) CVD: $PM_{2.5}$: 1.02 (1.00, 1.05) COPD: $PM_{2.5}$: 1.09 (1.00, 1.18) Lung Cancer: $PM_{2.5}$: 1.16 (1.03, 1.31)
Reference: Naess et al. (2007, 090736) **Period of Study:** 1992-1998 **Location:** Oslo, Norway	**Outcome:** Mortality: Lung cancer (162) COPD (490-496) Cardiovascular (390-459) Psychiatric causes (290, 292-302, 304, 306-319) Stomach cancer (151) Violence (800-999) **Study Design:** Multilevel cohort **Statistical Analyses:** WinBUGS **Age Groups:** 50-74	**Pollutant:** $PM_{2.5}$ **Averaging Time:** (Mo-yr) avg **Range Mean (SD):** 14.2 (3.6) **IQ Range (1st, 4th):** (6.6, 22.3) **Copollutant (correlation):** PM_{10}: r = 0.95| NO_2: r = 0.87	**Relative Risk (CI min, CI max)** **RR on All-cause mortality of $PM_{2.5}$ in Men Age 50-74** Primary Education: $PM_{2.5}$: 1.06 (1.00, 1.11) Individual: 1.34 (1.24, 1.43) Neighborhood: 1.22 (1.16, 1.28) Manual Class: $PM_{2.5}$: 1.06 (1.01, 1.12) Individual: 1.28 (1.20, 1.37) Neighborhood: 1.20 (1.14, 1.26) Income below median: $PM_{2.5}$: 1.05 (1.00, 1.12) Individual: 1.44 (1.35, 1.53) Neighborhood: 1.16 (1.11, 1.21) Not owner occupied: $PM_{2.5}$: 1.06 (1.00, 1.13) Individual: 1.24 (1.12, 1.36) Neighborhood: 1.11 (1.05, 1.17) Lives in flat dwelling:

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			$PM_{2.5}$: 1.04 (0.98, 1.11) Individual: 1.19 (1.09, 1.31) Neighborhood: 1.10 (1.04, 1.17) More than one person per room in dwelling: $PM_{2.5}$: 1.10 (1.02, 1.18) Individual: 1.05 (0.98, 1.13) Neighborhood: 1.01 (0.96, 1.05) **RR on All-cause mortality of $PM_{2.5}$ in Women Age 50-74** Primary Education Only: $PM_{2.5}$: 1.05 (1.00, 1.11) Individual: 1.32 (1.23, 1.42) Neighborhood: 1.18 (1.12, 1.24) Manual Class: $PM_{2.5}$: 1.07 (1.01, 1.13) Individual: 1.27 (1.18, 1.36) Neighborhood: 1.18 (1.12, 1.24) Income below median: $PM_{2.5}$: 1.05 (1.01, 1.10) Individual: 1.52 (1.41, 1.63) Neighborhood: 1.13 (1.09, 1.18) Not owner occupied: $M_{2.5}$: 1.07 (1.01, 1.14) Individual: 1.24 (1.12, 1.38) Neighborhood: 1.08 (1.02, 1.14) Lives in a flat dwelling: $PM_{2.5}$: 1.05 (0.99, 1.11) Individual: 1.21 (1.09, 1.34) Neighborhood: 1.09 (1.02, 1.15) More than one person per room in dwelling: $PM_{2.5}$: 1.11 (1.04, 1.19) Individual: 1.07 (0.99, 1.14) Neighborhood: 1.01 (0.96, 1.05) **RR for Interquartile Increase (MI) in $PM_{2.5}$ for different causes of death** CVD: Age and sex adjusted: 1.11 (1.07, 1.15) Primary education only: M1+ Individual: 1.07 (1.04, 1.11) M1+ Neighborhood: 1.03 (1.00, 1.07) Manual Class: M1+ Individual: 1.08 (1.04, 1.11) M1+ Neighborhood: 1.06 (1.02, 1.10) Income below Median: M1+ Individual: 1.07 (1.03, 1.11) M1+ Neighborhood: 1.02 (0.98, 1.05) Not owner occupied: M1+ Individual: 1.05 (1.01, 1.09) M1+ Neighborhood: 1.03 (0.99, 1.07): Living in a Flat dwelling M1+ Individual: 1.04 (1.00, 1.08) M1+ Neighborhood: 1.01 (0.97, 1.05) Crowded household: M1+ Individual: 1.10 (1.05, 1.14) M1+Neighborhood: 1.10 (1.06, 1.15) Pulmonary Cancer: Age and sex adjusted: 1.12 (1.05, 1.19) Primary education only: M1+ Individual: 1.09 (1.01, 1.17) M1+ Neighborhood: 1.05 (0.98, 1.13) Manual Class: M1+ Individual: 1.09 (1.01, 1.17) M1+ Neighborhood: 1.10 (1.06, 1.13) Income below Median: M1+ Individual: 1.09 (1.01, 1.17) M1+ Neighborhood: 1.02 (0.95, 1.10) Not owner occupied: M1+ Individual: 1.07 (1.00, 1.15) M1+ Neighborhood: 1.04 (0.97, 1.12) Living in a Flat dwelling: M1+ Individual: 1.03 (0.96, 1.11) M1+ Neighborhood: 1.00 (0.92, 1.08) Crowded household: M1+ Individual: 1.10 (1.03, 1.14) M1+Neighborhood: 1.11 (1.04, 1.20) COPD: Age and sex adjusted: 1.17 (1.09, 1.25)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			Primary education only: M1+ Individual: 1.13 (1.05, 1.22) M1+ Neighborhood: 1.09 (1.01, 1.19) Manual Class: M1+ Individual: 1.14 (1.05, 1.23) M1+ Neighborhood: 1.12 (1.04, 1.22) Income below Median: M1+ Individual: 1.13 (1.04, 1.22) M1+ Neighborhood: 1.06 (0.97, 1.15) Not owner occupied: M1+ Individual: 1.10 (1.02, 1.19) M1+ Neighborhood: 1.07 (0.99, 1.16) Living in a Flat dwelling: M1+ Individual: 1.08 (1.00, 1.18) M1+ Neighborhood: 1.03 (0.95, 1.13) Crowded household: M1+ Individual: 1.16 (1.07, 1.26) M1+Neighborhood: 1.16 (1.07, 1.26) Estimates for psychiatric diseases, genetic cancer and violent death
Reference: Nerriere et al. (2005, 088630) **Period of Study:** Grenoble (2001) Paris (2002) Rouen (2002-2003) Strasbourg (2003) **Location:** Four French Cities-Grenoble, Rouen, Paris, and Strasbourg	**Outcome:** Mortality: Lung Cancer (162) **Study Design:** Time-series **Statistical Analyses:** GIS **Age Groups:** 30-71 yr old nonsmoking adults	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 48-h avg **Mean Range:** 17 to 49 µg/m^3	**Increment:** 10 µg/m^3 **% Increase (Lower CI, Upper CI)** % increase in lung cancer deaths attributable to $PM_{2.5}$ exposure France: 8 (1, 16) Grenoble: 10 (3, 19) Rouen: 10 (2, 19) Strasbourg: 24 (4, 40)
Reference: Ozkaynak and Thurston (1987, 072960) **Period of Study:** 1980 **Location:** U.S.	**Outcome:** Total Mortality **Study Design:** Cross-sectional **Statistical Analyses:** Multiple regression analysis	**Pollutant:** Sulfate **Averaging Time:** Annual avg **Mean Range:** Sulfate: 11.1 (3.5)	**Range of estimated total mortality effects of air pollutions:** Sulfate: 4-9% "Sulfate concentration was consistently found to be a significant predictor of mortality in the models considered. Fine particle mass coefficients were also often found to be statistically significant in the mortality regressions."
Reference: Pope et al. (2004, 055880) **Period of Study:** 1982-2000 **Location:** Metropolitan areas in all 50 states in the U.S.	**Outcome:** Mortality: Cardiovascular Diseases (390-459) Diabetes (250) Respiratory Disease (460-519) **Study Design:** Prospective Cohort **Statistical Analyses:** Cox proportional hazards regression **Age Groups:** >30	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual avg **Mean (SD):** 17.1 (3.7) **Range (Min, Max):** NR	**Increment:** 10 µg/m^3 **Relative Risk (Lower CI, Upper CI)** All cardiovascular disease plus diabetes: $PM_{2.5}$: 1.12 (1.08, 1.15) Former Smoker: 1.26 (1.23, 1.28) Current Smoker: 1.94 (1.90, 1.99) Ischemic Heart Disease: $PM_{2.5}$: 1.18 (1.14, 1.23) Former Smoker: 1.33 (1.29, 1.37) Current Smoker: 2.03 (1.96, 2.10) Diabetes: $PM_{2.5}$: 0.99 (0.86, 1.14) Former Smoker: 1.05 (0.94, 1.16) Current Smoker: 1.35 (1.20, 1.53) All other Cardiovascular Diseases: $PM_{2.5}$: 0.84 (0.71, 0.99) Former Smoker: 1.22 (1.09, 1.38) Current Smoker: 1.78 (1.56, 2.04) Diseases of the respiratory system: $PM_{2.5}$: 0.92 (0.86, 0.98) Former Smoker: 2.16 (2.04, 2.28) Current Smoker: 3.88 (3.66, 4.11) COPD: $PM_{2.5}$: 0.84 (0.77, 0.93) Former Smoker: 4.93 (4.48, 5.42) Current Smoker: 9.85 (8.95, 10.84) All other respiratory diseases: $PM_{2.5}$: 0.86 (0.73, 1.02) Former Smoker: 1.54 (1.36, 1.74) Current Smoker: 1.83 (1.57, 2.12)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Pope et al. (2007, 091256) **Period of Study:** 1960-1975 **Location:** New Mexico, Arizona, Utah, and Nevada	**Outcome (ICD7&8):** Mortality: Cardiovascular (ICD 7: 400-468, 331, 332 ICD 8: 390-458) Respiratory (ICD 7: 470-527 ICD 8: 460-519) Influenza/ pneumonia (ICD 7: 480-483, 490-493, ICD 8: 470-474, 480-486) **Study Design:** Retrospective Cohort **Statistical Analyses:** Poisson regression model GAM SAS **Age Groups:** All smelter workers >18	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** NR **Range (Min, Max):** NR	The study does not present quantitative results Results are presented in figures. The References found that the strike-related estimated percent decrease in mortality was 2.5% (1.1-4.0),
Reference: Pope et al. (2009, 190107) **Period of Study:** 1978-1982, 1997-2001 **Location:** 211 U.S. counties and 51 metropolitan areas	**Outcome:** Increased life expectancy **Study Design:** Cross-sectional **Statistical Analysis:** Cross-sectional regression **Age Groups:** Adults ≥45 yr	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily, quarterly and annual **Mean (SD) Unit:** 1979-1983: 20.61 ± 4.36 µg/m^3 1999-2000: 14.10 ± 2.86 µg/m^3 **Range (Min, Max):** NR **Copollutant (correlation):** NR	**Increment:** 10 µg/m^3 **Regression Coefficient ± SD** 211 County Units Intercept: 1.75 ± 0.27 Reduction in $PM_{2.5}$: 0.61 ± 0.20 Change in Income: 0.13 ± 0.01 Change in Population: 0.06 ± 0.02 Change in Black Population: -2.70 ± 0.64 Change in Lung Cancer Mortality Rate: -0.06 ± 0.02 Change in COPD Mortality Rate: -0.08 ± 0.02 R: 0.53 51 Metropolitan Areas Intercept: 2.09 ± 0.36 Reduction in $PM_{2.5}$: 0.95 ± 0.23 Change in Income: 0.11 ± 0.02 Change in Population: 0.05 ± 0.02 Change in Black Population: -5.98 ± 1.99 Change in Lung Cancer Mortality Rate: 0.02 ± 0.03 Change in COPD Mortality Rate: -0.19 ± 0.05 R: 0.74

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Rainham et al. (2005, 088676) **Period of Study:** 1981-1999 **Location:** Toronto, Canada	**Outcome:** Total deaths (ICD9 <800), cardiorespiratory (390-459), non-cardiorespiratory (ICD9-NR) **Study Design:** Time-series **Statistical Analyses:** Generalized linear models were used **Season:** Winter (Dec-Feb) Summer (Jun-Aug) **Statistical Package:** S-Plus 6.1	**Pollutant:** $PM_{2.5}$ **Averaging Time:** NR **Mean (SD):** All yr: 17.0 (8.7) µg/m^3 Winters: 17.2 (6.8) Summers: 18.8 (10.2) Avg Winter values: Dry Moderate: 17.0 (1.0) Dry Polar: 17.5 (0.5) Dry Tropical: No Comparison Moist Moderate: 17.1 (0.8) Moist Polar: 17.5 (0.6) Moist Tropical: 16.5 (3.6) Transition: 16.7 (1.0) Avg summer values: Dry Moderate: 18.4 (0.9) Dry Polar: 19.0 (1.2) Dry Tropical: 18.5 (2.4) Moist Moderate: 19.2 (1.2) Moist Polar: 17.5 (2.0) Moist Tropical: 19.8 (1.1) Transition: 17.6 (1.5)	**Mortality risk for winter season and within winter synoptic weather categories** **RR Estimate [Lower CI, Upper CI]:** Winter: Total: 0.998[0.997, 1.000] Cardioresp: 0.998[0.996, 1.000] Other: 0.998 [0.996, 1.000] Dry Moderate: Total: 1.001[0.996, 1.007] Cardioresp: 1.005[0.998, 1.011] Other: 1.002 [0.998, 1.005] Dry Polar: Total: 0.998[0.995, 1.001] Cardioresp: 0.995[0.991, 0.999] Other: 1.002 [0.998, 1.005] Dry Tropical: NA Moist Moderate: Total: 0.998[0.993, 1.002] Cardioresp: 1.003[0.995, 1.010] Other: 0.997 [0.991, 1.004] Moist Polar: Total: 1.001[0.998, 1.005] Cardioresp: 1.002[0.997, 1.007] Other: 1.003 [0.999, 1.007] Moist Tropical: Total: 1.007[0.965, 1.203] Cardioresp: 1.123[1.031, 1.224] Other: 1.248 [1.123, 1.387] Transition Total: 1.003[0.996, 1.009] Cardioresp: 0.996[0.987, 1.004] Other: 0.997 [0.990, 1.004] **Mortality risk for summer season and within summer synoptic weather categories** **RR Estimate [Lower CI, Upper CI]:** Summer: Total: 1.000[1.000, 1.001] Cardioresp: 1.001[1.000, 1.002] Other: 1.001[1.000, 1.002] Dry Moderate: Total: 1.001[0.999, 1.002] Cardioresp: 1.002[0.999, 1.004] Other: 0.999[0.997, 1.002] Dry Polar: Total: 1.002[0.999, 1.005] Cardioresp: 0.996[0.991, 1.000] Other: 1.003[0.999, 1.007] Dry Tropical: Total: 1.016[1.006, 1.027] Cardioresp: 1.017[1.005, 1.030] Other: 1.017 [1.003, 1.031] Moist Moderate: Total: 1.002[1.000, 1.004] Cardioresp: 1.003[0.999, 1.006] Other: 1.004 [1.001, 1.006] Moist Polar: Total: 1.005[0.998, 1.011] Cardioresp: 1.008[0.997, 1.018] Other: 1.003 [0.995, 1.011] Moist Tropical: Total: 0.999[0.997, 1.001] Cardioresp: 0.996[0.993, 1.000] Other: 0.998 [0.995, 1.001] Transition: Total: 1.005[0.996, 1.014] Cardioresp: 1.007[0.994, 1.020] Other: 1.002 [0.996, 1.008]
Reference: Roman et al. (2008, 156921) **Period of Study:** 2006 **Location:** U.S.	**Outcome:** Mortality **Study Design:** Expert Judgment Study **Statistical Analyses:** Standard best practices for expert elicitation	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual avg **Mean (SD):** 4-30	Quantitative results are not presented in the text, but can be found graphically in Fig 3. "Most of the experts' central estimates fall at or above the 2002 ACS median (0.6% per µg/m^3) and below the original Six Cities median (1.2% per µg/m^3)."

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Schwartz, et al. (2008, 156921) **Period of Study:** 1979-1988 **Location:** Six U.S. metropolitan areas: Boston, Massachusetts Knoxville, Tennessee St. Louis, Missouri Steubenville, Ohio Madison, Wisconsin and Topeka, Kansas	**Outcome:** Mortality **Study Design:** Poisson regression with GAM **Statistical Analyses:** Weighted linear regression **Season:** all **Dose-response Investigated?** No **Statistical Package:** S-plus	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Daily **Mean (SD):** Boston-16.5 Knoxville-21.1 St. Louis-19.2 Steubenville-30.5 Madison-11.3 Topeka-12.2 SD not reported **Range (Min, Max):** (0,35) **Monitoring Stations:** 6	**PM Increment:** 10 $\mu g/m^3$ The difference between mean $PM_{2.5}$ concentrations of 10 $\mu g/m^3$ and 20 $\mu g/m^3$ is associated with about a 1.5% increase in deaths.
Reference: (Schwartz et al., 2008, 156963) **Period of Study:** 1979-1998 **Location:** Watertown, MA Kingston and Harriman, TN St Louis, MO Steubenville, OH Portage, Wyocena Pardeeville WI Topeka, KS	**Outcome:** Mortality: Nonaccidental (<800) **Study Design:** Cross-sectional **Statistical Analyses:** Cox proportional hazards regression penalized splines Bayesian Model Averaging **Age Groups:** >18	**Pollutant:** $PM_{2.5}$ **Averaging Time:** Annual avg **Mean (SD):** 17.5 (6.8) **Range (Min, Max):** (8, 40)	**Increment:** 10 $\mu g/m^3$ **Relative Risk (Lower CI, Upper CI)** **Estimated from Fig 4:** All Cause Mortality - Year before Death 0: 1.10 (1.00, 1.21) 1: 1.03 (0.98, 1.08) 2: 1.01 (1.00, 1.02) 3: 1.00 (0.99, 1.01) 4: 1.00 (0.99, 1.01) 5: 1.00 Lung Cancer Mortality - Year Before Death **Estimated from Fig 5** 0: 1.18 (1.00, 1.48) 1: 1.12 (0.98, 1.33) 2: 1.08 (0.92, 1.22) 3: 1.02 (1.01, 1.03) 4: 1.01 (1.00, 1.02) 5: 1.01 RR per 10 $\mu g/m^3$ increase of $PM_{2.5}$ exposure Level Of Increase **Estimated from Fig 3** 10 $\mu g/m^3$: 1.15 20 $\mu g/m^3$: 1.29 30 $\mu g/m^3$: 1.46 40 $\mu g/m^3$: 1.64
Reference: Tainio et al. (2005, 087444) **Period of Study:** 1997-Present **Location:** Helsinki, Finland	**Outcome (ICD10):** Mortality: Cardiopulmonary (I11-I70 and J15-J47) Lung Cancer (C34) Other causes **Study Design:** Time-series simulation **Statistical Analyses:** Monte Carlo Simulation **Age Groups:** All ages	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** 10.7 **Range (Min, Max):** NR	**Estimated Deaths Per Year (Min CI, Max CI) Associated with Primary $PM_{2.5}$** **Emissions from buses in Helsinki in 2020 for different bus strategies** Cardiopulmonary Mortality Current Fleet: 15.9 (0, 46.6) Modern Diesel: 7.9 (0, 23.0) Diesel with particle trap: 3.9 (0, 12) Natural gas bus: 2.3 (0, 6.8) Lung Cancer Mortality Current Fleet: 2.2 (0, 6.1) Modern Diesel: 1.1 (0, 3.0) Diesel with particle trap: 0.6 (0, 1.6) Natural gas bus: 0.3 (0, 0.9) Total Mortality Current Fleet: 18.1 (0, 55.0) Modern Diesel: 9.0 (0, 27.0) Diesel with particle trap: 4.4 (0, 14.1) Natural Gas Bus: 2.6 (0, 8.0)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Villeneuve et al. (2002, 042576) **Period of Study:** 1974-1991 **Location:** Six U.S. Cities: Steubenville, OH, St. Louis, MO, Portage, WI, Topeka, KS, Watertown, MA, Kingston/ Harriman, TN	**Outcome (ICD10):** Mortality: Nonaccidental (<800) **Study Design:** Prospective Cohort **Statistical Analyses:** Poisson, EPICURE **Age Groups:** All ages <60 ≥ 60	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24-h avg **Mean (SD):** Portage: 10.9 (7.2) Topeka: 12.1 (7.1) Harriman: 20.7 (9.4) Watertown: 14.9 (8.4) St. Louis: 18.7 (10.6) Steubenville: 28.6 (21.0) Overall: 18.6 **Range (Min, Max):** NR	**Increment:** 18.6 µg/m^3 **Relative Risk (Min CI, Max CI)** RR of all cause mortality for exposure of $PM_{2.5}$ by age group Exposure to $PM_{2.5}$ remained fixed over entire study period <60: 1.89 (1.32, 2.69) >60: 1.21 (1.02, 1.43) Total: 1.31 (1.12, 1.52) Exposure to $PM_{2.5}$ was defined according to 13 calendar periods* (no smoothing) <60: 1.52 (1.15, 2.00) >60: 1.11 (0.95, 1.29) Total: 1.19 (1.04, 1.36) Exposure to $PM_{2.5}$ was defined according to 13 calendar periods* (smoothed) <60: 1.43 (1.10, 1.85) >60: 1.09 (0.93, 1.26) Total: 1.16 (1.02, 1.32) Time dependent estimate of $PM_{2.5}$ received during the previous 2 yr <60: 1.42 (1.09, 1.82) >60: 1.08 (0.94, 1.25) Total: 1.16 (1.02, 1.31) Time dependent estimate of $PM_{2.5}$ received 3-5 yr before current yr <60: 1.35 (1.08, 1.67) >60: 1.08 (0.95, 1.22) Total: 1.14 (1.02, 1.27) Time dependent estimate of $PM_{2.5}$ received >5 yr before current yr <60: 1.34 (1.11, 1.59) >60: 1.09 (0.99, 1.20) Total: 1.14 (1.05, 1.23) * The calendar periods used were: 1970-1978, 1979, 1980, 1981, 1982, 1983, 1984, 1985, 1986, 1987, 1988, 1989, and 1990+. RR of all cause mortality and $PM_{2.5}$ exposure by city Portage: 1.16 (0.96, 1.39) Topeka: 1.06 (0.89, 1.27) Harriman Men: 1.04 (0.79, 1.36) Women: 0.96 (0.69, 1.31) All: 1.13 (0.95, 1.35) Watertown Men: 1.20 (0.95, 1.51) Women: 1.06 (0.78, 1.43) All: 1.32 (1.11, 1.51) St. Louis Men: 0.97 (0.76, 1.24) Women: 1.13 (0.86, 1.49) Steubenville Men: 1.39 (1.11, 1.74) Women: 1.22 (0.93, 1.61)
Reference: Willis et al. (2003, 089922) **Period of Study:** 1982-1989 **Location:** U.S. Metropolitan areas in all 50 states	**Outcome:** Mortality: All causes Lung Cancer (162) Cardiopulmonary (401-440, 460-519) **Study Design:** Prospective Cohort **Statistical Analyses:** Cox proportional hazards model **Age Groups:** All ages	**Pollutant:** Sulfates **Averaging Time:** Annual avg **Mean (SD):** 10.6 µg/m^3 **Range (Min, Max):** 3.6, 23.5 **Copollutant:** CO, NO_2, O_3, SO_2	All Cause, Metropolitan Scale: 1.25 (1.13, 1.37) All Cause, County Scale: 1.50 (1.30, 1.73) CPD, Metropolitan Scale: 1.29 (1.15, 1.46) CPD, County Scale: 1.75 (1.48, 2.08)
Reference: Zanobetti and Schwartz (2009, 188462) **Period of Study:** 1999-2005 **Location:** 112 U.S. Cities	**Outcome:** Mortality, all causes, excluding ICD codes S00-U99 **Study Design:** Time-series **Covariates:** Region, season	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 24 h **Mean (SD)** Birmingham AL - 16.5 Phoenix AZ - 11.4 LittleRock AR - 14.3	**Increment:** 10 µg/m^3 **Percent Increase (95% CI) in mortality by increment of $PM_{2.5}$, combined by season** All Cause Mortality Overall: 0.98 (0.75-1.22)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
	Statistical Analysis: Poisson regression **Age Groups:** All	Fresno CA - 19.4 Bakersfield CA - 21.7 Los Angeles CA - 19.9 Anaheim CA - 16.3 Rubidoux CA - 24.9 Sacramento CA - 13.0 El Cajon CA - 13.5 Denver CO - 10.3 Hartford CT - 11.6 New Haven CT - 13.7 Wilmington DE - 15.1 Davie FL - 8.4 Miami FL - 9.4 Jacksonville FL - 10.6 Pensacola FL - 12.4 Tampa FL - 11.9 Orlando FL - 10.3 Palm beach FL - 7.9 Pinellas FL - 10.4 Atlanta GA - 17.6 Chicago IL - 15.9 Gary IN - 15.3 Indianapolis IN - 16.3 Cedar Rapids IA - 11.0 Des Moines IA - 10.5 Davenport IA - 12.3 Louisville KY - 15.9 Baton Rouge LA - 13.4 Avondale LA - 12.3 New Orleans LA - 12.6 Baltimore MD - 15.6 Springfield MA - 12.3 Boston MA - 12.4 Worcester MA - 11.3 Holland MI - 12.1 Grand Rapids MI - 13.6 Detroit MI - 16.2 Minneapolis MN - 11.1 Kansas MO - 12.0 St Louis MO - 14.5 Omaha NE - 10.4 Elizabeth NJ - 14.7 Albuquerque NM - 6.7 New York NY - 14.8 Bath NY - 9.6 Durham NC - 14.3 Winston NC - 14.7 Greensborough NC - 14.2 Charlotte NC - 15.3 Raleigh NC - 14.3 Middletown OH - 16.4 Youngstown OH - 15.6 Cleveland OH - 16.4 Columbus OH - 16.2 Cincinnati OH - 17.1 Steubenville OH - 17.0 Toledo OH - 14.9 Dayton OH - 16.2 Akron OH - 16.0 Warren OH - 15.3 Oklahoma OK - 9.9 Tulsa OK - 11.1 Bend OR - 7.8 Medford OR - 9.9 Klamath OR - 10.6 Eugene OR - 8.0 Portland OR - 8.8 Gettysburg PA - 13.4 Pittsburgh PA - 15.7 State College PA - 13.2 Carlisle PA - 15.1 Harrisburg PA - 15.5 Erie PA - 13.1 Scranton PA - 11.8 Allentown PA - 14.2 Wilkes Barre PA - 12.8 Mercer PA - 14.1 Easton PA - 14.0	Winter: 0.56 (0.17-0.94) Spring: 2.57 (1.96-3.19) Summer: 0.25 (-0.13-0.63) Fall: 0.95 (0.56-1.34) CVD Overall: 0.85 (0.46-1.24) Winter: 0.70 (0.04-1.36) Spring: 2.18 (1.22-3.15) Summer: -0.03 (-0.75-0.69) Fall: 0.92 (0.17-1.68) MI Overall: 1.18 (0.48-1.89) Winter: 1.29 (-0.14-2.75) Spring: 2.12 (0.53-3.74) Summer: -0.03 (-1.46-1.42) Fall: 1.24 (0.12-2.36) Stroke Overall: 1.78 (0.96-2.62) Winter: 1.93 (0.34-3.54) Spring: 2.04 (-0.02-4.13) Summer: 1.64 (0.05-3.26) Fall: 1.69 (0.06-3.35) Respiratory Overall: 1.68 (1.04-2.33) Winter: 0.86 (-0.16-1.88) Spring: 4.62 (3.08-6.18) Summer: 0.78 (-0.49-2.06) Fall: 1.45 (0.19-2.72) **Percent Increase (95% CI) in mortality by increment in $PM_{2.5}$ combined by region** All Cause Mortality Humid Subtropical and Maritime: 1.02 (0.65-1.38) Warm Summer Continental: 1.19 (0.73-1.64) Hot Summer Continental: 1.14 (0.55-1.73) Dry: 1.18 (-0.70-3.10) Dry, Continental: 1.26 (-0.21-2.76) Mediterranean: 0.50 (0.00-1.01) CVD Humid Subtropical and Maritime: 0.78 (0.05-1.51) Warm Summer Continental: 1.43 (0.67-2.19) Hot Summer Continental: 0.43 (-0.53-1.40) Dry: 3.11 (-0.02-6.33) Dry, Continental: 1.67 (-0.75-4.16) Mediterranean: 0.16 (-0.46-0.79) MI Humid Subtropical and Maritime: 0.97 (-0.29-2.26) Warm Summer Continental: 1.50 (0.05-2.97) Hot Summer Continental: 0.64 (-0.96-2.28) Dry: 4.25 (-2.38-11.33) Dry, Continental: 0.60 (-7.42-9.32) Mediterranean: 1.85 (-0.66-4.41) Stroke Humid Subtropical and Maritime: 2.94 (1.59-4.32) Warm Summer Continental: 1.85 (0.04-3.69) Hot Summer Continental: 0.77 (-1.77-3.38) Dry: 1.82 (-6.98-11.45) Dry, Continental: 2.49 (-2.32-7.53) Mediterranean: 0.95 (-0.66-2.59) Respiratory Humid Subtropical and Maritime: 0.91 (-0.25-2.08) Warm Summer Continental: 2.12 (0.89-3.36) Hot Summer Continental:

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
		Philadelphia PA - 14.5 Washington PA - 14.7 Providence RI - 11.5 Charleston SC - 12.1 Taylors SC - 15.3 Columbia SC - 14.0 Spartanburg SC - 14.2 Nashville TN - 14.0 Knoxville TN - 16.0 Memphis TN - 13.5 San Antonio TX - 9.4 Dallas TX - 12.9 El Paso TX - 9.2 Houston TX - 12.9 Port Arthur TX - 11.5 Ft Worth TX - 12.2 Austin TX - 10.4 Salt Lake UT - 11.5 Provo UT - 9.5 WDC VA - 15.2 Annandale VA - 14.0 Dumbarton VA - 13.6 Chesapeake VA - 12.7 Norfolk VA - 12.7 Richmond VA - 14.3 Seattle WA - 10.1 Tacoma WA - 11.2 Spokane WA - 9.1 Dodge WI - 11.1 Milwaukee WI - 13.2 Waukesha WI - 13.2 **Range (Min, Max):** NR **Copollutant (correlation):** NR	3.36 (1.95-4.79) Dry: 5.81 (-0.04-12.00) Dry, Continental: -0.31 (-5.89-5.61) Mediterranean: 1.06 (-0.36-2.50)
Reference: Zeger et al. (2007, 157176) **Period of Study:** 2000-2002 **Location:** 250 largest U.S. counties	**Outcome:** Mortality **Study Design:** Retrospective Cohort (MCAPS) **Statistical Analyses:** Log-linear regression models (GAM) **Covariates:** Age, gender, race, county-level SES, education and COPD SMR **Age Groups:** 65+ 65-74, 75-84, 85+	**Pollutant:** $PM_{2.5}$ **Averaging Time:** 3-yr avg	**Increment:** 10 µg/m^3 65+: 1.076 (1.044, 1.108) Eastern U.S.: 1.125 (1.091, 1.159) Central U.S.: 1.196 (1.115, 1.277) Western U.S.: 1.029 (0.994, 1.064) 65-74: 1.156 (1.117, 1.196) 75-84: 1.081 (1.042, 1.121) 85+: 0.995 (0.956, 1.035)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Reference: Zeger et al. (2008, 191951)	**Outcome:** Mortality	**Pollutant:** $PM_{2.5}$	**Increment:** 10 µg/m^3
Period of Study: 2000-2005	**Study Design:** Retrospective Cohort	**Averaging Time:** Annual	**Relative Risk (Min CI, Max CI) lag**
Location: 4568 zip codes in urban areas	**Statistical Analysis:** Log-linear regression model	**Median (SD) Unit:**	Risk estimate for increase in mortality per increase in $PM_{2.5}$, all ages
	Age Groups: ≥65	Eastern: 14.0 µg/m^3	Eastern Region Age: 1.155 (1.130-1.180) Age + SES: 1.105 (1.084-1.125) Age + SES + COPD: 1.068 (1.049-1.087)
		Central: 10.7 µg/m^3	Central Region Age: 1.178 (1.133-1.222) Age + SES: 1.089 (1.052-1.125) Age + SES + COPD: 1.132 (1.095-1.169)
		Western: 13.1 µg/m^3	Western Region Age: 1.003 (0.981-1.025) Age + SES: 0.997 (0.978-1.016) Age + SES + COPD: 0.989 (0.970-1.008)
		All: 13.2 µg/m^3	Risk estimate for increase in mortality per increase in $PM_{2.5}$, ages 65-74 Eastern Region Age: 31.1 (26.8-35.5) Age + SES: 17.3 (14.6-20.0) Age + SES + COPD: 11.4 (8.8-14.1) Central Region Age: 39.0 (29.7-48.2) Age + SES: 16.5 (10.9-22.1) Age + SES + COPD: 20.4 (15.0-25.8) Western Region Age: 6.0 (2.3-9.6) Age + SES: -2.1 (-5.0-0.8) Age + SES + COPD: -1.5 (-4.2-1.1)
		Range (IQR):	
		Eastern: 12.3-15.3	
		Central: 9.8-12.2	
		Western: 10.4-18.5	
		All: 11.1-14.9	Risk estimate for increase in mortality per increase in $PM_{2.5}$, ages 75-84 Eastern Region Age: 17.6 (14.9-20.4) Age + SES: 12.4 (10.1-14.6) Age + SES + COPD: 8.9 (6.8-11.0) Central Region Age: 17.5 (12.7-22.2) Age + SES: 8.8 (4.6-13.0) Age + SES + COPD: 12.0 (7.6-16.4) Western Region Age: 0.4 (-2.0-2.7) Age + SES: 0.3 (-1.8-2.5) Age + SES + COPD: -0.2 (-2.2-1.9)
		Copollutant (correlation): NR	Risk estimate for increase in mortality per increase in $PM_{2.5}$, aged ≥85 Eastern Region Age: -1.4 (-3.5-0.8) Age + SES: 1.4 (-0.7-3.5) Age + SES + COPD: 1.7 (-0.3-3.7) Central Region Age: -2.1 (-5.9-1.6) Age + SES: -0.7 (-4.2-2.8) Age + SES + COPD: -0.3 (-4.0-3.3) Western Region Age: -5.2 (-7.2-3.2) Age + SES: 0.9 (-0.8-2.7) Age + SES + COPD: -0.5 (-2.5-1.5)

[1]All units expressed in µg/m^3 unless otherwise specified.

Table E-34. Long-term exposure - central nervous system outcomes - PM.

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Author: Calderón-Garcidueñas et al. (2008, 192369) **Period of Study:** NR **Location:** Mexico City (polluted city) and Tlaxcala and Veracruz (control cities), Mexico	**Outcome (ICD9 and ICD10):** COX2 (cyclooxygenase), IL-1β, CD14 in lungs, OB (olfactory bulb), frontal cortex, hippocampus, substantia nigrae, periaqueductal gray and vagus nerves **Age Groups Analyzed:** Subjects 2-45 yr of age mean=25.1 ± 1.5 yr **Study Design:** Cross-sectional **N:** 47 deceased subjects with complete autopsies and neuropathological examinations (each subject had to be considered clinically healthy and cognitively and neurologically intact prior to death) (primarily cause of death: accidents resulting in immediate death) **Statistical Analyses:** NR likely used T-tests in addition, stated using "parametric procedure that considers the differences among variances of the variables of interest" **Covariates:** Age, gender, place of birth, place of residency, occupation, smoking habits, clinical histories, cause of death, and time between death and autopsy **Season:** NR **Dose-response Investigated? (Yes/No):** No **Statistical package:** Stata	**PM Size:** No measure of PM used Mexico City as the "polluted city" and Tlaxcala and Veracruz as the "control cities" **Averaging Time:** NA **Mean (SD):** NA **Percentiles:** NA **Range (Min, Max):** NA **Unit (i.e. μg/m^3):** NA **Number of Monitoring Stations:** NA **Co-pollutant (correlation):** NA	**PM Increment:** NA **Effect Estimate [Lower CI, Upper CI]:** RT-PCR sample results from Control and Mexico City (MC) lung, CNS, PNS (peripheral nervous system) tissues and p-value for the difference between the means Concentrations are normalized to the amount of GAPDH cDNA COX2 (cyclooxygenase-2) lung Controls: 15.9± 6.7 x 106 MC residents: 42.3± 7.4 x 106 P-value: 0.015 IL-1β lung Controls: 3.08±1.87 x 106 MC residents: 4.51± 2.6 x 106 P-value: 0.60 COX2 OB (olfactory bulb) Controls: 12.9± .0 x 105 MC residents: 38.7± 5.5 x 105 P-value: 0.0002 IL-1β OB Controls: 3.4± 0.8 x 104 MC residents: 7.7± 1.0 x 104 P-value: 0.003 CD14 OB Controls: 0.01± 0.001 MC residents: 0.04± 0.01 P-value: 0.04 COX2 frontal Controls: 2.6± 0.4 x 105 MC residents: 5.0± 0.7 x 105 P-value: 0.008 IL-1β frontal Controls: 0.6± 0.2 x 104 MC residents: 6.2± 1.3 x 104 P-value: 0.0002 COX2 hippocampus Controls: 1.9± 0.5 x 105 MC residents: 1.6± 8.7 x 105 P-value: 0.1 IL-1β hippocampus Controls: 1.8±0.2 x 104 MC residents: 3.0±0.5 x 104 P-value: 0.06 COX2 substantia nigrae Controls: 0.16± 0.06 MC residents: 0.97± 0.2 P-value: 0.03 IL-1β substanita nigrae Controls: 0.01± 0.005 MC residents: 0.09± 0.03 P-value: 0.06 CD14 substantia nigrae Controls: 0.02± 0.005 MC residents: 0.03± 0.007 P-value: 0.7 COX2 periaqueductal gray Controls: 0.10± 0.03 MC residents: 0.45± 0.12 P-value: 0.12 IL-1β periaqueductal gray Controls: 0.009± 0.003 MC residents: 0.07± 0.02 P-value: 0.09 COX2 left vagus Controls: 0.65± 0.18 MC residents: 2.68± 0.82 P-value: 0.03 COX2 right vagus Controls: 0.43± 0.09

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
			MC residents: 3.68± 0.8 P-value: 0.0002 IL-1β left vagus Controls: 0.1± 0.03 MC residents: 1.3± 0.73 P-value: 0.06 IL-1 β right vagus Controls: 0.15± 0.09 MC residents: 0.87± 0.53 p-value: 0.66 CD14 left vagus Controls: 0.07± 0.01 MC residents: 0.79± 0.41 P-value: 0.01 CD14 right vagus Controls: 0.05± 0.01 MC residents: 0.31± 0.1 P-value: 0.02 Distribution of subjects with expression of Aβ42 as a function of age and residency Groups: No (%) with Aβ42 expression Controls <25yr APOE 3/3 (n=6): 0 (0) Controls >25yr APOE 3/3 (n=3): 0 (0) MC E2 or E3 <25yr (n=17): 10 (58.82) MC E2 or E3 >25yr (n=10): 8 (80) MC E4 (n=8): 8 (100) Controls E4 (n=3): 2 (66) Distribution of subjects with expression of α-synuclein as a function of age and Residency Groups: No (%) with α-synuclein expression Controls <25yr APOE 3/3 (n=6): 0 (0) Controls >25yr APOE 3/3 (n=3): 0 (0) MC E2 or E3 <25yr (n=17): 4 (23.5) MC E2 or E3 >25yr (n=10): 3 (30) MC E4 (n=8): 2 (25) Controls E4 (n=3): 0 (0)
Reference: Chen and Schwartz (2009, 179945) **Period of Study:** 1989-1991 **Location:** U.S.	**Outcome:** Change in central nervous system function **Study Design:** Panel **Covariates:** Age, sex, race/ethnicity, individual socioeconomic position, lifestyle factors, household and neighborhood characteristics, conventional CVD risk factors **Statistical Analysis:** Pearson Chi-square tests and t-tests, as appropriate **Statistical Package:** STATA **Age Groups:** 20-59 yr	**Pollutant:** PM_{10} **Averaging Time:** 1 yr **Mean (SD) Unit:** 37.2 ± 12.8 μg/m^3 **Copollutant:** O_3	**Increment:** 10 μg/m^3 **Regression Coefficient β (95% CI)** Crude SRTT: 2.14 (-0.08-4.36) SDST: 0.08 (0.04-0.13) SDLT Trials: 0.22 (0.13-0.31) SDLT Total: 0.44 (0.23-0.65) Model 1: adjusted for age, sex, race/ethnicity SRTT: 2.03 (-0.15-4.20) SDST: 0.10 (0.05-0.15) SDLT Trials: 0.23 (0.14-0.32) SDLT Total: 0.48 (0.27-0.68) Model 2: Model 1 + socioeconomic factors SRTT: -0.11 (-2.38-2.16) SDST: 0.01 (-0.04-0.06) SDLT Trials: 0.01 (-0.08-0.10) SDLT Total: -0.07 (-0.27-0.13) Model 3: Model 2 + lifestyle factors SRTT: -0.36 (-2.58-1.85) SDST: 0.00 (-0.04-0.05) SDLT Trials: 0.09 (0.00-0.17) SDLT Total: 0.12 (-0.07-0.31)

Study	Design & Methods	Concentrations[1]	Effect Estimates (95% CI)
Author: Suglia et al. (2008, 157027) **Period of Study:** 1986-2001 **Location:** Boston, Massachusetts	**Outcome (ICD9 and ICD10):** Cognition: Kaufman Brief Intelligence Test, K-BIT (vocabulary and matrices subscales and composite IQ score) Wide Range Assessment of Memory and Learning, WRAML (psychometric instrument with subscales on verbal memory, visual memory, learning, and overall general index scale) All cognition scores have a mean of 100 and SD=15. **Age Groups Analyzed:** Cognitive tests administered when children were 8-11 yr of age **Study Design:** Cross-sectional **N:** 202 children **Statistical Analyses:** Linear regression **Covariates:** Child's age at cognitive assessment, gender, primary language spoken at home, and maternal education (model 1 "Demographic factors") Sensitivity analyses performed with further adjustment for in-utero and postnatal secondhand tobacco smoke exposure (via questionnaire during follow-ups and urinary cotinine levels) (model 2) Birth weight (model 3) and blood lead level (model 4) **Season:** Separate land-use regression models were fit for the warm (May-Oct) and cold (Nov-Apr) seasons Used avg of two seasons as measure of avg lifetime BC exposure **Dose-response Investigated? (Yes/No):** No **Statistical package:** SAS (v9.0)	**PM Size:** Black carbon (BC) **Averaging Time:** Lifetime exposure Estimated 24 h measures of traffic using a spatiotemporal land-use regression model using data from >80 locations in Greater Boston (6021 pollution measurements from 2127 unique exposure days) Predictors in the land-use regression analysis were the BC level at a central station (to capture avg concentrations on that day), meteorological conditions, weekday/weekend, and measure of traffic activity (GIS-based measures of cumulative traffic density within 100m, population density, distance to nearest major roadway, % urbanization) Used the avg of the cold and warm seasons as the measure of avg lifetime BC exposure **Mean (SD):** 0.56 (0.13) μg/m^3 **Percentiles:** NR **Range (Min, Max):** NR **Unit (i.e. μg/m^3):** **Number of Monitoring Stations:** >80 locations **Co-pollutant (correlation):** NA	**PM Increment:** 0.4 μg/m^3 **Effect Estimate [Lower CI, Upper CI]:** Change in subscale score (95%CI) per IQR (0.4 μg/m^3) increase in log BC level K-BIT Vocabulary: Adj for demographic factors: -2.0 (-5.3, 1.3) Adj for above factors + secondhand smoke: -2.0 (-5.3, 1.4) Adj for above factors + birth weight: -2.0 (-5.4, 1.3) Adj for above factors + blood lead level: -2.2 (-5.5, 1.1) Matrices: Adj for demographic factors: -4.2 (-7.7, -0.7) Adj for above factors + secondhand smoke: -4.0 (-7.5, -0.4) Adj for above factors + birth weight: -4.0 (-7.6, -0.5) Adj for above factors + blood lead level: -4.0 (-7.6, -0.5) Composite: Adj for demographic factors: -3.4 (-6.6, -0.3) Adj for above factors + secondhand smoke: -3.3 (-6.4, -0.1) Adj for above factors + birth weight: -3.3 (-6.5, -0.2) Adj for above factors + blood lead level: -3.4 (-6.6, -0.3) WRAML Verbal: Adj for demographic factors: -1.1 (-4.6, 2.3) Adj for above factors + secondhand smoke: -1.2 (-4.7, 2.3) Adj for above factors + birth weight: -1.3 (-4.7, 2.2) Adj for above factors + blood lead level: -1.3 (-4.8, 2.2) Visual: Adj for demographic factors: -5.2 (-8.6, -1.7) Adj for above factors + secondhand smoke: -5.3 (-8.8, -1.8) Adj for above factors + birth weight: -5.3 (-8.8, -1.8) Adj for above factors + blood lead level: -5.4 (-8.9, -1.9) Learning: Adj for demographic factors: -2.7 (-6.5, 1.1) Adj for above factors + secondhand smoke: -2.6 (-6.5, 1.2) Adj for above factors + birth weight: -2.6 (-6.5, 1.3) Adj for above factors + blood lead level: -2.8 (-6.6, 1.1) General: Adj for demographic factors: -3.7 (-7.2, -0.2) Adj for above factors + secondhand smoke: -3.7 (-7.3, -0.1) Adj for above factors + birth weight: -3.8 (-7.4, -0.2) Adj for above factors + blood lead level: -3.9 (-7.5, -0.3)

[1]All units expressed in μg/m^3 unless otherwise specified.

Annex E References

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Annex F. Source Apportionment Studies

Table F-1. Epidemiologic studies of ambient PM sources, factors, or constituents

Reference: Andersen et al. (2007, 093201) **Location:** 1 monitor in Copenhagen, Denmark/ 6 yr, but apportionment done for 1.5 yr only (2002-2003) **Particle Size:** PM_{10}	**Subjects:** NR **Exposure:** NR	**N:** NR	**Number of Constituents considered for grouping:** 31	**Grouping method:** PCA + PMF/CMB hybrid (COPREM) **# of groups:** 12, but only 6 used in relating to health effects, and CO, NO_2	**Groups/Factors/ Sources:** Road, vehicle, salt, biomass, oil, coal, rock, lime, $NaNO_3$, NH_4NO_3, $(NH_4)_2SO_3$, (NH_4SO_4)	**PM variables used:** Mass contribution of sources
	Results: Single pollutant models: Biomass, secondary compounds, oil, and crustal significantly associated with CVD HA (4-day ma). Biomass and secondary components significantly associated with respiratory HA (5-day ma). No significant effects for asthma HA in children (6-day ma). **Two pollutant models:** Crustal effect for CVD admissions remained robust. Biomass effect for respiratory admissions was highest. Effect of vehicle source remained robust for asthma admissions in children in presence of other PM_{10} sources.					
Reference: Bell et al. (Bell et al., 2009, 191007) **Location:** $PM_{2.5}$: 2000-2005 (6 yr)/106 US counties/EPA composition data PM_{10}: 1987-2000/100 counties/EPA composition data **Particle Size:** PM_{10}, $PM_{2.5}$	**Subjects:** NR **Exposure:** NR	**N:** NR	**Number of Constituents considered for grouping:** 16 elements + NO_3, SO_4, EC, OC	**Grouping method:** NR **# of groups:** NR	**Groups/Factors/ Sources:** NR	**PM variables used:** Every component (16 elements + NO_3, SO_4,EC, OC)
	Results: Mortality: Ni significantly increased PM_{10} mortality risks. However, effect of Ni was not significant when New York City was removed, in a sensitivity analysis conducted by selectively removing cities from the overall estimate. **Hospital Admissions:** CVD and respiratory HAs higher in counties with higher EC, Ni, and V $PM_{2.5}$. In CVD association between $PM_{2.5}$, RR and V robust to inclusion of EC or V, and V robust to inclusion of EC.					
Reference: Cakmak et al. (2009, 191995) **Location:** 1 monitor in Santiago, Chile **Particle Size:** $PM_{2.5}$	**Subjects:** NR **Exposure:** 1998-2009 (8.3 yr)	**N:** NR	**Number of Constituents considered for grouping:** 16 elements + CO, NO_2, SO_2, EC, OC	**Grouping method:** PCA **# of groups:** 4	**Groups/Factors/ Sources:** Vehicle (CO, NO_2, EC, OC), Soil (Al, Ca, Fe, Si), Combustion (Cr, Cu, Fe, Mn, Zn), Factor 4 (Br, Cl, Pb)	**PM variables used:** individual components, then groupings
	Results: Individual components: EC, OC only stat. sign. risk estimates for total, cardiac, and respiratory mortality for 1-day lag after adjustment for other elements. **Groupings:** Lag 1. Vehicle factor: Increased total mortality, cardiac mortality, and respiratory mortality. Soil factor: increased cardiac mortality and respiratory mortality (but smaller than vehicle factor RRs). Combustion factor: greatest RR for respiratory mortality, but significant for total and cardiac mortality. Factor 4: increased total, cardiac, and respiratory mortality. Point estimates for Factor 1 significantly different from Factors 3 and 4. Elderly had higher risk estimates for combustion and soil sources. No significant effect modification by gender or season.					
Reference: Franklin et al. (2008, 097426) **Location:** STN/25 communities/2000-2005 (6 yr) **Particle Size:** $PM_{2.5}$	**Subjects:** NR **Exposure:** NR	**N:** NR	**Number of Constituents considered for grouping:** 15 elements + EC, OC, NO_3	**Grouping method:** NR **# of groups:** NR	**Groups/Factors/ Sources:** NR	**PM variables used:** Every component
	Results: The $PM_{2.5}$-mortality association was significantly modified by Al, As, Sulfate, Ni, and Si. When including a combination of species proportions and using backwards elimination Al, sulfate, and Ni remained significant. Al and Ni explained most of the residual heterogeneity.					

Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISA) and the Integrated Risk Information System (IRIS).

Reference: Gent et al. (2009, 180399) **Location:** 2 monitors in New Haven, CT/ 3.5 yr **Particle Size:** $PM_{2.5}$	**Subjects:** Children with physician diagnosed asthma and symptoms or medication use in previous 12 mo, and resided within 30km of New Haven county monitor **Exposure:** NR	**N:** 149 children	**Number of Constituents considered for grouping:** 17 elements + EC	**Grouping method:** PCA **# of groups:** 6	**Groups/Factors/ Sources:** Vehicle (EC, Zn, Pb, Cu, Se), road dust (Si, Fe, Al, Ca, Ba, Ti), sulfur (S, P), biomass burning, (K) oil (V, Ni), sea salt (Na, Cl) In addition, effects of NO_2, CO, SO_2, and O_3 were included in the health outcomes model	**PM variables used:** Groupings and individual elements
	Results: Overall: Trace elements originating from motor vehicle, road dust, biomass burning, and oil sources associated with symptoms and/or medication use. No associations with S or sea salt. **Specific Results:** $PM_{2.5}$ mass from motor vehicle or road dust associated with increased odds of respiratory symptoms or inhaler use. Reduced odds of wheeze or inhaler use with same day S. Significant reductions odds of wheeze with biomass burning. **Co-pollutant:** Positive effects of motor vehicles and road dust on wheeze were robust to the inclusion of gaseous copollutants. However, NO_2 increases association with wheeze.					
Reference: Ito et al. (2006, 088391) **Location:** Washington, DC **Particle Size:** $PM_{2.5}$	**Subjects:** NR **Exposure:** NR	**N:** NR	**Number of Constituents considered for grouping:** NR	**Grouping method:** Comparison of: PMF; (absolute) PCA; UNMIX **# of groups:** 6-10 **Groups/ Factors/ Sources:** Different research groups gave different names to sources	**Sources for which association with health was analyzed:** Soil, traffic, Secondary SO_4, NO_3 (Washington, DC only), residual oil (Washington, DC only), Wood smoke/ biomass combustion, Sea salt, incinerator (Washington, DC only), primary coal (Washington, DC only), Cu smelter (Phoenix only)	**PM variables used:** Mass contribution of sources
	Results: Overall, $PM_{2.5}$ effects observed at lag 3. Lag structure of association varied across source types, but consistent across investigators for total (nonaccidental mortality): soil factor - mostly positive at various lags (not significant); secondary sulfate - strongest association at lag 3; nitrate - mostly negative except at lag 3; residual oil - strongest association at lag 2 (not significant); wood-burning - increasing association as lag increases (not significant); incinerator - significant negative associations at lag 0; primary coal - significant association at lag 3.					
Reference: Laden et al. (2000, 012102) **Location:** Monitors in 6 Eastern US cities (Harvard Six Cities Study) **Particle Size:** NR	**Subjects:** NR **Exposure:** NR	**N:** NR	**Number of Constituents considered for grouping:** 15 elements	**Grouping method:** PCA **# of groups:** 8	**Groups/ Factors/ Sources:** Soil/crustal (PM fine), mobile vehicle exhaust (PM fine), coal (PM fine), fuel oil; metals, salt manganese, residual	**PM variables used:** Tracers: Si, V, Cl, Pb, Se
	Results: Lag 0-1 avg for all results. Overall 6 cities, mobile source factor (using Pb as tracer) had greatest association with daily mortality (3.4%) with 10 µg/m3 increase. The greatest effects for mortality due to mobile sources were observed in Madison (Portage), Knoxville (Kingston-Harriman), and St. Louis, although the Madison results were not statistically significant. The coal source factor was only significant in Boston (Watertown) - 2.8% increase in mortality and the overall percent increase was also significant (1.1%). Deaths from pneumonia attributable to coal combustion sources was 7.9% (CI 3.1-12.7%) and statistically significant. The crustal factor was not associated with mortality in any city, although this factor was not a significant predictor in the regression model for Boston (Watertown) due to its low contribution to $PM_{2.5}$ mass. For specific elements included simultaneously, S, Pb, and Ni were significantly associated with overall mortality (3.0, 1.6, 1.5%, respectively). Boston had the greatest percent increase in mortality for S (7.9%), Knoxville for Pb (15.0%), and Steubenville for Ni (8.2%), although the CIs are all quite large. **Reanalysis results: (Schwartz, 2003, 042811)** Effects changed slightly. New percent increases in mortality for combined cities are 3.5 and 0.79 for traffic and coal, respectively. The coal factor in Boston decreased to 2.1% increased mortality. A residual oil factor in Boston and Steubenville resulted in at 22.9% increase in daily deaths (but was not significant in the original analysis).					
Reference: Lanki et al. (2006, 088412) **Location:** Monitors in Helsinki, Finland, Amsterdam,The Netherlands and Erfurt, Germany **Particle Size:** UF/$PM_{2.5}$	**Subjects:** NR **Exposure:** NR	**N:** NR	**Number of Constituents considered for grouping:** 13 elements	**Grouping method:** Absolute PCA **# of groups:** 5	**Groups/ Factors/ Sources:** Crustal; long range transported; oil combustion; soil; traffic	**PM variables used:** Tracers: Si (crustal); S (long-range transport); Ni (oil combustion); Cl (salt); ABS (local traffic).
	Results: Highest observed effects were for crustal sources and salt at lag 3 (when analyzing sources), but not consistent or significant. In multipollutant models only ABS associated with ST-segment depression, but wide CIs. When examining indicator elements of a source, local traffic found to be the most toxic, but when examined per IQR long-range transport and traffic had similar effects.					

	Results: All had significant associations with mortality. Traffic density and EC had the largest effects.					
Reference: Lippmann et al. (2006, 091165) **Location:** U.S. **Particle Size:** PM_{10} for risk estimates, $PM_{2.5}$ for speciation data	**Subjects:** NR **Exposure:** NR	**N:** NR	**Number of Constituents considered for grouping:** NR	**Grouping method:** No grouping was performed # **of groups:** NR	**Groups/ Factors/ Sources:** NR	**PM variables used:** Mass contribution of 16 constituents
	Results: The strongest predictions of the variation in PM_{10} risk estimates across the 90 NMMAPs MSAs was for Ni and V. Elevated, but nonsignificant increases were associated with EC, Zn, $SO_4$2-, Cu, Pb, and OC. Al and Si had the lowest values.					
Reference: Mar et al. (2000, 001760) **Location:** 1 monitor in Phoenix, AZ **Particle Size:** NR	**Subjects:** Elderly only **Exposure:** NR	**N:** NR	**Number of Constituents considered for grouping:** 10 elements, OC, EC, CO, NO_2; SO_2	**Grouping method:** Unspecified type of factor analysis # **of groups:** 3 or 5	**Groups/ Factors/ Sources:** Motor exhaust/road dust, soil, vegetative burning, local SO_2, regional SO_4	**PM variables used:** First used individual constituents: S, Zn, Pb, K, OC, EC, TC (AL+Si+Ca+Fe+Ti), then factor scores
	Results: Cardiovascular mortality associated with $PM_{2.5}$ mass on lag 1 and 4 (6 and 4%, respectively). EC and TC associated with CV mortality for lag 1 (RR = 1.05); OC was weakly associated with CV mortality for lags 1 and 3. For total mortality, regional sulfate was positively associated at lag 0, but negatively associated at lag 3. The local SO_2 and the soil factors were negatively associated with total mortality. For CV mortality, secondary sulfate was positively associated at lag 0, motor vehicle at lag 1, and vegetative burning at lag 3. **Reanalysis results** (Mar, 2003): Similar associations were observed.					
Reference: Mar et al. (2006, 086143) **Location:** Phoenix, AZ **Particle Size:** $PM_{2.5}$	**Subjects:** NR **Exposure:** NR	**N:** NR	**Number of Constituents considered for grouping:** NR	**Grouping method:** Comparison of: PMF (absolute); PCA; UNMIX # **of groups:** 6-10 **Groups/ Factors/ Sources:** Different labs gave different names to sources (see Hopke et al, table 2)	Sources for which association with health was analyzed: Soil, Traffic, secondary SO_4, NO_3, (Washington, DC only), residual oil (Washington, DC only), woodsmoke/ biomass combustion, sea salt, incinerator (Washington, DC only); primary coal (Washington, DC only); Cu smelter (Phoenix only)	**PM variables used:** Mass contribution of sources
	Results: Using daily $PM_{2.5}$ data found the following associations with cardiovascular mortality: Secondary sulfate - greatest effect observed for all sources and at lag 0; traffic - associated at lag 1; copper smelter associated at lag 0; sea salt - had the greatest statistical significance and observed at lag 5; biomass/wood burning - less consistent lag structure but greatest association at lag 3; soil - did not show an association or consistent lag structure. For total (nonaccidental) mortality associations were weaker and consistently observed for only: copper smelter - lag 0; sea salt - lag 5.					
Reference: Ostro et al. (2007, 091354) **Location:** Monitors in 6 CA counties, some with 2 monitors, for 4 yr **Particle Size:** $PM_{2.5}$	Subjects NR **Exposure:** NR	**N:** NR	**Number of Constituents considered for grouping:** 15 elements, EC, OC; NO_3; SO_4, $PM_{2.5}$ mass	**Grouping method:** No grouping was performed # **of groups:** NA	**Groups/ Factors/ Sources:** NR	**PM variables used:** Mass contribution of every constituent
	Results: Effects were greater during the winter months. In the all year analysis, at 3-day lag associations observed for EC, OC, NO_3 and Zn. During winter months (Oct -March) effects observed for most species for both all-cause and cardiovascular mortality at lag 3 (EC, OC, SO_4, Ca, Fe, K, Mn, Pb, S, Si, Ti, Zn) and (OC, NO_3, SO_4, Fe, Mn, S, V, Zn), respectively.					
Reference: Ostro et al. (2009, 191971) **Location:** Monitors in 6 CA counties, some with 2 monitors/4 yr **Particle Size:** $PM_{2.5}$	Subjects NR **Exposure:** NR	**N:** NR	**Number of Constituents considered for grouping:** 9 elements,EC, OC, $PM_{2.5}$ mass, SO_4, NO_3	**Grouping method:** No grouping was performed # **of groups:** NA	**Groups/ Factors/ Sources:** NR	**PM variables used:** Mass contribution of every constituent
	Results: The following associations were observed with cardiovascular mortality: $PM_{2.5}$ (lag 3); EC (lag 2); NO_3 (lag 3); SO_4 (lag 3); Fe (lag 2); K (lag 2); S (lag 3); Ti (lag 2); Zn (lag 3).					

Reference: Peng et al. (2009, 191998) **Location:** 119 urban communities STN data/2000-2006 **Particle Size:** $PM_{2.5}$	**Subjects:** Medicare enrollees 65 or older **Exposure:** NR	**N:** NR	**Number of Constituents considered for grouping:** SO_4, NO_3, Si, EC, OCM, Na, NH_4	**Grouping method:** NR # **of groups:** NR	**Groups/Factors/ Sources:** Only suggested in discussion	**PM variables used:** Tracers
	Results: CVD HAs: EC associated with same-day CVD HAs in single and multi-pollutant models. In single pollutant models associations also observed for sulfate, nitrate, OCM, and ammonium. However, the sulfate, nitrate, OCM, and ammonium associations were reduced in the multi-pollutant models. **Respiratory HAs:** OCM associated with same-day respiratory HAs in single and multi-pollutant models. Some evidence for sulfate associations at one and two-day lag.					
Reference: Penttinen et al. (2006, 087988) **Location:** Helsinki 1996-1997 (7 mo) **Particle Size:** $PM_{2.5}$	**Subjects:** Adult asthma subjects, max 2 km from single monitor **Exposure:** NR	**N:** 78	**Number of Constituents considered for grouping:** Unknown	**Grouping method:** PCA # **of groups:** 6	**Groups/Factors/ Sources:** Long range (PM mass, S, K, Zn), local combustion-traffic (Cu, Zn, Mn, Fe), soil (Si, Al, Ca, Fe, Mn), oil (V, Ni), salt (Na, Cl), unidentified	**PM variables used:** every component individually, then groupings
	Results: Long range $PM_{2.5}$ associated with decreased mean PEF in the morning at lag 1. Local combustion $PM_{2.5}$ associated with decreased mean PEF in the evening for lag 1. Local combustion $PM_{2.5}$ associated with decreased mean PEF in the afternoon and evening for 5-day mean lag. Negative significant association between long-range $PM_{2.5}$ and asthma symptom prevalence at lag 3. Sea-salt $PM_{2.5}$ negatively associated with bronchodilator use at lag 3 and 5-day mean lag. Sea-salt $PM_{2.5}$ negatively associated with corticosteroid use for 5-day mean lag. Unidentified $PM_{2.5}$ negatively associated with corticosteroid use at lag 1. Most consistent negative responses for local combustion, although not always significant. No consistent or significant associations between 5-day avg concentrations of elements and PEF, cough, asthma symptoms, or medication use.					
Reference: Riediker et al. (2004, 091261) **Location:** Inside 9 state police patrol cars **Particle Size:** $PM_{2.5}$	**Subjects:** Healthy male young police officers **Exposure:** 4 consecutive days	**N:** 9	**Number of Constituents considered for grouping:** 10 elements; 3 gaseous pollutants; 2 physical variables	**Grouping method:** PCA # **of groups:** 4 when 13+2 constituents included; 3 when only 9 "PM-associated" constituents included	**Groups/ Factors/ Sources:** Soil; automotive steel wear; gasoline combustion; speed-changing traffic	**PM variables used:** Mass contribution or score of sources
	Results: Using two different factor analysis models found most significant effects (MCL, SDNN, PNN_{50}, supraventricular ectopic beats, % neutrophils, % lymphocytes, MCV, von Willebrand Factor, and protein C) were for "speed-change factor" (i.e., Cu, S, aldehydes). Some associations observed for "crustal" and none for "steel wear" and "gasoline."					
Reference: Sarnat et al. (2008, 097972) **Location:** 1monitor in Atlanta. GA for 2 yr **Particle Size:** $PM_{2.5}$	**Subjects:** NR **Exposure:** NR	**N:** NR	**Number of Constituents considered for grouping:** NR	**Grouping method:** Comparison of: PMF, CMB-LGO, "a priori decision" # **of groups:** 9,11 (6 of them common between methods)	**Groups/ Factors/ Sources:** gasoline, diesel, wood smoke/ biomass burning, soil, secondary SO_4/ammonium sulfate, secondary nitrate/ ammonium nitrate, metal processing, railroad, bus and highway, cement kiln, power plants, other OC, ammonium bisulfate	**PM variables used:** Mass contribution or score of sources, and tracers
	Results: Sulfate secondary associated with 1.2-2.0% increase in RD visits, significant negative association RD visits and primary emissions from coal-fired power plants. CVD significantly associated with other OC (1.014), biomass (1.033), diesel and gas for CMB-LGO. For PMF and CVD visits: diesel (1.025), gas, wood smoke, metal processing (1.013). Year-long associations: PMF diesel, EC, CMB-LGO gas, Zn and biomass combustion sources (CMB-LGO biomass burning, PMF wood smoke, and K). Diesel and gas sources association with RD in the warm season (1.2-2.1% per IQR).					
Reference: Schreuder et al. (2006, 097959) **Location:** 1monitor in Spokane, WA for 7 yr **Particle Size:** $PM_{2.5}$	**Subjects:** NR **Exposure:** NR	**N:** NR	**Number of Constituents considered for grouping:** 11 elements, TC, NO_3	**Grouping method:** Comparison of: PMF, UNMIX, Multilinear Engine # **of groups:** 8	**Groups/ Factors/ Sources:** Vegetative burning; As-rich Vehicle; SO_4; NO_3; Soil; Cu-rich; Marine	**PM variables used:** Tracers: TC (vegetative burning); As (As-rich); Zn (vehicle); Si (soil)
	Results: Si, As, and Zn were not associated with any health outcomes; while an IQR increase in TC (vegetative burning) was associated with a 2% increase in respiratory ED visits.					

Reference: Tsai et al. (2000, 006251) **Location:** 3 NJ sites for 2 summers (ATEOS study) **Particle Size:** NR	**Subjects:** NR **Exposure:** NR	**N:** NR	**Number of Constituents considered for grouping:** 8 metals, IPM, FPM, SO_4, CX, DCM, ACE, CO	**Grouping method:** Unspecified type of factor analysis # **of groups:** 5	**Groups/ Factors/ Sources:** Oil burning, motor emissions, resuspended dust, secondary aerosol, industrial sources	**PM variables used:** individual constituents, then factor scores, then tracers
	Results: RR associated with 10 µg/m3 increases: Newark - 1.03 for industrial and total daily deaths; 1.02 for sulfate and total daily deaths; 1.04 for sulfate and cardiopulmonary deaths. Camden - 1.11 for oil burning sources and total daily deaths; 1.10 industrial and total daily deaths; 1.12 for oil burning sources and cardiopulmonary daily deaths; 1.02 for sulfate and cardiopulmonary daily deaths					
Reference: Yue et al. (2007, 097968) **Location:** 1monitor in German city, 30.000 samples **Particle Size:** UF/$PM_{2.5}$	**Subjects:** Adult males **Exposure:** CAD	**n:** 56, data collected 12 times over 6 mo for every subject, but extended period of missing PM data	**Number of Constituents considered for grouping:** Apportionment based on particle size distribution.	**Grouping method:** PMF # **of groups:** 5	**Groups/ Factors/ Sources:** Airborne soil, local traffic, local fuel combustion, remote traffic (diesel), secondary aerosols	**PM variables used:** Mass contribution or score of sources
	Results: Overall, repolarization parameters influenced by traffic-related particles; vWF increased in response to traffic-related particles and combustion-generated aerosols. All source factors contributed to increasing CRP levels.					

Table F-2. Human clinical studies of ambient PM sources, factors, or constituents

Study: Gong et al. (2003, 042106) **Location:** Los Angeles, CA **Particle Size:** $PM_{2.5}$	**Subjects:** Adult 18-45, healthy vs. asthmatic **Exposure:** CAPs, healthy and asthmatic subjects exposed at different times	**N:** 12 healthy, 12 asthmatic	**Constituents considered for grouping:** 7 elements, EC, NO_3, SO_4	**Grouping method:** PCA # **of groups:** 4 (note: OC data was unavailable)	**Groups/ Factors/ Sources:** Crustal (Al Si CA K Fe),S (2 metrics of SO_4 + elemental S), Total Mass+NO_3, EC	**PM variables used:** Total mass, then tracers: SO_4, EC, Fe
	Results: Fe and EC associated with a decrease in ST-segment voltage 2 days post-exposure. EC associated with an increase in ST-segment voltage immediately following exposure. Sulfate content associated with a decrease in systolic BP 4 h post-exposure.					
Study: Gong et al. (2005, 087921) **Location:** Los Angeles, CA **Particle Size:** $PM_{2.5}$	**Subjects:** Elderly, COPD vs. healthy/ CAPs **Exposure:** NO_2 (full factorial)	**N:** 6 healthy, 18 COPD	**Constituents considered for grouping:** 7 elements + EC	**Grouping method:** PCA # **of groups:** 3 (note: OC was unavailable)	**Groups/ Factors/ Sources:** Crustal (Al Si CA K Fe), S (= SO_4),Na	**PM variables used:** Total mass, then tracers:, SO_4, Si, Fe, EC
	Results: Mass concentration of CAPs not observed to significantly affect lung function. However, sulfate content was associated with a decrease lung function (FEV_1 and FVC), which was enhanced by coexposure to NO_2.					
Reference: Huang et al. (2003, 087377) **Location:** Chapel Hill, NC **Particle Size:** $PM_{2.5}$	**Subjects:** Healthy adults **Exposure:** CAPs	**N:** 35 male; 2 female	**Constituents considered for grouping:** 8 elements and SO_4	**Grouping method:** PCA # **of groups:** 2	**Groups/ Factors/ Sources:** Fe/SO_4/Se/V/Zn/Cu	**PM variables used:** Factor scores, then mass contribution of all 9 constituents
	Results: Associations observed between sulfate,Zn, and Se content and increases in BAL neutrophils. Increases in fibrinogen associated with Cu, Zn, and V content.					
Reference: Urch et al. (2004, 055629) **Location:** Toronto, Canada **Particle Size:** $PM_{2.5}$	**Subjects:** Healthy adults 19-50 yr/CAPs **Exposure:** O_3	**N:** 23	**Constituents considered for grouping:** unknown	**Grouping method:** No grouping was performed # **of groups:** NA	**Groups/ Factors/ Sources:** NR	**PM variables used:** Every constituent in univariate analysis, then OC and SO_4 in multivariate analysis
	Results: CAPs-induced increase in diastolic BP significantly associated with carbon content of the particles.					
Reference: Urch et al. (2004, 055629) **Location:** Toronto, Canada **Particle Size:** $PM_{2.5}$	**Subjects:** Healthy adults/CAPs **Exposure:** O_3	**N:** 24	**Constituents considered for grouping:** 14 elements, EC, OC	**Grouping method:** No grouping was performed # **of groups:** NA	**Groups/ Factors/ Sources:** NR	**PM variables used:** Every constituent in univariate analysis, then OC and SO_4 in multivariate analysis
	Results: Both organic and EC content of CAPs associated with an increase in brachial artery vasoconstriction.					

Table F-3. Toxicological studies of ambient PM sources, factors, or constituents

Reference: Batalha et al. (2002, 088109) **Location:** Boston, MA **Particle Size:** $PM_{2.5}$	**Subjects:** Rats **Exposure:** CAPs (3-day mean CAPs concentration range: 126.1-481.0 µg/m3) CAPs (3-day mean CAPs concentration range: 126.1-481.0 µg/m3)	**N:** 7-10 rats × 2 levels CAPs × 2 levels SO_2 × 6 runs in different seasons	**Constituents considered for grouping:** 20 elements; OC; EC	**Grouping method:** Previous study in same city (Clarke et al., 2000, 013252) and PCA of this experiment's data # **of groups:** 4	**Groups/ Factors/ Sources:** V/Ni, S, Al/Si, Br/Pb	**PM variables used:** 4 tracers (Si, SO_4, V, Pb) and EC, OC in univariate step. 4 tracers (Si, SO_4, V, Pb) in multivariate step
	Results: Univariate analyses for first day not significant for L/W ratio. Univariate analyses for second and third day and second+third day mean were similar. Presented second+third day mean regression data. CAPs mass, Si, Pb, SO_4, EC, OC significant for decreased L/W ratio in normal+CB rats exposed to CAPs. Si, SO_4 significant for decreased L/W ratio in normal rats. Si, OC significant for decreased L/W ratio in CB rats. Multivariate analysis using normal+CB rats for Si, SO_4, V, Pb - only Si remained significant with decreased L/W ratio.					
Reference: Becker et al. (2005, 088590) **Location:** Chapel Hill, NC; repeated sampling for 1 yr **Particle Size:** PM_{10}	**Subjects:** Normal human bronchial epithelial and human AM **Exposure:** (2-3X105 cells/mL; 11 or 50 µg/mL)	**N:** NR	**Constituents considered for grouping:** 12 elements	**Grouping method:** PCA # **of groups:** 2	**Groups/ Factors/ Sources:** Cr/Al/Si/Ti/Fe/Cu ("crustal"), Zn/As/V/Ni/Pb/ Se	**PM variables used:** NR
	Results: Cr/Al/Si/Ti/Fe/Cu associated with IL-8 release in normal human bronchial epithelial cells and IL-6 release in AM. Zn/As/V/Ni/Pb/Se not associated with any endpoints. Stepwise linear regression with individual constituents Fe and Si associated with IL-6 release in AM. Cr associated with IL-8 release in NHBE cells.					
Reference: Clarke et al. (2000, 013252) **Location:** Boston, MA **Particle Size:** $PM_{2.5}$	**Subjects:** Dogs **Exposure:** CAPs (avg for all studies, paired: 203.4, crossover: 360.8 µg/m3) repeated exposure with several weeks in between	**N:** 10 dogs, 20 paired exposures, 24 crossover	**Constituents considered for grouping:** 19 elements, black C	**Grouping method:** PCA # **of groups:** 4 for exposure in paired runs,6 for exposure in crossover runs	**Groups/ Factors/ Sources:** V/Ni, S, Al/Si, Br/Pb, S, Na/Cl, Cr	**PM variables used:** All elements, then factor scores
	Results: No significant differences between baseline, sham, or CAPs group for BAL cell differential percentages. Total BAL protein increased with CAPs compared to sham. No significant hematological effects with CAPs exposure. Mixed linear regression analyses (statistics not provided): Al and Ti (3-day avg. concentrations) associated with dose-dependent decreases in BAL AM and increases in BAL PMN percentages. Sulfate associated with increased WBC. BC, Al, Mn, Si, Zn, Ti, V, Fe, Ni associated with increased blood PMN. Na associated with increased blood lymphocytes. Al, Mn, Si associated with decreased blood lymphocytes. CAPs mass and BC associated with decreased blood eosinophils. CAPs mass associated with decreased platelet count. Regression using results of factor analysis: None for 3-day avg. concentration for BAL parameters. V/Ni for increased AM percentage and Br/Pb for increased PMN percentage for 3rd-day only concentration. V/Ni and Al/Si for increased blood PMN percentage and decreased blood lymphocyte percentage. Al/Si also for increased WBC counts. Na/Cl for increased blood lymphocyte percentage. S for decreased RBC and hemoglobin.					
Reference: Duvall et al. (2008, 097969) **Location:** 5 US cities **Particle Size:** $PM_{2.5}$	Subjects Primary human airway epithelial cells (100,000 cells/mL; dose not provided) **Exposure:** NR	**N:** NR	**Constituents considered for grouping:** NR	**Grouping method:** CMB, but not on coarse and ultrafine # **of groups:** 6 or 7	**Groups/ Factors/ Sources:** Mobile, residual, oil, wood, soil, secondary SO_4, secondary NO_3	**PM variables used:** Mass contribution of constituents, then mass contribution of sources
	Results: Linear regression with individual constituents: Sulfate associated with increased IL-8 mRNA expression. Sr associated with increased COX-2 and decreased HO-1 mRNA expressions. K associated with decreased HO-1 mRNA expression. Linear regression with sources: Significance levels not provided.					

Reference: Godleski et al. (2002, 156478) **Location:** Boston, MA **Particle Size:** NR	**Subjects:** Rats **Exposure:** CAPs (3-day mean CAPs concentration range: 126.1-481.0 µg/m3)	**N:** 7-10 rats × 2 levels CAPs × 2 levels SO_2 × 6 runs in different seasons	**Constituents considered for grouping:** 20 elements, OC, EC	**Grouping method:** Previous study in same city (Clarke et al.), and PCA of this experiment's data **# of groups:** 4	**Groups/ Factors/ Sources:** V/Ni, S, Al/Si/Ca, Br/Pb	**PM variables used:** 4 tracers (I, SO_4,V, Pb) and EC, OC
	Results: Increased percent of PMNs in BALF in CAPs-exposed rats at 24 h. CAPs affected lung tissue mRNA involved in pro-inflammation, immune, and vascular endothelial responses. Linear regression: Increased PMN associated with CAPs mass, Br, Pb, SO_4, EC, and OC.					
Reference: Gurgueira et al. (2002, 036535) **Location:** Boston, MA **Particle Size:** $PM_{2.5}$	Subjects Rats (Sprague Dawley) **Exposure:** CAPs (avg. mass concentration 600 µg/m3); also carbon black and ROFA	**N:** 13 experiments (1 rat/group at each time point)	**Constituents considered for grouping:** 20 elements	**Grouping method:** No grouping was performed **# of groups:** NA	**Groups/ Factors/ Sources:** NR	**PM variables used:** Mass contribution of every constituent
	Results: Increased oxidative stress in heart and lungs following CAPs exposure (and ROFA exposure). Univariate regression: Mn, Zn, Fe, Cu, and Ca most significant responses for lung (r^2>0.40). Al, Si, Ti, Fe, and total mass most significant response for heart (r^2>0.49).					
Reference: Kodavanti et al. (2005, 087946) **Location:** RTP, NC **Particle Size:** $PM_{2.5}$	Subjects Rats (SH and WKY) **Exposure:** CAPs (144-2758 µg/m3)	**N:** 6 1-day , 1-strain runs, 7 2-day, 2-strain runs, 4-9 rats per run.	**Constituents considered for grouping:** NR	**Grouping method:** No grouping was performed **# of groups:** NA	**Groups/ Factors/ Sources:** NR	**PM variables used:** Mass contribution of every constituent
	Results: No significant correlations between biologic responses and exposure variables (i.e., CAP mass, OC, inorganic C, sulfate, and other major elemental constituents). Al, Cu, Zn correlated with biologic responses when constituents normalized per unit mass of CAP (µg/mg). Zn correlated with plasma fibrinogen in SH rats (p = 0.0023).					
Reference: Lippmann et al. (2005, 087453) **Location:** Rural location upwind from New York City **Particle Size:** $PM_{2.5}$	**Subjects:** Mice (C57 and ApoE) **Exposure:** CAPs (avg. mass concentration 113 µg/m^3)	**N:** C57: 3-6 mice/group $ApoE^{-/-}$: 9-10 mice/group	**Constituents considered for grouping:** 19 elements + OC, EC, NO_3	**Grouping method:** (Absolute) PCA **# of groups:** 4	**Groups/ Factors/ Sources:** Regional SO_4 (S/Si/OC); Resuspended soil (CA/Fe/Al/Si);RO power plants (V/Ni/Se); traffic and unknown	**PM variables used:** Mass contribution of sources
	Results: ApoE null mice: Resuspended soil associated with decreased HR during exposure, but increased HR after exposure. Secondary sulfate associated with decreased HR after exposure. Residual oil associated with increased RMSSD and SDNN in afternoon following exposure. Secondary sulfate associated with decreased RMSSD and SDNN in night following exposure. Resuspended soil associated with increased RMSSD at night following exposure. PM mass associated with decreased HR during exposure and decreased RMSSD at night following exposure. **C57 mice:** Motor vehicle/other source category associated with decrease in RMSSD in afternoon following exposure					
Reference: Lippmann et al. (2006, 091165) **Location:** Rural location upwind from New York City **Particle Size:** $PM_{2.5}$	**Subjects:** Mice ($ApoE^{-/-}$) **Exposure:** CAPs (avg. mass concentration 85.6 µg/m^3)	**N:** 12 $ApoE^{-/-}$ mice (6/group)	**Number of Constituents considered for grouping:** NR	**Grouping method:** No grouping was performed **# of groups:** NR	**Groups/ Factors/ Sources:** NR	**PM variables used:** Mass contribution of every constituent in CAPs portion of study, contribution of 16 constituents in epi portion
	Results: Lag for HR elevations on 14 days with wind from NW was same day. Lag for SDNN reduction on 14 days with wind from NW was 0, 1 and 2. GAM analysis: B coefficient significant for Ni and HR (but not V, Cr, or Fe). B coefficient significant for Ni and log SDNN (but not V, Cr, or Fe).					

Reference: Maciejczyk and Chen (2005, 087456) **Location:** Rural; upwind from New York City **Particle Size:** $PM_{2.5}$	**Subjects:** NR **Exposure:** CAPs (90,000/well; 300 µg/mL)	**N:** 110 samples	**Constituents considered for grouping:** 19 elements + OC, EC, NO_3	**Grouping method:** (Absolute) PCA # **of groups:** 4	**Groups/ Factors/ Sources:** Regional SO_4 soil; unknown oil combustion	**PM variables used:** Mass contribution of sources
	Results: Correlation: V and Ni positively correlated with NF-κB. Oil combustion correlated the greatest with NF-κB (0.316). Significance not provided. Only 2% of mass contribution originates from this source.					
Reference: Nikolov et al. (2008, 156808) **Location:** Boston, MA **Particle Size:** NR	**Subjects:** Dogs **Exposure:**	**N:** 8 dogs, 24 exposure-days in 1997-98; 4 dogs, 21 exposure-days in 2001-2002	**Constituents considered for grouping:** 13 elements, BC, EC, OC	**Grouping method:** Compared 3 factor-analytic models within a SEM model # **of groups:** 4	**Groups/ Factors/ Sources:** Oil Combustion V/Ni; power plants S ;road dust Al/Si ;motor vehicles BC/OC/EC	**PM variables used:** Mass contribution of every constituent
	Results: Univariate response for respiratory outcomes: road dust and oil combustion associated with decreased respiratory frequency; motor vehicles associated with increased respiratory frequency; motor vehicles associated with increased PEF; road dust associated with decreased penh and motor vehicles associated with increased penh. **Multivariate responses for respiratory outcome:** Road dust associated with decreased respiratory rate; Motor vehicles associated with increased airway irritation.					
Reference: Rhoden et al. (2004, 087969) **Location:** Boston, MA **Particle Size:** $PM_{2.5}$	**Subjects:** Rats (Sprague-Dawley) **Exposure:** CAPs (avg. mass concentration range 150-2520 µg/m3) acetylcysteine full factorial	**N:** 4-8 rats (1-2 per group - sham, CAPs, sham/NAC, CAP/NAC) 10 exposures	**Constituents considered for grouping:** 20 elements	**Grouping method:** No grouping was performed # **of groups:** NA	**Groups/ Factors/ Sources:** NR	**PM variables used:** Mass contribution of every constituent
	Results: Increased oxidative stress and inflammation in lungs of CAPs animals that was attenuated with NAC. **Univariate regression:** Al, Si, Fe, K, Pb, and Cu most significantly correlated with lung TBARS. No significant correlations for lung carbonyls or lung PMN.					
Reference: Saldiva et al. (2002, 025988) **Location:** Boston, MA **Particle Size:** $PM_{2.5}$	**Subjects:** Rats (Sprague-Dawley **Exposure:** CAPs (3-day avg. mass concentration range 126.1-481 µg/m3)	**N:** 7-10 rats/group (air/sham, SO_2/sham, air/CAP, SO_2/CAP) × 6 runs in different seasons	**Constituents considered for grouping:** 15 elements (used Clarke 2000 to select tracers)	**Grouping method:** Previous study in same city (Clarke et al. 2000) # **of groups:** 6	**Groups/ Factors/ Sources:** V/Ni S Al/Si Br/Pb Na/Cl Cr	**PM variables used:** Mass contribution of 8 elements in univariate step. Tracers (Si, SO_4, V, Pb, Br, Cl) and EC, OC in multivariate step.
	Results: Increased percent and number of PMN in majority of air and SO_2 rats exposed to CAPs, but significance levels not provided. Other responses (protein, LDH, NAG) were variable and depended upon the CAPs exposure. No CAPs effect on histopathology. **Linear regression:** V, Br, Pb, SO_4, EC, OC, Si, CAP mass associated with increased PMN and lymphocytes for normal+CB rats. Only V not associated with PMN in normal rats. Lymphocyte response due to CB rats, but not observed for SO_4 , Si, or mass in this group. Br, Pb, SO_4, EC, OC, Si associated with increased total protein in CB rats. Cl and V associated with decreased LDH in CB rats. No BAL effects in normal rats exposed to CAPs. V, Br, Pb, EC, OC, and Cl associated with increased neutrophil density in lungs of normal rats.					
Reference: Seagrave et al. (2006, 091291) **Location:** 4 SE US sites for 2 seasons **Particle Size:** $PM_{2.5}$	Subjects Rats (Fisher 344) **Exposure:** 0.75, 1.5 and 3 mg/rat via intratracheal instillation	**N:** 5 rats/dose	**Constituents considered for grouping:** NR	**Grouping method:** CMB # **of groups:** 13	**Groups/ Factors/ Sources:** secondary NO_3; secondary NH_4; secondary SO_4; coke production; vegetative detritus; natural gas combust; road dust; wood combust; meat cooking gasoline; diesel other OM; other mass	**PM variables used:** Mass contribution of every constituent, then mass contribution of sources
	Results: Potency depended upon season and site of sample collection. In general, effects were greater in the winter. **PLS analysis**: 2 major constituents identified (OC, Pb, hopanes/steranes, nitrate, As for first and major metal oxides for the second), gasoline most important predictor for both constituents, with diesel influencing second constituent and nitrate influencing first constituent. First constituent affected cytotoxic responses, second constituent affected inflammatory responses.					

Reference: Veranth et al. (2006, 087479) **Location:** 8 sites in the western US **Particle Size:** $PM_{2.5}$	**Subjects:** BEAS-2B cells (35000 cells/cm2; 10, 20, 40, 80 µg/cm2) **Exposure:** Loose surface soil sweepings through mechanical tumbler and cascade impactor	**N:** 6; 16 runs over 6 mo	**Constituents considered for grouping:** 13 elements, TC, 5 OC variables, 4 EC variables, 2 ions, EU, one ratio (Ca: Al), OP, CO_3	**Grouping method:** PLS **# of groups:** NR	**Groups/ Factors/ Sources:** NR	**PM variables used:** Mass contribution every constituent (?)
	Results: Dose-related increase in IL-6 and decreases in cell viability for all soil types. IL-8 responses more variable and dependent upon soil type. Univariate correlations. Low correlations for all constituents tested with IL-6. Highest correlations for EC1 (R^2 = 0.50) and pyrolyzed OC (R^2 = 0.46), then Ca/Al (R^2 = 0.21). Carbonate carbon, EC3, and Sr correlated with IL-8 (R^2 = 0.27, 0.13, and 0.25, respectively). EC and Ni correlated with IL-8 trend over the range of 10-80 µg/cm2 (R^2 = 0.39 and 0.27, respectively). Multivariate redundancy analysis OC1, OC3, OC2, EC2, Br, EC1, Ni correlated with IL-8 release, decreased viability, and decreased IL-6 at low and high doses. Ni, EC1, and EC2 correlated with IL-6 release at the high dose, decreased IL-6 at the low dose, decreased IL-8 release, and decreased viability. Br was negatively associated.					
Reference: Wellenius et al. (2003, 055691) **Location:** Boston, MA **Particle Size:** $PM_{2.5}$	**Subjects:** Dogs **Exposure:** CAPs (avg. mass concentration range 161.3-957.3 µg/m^3) repeated exposure with several weeks in between	**N:** 6 dogs, 20 exposures	**Constituents considered for grouping:** 15 elements (+EC OC?) (used Clarke et al. 2000)	**Grouping method:** Previous study in same city (Clarke et al. 2000) **# of groups:** 6 (but did not use all in analysis of health effects)	**Groups/ Factors/ Sources:** V/Ni S Al/Si Br/Pb Na/Cl Cr	**PM variables used:** Univariate: Mass Number Ni, S, Si, BC Multivariate: Ni, S, Si , BC
	Results: ST-segment elevation increased with CAPs. **Univariate regression:** Si and Pb associated with peak ST-segment elevation and integrated ST-segment change.CAPs mass or number concentration were not associated with any change. **Multivariate regression:** Si associated with peak ST-segment elevation and integrated ST-segment change.					
Reference: Zhang et al. (2008, 192008) **Location:** Metro area of Denver, CO/ 45 samples through 1 yr **Particle Size:** 2.5; filtered to 0.22 um	**Subjects:** Alveolar macrophage cell line (NR8383); 1 ×106 cells/ml **Exposure:** Soluble components exposure concentration range from 20-200 pg of PM/cell	**N:** 45 PM samples, 3 runs	**Constituents considered for grouping:** 43 + EC, OC	**Grouping method:** PMF **# of groups:** 9	**Groups/Factors/ Sources:** Mobile, water soluble carbon, sulfate, soil, iron, Cd and Zn point source, Pb, pyrotechnics, platinum	**PM variables used:** Mass contribution of sources
	Results: Started with regression on 9 sources, then 3 (water-soluble carbon factor, soil dust source, iron source). Soil dust source was not significant. Final regression model excluded 3 days of outliers (Fe source most significant, then water-soluble carbon factor, then soil dust source) for ROS effects, with adjusted R^2 of 0.774. Fe source likely associated with industrial source and includes high loadings of water-soluble Fe and Ti (not identified); water-soluble C factor derived from both secondary organic aerosol and biomass smoke (largely consists of polar organic compounds); soil dust source identified by water-soluble resuspended dust elements and contains Mg and Ca.					

Annex F References

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Note: Hyperlinks to the reference citations throughout this document will take you to the NCEA HERO database (Health and Environmental Research Online) at http://epa.gov/hero. HERO is a database of scientific literature used by U.S. EPA in the process of developing science assessments such as the Integrated Science Assessments (ISA) and the Integrated Risk Information System (IRIS).

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